FEATURED ARTICLES

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Ever watched a typical coming of age movie where the main actors drink an excessive amount of alcohol and do dangerous, yet amusing, things? Although not obvious in all movies, alcohol is actually an addictive substance and lends itself to many dangers. In regards to the brain, alcohol changes brain functioning as it alters the prefrontal cortex, cerebellum, and hippocampus. With this, various chemicals such as dopamine, glutamate, and GABA are impacted by alcohol and slow down the brain’s normal reactions and functions. Moreover, overconsumption can lead to side effects such as confusion, amnesia, and loss of motor control. Read on to find out more about the way in which alcohol can affect the brain and the long-term effects of chronic alcohol consumption in relation to neurological disorders.

Neurological Manifestations of Menopause  Alisha Chunduri  pages 13-16

A series of intricate hormonal changes helps regulate a crucial period of a woman’s life: menopause. It is a distinctive period in a woman’s life when she is not able to get pregnant naturally, causing insomnia, depression and weight gain. These symptoms have been associated in the past though with a neural basis, rather than a hormonal problem. To learn more about its neurodegenerative, sleep and behavior impact, make sure to read Alisha’s article about the neurological manifestations behind menopause!

The Effects of Cocaine Exposure on Pregnant People and Fetuses  Maya Sharma  pages 17-23

Did you know that substance abuse affects over 33 million people in the USA alone? Even though addiction is a serious epidemic with harmful effects on the person, it has an equally devastating impact on their fetus if they are pregnant; including, restrictions on fetal circulation and weak organ growth. In addition to this, pregnant people experience several neurological issues, high blood pressure, and serious damage to their nervous system. To find out more about these traumatic effects, read author Maya Sharma’s, “The Effects of Cocaine Exposure on Pregnant People and Fetuses,” where she discusses these adverse effects in detail.

DISEASES AND DISORDERS

Body Dysmorphia: A Neurological Perspective  Laura Maisvoreva  pages 24-27
Body dysmorphic disorder (BDD), also known as body dysmorphia, is a mental illness marked by an abnormal preoccupation with one’s appearance. These aesthetic concerns usually stem from a desire to conform to a social ideal of beauty, as well as any face or body irregularities that cause insecurity and dissatisfaction with one’s appearance. While BDD has a strong social connection, researchers have discovered that it also has a neurological connection, and this link to brain function and structure is a solid sign of why BDD has perceptual implications. The author, Laura Maisvareva, provided a neurological breakdown of Body Dysmorphia in Body Dysmorphia: A Neurological Perspective. This is undoubtedly one of the most interesting and educational articles in the IYNA journal’s July issue.

Neurofibromatosis 2 (NF2): An Overview  Shreya Gurusankar  pages 28-32

Did you know that benign tumors can form at any point along the nervous system? If not, this article talks about a genetic disorder called Neurofibromatosis that causes exactly that. This disorder is characterized by primarily three types of tumors: schwannoma tumors, meningioma tumors, and ependymoma tumors, which are often non-cancerous or benign tumors. These are accompanied by symptoms like a compromised sense of balance, high rates of hearing, vision and smell loss, risk of seizures, and headaches depending on the level of severity and the type of tumor. This article further examines the types of tumors of NF2, symptoms, neurological causes, and the diagnostic methodology and treatment. It also provides distinctive insights into current research of NF2, discussing the factors behind the faulty gene and the tumor growths. If this intrigues you and prompts you to find out more about Neurofibromatosis, tune into the latest IYNA journal and get your hands on this article and many more!

St. John’s Wort’s Effect on Depression  Sadra Marjai  pages 33-39

Did you ever think that there are some plants with properties able to treat depression? If not, this article talks exactly about that. Hypericum Perforatum, also known as St. John’s Wort, is the plant which possesses this great medicinal purpose, by being able to increase the levels of serotonin and norepinephrine in the brain, promoting anti-depressive behaviour. The main active components of this plant are Hypericin and Hyperforin. The attractive perspective of treating a mental condition which affects so many people is however accompanied by the adverse effects which the use of this plant could cause – namely Serotonin Syndrome, a potentially life-threatening complication caused by excessive serotonin levels in the body. If you wish to find out more about depression and the potential to treat it using herbal remedies, check out the latest IYNA journal and many more intriguing articles!

Transcranial Magnetic Stimulation: A Treatment for Depression  Arya Reddy  pages 40-44

Experts estimate that 2-4% of the population, or 264 million people worldwide, are affected by some form of depression. Yet, treatments and therapies for depression are not as easily found. A novel treatment method, repetitive transcranial magnetic stimulation (rTMS), uses magnetic pulses to stimulate neural activity, ridding some of the effects of depression. The treatment is quite literally a new wave in the realm of
depression therapies. However, as with any therapy, rTMS comes with its own plate of side effects and risks worth considering. Regardless, the immense potential of rTMS is enough to delight researchers and experts, as well as hopeful patients battling depression. Make sure to read the rest of this article to discover more about this hopeful treatment!

**NEUROSCIENCE AND SOCIETY**

A Cycle of Stress: A Study of Increased COVID-19 Exposure Through Body-Focused Repetitive Behaviors

Hannah Pescaru

Body-focused repetitive behaviors (BFRBs) affect about 5% of the American national population and are behaviors where the individual repeatedly fidgets with their/his/her own body in ways that produce lasting physical and psychological damage. These include trichotillomania (hair-pulling), dermatillomania (skin-picking), and onychophagia (nail-biting). Research indicates that damage or lesion to corticostriatal circuits and the basal ganglia can inflict hyperactivity and abnormal repetition of behavior.

Do BFRBs seemingly increase the pain tolerance in patients suffering from them? What could the COVID-19 pandemic inflict on individuals with BFRBs? This article provides significant insights on the implications of the pandemic on BFRBs affected individuals and also discusses possible treatment options. If you wish to find out the answers to the questions posed above, check out the latest IYNA journal to find them out, and many more intriguing articles!

How Listening to Music Affects the Human Brain

Mark Messak

Throughout human history, music has been a constant factor in civilizations across the world. Stemming from the proto-language of Neanderthals, it evokes a wide range of emotions, ranging from joy to sorrow. In How Listening to Music Affects the Human Brain, author Mark Messak explores how music interacts with and enhances specific regions of the brain, such as the hippocampus and the amygdala. Using functional magnetic resonance imaging (fMRI), researchers discovered evidence for the separation of neural processing between music and speech. Currently, music is used as a therapeutic Parkinson’s disease and other neurological disorders. However, musical subgenres like hard rock and acid rock have been linked to reduced memory capabilities. Furthermore, scientific studies have suggested that disharmonic music is associated with negative changes in mood. Interested in learning more about the relationship between mind and melody? Be sure to check out this article in the latest IYNA journal!

Particulate Matter: Its Detrimental Effects on the Brain

Kathyayini Mendu

What comes to mind when you hear pollution? The idea of coughing or birds stuck in plastic bags may come to your mind. Though these are horrifying images, there is another disadvantage to air pollution: its grueling effects on the brain. The brain, the control center, may be severely affected at all ages by pollution. In their article, Particulate Matter: Its Detrimental Effects on the Brain, author Kathyayini Mendu discusses the current knowledge on the correlation between pollution and brain impact. Pollution appears to be associated
with loss of certain brain matter, slow growth, and even development of early Alzheimer’s disease and dementia. If you are interested in learning more and taking a more proactive approach to the effects of pollution, check out this article in the June issue of IYNA!
Dear Readers,

Welcome to the sixth installment in the fourth season of the IYNA Journal! While everyone has been reveling in the sweltering dog days of summer and has been starting to enjoy what seems to be the beginning of the transition back to normal in light of recent vaccination efforts, staff members at the IYNA Journal have been working diligently to provide you some first-rate neuroscience articles, covering pertinent issues in an accessible manner. Some of you may have noticed a change in the Contributors page as well as the stark absence of a published issue last month. The IYNA had a staff reorganization to better meet the goals of our community, so we want to give a shoutout to everyone in the Journal Department for enduring these frantic past few weeks. We would like to give a special shoutout to a few of our senior editors who filled in for the journalist role, for which our lovely managing editor is reviewing applications at this time. We appreciate everyone’s flexibility these past couple of months, and we hope to return to our regularly scheduled programming, which includes our monthly release of new issues.

Since many of you are students who are just now breaking free from the tests and schoolwork that plague the academic year, we would like to thank you for choosing to spend your newly acquired free time by supporting the work of young neuroscientists. We would like to give a special shout-out to Sadra Marjai and Shreya Gurusankar, who are the featured authors of “St. John’s Wort’s Effect on Depression” and “Neurofibromatosis 2 (NF2): An Overview,” respectively.

Once again, we would like to recognize and thank all of our dedicated editors—both veteran and neophytic—for being the reason that this issue is the success that it is. You can see all of their names and positions on our Contributors page. If you have any questions, comments, or suggestions for us, please feel free to reach out to the Editor-in-Chief directly at swagle@youthneuro.org. We hope you enjoy reading this issue as much as we enjoyed editing it!

Best Regards,
Sojas Wagle - IYNA Journal Editor-In-Chief
Annie Pan - Head of Assembly
Ashley Thommana - Managing Editor
Haris Rana - Senior Editor
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Kunal Dhirani - Senior Editor
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Gasser Alwasify - Senior Editor
Sampath Rapuri - Senior Editor
Nicholas Aderinto - Senior Editor
Alcohol and the Brain: An Overview
Teo Richard

Abstract
Alcohol is an addictive substance, posing many dangers. It changes the very functioning of the brain, altering the hippocampus and prefrontal cortex and leading to cerebellar degeneration. Alcohol-induced shifts in levels of thiamine may lead to disorders involving confusion, loss of motor control, and even amnesia. In addition, levels of dopamine, GABA, glutamate, and other chemicals are affected by alcohol, slowing down the brain, altering shapes of receptors, and eventually disrupting the brain's homeostasis to such an extent that addiction is formed. This article gives an overview of significant ways alcohol can affect the brain, along with detrimental long-term effects of chronic alcohol consumption including hepatic encephalopathy and other neurological conditions.

Stages of Alcohol Consumption

Alcohol consumption can generate pleasurable effects at low levels but can also lead to depression and memory loss beyond 0.05 BAC (blood alcohol content). At around 0.2 BAC, significant confusion begins to set in, and an increasing lack of coordination presents itself. For reference, the federal limit in the U.S. to drive is 0.08 BAC. Serious symptoms of blood alcohol poisoning appear at around 0.3 BAC, and the brain and body are impaired. Reaching a BAC of 0.35, a coma may be induced. Death is possible over 0.45 BAC [1]. Weight and other factors affect BAC and the severity of alcohol consumption symptoms [2].

Dopamine

Dopaminergic (dopamine-mediated) neurons are part of three main circuits: the nigrostriatal system, mesolimbic system, and mesocortical system. The mesolimbic system is especially significant because behaviors caused by incentive stimuli are controlled here [3]. Furthermore, this system contains the nucleus accumbens (NAc), which plays an integral part in motivating behavior related to rewards [4]. Specifically, the NAc itself is believed to play an integral part in fostering alcohol dependency. Studies have
demonstrated that the levels of dopamine in the NAc increase not only when consuming alcohol, but also when simply thinking about it [3]. Interestingly, repeated presentation of any stimuli does not correlate to repeated dopamine production in similar amounts. Instead, the levels of dopamine drop [5].

This drop in dopamine may be explained by the brain’s need to maintain homeostasis, an idea that goes hand in hand with addiction. This idea is expressed in the Himmelsbach hypothesis, which demonstrates neuroplasticity, the idea that the brain can adapt. When first exposed to alcohol, the balance of the brain is disrupted. Over time, the brain attempts to return to the previous state of equilibrium, creating tolerance for alcohol.

Gradually, more and more alcohol is needed to produce the desired effects. When consumption is cut off or reduced drastically, the balance of the brain becomes steeply tilted as the new equilibrium is disrupted, creating a need for alcohol to reestablish homeostasis. Cutting off the addictive substance nearly always results in withdrawal symptoms, making relapses hard to avoid. It is important to note that the Himmelsbach hypothesis is not confined to just dopamine imbalances, as it includes other imbalances such as changes in GABA and glutamate. The Himmelsbach hypothesis is seen in almost all addictive substances, not just alcohol [6].

GABA

Gamma-aminobutyric acid (GABA) is an inhibitory neurotransmitter, meaning that it slows down the brain by inhibiting electric signals. This is unlike dopamine, which exhibits both excitatory and inhibitory effects. Alcohol affects GABA by binding to both GABA-producing (presynaptic) and signal to receive (postsynaptic) neurons, increasing production of GABA and activity in its receptors. Neuroactive steroids likely play an important role in the change in GABA as one subtype of GABA receptors, GABA₄, is regulated by these steroids. Alcohol is strongly correlated to a significant increase in neuroactive steroids, meaning that these steroids may act as middlemen in the effects alcohol holds over GABA [3].

Coordination, reaction time, and processing are all related to GABA, which helps explain the lack of these functions after alcohol exposure [7]. Alcohol causes increased activation of GABA, which slows down electrical signals in the brain, which in turn slows functions like coordination, reaction time, and processing. It also clarifies why initial exposure to alcohol results in a “buzz,” but as time goes on, exhaustion sets in.

Glutamate

Glutamate is an important excitatory neurotransmitter and, unlike GABA, promotes electrical signals [3]. If GABA acts as the brakes, glutamate acts like the accelerator. Important glutamate receptors include N-methyl-D-Aspartate (NMDA) and AMPA/kainate receptors. Alcohol inhibits these receptors by inhibiting their ion flow. However, non-NMDA receptors typically require a higher alcohol concentration than NMDA receptors to be affected [8].
Such inhibition of NMDA is likely to cause negative effects in offspring. Studies on rats demonstrate that when alcohol is consumed during gestation, NMDA function is inhibited in the offspring. NMDA is also important in neuroplasticity. Maternal consumption of NMDA in rats has caused NMDA-related plasticity to be reduced in offspring. Studies have shown that these offspring may be affected after only a single exposure to alcohol [8].

**Hippocampus**

The hippocampus is heavily involved in the formation of memories, which are important for recognition, learning, and emotions [9]. Typically, alcohol does not affect previously formed memories, but rather impacts the formation of new memories [10]. When people think of alcohol's effect on memory, they often think of blackouts. Blackouts are certainly a prominent effect of alcohol, but there is additional potential for long-term hippocampal damage.

In the hippocampus, alcohol binds to receptors for neurotransmitters such as GABA, glutamate, serotonin, acetylcholine, and glycine [10]. It alters the shapes of these receptors, resulting in a reduction of electrical activities in the associated neurons, which inhibits the formation of new memories [11]. This reduction of electrical activities is well demonstrated in a study performed on rats. Around 45 to 60 minutes after an alcohol injection, cell activity within the hippocampus went down to effectively none. After around seven hours, activity was normal once more [10].

Reduction in total hippocampal volume is also correlated to long-term alcohol intake, a potential long-term damage. Older studies have typically not found conclusive results. However, new studies do support this hypothesis [12]. Hippocampal volume deficits are shown to be independent of total brain volume, meaning that the small sizes of the hippocampus in alcoholics are unrelated to the volume of other intracranial structures [13].

**Thiamine Deficiency**

Thiamine (vitamin B1) is an essential nutrient in all tissues. It must be consumed, meaning that all thiamine is absorbed, not produced. Chronic alcohol drinkers typically do not eat a balanced diet, meaning that they do not take in a sufficient amount of thiamine-rich foods like meat, poultry, nuts, and whole grains. Additionally, over time, alcohol suppresses the absorption of thiamine in cells, causing malabsorption [19]. Regular symptoms of thiamine deficiency include constipation, appetite loss, and fatigue [20]. However, long-term thiamine deficiency may cause serious brain damage.
It is common for alcohol to cause thiamine deficiency over the long term, and in countries where malnutrition is uncommon, alcohol consumption is one of the most common causes of thiamine deficiency. While these disorders are caused specifically by the deficiency in thiamine itself, alcoholics are the most common type of person to develop them should they live in an affluent country [19].

**Wernicke’s Encephalopathy and Korsakoff’s Syndrome**

Wernicke’s encephalopathy (WE) is a neurological disorder that generally causes lesions in the thalamus and hypothalamus resulting from thiamine deficiency [21]. It is characterized by symptoms including paralysis of nerves within the eye (oculomotor disturbances), extreme confusion, and severe impairment of coordination of movement significantly in the lower body (ataxia). It is unusual that a WE patient would present all three symptoms at once, meaning that encephalopathy may be inappropriately overlooked [19].

It is relatively common that WE patients develop Korsakoff’s syndrome, a disorder that causes damage in parts of the brain associated with memory [21]. Wernicke-Korsakoff Syndrome (WKS) patients often exhibit both retrograde amnesia (inability to recall old memories), but most significantly anterograde amnesia (inability to acquire new memories) [19]. Anterograde amnesia is known to stem from diencephalic lesions, often in anterior thalamic nuclei, which work with the hippocampus [17]. However, deficits in the hippocampal volume are shown to be strongly correlated to amnesia in WKS [18].

WE and WKS may be treated by taking thiamine supplements, and this treatment may fully reverse many symptoms. However, this is not a perfect cure by any means. In the gravest cases, patients may present persisting symptoms of severe WKS despite treatment [19].

**Cerebellar Degeneration**

The number of alcoholics with cerebellar damage lends evidence to the idea that the cerebellum is especially sensitive to thiamine deficiency. Cerebellar degeneration is more common than WE and leads to atrophy of parts of the cerebellum. The cerebellum is important in muscle coordination and cognitive and sensory functioning. Consequently, shrinkage in the cerebellum results in decreased abilities in coordinating movements along with twitching in the eyes [19].

**Hepatic Encephalopathy**

Hepatic encephalopathy (HE) occurs in patients with liver failure. The liver is quite an important organ in terms of making sure the brain works properly. It removes toxins from the blood and toxins built up by the brain itself, as well as supplying nutrients to the brain [19]. When the liver is unable to properly remove toxins, the toxins builds up and can travel to the brain. General symptoms include difficulties in remaining alert, sleeping, and focusing. Lethargy, slurred speech, and reduced abilities to perform mental or physical tasks may also manifest [20].
Liver complications may not always stem from alcohol, but alcohol is a common cause. Alcoholic liver disease may appear in many forms: fatty deposits in liver cells (steatosis), inflammation of liver tissues (hepatitis), formation of scar tissue on the liver (fibrosis), or destruction of liver structures (cirrhosis) [19]. Patients with cirrhosis are often more likely to express symptoms like a reduced frequency of brain waves, difficulties in neuropsychological tests, and asterixis (hand tremors).

HE does not cause direct damage to neurons but instead harms astrocytes, which are support cells that help maintain an appropriate amount of fluid surrounding neurons and remove toxins from the brain [19]. Brains of patients with HE often contain abnormal astrocytes, which generally occur in pairs or triplets and have enlarged and glassy nuclei. These are referred to as Alzheimer type II astrocytes, and often have functional abnormalities [21]. The following two specific neurotoxins have been confirmed in their contributions to HE.

**Ammonia**

Permeability-surface area product (PS) describes the variable that determines how much ammonia may enter the brain. Positron emission tomography has shown that in patients with cirrhosis, PS increases, meaning that a greater amount of ammonia from general circulation may enter the brain. Ammonia that has reached brain cells may only be eliminated with the enzyme glutamine synthetase. Astrocytes are brain cells with this enzyme, meaning that neurons are helpless against this increased amount of ammonia. Ammonia causes damage by inhibiting nerve signal transmissions, impairing the metabolism of the brain, and altering genes involved in the production, structure, and interactions of brain cells [21].

Treatments to reduce ammonia levels in the brain include attempting to reduce natural ammonia production by giving the patient sugar molecules or antibiotics. Patients may also use artificial livers or liver transplants [21].

**Manganese**

Magnetic resonance imaging has demonstrated a high amount of signal hyperintensities in over 80% of patients with cirrhosis, mostly in the globus pallidus, which is involved in motor functions. The signal hyperintensity is caused by high manganese levels in this part of the brain as a result of the liver failing to function properly. Manganese can alter receptors and even cause Alzheimer’s type II changes in astrocytes. Manganese entering the brain likely accounts for the lack of motor control frequently exhibited in alcoholics and much of the change in astrocytes [21].
Prefrontal Cortex

The prefrontal cortex (PFC) is complex. However, generally, its role is to take information from other places in the brain and use this information to develop certain responses. Studies have shown a correlation between ethanol (alcohol) intake and a lack of ability to perform tasks requiring the PFC. For example, when social drinkers became intoxicated, they performed worse on spatial and planning tasks than when not inebriated. Parts of the PFC associated with language also showed less activation, and performance on language tasks worsened [22].

Over time, the very structure of the PFC will change. Reduced amounts of gray and white matter are prevalent, along with reduced amounts of N-acetylaspartate, an important metabolite in the brain. The soma (cell body of a neuron) decreases in size, along with a decrease in the overall volume of the PFC. This shrinkage is likely due to either atrophy or dendritic retraction (decrease in dendrite size) because no heavy cell loss has been shown to be correlated to the shrinkage. It is not known whether this structural change may be reversed. Evidence suggests that it cannot be; in one study, patients abstained from alcohol for 6-9 months in rehab but did not emerge with increased frontal lobe volume [22].

Conclusion

Chronic alcohol users face multiple types of brain damage. Production of dopamine will increase, which aids addiction. The activity of GABA increases, slowing the brain down as a whole. Glutamate is inhibited, increasing the sluggishness of the brain. The Himmelsbach hypothesis explains how these changes make addiction hard to avoid after long-term use. Thiamine deficiency may lead to dangerous disorders like Wernicke’s encephalopathy and Korsakoff’s Syndrome. Liver failure increases the risk for hepatic encephalopathy, in which increased levels of ammonia and manganese are especially significant. Hippocampal damage is a serious issue and is the cause of blackouts that many drinkers experience. Finally, damage to the prefrontal cortex may occur and may not be reversible.

References


Neurological Manifestations of Menopause
Alisha Chunduri

Abstract
With the onset of 12-45 years of age, a female goes through various menstrual phases from menarche to menopause. Release of the endometrial lining in a rhythmic manner when the egg does not get fertilized is essential for women’s health. The hormone release is regulated on the basis of this menstrual rhythm. As the ovaries age, menstruation becomes irregular, causing women to suffer from various symptoms, including insomnia, depression, and weight gain. These symptoms occur because of hormonal imbalances in aging women. Often, these symptoms are more neurological due to fluctuating neuroendocrine regulations. This article is an exploration of the neurological symptoms of menopause with an emphasis on sleep, behavioral and neurodegenerative impact in comparison to the pre-menopausal period.

Menopause

After a span of 12 months without a menstrual period, women are considered to have entered menopause. Most menopausal cases are diagnosed in the 40s or 50s. It is usually natural and a result of aging. The end of reproductive years is marked by the stages of perimenopause, menopause, and postmenopause.

Perimenopause occurs eight to ten years before menopause. This is followed by menopause and postmenopause, which is the after level of menopause. This natural biological process is accompanied by physical and psychological symptoms like irregular periods, followed by night sweats, mood changes, sleep disruptions, changed metabolism, and vaginal dryness. These symptoms vary from woman to woman. Postmenopause occurs a year after the menopause, for the rest of the life. Due to significantly decreased hormone
production, various body systems are affected leading to symptoms including hot flushes, mood swings, dry vagina, mental confusion, osteoporotic symptoms, depression, and insomnia. The hormonal aspect of the transition depends on the changes in the production of the ovarian hormones estrogen (the hormone that is responsible for a female's sexual and reproductive functioning) and progesterone. These changes manifest in symptoms like the weakening of bones, energy loss, and weight gain [1].

Changes in Sleep and Circadian Rhythm

Melatonin secretion by the pineal gland is an underlying mechanism of the circadian rhythm. With aging, the level of melatonin gradually decreases. The underlying reasons for this decrease vary with gender and age. Studies show that menopause is associated with fluctuating levels of melatonin. This is a plausible cause of sleep disruption in the menopausal phase. The circadian rhythm of melatonin secretion is correlated with normal sleep patterns [2]. Sleep deprivation can lead to consequences that are detrimental to human health. In fact, various conditions including increased risk of diabetes, obesity, hypertension, heart attack, and stroke are associated with sleep loss and sleep disorders [3]. In addition, women tend to experience higher sleep problems post-menopause compared to pre-menopause. Hot flushes, a symptom of menopause, have shown a circadian rhythm in its occurrence. Other studies looked at the suppression of Luteinizing hormone by melatonin. A possible explanation is that the pulsatile release of Gonadotropin-releasing hormone and Luteinizing hormone is by the same hypothalamic pulse generator. This could lead to hot flushes. Hence, there is a chance of relief from the hot flushes in postmenopausal women with supplemental melatonin, as it can suppress the pulse generator [4].

Behavioral Effects

Behavioral symptoms vary from woman to woman. The transition into old age, improper sleep, hot flushes, and other symptoms leading to discomfort can make a woman feel unstable in terms of mood. Sudden and extreme bursts of panic, anger, restlessness, anxiety, and depression are variably experienced. The underlying chemical changes include altered estrogen levels. In menopause, there is a reduction in the ovaries’ production of estrogen, which also controls the amount of serotonin produced in the brain. Their production is positively correlated; decreased estrogen production implies that there is decreased serotonin production. The biological function of serotonin is complex and is involved in regulating mood and cognition [5]. Thus, overall, serotonin impacts the happiness and wellbeing felt by a woman. The control of psychological symptoms develops gradually as one becomes habitual of the transition. Other ways to manage the emotional symptoms include meditation, consumption of a balanced diet, and regular exercise.

Neurodegenerative Effects

Research shows that symptoms of neurological disorders, such as Alzheimer’s disease and multiple sclerosis, are worsened in postmenopausal women [6]. Estrogen receptors are located in the prefrontal cortex, amygdala, cingulate cortex, retrosplenial cortex, and various subfields of the
hippocampus that are associated with learning, memory, emotion. Decrease of the same estrogen hormone in menopause, can be the underpinning of the neurodegenerative impacts in this phase.

Findings show the protective role of estrogen in neurodegenerative diseases, including Alzheimer’s disease. Estrogen’s role as an antioxidant is essential because there is a high level of oxidative stress in AD neuropathology [7]. There is genetic evidence linking menopausal loss of estrogen and increased risk for AD in women. A genetic overlap was found between the genes upregulated by estrogen and genes downregulated in the human postmortem AD brain [8]. There is a disruption in multiple systems in the menopausal transition. Studies have shown that the removal of ovaries before menopause triggers neurological symptoms that are similar to perimenopause. Restoring the estrogen levels has reversed the symptoms. Estrogen signaling receptors are involved in supporting the neurons’ energy demands. Glucose metabolism regulates depression and anxiety brain regions in complicated networks. Postmenopausal women with depression have hypometabolism and hypermetabolism in the pons, and the middle and inferior frontal gyri respectively [9].

Conclusion

The complications caused by the transition of phases in a woman’s life can be bothersome. Adapting to this change should be given importance in order to make the symptoms more bearable. The magnitude of impact due to hormonal changes can be mitigated via medication prescribed by a doctor. Additionally, lifestyle changes such as yoga, meditation, and a healthy diet (with natural supplements like flax seeds, vitamin E, and melatonin) can significantly improve one’s lifestyle.

References


The Effects of Cocaine Exposure on Pregnant People and Fetuses

Maya Sharma

Abstract
Substance abuse is a huge problem in the United States. In fact, over 33 million people suffer from it [1]. It is estimated that the economic cost of abuse of illicit drugs is about $193 billion [2]. The impact of such abuse can be especially adverse for the expectant people and their children. This paper discusses the effects of the use of cocaine during pregnancy on the pregnant person and the fetus. Cocaine is a powerful vasoconstrictor that damages blood flow to the offspring and also causes damage to the monoaminergic synapses in the developing brain. The effects of fetal exposure to cocaine are usually connected to the neurological and developmental abnormalities found in the offspring [3]. The long-term effects of cocaine are more devastating on the fetus compared to the pregnant person as the latter have more opportunities to recover from the exposure through rehabilitation centers and hospitals, whereas the impact of cocaine is felt by the offspring throughout their early childhood and youth.

Background
Cocaine is a very powerful and addictive stimulant drug that impacts the central nervous system (CNS). Coca is one of the oldest and most dangerous stimulants of natural origin. In 1859, cocaine was first isolated by a German chemist named Albert Niemann. Over a hundred years ago, the purified cocaine hydrochloride chemical was separated from its plant. Its original use was in a purified form and was the main active ingredient in lots of elixirs and tonics (medicinal solutions) that emerged to treat a variety of diseases in the early 1900s. However, lately, research has shown that cocaine can be a powerfully addictive substance that can change brain structure and function if used constantly [4].

Cocaine is a teratogen, which means that it is a key factor that causes deficiencies in fetuses during prenatal development. Exposure to cocaine has many dire effects on the fetus and the embryo [5]. Cocaine is one of the most used drugs in the United States, especially for illegal recreational use. As reported by the National Survey on Drug Use and Health, the abuse of cocaine in the United States has been relatively still ever since the early 2000s. In 2016, over 5.1 million
individuals older than 12 were said to acknowledge using cocaine during the previous year, and in the same year, 1.9 million people admitted to using cocaine at least one time within the last month [6]. By 2018, these numbers increased to 5.5 million [7]. Since the early 1980s, many studies have advanced the knowledge on cocaine’s destructive impacts of maternal cocaine use on fetal and embryonic development.

The cocaine molecule has seventeen carbon, twenty-one hydrogen, one nitrogen, and four oxygen atoms. Its structure is composed of three parts: hydrophilic (water-loving), lipophilic (lipid-loving), and aliphatic (where carbon atoms form open chains) groups. It can be either found as a hydrochloride salt or a “base”. The hydrochloride salt is the powdered form of cocaine and can be taken intranasally while the “base” form includes any form of cocaine that is not neutralized by acids in order to create the hydrochloride salt [5]. Also, this form spreads faster than cocaine hydrochloride does in the human body [8].

Impact of Cocaine on Pregnant People

Statistically speaking, the probability that a pregnant person addicted to cocaine is of childbearing age is quite high. It is estimated that roughly 5% of pregnant people use addictive substances and there are approximately 750,000 cocaine-exposed pregnancies every year. During pregnancy, people go through cardiovascular changes and exposure to cocaine accentuates these changes further which leads to problems such as high blood pressure, miscarriage, preterm labor, and psychological breakdown [10].

The complete impact on the pregnant person from cocaine exposure depends on a number of factors such as the amount and duration of drug use, the quality of prenatal care, socioeconomic conditions, nutrition, other diseases, and physiological conditions. Sustained periods of cocaine exposure can have devastating effects on the pregnant person [10].

Cocaine stimulates the CNS by increasing nerve cells’ uptake of norepinephrine and dopamine, chemicals that are required in the transmission of neurological signals. Increased levels of dopamine can lead to a sense of ecstasy, improved alertness and energy, and reduced fatigue. However, an accumulation of norepinephrine allows cocaine to collect at nerve terminals, and in a pregnant person, this can lead to vasoconstriction (constriction of the maternal blood vessels) as well as hypertension (high blood pressure) where the placenta and uterus are attached. Since there is a disruption of blood flow to the uterus and placenta, maternal tachycardia (an abnormally high heart rate) can occur. There is also a risk for ventricular arrhythmias (irregular heartbeat) and amnion (the innermost membrane enclosing the embryo) rupture which then causes defects in the fetus’s limbs [10].
Exposure of cocaine to a pregnant person can increase the toxicity of the drug as serum cholinesterase, which is in part responsible for degrading cocaine, is reduced in maternal blood serum during pregnancy. This means that an equal dose of cocaine in a non-pregnant person is elevated and a longer dose in a pregnant person. Additionally, the risk of spontaneous abortion (involuntary abortion), uterine rupture, and premature labor and delivery increases. Maternal cocaine use can also increase the risk of death of a fetus in the uterus which can have an adverse psychological impact on the carrier. Complications like these arise from vasoconstriction in the placenta and the resulting decrease in supplied oxygen to the fetus. The decrease in supplied oxygen to the fetus, in turn, increases the carrier’s blood pressure, hence, increasing activity in the uterus. This series of events can result in fetal anomalies such as fetal intracranial hemorrhage (bleeding in the fetus’s skull) and fetal hypoxemia (oxygen deficiencies in the fetal tissues). These complications result not only from the exposure of cocaine to the pregnant person but also because of cocaine’s low molecular weight and hydrophilic and lipophilic nature, which makes it easy for it to cross the placenta and enter into the fetus [10].

Thus, the effects of cocaine exposure on the pregnant person include neurological issues, high blood pressure, and has impacts on the nervous system. Consequently, maternal exposure to cocaine has a direct effect on fetal circulation. However, for the fetus, the impacts are much more severe as cocaine exposure damages its development in a way that can sometimes be fatal.

**Impact of Cocaine on the Fetus**

The beginning stages of pregnancy are when the embryos develop quickly. This is also the period where teratogenic substances do the most harm to the development of the embryo, specifically, during the third and eighth weeks of gestation [10].

Maternal exposure to cocaine has a variety of effects on the fetus that range from cardiac and gastrointestinal (relating to the stomach and intestine) deficiencies to tissue death due to inadequate blood supply [10].

Restriction of fetal circulation can have various effects on the growth of organs and other anatomy. Some of the common defects of fetal exposure to cocaine that have been observed in both human and animal fetuses involve the death of certain parts of the brain and intestine because of inadequate blood supply, swelling in the kidneys because of hydronephrosis (urine backup), many cephalic (relating to the head) and cardiac disorders, cleft palate and lip, Down syndrome, obstructive genitourinary defects and gastroschisis (when the fetus’s intestines protrude from their body) [10].

Maternal exposure to cocaine can lead to various types of neurological damage in the fetus. For example, in the child’s early infancy, they can present signs of irritability and hypertonia which is a condition where the CNS diminishes the ability of muscles to stretch. If cocaine is exposed to the fetus early in its development, the result is an intrusion with neurotransmitters (chemicals
involved in attention and arousal). This causes children to suffer from a short attention span and a loss of visual memories. Effects of prenatal cocaine exposure for mature children are limited, however, research has provided a link between fetal exposure to cocaine and inattentiveness in older children [10].

Furthermore, Cyclin A, a protein that regulates cell division is thought to be inactivated by fetal exposure to cocaine. When Cyclin A gets inactivated, the development of nerve cells stops in the fetus. If the development of nerve cells gets disturbed at an early stage of the fetus's development, then the neural tube (the brain and spinal cord in their earliest developmental stage), might fail to close correctly implying that the cells that form the forebrain and its overlying skull and scalp might not be produced. This results in a condition called anencephaly, or “without brain” and in most cases, the fetus ends up in stillbirth or only survives for a few hours after delivery. A less critical defect involves various degrees of a condition called spina bifida, or “split spine,” a spinal defect where part of the spinal cord is exposed through the backbone since it is missing some of its bony protection [11].

The list of the effects from prenatal cocaine exposure is long, but mainly the effects are commonly associated with neurological and developmental abnormalities in the offspring. Also, cocaine affects the monoaminergic (usually serotonin and norepinephrine) synapses in the developing brain causing changes in neurophysiology and the anatomy of the offspring. Another key point about prenatal cocaine exposure is that cocaine is a powerful vasoconstrictor and many of the medical and neurological problems that the child deals with in-utero are because of the damaged blood flow through the cerebral and placental vasculature that they experience [12].

As discussed above, the fetal impact from cocaine exposure can be long-lasting for the child. The comparison of the effects on the pregnant person and the fetus is discussed in the next section.

Comparison

While both the fetus and the pregnant person face similar risks of cocaine exposure, comparatively, the consequences are more severe for the fetus. The adult body can prove to be more resilient and there are more opportunities for understanding the effects of cocaine on their own body, diagnosing the problems, and putting the pregnant person on a course correction through medicine and rehabilitation. Cocaine’s exposure is prolonged in the fetus (compared to the carrier) because of the slow rate that fetuses metabolize cocaine [10]. Dr. Emily Fay from the University of Washington Medicine who specializes in maternal-fetal medicine says, “there are definitely ways for the mom to get sober, to maintain her sobriety... in general, moms can do quite well to stop using cocaine and get into adequate treatment” (Fay). As Dr. Fay clearly states, addiction is treatable, whereas treating the effects of fetal cocaine exposure is a much harder problem to solve. In addition to the risks discussed above, kids exposed to cocaine in-utero can become victims of cocaine addiction later in life [13].
As is clear from the discussion above, both the pregnant person and baby have the potential of suffering adverse effects for long durations of time as a result of cocaine exposure. However, the impact is far more severe on the fetus. Dr. Ira J. Chasnoff says, “While a single dose of cocaine and its metabolites clear out of an adult body within 48 hours, an unborn baby is exposed for four or five days”. This means the same dose of cocaine on a pregnant person has a longer-term effect on the fetus. Jane Schneider, a physical therapist in Chicago says, “cocaine babies are 40 times as likely to suffer delays in motor development as infants not exposed to drugs before birth”. Not only is the child’s development disturbed, but they have to live with damaging effects like deformities that last a lifetime, whereas the pregnant person might only suffer from short-term consequences, however debilitating they might be. An example of these long-term consequences on the fetus is stated by Dr. Chasnoff, “the drug precipitated labor and the baby, a boy, was born with limited use of his right arm and leg. He had suffered a cocaine-induced stroke that damaged a large segment of his brain just before he was born”. The baby boy was exposed to cocaine during fetal development. This baby will have suffered the long-term effects of deformities, while the pregnant person only suffers from effects that can be reversed in rehab centers or hospitals [13].

The fetus suffers from the challenge of facing the consequences of cocaine exposure through different stages of child development. Speaking from her medical experience, Dr. Fay notes, “it does seem like getting a mom clean and sober is an easier treatment than a baby who might need several years of early intervention,” (Fay). However, it is not about picking sides. As Dr. Fay further states, “We definitely need more programs and providers to help [pregnant people] maintain sobriety and support them, as well as more support for children who were drug-exposed in utero,” we need effective programs to address both sides of the issue.

Future Work to Improve Treatment for Cocaine Exposure

The understanding of the negative impact of cocaine on the pregnant person and the fetus has improved significantly over the last three decades. It is clear that the probability of normal birth and subsequent normal life reduces as a result of the exposure. The impacts on the pregnant person are much more observable. The pregnant person is able to communicate their symptoms to a doctor contemporaneously than a fetus can and thus is more treatable. The fetus and the child can face the consequences of their circumstances for a long period of time.

The screening for the drug impact on the fetus is rather limited, especially during the first trimester. Usually, drug testing has happened using ELISAs (Enzyme-Linked Immunoassay which detects and quantifies substances such as peptides, antibodies, hormones, and proteins), which has proved to be cheap and easy to execute in a general lab. In addition, ELISA is a reliable tool for testing cocaine metabolites in the urine. However, for testing other drugs, ELISA
has been known to give false positives and negatives. Better screening methods need to be
developed so that the feedback can be given to families in real-time to improve the quality of
awareness. Such screening is fraught with significant public health, ethical, and legal considerations
but can lead to better understanding of the impact of cocaine on the fetus and the pregnant person
during and after pregnancy. The new data can also help researchers come up with the correct
antibodies, medicine, and necessary strategies to reverse the damage that is experienced by the fetus
when exposed to cocaine [14]. However, “if we want the next generation to be fit, healthy and
adjusted, health care policy needs to be addressed,” says Dr. Dotun Ogunyemi. To avoid the
exposure to cocaine in the first place, better policies need to be formulated to eliminate cocaine
exposure for pregnant people [16].

References

By State. Substance Abuse and Mental Health Services

Drug Abuse. https://archives.drugabuse.gov/trends-statistics/costs-substance-a-

Cocaine as a Teratogen. The Embryo Project Encyclopedia.
https://embryo.asu.edu/pages/cocaine-teratogen. Retrieved:
23/04/2021.

medicine and its importance to the discovery of the different
24/04/2021.

Monitoring Centre for Drugs and Drug Addiction.

Drug-Related Risks And Outcomes. Center for Disease Control.
https://www.cdc.gov/drugoverdose/pdf/pubs/2018-cdc-drug-surve-

Indicators in the United States: Results from the 2018 National
Survey on Drug Use and Health. Substance Abuse and Mental
Health Services Administration.


[10] NIDA. (29/09/2020). What are the effects of maternal cocaine
use? National Institute on Drug Abuse.
https://www.drugabuse.gov/publications/research-reports/cocaine/

Brain. National Center for Biotechnology Information.
23/04/2021.

syndrome. MedLink.


Know That There's A Drug In The Blood Or Urine? The Truth
About Forensic Science.
https://thetruthaboutforensicscience.com/gc-ms-machine-know-t

Their Neonates for Illicit Drug Use: Consideration of the
Integrated Technical, Medical, Ethical, Legal, and Social Issues.
Frontiers.

[16] Boerner, Leigh Krietsch. (03/02/2011). Just how bad is cocaine
use during pregnancy? Reuters.
DISEASES AND DISORDERS
Body Dysmorphia: A Neurological Perspective
Laura Maisvoreva

Introduction
Body dysmorphic disorder (BDD), also referred to as body dysmorphia, is defined as a mental illness characterized by an unhealthy obsession with one's appearance [1]. These cosmetic concerns generally arise from a need to fit within a social standard that defines beauty and any facial or body anomalies that lead to insecurity and discontent with one's appearance. While a strong social connection exists, it has been found that BDD has a neurological connection also, and this connection to brain function and structure is a good indicator of why the perceptual implications of BDD exist.

What Is Body Dysmorphia?

Body dysmorphia is a perceptual impairment that causes individuals to have distorted perceptions of their appearance, often leading to depression and emotional distress [2]. People with BDD have been described to obsess over their appearance. Other symptoms of the disorder include a continual or habitual comparison to others, avoidance of mirrors, and obsessive or compulsive behaviors to alter one's physical appearance [3].

The media has been criticized for its association with how people perceive themselves and others. Social implications involve withdrawal from social settings, isolation, or avoidance because of the fear of judgement or failure to conform to a societal standard. In an age where uploading images of oneself online is popular, the obsession people with BDD have with appearance can only increase. One can only imagine the psychological impact individuals with pre-existing insecurities...
feel when constantly being bombarded with images of other people, increasing pressure to conform for praise, approval or acceptance. Social media alone is not considered a cause of BDD, but it can exacerbate the symptoms experienced in the condition, increasing its severity. This phenomenon has been termed ‘Social Media Dysmorphia’ [5]. One study confirms that the use of social networking is proportional to the extent of body dissatisfaction experienced in BDD; increased or popularization of social networking exacerbates the symptoms and feelings associated with BDD and is a ‘risk factor in the development of BDD symptoms’ [6]. A Florida House Experience study found that a staggering 87% of women and 65% of men in their study compare themselves to others on social media [7].

Antisocial behavior is not the worst outcome associated with BDD; people with BDD can be driven to self-harm, commit suicide, avoid people, or undergo unnecessary cosmetic procedures such as plastic surgery, to ‘repair’ their ‘flaws’ and increase their self-esteem and confidence. BDD is a serious condition that can severely affect people and drive them to make irrational decisions based on an unrealistic or untrue perception of themselves. While many blame the media for its contribution to either initiating the onset of BDD or worsening its symptoms, an understanding has been reached that BDD also does have a neurological basis and that some individuals may be predisposed to experience BDD without the influence of media or pressures exerted by society.

**Inside the Brain: What Goes On in BDD?**

It has been said that people with BDD have ‘abnormal visual processing’ due to disruptions in the visual cortex [8]. One study discovered that individuals with BDD had reduced activity in the visual cortex, leading to impaired visual processing [8]. These cortical disruptions are the reason why the perception of self is flawed within individuals who suffer from BDD. Hyperactivity has also been found in other regions of the brain such as the temporal lobes and prefrontal cortex, contributing to other symptoms experienced in BDD.

Subjects studied for neurological function in BDD have been found to utilize the left side of their brain more to process information, namely in the lateral prefrontal cortex and lateral temporal lobe [9]. Generally, the left hemisphere of the brain is more analytical and logical, functioning to rationalize issues and reason [9,10]. The lateral prefrontal cortex is responsible for multiple cognitive processes, and its association with BDD could be in its function that deals with ‘attentional selection’ [10]. The lateral temporal lobe accommodates the cerebral cortex and is responsible for visual processing. Hyperactivity in these areas of the brain causes an individual to be overly attentive to minor details, analysing something beyond what is apparent. In BDD, such brain function could lead to delusional processing, especially of images, leading to the obsessive behavior characterized in BDD. The condition has also been said to be associated with the obsessive compulsive disorder and other eating disorders that relate to overthinking [11]. Minor details that are normally hardly noticeable appear to be far more prominent in people with BDD, to such proportions that these issues define who they think they are or what they appear like to others, independent of anything they may otherwise have been told.
The Role of Serotonin

The role of serotonin in BDD has been debated, and conclusive evidence of a direct relationship is yet to be illuminated. However, current research suggests how this neurotransmitter is implicated in BDD, especially considering how it helps to alleviate the symptoms.

Figure 2 shows how serotonin works in BDD. First, it is released from the presynaptic neuron and enters the synaptic cleft. It then binds to receptors on the postsynaptic neuron and is taken into the neuron. Unused serotonin can be taken back up into the presynaptic neuron (reuptake) or degraded by monoamine oxidase. In BDD, the normal process of serotonin release, use, and reuptake is imbalanced, and an improper equilibrium exists between all three processes. Research suggests diminished levels of serotonin contribute to the symptoms experienced in BDD [12], and serotonin reuptake inhibitors have been proved to be effective in improving the condition by increasing the amount of the neurotransmitter available for brain function. One case report confirms this; a man suffering from BDD reported feeling less concerned about his appearance after an administration of fluoxetine, a serotonin reuptake inhibitor [13]. Many others who have been prescribed such medication have reported similar experiences, indicating that serotonin is involved, at least in some way, in the symptomatology of BDD.

Conclusion

The causes of BDD have popularly been attributed to social issues and press media for a long time, especially with the growth of technology. The popularization of social media greatly increases the insecurity experienced by people who use it most. It is evident, however, that some individuals may be predisposed to developing BDD independent of social media's influence. Ultimately, neurophysiological make-up plays an important role in the degree to which the disorder is experienced.
References


Neurofibromatosis 2 (NF2): An Overview

Shreya Gurusankar

Abstract

Neurofibromatosis is a genetic disorder that causes the formation of tumors on top of nerve tissues, which comprises large growth of masses of tissues due to the collection of cells. These extraneous tumor growths can be found anywhere along the nervous system, including the brain, nerves, and even the spinal cord. The implications of this disease range in severity, as tumors are often not cancer-causing, but can later become cancerous due to complications. Because of the expansive nature of the disease’s effects on the entire nervous system, neurofibromatosis is classified into two types - neurofibromatosis 1 (NF1) and neurofibromatosis 2 (NF2) - based on their differing implications and causes. This article will explore Neurofibromatosis 2 (NF2), the much rarer form of neurofibromatosis whose tumor growth spans across nerves connected to the brain, leading to prolonged neurological and nervous system damage.

Types of Tumors

NF2 is primarily caused by the growth of slow-growing, non-cancerous tumors that affect “the cranial, spinal, and peripheral nerves” and consequently cover the brain and the spinal cord [1][3]. The three main types of tumors seen in NF2 correspond with the signs and symptoms experienced by individuals with the condition.

The first and most common type of tumor is known as schwannoma tumors. These are made up of accumulated Schwann cells, whose function is producing myelin, the protective insulating layer surrounding nerve cells. Schwannomas are most frequently seen on the eighth cranial nerves, also known as vestibulocochlear nerves, in the brain (see fig. 1) [4]. These nerves have two main branches: the acoustic and the vestibular branches. The acoustic branch is responsible for carrying signals for hearing and comprehension into the brain, while the vestibular branch is responsible for maintaining one’s sense of position and balance. As such, people with NF2...
often have a compromised sense of balance, high rates of hearing loss, and an inability to balance themselves properly. It is notable that while vestibular schwannomas are the most common in cases of NF2, schwannoma tumors can grow on any cranial or peripheral nerve. Hence, people with NF2 often experience symptoms that are directly related to a variety of sensational abilities and feel strong sensations of pain or numbness in such areas. For example, they experience losses in vision, dizziness, etc [5]. Like other tumors, schwannomas may also be seen on the skin as “bumps” underneath the surface. While these tumors are usually non-cancerous, their severity is variable and may require treatment if the tumor growth becomes uncontrollable [3].

The second type of tumor is called a meningioma, a type of slow-growing tumor that grows on the tissue enclosing the brain and the spinal cord. Notably, people with NF2 have a significantly higher incidence of meningiomas, as they are able to grow multiple tumors on the brain and spinal cord [3]. As these tumors continue to grow, they pose the risk of compromising one’s nervous system capacity and risks of seizures, vision loss, smell loss, etc., as a result of heightened pressure caused by the growths on the central nervous system [6]. As a result, medical professionals aim to intervene earlier in a patient’s childhood when meningioma tumors are detected, in order to prevent future suppression of the individual’s bodily capabilities and brain function.

The last main tumor that is observed in cases of NF2 are the ependymoma tumors. These tumors grow within the brain or the spinal cord as opposed to on its surface. Additionally, the tumours only spread within these parts of the nervous system and not outside of it. For example, certain ependymoma tumors in the brain are found growing in the ventricles of the brain (see figure 2) as opposed to on the skull’s surface [7]. Therefore, in severe cases, these tumors can lead to headaches, dizziness, or nausea, due to their interference with the brain’s composition [8]. In children, ependymomas are more likely to occur in the lower half of the brain, while in adults, they are more frequently found in the spinal cord [8]. This is also shown in figure 2, where the ependymoma found in the brain is noted as being in a “pediatric patient.” In cases where these tumors become cancerous or pose significant implications on the patient, they can be removed surgically or by means of chemotherapy.

Signs, Symptoms, and Diagnostic Methodology
Often, NF2 symptoms are detected only in adulthood. Early-onset NF2 in children is usually only noticed through the presence of tumors in the central nervous system. Later, immediate treatment or intervention is encouraged to prevent the intensification of symptoms.

Among all symptoms of NF2, the most common is hearing loss or excessive ringing sounds in one’s ears. This is caused by vestibular schwannomas that prevent signals from being adequately transmitted through the acoustic branches of the eighth cranial nerves. Other symptoms also include issues with bodily balance (another direct result of vestibular schwannomas), seizures, loss of eyesight, or growth of tumors beneath the skin.

However, it is notable that the majority of the above symptoms are quite universal, as they may be applicable to a wide range of medical and neurological conditions. As such, in order to accurately diagnose NF2, neurologists adhere to a methodology to standardize and ensure accuracy in diagnosis. Firstly, they will check for the presence of vestibular schwannomas, the most common indicator, often used as the “hallmark” of NF2 [9]. Since the disease is genetic, they will check for any family members who may have had the same or related conditions (from which a plausible mutation could have been passed down). They will also check for the presence of the other types of tumors, including meningiomas and ependymoma tumors, as either could be the cause of NF2-related symptoms [3]. Moreover, to ensure that the symptoms are not one-off occurrences, they will often run clinical tests, including hearing tests, eyesight examinations and MRIs to confirm the presence of suspected tumors or symptoms [10].

Etiology

NF2 is a genetic disease and is caused by a faulty or a mutated NF2 gene [10]. The faulty NF2 gene is what leads to the uncontrolled growth of tumors within the brain and spinal cord, as the original gene (neurofibromin 2 merlin) is a tumor suppressor gene [11]. 50% of all NF2 cases arise from the gene passing from parent to child, which is of a relatively high likelihood given that only one parent needs to have the faulty gene in order for the child to be at risk of developing the disorder, meaning that the gene is a dominant gene [10].

However, there are also cases in which the faulty NF2 gene arises spontaneously without having been passed down in the familial gene pool. The reasons for this are unknown; hence, the cause is listed as a “spontaneous mutation” [11].

Treatment

Unfortunately, there is currently no known cure for NF2, and thus, doctors treat the condition on a day-to-day basis, given how its severity can vary unpredictably. As a result, the methodology of “regular monitoring and treating any problems as they occur” has been utilized to provide maximally effective treatments to patients on a case-by-case basis [10]. Surgery or radiation therapy can be used to remove tumors if their growth is uncontrollable and if they pose significant
risks to the functioning of the central nervous system. However, this option is known to be quite risky, as there is a high likelihood of surgical processes causing “further injury to nerves and additional neurological problems”, including complete loss of hearing [10] [11]. As a result, neurologists must carefully weigh the potential benefits of conducting the surgery against the risks based on the severity and individual scenario of the patient.

NF2 is a disease that increases in severity as one ages. This worsening occurs at different rates for different individuals. However, it can be generalized that most NF2 patients will eventually experience complete hearing loss and very limited levels of mobility. As such, it is recommended that in order to offset the impacts of NF2, patients are afforded mobility devices and hearing aides as a form of “treatment” to the disorder [10].

Ongoing Research

Currently, research into NF2 is ongoing in order to understand more about the causative factors behind the faulty gene and the tumor growths. For example, the National Institute of Neurological Disorders and Stroke is conducting ongoing studies on patients with NF2 (including MRI, blood collection, and genetic sequencing) with the aims of “identifying imaging biomarkers of hearing loss, attempting to discover the mode of peripheral neuropathy in patients with NF2, as well as attempting to discover previously unknown serum biomarkers associated with high tumor burden” [12]. In other words, this study aims to find tangible processes and phenomena associated with hearing loss, discover how common it is for patients with NF2 to have damaged nerve signal transportation networks (known as peripheral neuropathy), and determine specific proteins or “biomarkers” associated with the high incidence of tumors present in patients with NF2.

Moreover, there is also ongoing research into potential drugs and treatments for NF2, which is important given the high incidence of the disease and the lack of tangible and reliable treatments. For example, there is currently an ongoing study on the potential “effectiveness” and “tolerability” of Icotinib (a growth-inhibiting drug) as an inhibitor of the growth of tumors and vestibular schwannoma, thereby helping to reduce the severe and lasting impacts of continued tumor growth in patients with NF2 [9].

The above are just two examples of the broad ongoing research into the field of Neurofibromatosis, specifically NF2. The sheer breadth of this disease and the general lack of knowledge regarding its spontaneous causes and possible treatments have been a cause of concern for the neuroscientific research community. As such, ongoing research efforts hope to yield tangible outcomes to mitigate the effects of this disease.

Conclusion

With an incidence rate of 0.0023% (one out of every 40,000 births, NF2 has always been relatively obscure [11]. However, understanding the types of tumor growths and its correlations with
the symptoms and diagnosis of NF2 have helped to provide neurologists with a methodology to help understand and monitor the disease in patients, especially given the nature of the disease. However, it is hoped that the increase in research efforts into the causes and potential treatments can help mitigate and minimize the negative impacts of this disease on patients in the future.

References


St. John’s Wort’s Effect on Depression
Sadra Marjai

Abstract
One of the main responsibilities of neuroscience in the past decades has been to elucidate the boundaries of science and distinguish it from pseudoscience. The ever-increasing knowledge in different branches of neuroscience and the advent of newer technologies have helped neuroscientists gain insight into the effects of substances on the brain. Traditional medicine and medicinal herbs have been used for millennia to treat ailments and maladies. Many of those treatments have lost their applicability, while others have found a spot for themselves in modern medicine. Hypericum Perforatum (St. John’s Wort) is a medicinal herb that has long been used to treat depression and other diseases. By recent advances in science, its bioactive ingredients have been discovered and studied, enabling its role in treating depression and its potential side effects to be scrutinized. The aim of this article is to present a short neuro-scientific approach to depression and its treatment possibilities and to investigate the biochemical function of Hypericum Perforatum (St. John’s Wort) in treating depression.

Hypericum Perforatum (St. John’s Wort)

Hypericum Perforatum (see Figure 1) is a flowering shrub. This perennial herb produces small yellow flowers by the early and mid-summer. This plant has medical applications and has been used to treat depression, obsession, anxiety, and insomnia for the past two thousand years [1]. The botanical name, Hypericum, has a Greek origin and refers to the plant’s supposed ability to protect from demons and ward off evil spirits. Great ancient physicians, such as Hippocrates, Galen, and Pliny, have appreciated the plant’s medicinal application including its
psycho-modulatory effects [2]. This plant blossoms around St. John’s birth date, on June 24th, and is named in honor of John the Baptist. Medieval Christians used to hang the flower on stall doors or over religious icons during their feasts to protect themselves against diseases and ailments [3]. Nowadays, drug-producing companies, especially in Europe, produce standard formulations of this herb. It can be bought as a dietary supplement in grocery stores or ordered online through Amazon. Annual sales of it around the globe exceed billions of dollars. In Germany, it outsells antidepressants such as fluoxetine by as much as 20 to 1. *Hypericum Perforatum* contains many bioactive ingredients but the two most active ingredients are hypericin (a naphthodianthrone) and hyperforin (a lipophilic phloroglucinol). These two compounds have been studied thoroughly in vitro and in vivo contexts to evaluate their psycho-modulatory effects, particularly in treating depression [4]. In this review, the pharmacological effects of this herbal plant and its bioactive ingredients on neural tissues and its role in treating depression are studied [5].

**About Depression**

Depression is a mood disorder during which the mood becomes depressed and one loses interest and enjoyment in activities. It can be accompanied by physical impairment, cognitive disability, and impaired social performance. Its severity and duration may vary from person to person and accordingly it can fall into specific categories described in standard classification systems such as DSM-5 or ICD-10 [6,7]. Depression is pretty common as more than 264 million people worldwide are affected [8]. Some great historical figures struggled with depression during their lives such as Abraham Lincoln, Sigmund Freud, Franz Kafka, and Virginia Woolf.

According to WHO, depression is the "leading cause of disability worldwide" and interferes with daily activities, sleep, and thinking [8]. Depressed people may overeat or lose appetite. They may have trouble concentrating or making decisions; they may feel worthless or guilty, experience pain, experience suicidal ideation, or hurt themselves. Currently, it is known that mood disorders such as depression are cerebral dysfunctions and are the result of molecular biological abnormalities in the brain [6].

**Magnetic Resonance Imaging (MRI)**
Brain scanning devices and neuroimaging methods provide useful information about brain activity in mood disorders. Magnetic Resonance Imaging (MRI) sequences have been used to study brain changes in depression. Diffusion tensor imaging (DTI), high-resolution structural imaging (3D-T1), and functional MRI (fMRI) are among MRI sequences that have been specifically used in this regard. DTI scrutinizes the white matter microstructure, 3D-T1 studies brain morphology and the thickness of gray matter, and fMRI shows brain activity in different parts of the brain. MRI studies in depression have shown structural brain changes and abnormal brain activity in several regions, including the frontal lobe, thalamus, striatum, and parietal lobe [9]. Neuroscientists have also discovered a decrease in myelinated axons, a smaller amygdala, a smaller hippocampus and large fluid-filled lateral ventricles in patients with depression [10]. Brain regions are interconnected and form complex networks. Impairment in these connections, especially circuits connecting cortical to the subcortical area, can be the leading cause of diseases such as depression (Fig.2) [11].

**Positron Emission Tomography (PET)**

Positron Emission Tomography, also known as PET scan, is another imaging modality used for evaluating brain function and activity in mood disorders. It is a functional imaging technique that uses radioactive tracers to study metabolic activities and physiologic processes such as blood flow in the brain. PET studies in patients with all types of depression have shown decreased metabolic activities in the frontal lobe. The severity of decreased metabolism in the brain correlates with the severity of depression and normalizes when the mood returns to normal with treatment. Abnormal metabolic activity is also discovered in some other brain areas, including the temporal lobes, the cingulate gyrus, and the amygdala [12].

**Brain Chemistry**

Neurotransmitters are a series of chemicals in the body that transmit messages between nerve cells or from nerve cells to other cells such as muscle cells or gland cells. Monoamines are a group of neurotransmitters in the brain involved in the regulation of mood, emotion, and memory. Dopamine, norepinephrine, and serotonin (5-HT) are the three main monoamine neuromodulators in the body. Neuroscientists have discovered a strong correlation between mood and the levels of these monoamines in the brain. For example, norepinephrine that boosts mood and increases arousal is decreased significantly in depression. Serotonin (5-HT), another monoamine neurotransmitter, is also in short supply in depressed patients [13].
By knowing the biochemistry behind mood disorders in the brain, neuroscientists search for ways to correct disturbances in neurotransmitter levels and compensate for monoamine deficiencies. Aerobic exercises such as walking, running, biking, and swimming can boost mood by increasing serotonin levels in the cerebral cortex and brainstem [14]. Neuroscientists have also discovered the role of sunlight, massage, and even remembering happy memories in increasing brain serotonin levels [15,16,17]. Antidepressant drugs such as fluoxetine (Prozac) also elevate arousal and mood by increasing the availability of serotonin and norepinephrine in nerve synapses.

**St. John’s Wort’s Effects on the Brain**

Any compound that increases the level of serotonin and norepinephrine in interneuron synapses is potentially capable of elevating mood and treating depression. Monoamine oxidases (MAO) A and B are outer mitochondrial membrane proteins. These proteins catalyze the oxidation and degradation of amines, including monoamine neurotransmitters, serotonin, norepinephrine, and dopamine. Drugs that inhibit the activity of monoamine oxidase can increase the amount of monoamine neuromodulators in the synaptic cleft and can clinically be used for the treatment of depression. Isocarboxazid (Marplan), phenelzine (Nardil), and selegiline (Emsam) are some examples of the MAO inhibitor (MAOI) drugs prescribed for the treatment of atypical depression and treatment-resistant depression [18].

Hypericin is one of the main ingredients of St. John’s Wort. It was once thought to be the main antidepressant constituent of this plant. It works by inhibiting enzymes MAO A and MAO B. Therefore, monoamine levels such as serotonin and norepinephrine increase in the synaptic cleft and help treat depression [19]. Later studies showed that hypericin’s ability to inhibit MAO was lower than what was first presumed and the level of hypericin necessary to obtain significant MAO inhibition was far greater than that likely to be found in human brain tissue at normal doses [20].

After being released by a presynaptic nerve cell, monoamine neuromodulators attach to and activate receptors at postsynaptic dendrites. Some of the serotonin released in the synapses is reuptaken and deactivated by presynaptic axons. Selective Serotonin Reuptake Inhibitors (SSRI) are the main synthetic antidepressants that increase serotonin at the synaptic level by inhibiting its reuptake by presynaptic nerve cells [21]. Fluoxetine (Prozac), fluvoxamine, paroxetine, sertraline, and citalopram are the five major SSRIs. They have a very low affinity for neurotransmitter receptors (post-synaptic) and a high affinity for 5-HT reuptake transporters (pre-synaptic) [22].

Hyperforin, the other main ingredient of St. John’s Wort, inhibits serotonin reuptake, like SSRIs. Unlike synthetic antidepressants that block 5-HT receptors, it inhibits serotonin reuptake by an increase in sodium uptake by presynaptic neurons and elevating intracellular concentrations of sodium (Na⁺) and calcium (Ca²⁺). The loss of the Na⁺ and Ca²⁺ gradient between the neuron and the synaptic cleft decreases reuptake of the monoamine neurotransmitter and increases their level in the synaptic space [23]. This different mechanism of action may lead to a new class of antidepressants in
future. Hyperforin also has shown to increase 5-HT receptors in rat brains, indicating a possible long-term therapeutic benefit [24].

Potential Toxicity of St. John’s Wort

The human body is a complex structure with many systems working together to maintain one’s health. Brain and the nervous system function in collaboration with other body parts, affecting and being affected by other organs. Synthetic pharmaceuticals and medicinal herbs used to treat mood disorders such as depression are ingested by the body and can affect not only the brain and nervous system but the whole body.

St. John’s Wort is found to induce Cytochrome p450. Cytochrome p450 is a large and diverse family of enzymes that metabolize and degrade drugs and toxic compounds. By inducing Cytochrome p450, St. John’s Wort can weaken the effect of medications that are metabolized and degraded by Cytochrome p450 such as birth control pills, digoxin (a heart medication), oxycodone (a pain medicine), some HIV drugs (such as indinavir), some cancer medications, and Warfarin (an anticoagulant or blood thinner). By decreasing the therapeutic level of these medications, some clinically adverse outcomes may happen. In addition, concomitant use of St. John’s wort with other antidepressants that increase serotonin level in the body can result in serotonin syndrome, which is a potentially life-threatening condition with symptoms including agitation, diarrhea, fast heartbeat, high blood pressure, hallucinations, and increased body temperature due to elevated serotonin level in the body [25].
Conclusion

Hypericum Perforatum or St. John’s Wort is a medicinal herb that has long been used for treating depression and some other psychological disorders. The serotonin level in the synaptic cleft is increased by the effect of its two main bioactive ingredients:

1. Hypericin: acts as a MAOI and blocks degradation of serotonin and other monoamine neurotransmitters
2. Hyperforin: functions similar to SSRIs but with a different mechanism and inhibits serotonin reuptake by presynaptic nerve cells.

Hyperforin is now considered the main anti-depression constituent of St. John’s Wort; hypericin’s activity is shown to be less than what was once presumed. St. John’s Wort induces a cytochrome p450 enzyme that is responsible for the degradation of many prescription drugs and can weaken their efficacy. Concomitant use of St. John’s Wort with other antidepressants can lead to serotonin syndrome that is potentially a life-threatening condition. Today, St. John’s wort is available by prescription in Europe, especially in Germany. In the US, the Food and Drug Administration (FDA) has not approved the substance for depression or any other medical condition.

References


Transcranial Magnetic Stimulation: A Treatment for Depression

Arya Reddy

Abstract

Depression is currently one of the most common mental health disorders. Mechanism-based therapies for this condition, however, remain elusive. Repetitive transcranial magnetic stimulation (rTMS), a non-invasive technique that uses a pulsed magnetic field to induce electrical activity in the brain, is thought to be an essential therapy for depression [7]. rTMS is a new and emerging technology that utilizes magnetic waves to stimulate the brain and help people become less depressed. The treatment sends currents through a coil to create a magnetic field that affects the nerves. This article discusses the mechanisms, side effects, and the future scope of TMS treatment.

Depression

Depression is a mood disorder characterized by a constant feeling of sadness and lack of motivation. It changes how a person acts, perceives, and responds to stimuli and can cause a host of mental and physical symptoms. A person suffering from depression might find it challenging to carry out day-to-day tasks and may feel undue sadness, sometimes to the extent that they believe life isn't worth living [3]. Depression can vary in severity from moderate, temporary depression to extreme, long-term depression. Medical depression, also known as major depression or major depressive disorder, is a more extreme type of depression. It’s not the same as sadness that might be brought about by a tragedy, such as a loved one’s death or by a medical illness. Symptoms are typically severe enough to trigger difficulties in intimate relationships or everyday activities such as work, education, and social interactions [4].

Current Treatments for Depression

The majority of people who have been diagnosed with depression respond well to medication and psychotherapy. A primary care physician or therapist typically prescribes medications to alleviate symptoms. Many individuals suffering from depression, on the other hand, benefit from visiting a therapist, counselor, or other mental health specialists. Some available antidepressants are selective serotonin reuptake inhibitors (SSRIs), Serotonin-norepinephrine...
reuptake inhibitors (SNRIs), atypical antidepressants, tricyclic antidepressants, and Monoamine oxidase inhibitors (MAOIs) [5]. Psychotherapy is a common term for consulting with a therapist, psychologist, or other mental health specialist for mental health issues. Psychotherapy teaches patients how to take control of their lives and deal with difficult circumstances using positive coping mechanisms. A mix of many approaches is commonly used to treat depression [6].

**Transcranial Magnetic Stimulation (TMS)**

TMS (transcranial magnetic stimulation) is a non-invasive therapy for depression that uses magnetic fields to activate nerve cells in the brain. TMS is commonly used when all other depressive therapies have failed. Repetitive TMS, or rTMS, is a therapy for depression that requires the delivery of repetitive magnetic pulses [8]. TMS systems work entirely outside of the body, affecting central nervous system function by delivering strong magnetic fields to various brain regions linked to depression such as the limbic system. TMS does not require anesthesia, and the side effects are usually minuscule compared to antidepressants and electroconvulsive therapy (ECT) [2].

**Mechanism**

TMS is a non-invasive tool that modulates neuronal processing in the brain by causing a brief discharge of electric current through a stimulated coil. This generates a magnetic field that causes neuron membrane potentials to depolarize in cortical tissue under the coil, affecting the associated nerve loop function. The effects of TMS are linked to context-dependent variables such as total pulses, stimulus frequency and strength, time period between each pulse, and regions on the cortex. Different forms and variations of stimulation, as well as the targeted brain area, can have different biochemical effects. In fact, certain stimulus models may have long-term effects on neuronal function that can continue well after the therapy time has finished [7]. Consequently, during a TMS treatment, an electromagnetic coil is positioned near the forehead. The electromagnet sends a painless magnetic shock to nerve cells in the part of the brain that controls mood and depression. This is intended to stimulate brain areas that are underactive in depression [8].

**Treatment Process**
In most cases, repetitive TMS is performed in a doctor’s office or laboratory and only shows success after a number of therapy sessions. In most cases, meetings are held five days a week for four to six weeks. The doctor determines the best location for the magnets to be placed on the head and the best dosage of magnetic energy for the patient before therapy begins. The duration of the first consultation is usually about 60 minutes. During the first visit, the patient is taken to a recovery area, where they receive treatment. To emit soothing pulses, an electric coil is positioned against the head and turned on and off repeatedly. This produces a tapping or clicking sound that lasts for a few seconds before stopping. A clicking feeling can also develop on the forehead. The term “mapping” refers to this stage of the process. By increasing the magnetic dosage until the patient’s fingertips or hands twitch, the doctor decides the amount of magnetic energy needed. This is referred to as the motor threshold, and it acts as a criterion for deciding the optimal dosage for the patient. Based on the symptoms and side effects, the level of stimulus is increased during therapy [1].

**Side Effects**

rTMS is well-tolerated and has few adverse effects, with only a limited number of patients opting to avoid therapy due to them. Headaches are the most frequent side effect, reported by around half of patients infected with rTMS. However, this is a minor side effect and usually goes away as the therapy progresses. These headaches can be treated with over-the-counter pain relievers. With rTMS pulses, about a third of patients can experience unpleasant scalp stimuli or facial twitching. This, too, appears to fade with time, though changes in coil orientation and stimulus settings may be made right away to alleviate pain. Since the rTMS system is quite loud, the patients are given earplugs to wear during the procedure. However, some patients may continue to have hearing difficulties after treatment. If earplugs are used during therapy, there is no indication that these symptoms are lasting. Many of the adverse effects of antidepressant drugs, such as gastrointestinal irritation, dry mouth, sexual impairment, weight gain, and sedation, have not been linked to rTMS. Seizures are the most severe side effect of rTMS, although they are highly rare. Even though rTMS is a safe technique, it is worth noting that since it is a modern medication, there could be unforeseeable complications [8].

**Contraindications**

rTMS should not be used on patients who have any form of non-removable metal in their heads (except braces or dental fillings). Failure to adhere to this rule can cause the object to heat up, shift, or malfunction, resulting in serious injury or death. A list of metal implants that can prohibit a patient from having rTMS is as follows: aneurism clips or coils, stents in the neck or brain, deep brain stimulators, electrodes to monitor brain activity, metallic implants in the ears and eyes, shrapnel or bullet fragments in or near the head, facial tattoos with metallic or magnetic-sensitive ink, and other metal devices or objects implanted in or near the head [8].

**Future Scope**
There is currently no definitive data to justify the use of rTMS as a substitute treatment for depression. Although promising outcomes have been documented in both open and randomized controlled trials, the best treatment criteria for individual therapy, such as stimulation location, severity, frequency, and length, are still uncertain [7]. Although these TMS applications are commonly used in clinics around the world, they are still relatively recent and innovative strategies that just scratch the surface of what potential applications may bring. Many future implementations are either in the proof-of-concept stage or are entirely unknown. There have been many studies concerning the protection and effectiveness of noninvasive stimulatory therapies for depression and brain imaging, but other uses have not been examined as extensively. Some of these future implications show that this form of therapy will become even less invasive. TMS has a wide variety of benefits, including the treatment of psychiatric conditions such as obsessive-compulsive disorder (OCD) and addiction. Applications to help understand the interconnectedness of neuronal processes are another possibility. Most experiments that have been or are currently being conducted to assess the efficacy of TMS for uses other than those listed are still in the proof of concept stage, with limited numbers of participants and no control groups to compare against [9].

Conclusion

Depression is one of the most common mental health problems today. Many treatments for depression such as mechanism-based treatments are also a long way off. The non-invasive technique of repetitive transcranial magnetic stimulation (rTMS), which uses a pulsed magnetic field in the brain to stimulate electrical activity, is considered to be an effective treatment for depression. The key findings of clinical and basic research on rTMS for depression, including its antidepressant potency, basic mechanisms, and ability to regulate neuronal functions, neurotransmitters, and brain networks, as well as synaptic and molecular pathways, indicate that it may be a promising choice for treating depression [7].

References


NEUROSCIENCE AND SOCIETY
A Cycle of Stress: A Study of Increased COVID-19 Exposure Through Body-Focused Repetitive Behaviors

Hannah Pescaru

Abstract

Body-focused repetitive behaviors (BFRBs), impacting up to 5% of the American national population, are behaviors in which a person uncontrollably fidgets with his or her body in ways that cause physical damage. They can often be dismissed as bad habits; however, BFRBs are actual disorders and much harder to treat due to changes in brain anatomy and external stressors. These disorders leave the individual more susceptible to infection through increased contact with the facial region and orifices. In this literature review and synthesis, a potential link between body-focused repetitive behaviors and COVID-19 exposure is discussed. The added stress and anxiety of contracting the virus results in an increase of severity and frequency of these disorders, which, in turn, further increases the risk of COVID-19 infection. The end result is a complex cycle in which an individual is trapped between the stress of his or her conditions. Methods of prevention are also discussed in order to promote individual safety during the pandemic.

Neurobiology

Body-focused repetitive behaviors (BFRBs), estimated to impact up to 5% of the national population, are behaviors in which an individual repeatedly fidgets with his or her own body in ways that produce lasting physical and psychological damage [1]. BFRBs—including trichotillomania (hair-pulling), dermatillomania (skin-picking), and onychophagia (nail-biting)—can be subclinical and relatively...
common, but they can also be more severe, albeit rarer [2]; pathological manifestations of BFRBs can be conceptualized as disorders [3].

Although BFRBs are still a relatively novel topic in the research world, some studies have suggested a predisposition to the disorders through genetics or experienced stress [6][7]. Modern imaging studies have also been conducted to research the anatomical differences in the brains of BFRB groups and control groups. One such study provided evidence for cortico-basal ganglia circuit dysfunction in obsessive-compulsive-spectrum disorders [8]. As corticostriatal circuits and the basal ganglia are both responsible for regulating impulsive motor behavior, damage or lesions to any part of these circuits could lead to their hyperactivity and abnormal repetition of behavior [8][9][10][11]. This dysfunctional impulsivity can lead to a dysregulation in the brain’s dopamine reward system, increasing feelings of pleasure, gratification, or emotional release in BFRB patients when engaging in their behaviors [12][13].

Another studied characteristic of these behaviors is their ability to seemingly increase pain tolerance in their patients. A recent study conducted by Professor Jon Grant compiled evidence that individuals with a BFRB (specifically dermatillomania) were able to withstand higher levels of pain as compared to those in control groups; while still reporting similar levels of pain intensity, individuals with dermatillomania experienced dampened autonomic responses [13]. These results can be extrapolated to other BFRBs and can potentially explain why these individuals actively and subconsciously continue to engage in these painful behaviors. According to the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders, the diagnostic criteria for body-focused repetitive behaviors also involves identifying a patient’s impairment in function from engaging in his or her behaviors as well as repeated attempts to reduce or stop them.

These studies give a brief background on BFRBs and demonstrate how difficult it may be for patients to stop engagement. However, as stress is hypothesized to exacerbate these behaviors, the added anxiety induced by the COVID-19 pandemic could greatly increase this difficulty [3]. Furthermore, since the spread of the COVID-19 virus is expedited through contact with one’s face and orifices, individuals with BFRBs could be at a greater risk for contracting the virus. Humans are intrinsically prone to touching their faces 10-20 times an hour, but individuals with BFRBs are at an even greater risk because of their compulsions [4]. These two phenomena, acting together, could potentially create a complex cycle in which BFRB patients stress over their chances of being infected with COVID-19, increasing their BFRB engagement, resulting in an even higher risk of infection.

**Implications During the COVID-19 Pandemic**

Body-focused repetitive behaviors are already associated with increased sensory sensitivity, indicating potential abnormalities in the sensory process [2]. This sensory sensitivity could potentially indicate that individuals with BFRBs are already more prone to feelings of anxiety and stress after consuming media covering COVID-19. BFRBs were also found to be maladaptive emotional regulation mechanisms, with higher feelings of perceived stress leading to greater disease severity. Trichotillomania specifically was shown to increase in severity in patients that have
experienced past traumatic events [1][5][14][15]. Individuals with BFRBs demonstrated an increased reaction time in which to control these feelings of stress [16]. The synthesis of these studies offers an explanation as to how body-focused repetitive behaviors are exacerbated by feelings of stress and anxiety.

Simultaneously, body-focused repetitive behaviors, specifically onychophagia, were shown to increase the risk of infection of Enterobacteriaceae [17][18]. Onychophagia is characterized by the practice of keeping one’s hands close to the mouth from a few seconds to half a minute [19]. In this time, the fingers act as carriers of microorganisms from the external oral environment into the oral cavity, whose warm and moist environment can support the growth of these microorganisms [17][18]. This data can be extrapolated to the transmission of the COVID-19 virus, which is highly contagious and can last on surfaces from a few hours to days. In fact, a 2020 study has provided evidence for an increased chance of being diagnosed with a general psychiatric disorder three months after infection with COVID-19. Correspondingly, a diagnosis of a general psychiatric disorder the previous year, before the pandemic’s outbreak, was found to be associated with a 65% higher chance for contracting COVID-19 in the present period, regardless of known physical health risk factors [20].

In summary, individuals with body-focused repetitive behaviors are already more affected stress-wise by the media concerning the current pandemic, but the increased engagement in these behaviors further increases their risk for contracting COVID-19. As a result, during the pandemic, these individuals are experiencing a cycle in which their own behaviors aggravate their conditions mentally, emotionally, and physically.

**Possible Treatments**

These results show that individuals with body-focused repetitive behaviors are at risk of worsening their mental and physical health by themselves. Consequently, potential prevention methods must be discussed in order to protect this population from the stress of COVID-19 infections. For the best possible result, patients should consult their primary care physician to identify what treatment is best for them. One possibility for general prevention and treatment for BFRBs is therapy, including pharmacotherapy, psychotherapy, and cognitive-behavioral therapy. Pharmacotherapy can include treatment with drugs such as n-acetylcysteine and clomipramine, although data researching these substances is limited [21][22]. Cognitive-behavioral therapy, most commonly habit reversal therapy, is also proven to be efficacious in affected individuals [23]. This primarily behavioral therapy involves awareness training, stimulus control, and competing response training. Essentially, work must be done by each individual to identify and suppress his or her personal triggers, as well as find behavioral substitutes, such as sitting on their hands to prevent engagement in the BFRB [22]. Loved ones also play a critical role in an affected individual’s treatment. By establishing a supportive and positive environment, loved ones can offer vital encouragement to boost the individual’s self-confidence [24].
For onychophagia specifically, aversive therapy can include using olive oil or bitter-tasting polish in order to deter individuals from biting or chewing on their fingers [24]. However, especially during the COVID-19 pandemic, this solution can be harmful as it would still potentially involve contact with the oral cavity. One specific solution is wearing a smart device that would alert the user when their hands are unintentionally brought up to the face. Humans are naturally prone to touching their faces 10-20 times an hour, increasing their risk of viral infection. Thus, these devices could be a harmless, effective way to avoid that contact [4].

For general COVID-19 prevention, all individuals should continue with handwashing, cleaning high-touch surfaces, and wearing masks to avoid the spreading of particles. Not only would this ultimately help the individual with a BFRB by reducing the possibility of exposure, but it would also protect family and friends from the transmission.

To conclude, individuals with body-focused repetitive behaviors are more inclined to touch their faces and facial orifices than the average person, increasing the risk of contracting COVID-19. This added anxiety and pressure further contribute to behavior engagement, resulting in a cycle of immense stress for the individual’s health in a time when the world is already suffering under the stress of a global pandemic.

References


How Listening to Music Affects the Human Brain
Mark Messak

Abstract
Music is a fundamental attribute of humankind. It has existed in our cultures throughout history. The human brain and nervous system are hard-wired to recognize and distinguish music from other kinds of noises. Music affects brain function and human behavior in various ways, including reducing stress, pain, and symptoms of depression while enhancing cognitive and motor skills, spatial and temporal learning, and neurogenesis which is the brain's ability to produce neurons. Research further shows that people with neurodegenerative diseases such as Alzheimer's and Parkinson's respond positively to music.

Introduction
Music, like language, is a ubiquitous aspect of society. Like every other art form, music has always been viewed from an aesthetic perspective. Its healing power has been documented in various music traditions across the world. The current belief is that today's language emerged via a proto-language driven by gestures and framed by auditory elegance. Singing, an integral part of many music forms, is performed by the flexibility that resulted from expanded anatomical developments, not only of the brain but also of our facial, pharyngeal, and laryngeal muscles. Around the same time (to an accuracy of several thousand years), the human brain was bicameral with the two cerebral hemispheres cooperating coordinating the life of the individual coherent with the surrounding environment. The brain became differently balanced concerning the functions of the two sides: pointing and suggestion (left) versus urgency and longing (right). These findings support that both music and spoken language, the first musical
instrument used by our ancestors *Homo neanderthalensis*, evolved from a proto-language [9].

There’s no doubt that music affects our emotions and feelings. Different types of songs evoke different feelings and can change one’s mood in just a second. For instance, some songs can make someone weep, while others can make them feel over the moon with joy. Scientists have spent years trying to understand this phenomenon, ultimately finding the answer in our brain. Before we explore the effects of music, we first need to know how it travels from our ears to our brains [3].

When the waves from a musical instrument enter the outer ear and reach the middle ear, they cause the eardrum and some tiny bones to vibrate. These longitudinal waves then pass to the inner ear. The snail-shaped cochlea is found in the inner ear and contains about 20 to 30 thousand tiny hair cells that can interact with different tones and pitches due to their different sizes. The inner ear and cochlea convert the vibrations to electrical signals allowing the brain to understand them. These signals are finally transferred by the neurons found in the cochlear nerve system to the auditory complex in the brain’s temporal lobe, where they are processed by the brain until they resemble what we know as music [2,3].

**The Brain and Music**

A better understanding of how and why humans are so moved by music can emerge from a more in-depth look at how the brain functions. Music causes structural and functional changes within the brain, both with immediate exposure and over several weeks, months, and years. The very fact that music is processed by numerous areas of the brain (ranging from the cortex to the limbic system, to the neuroendocrine and even autonomic nervous system) emphasizes the wide-reaching impact music has not only on our brain but also on our bodies. Music activates every area of the brain that scientists have so far mapped [1]. There is no brain area known that music does not touch in some way, and these different parts of the brain have their unique musical functions, whether we are listening to music or performing it.

Twelve regions of the brain are closely related to processing music and bringing about neurological changes. They are the frontal lobe, the temporal lobe, Broca’s area, the Wernicke’s area, the occipital lobe, the cerebellum, the nucleus accumbens the amygdala, the hippocampus, the hypothalamus, the corpus callosum, and the putamen. Given our understanding of the biological processes of the brain, it appears that our evolutionary and instinctive response to music can shape brain structure and our performance to reduce the severity of joint disease and improve wellness in a population [2].

**How Music Affects Different Parts of the Brain**
Our brain could be considered the most important thing in our body that is affected by listening to music. When one feels happy while listening to music, the pleasure centers in the brain are activated, producing more dopamine that makes you pleased and activates the reward centers of the brain. This response to music has led some scientists to believe that music is similar to drugs. After all, it stimulates the substantia nigra, which produces a protein, and the nucleus accumbens, which plays a central role in the reward circuit. Music may also increase neurogenesis within the hippocampus, allowing the production of new neurons and improving memory [i].

In addition to making one feel pleasant, music may influence brain development itself. For example, learning how to play a new instrument increases the gray matter volume in some parts of the brain [7]. Additionally, playing music may increase the function of Broca’s area, which enables us to communicate and cooperate with other people better. Furthermore, music can enhance the functions of the frontal lobe in decision-making and planning [7].

Scientists have also discovered that people with Alzheimer’s disease never forget the musical instruments they play or even the rhythms that they know [6]. Since scientists identified that the rhythms of music and melodies are all stored in the cerebellum, they concluded that Alzheimer’s disease does not affect this region of the brain. This conclusion has been proven by many other experiments and research that show that procedural memory (responsible for playing musical instruments) is usually the least affected by Alzheimer’s disease [i].

The answer to how music can change people’s moods based on its type is found in part of a brain called the amygdala. The amygdala stimulates the emotions to perceive, recognize, and interact with different types of music. The basolateral amygdala, which is the center of the region, is the primary way in which sound enters to be processed along with other sensations, and it responds to both music that makes us happy and fearful [1,9].

One of the greatest influences of music in the brain is that it may increase the neurogenesis in the hippocampus, which is responsible for our navigation as well as regulation of our emotional response, allowing the production of new neurons, which leads to improving memory [i].

**Functional Magnetic Resonance Imaging**

Functional Magnetic Resonance Imaging (fMRI) is a technique that is used for mapping brain activity in a safe way. It does so by imaging metabolic function as well as blood flow to different parts of the brain. This is the main difference between fMRI and MRI, which instead scans for anatomical functions [4].
The scanner consists of a doughnut-shaped magnet with a tunnel in its center and a table on which the patients can slide into the machine. The waves are produced to interact with the magnetic position of the atoms in the brain and are sent into a computer that produces an image that can be converted into a 3-dimensional shape, which can be used to examine brain diseases and disorders [5].

When this technique was used to see music response on the brain, scientists found that a region in the superior temporal gyrus (STG) responds to a musical stimulus. The finding supports the idea that there is not only one particular area that analyzes music. Instead, different parts of the brain can and do respond to it. This experiment also confirmed that there are regions in the STG that respond to music more than voice. These findings provide further support for the neural separation of music and speech within the temporal lobe [10].

How Music Is Used in Neurological Treatments

As music has a significant influence on different parts of the brain, scientists have used it as a method to treat the symptoms of neurological disorders. The types of music therapies are numerous, and it is hard to capture them all. However, the most famous method of music therapy is Neurologic Music Therapy or NMT. NMT is an evidence-based method that uses techniques to treat the brain using specific elements such as rhythm, melody, and dynamics, as these elements can make new neural connections that enhance the brain and treat some disorders [8].

Music can increase dopamine levels inside the brain, so it can also temporarily stop the symptoms of Parkinson’s disease. Rhythmic music, for instance, has been used to help Parkinson’s patients who require assistance in moving in tasks like getting up and down and walking. Unfortunately, after the music stops, the symptoms return [1].

The Negative Implications of Music

Nothing in the world is ideal. In addition to advantages, there are disadvantages associated with music too. While music can treat or even reduce the symptoms of some disorders, it can also negatively affect our brain and nervous systems.

Contrary to classical music which enhances memory, some types of music like hard rock or acid rock music can inhibit some people’s ability to store information in their brain. Rock music is also a type of music that can stimulate the adrenal hormones from the medulla and increase the levels of adrenaline to a point where it negatively affects the heart and further causes disorders [11].

An experiment done on mice to see the influence of disharmonic music supports that this type of music can negatively affect memory. Two scientists, a physicist, and a neurologist divided the 36 mice into three groups: a control group that did not listen to any music, a group that listens to harmonic music, and a group that listens to disharmonic music. They then put the mice in a maze that they had previously passed through three weeks before the experiment [11].
The scientists observed that the control group and the group that had listened to the harmonic music were able to pass through the maze again successfully. However, the group who listened to the disharmonic music was not able to pass the maze again as they did not memorize it. Furthermore, these mice also exhibited aggressive behaviors. So, the scientists concluded that disharmonic music negatively affected the memory as well as killed some neurons and changed the mood of the organism negatively [11].

Conclusion

Through music, we can learn a lot about our human origins and the human brain. Music is a potential method of therapy and a way to access and stimulate specific brain circuits. There is also a link between musical creativity and psychopathology [9]. Overall, the functionality of the brain and its attributes are affected by various exposures and experiences. Our daily feelings of happiness, anxiety, sadness and various forms of modesty can be influenced by music. Music has also shown its influence on various diseases, including providing excellent benefits for Alzheimer’s patients by reducing their symptoms. Music enhances different brain parts like the frontal lobe, responsible for rational thinking and decision making. Broca’s area, which is the speech center for the human brain, can also be enhanced through music listening, improving communication skills and ability. Interestingly, the occipital lobe, an area of the brain that is responsible for vision processing, can also be activated by listening to music. Many other brain parts are connected and are affected by music experiences. As seen in this article, our brains are greatly affected by music. So, will you think of how your brain functions the next time you listen to music?

Glossary

- **Proto-Language**: a hypothetical parent language that is lost and it is believed that actual languages are derived from it.
- **Cochlea**: a spiral-shaped cavity in the bony labyrinth of the inner ear that converts the vibrations of the cochlear fluid produced by hearing sound into neural signals.
- **Substantia nigra**: a basal ganglia structure in the midbrain that mainly produces dopamine and the death of its neurons causes Parkinson’s disease.
- **Parkinson’s disease**: a brain disorder that causes tremors, stiffness, difficulty walking, balance and coordination.
- **Nucleus accumbens**: a region in the basal forebrain that is a part of the reward system.
- **Alzheimer’s disease**: a form of dementia that primarily affects memory.
- **Basolateral amygdala**: a complex that consists of lateral, basal, and accessory-basal nuclei of the amygdala that stimulates the fear response.
- **Superior temporal gyrus**: one of three gyri in the temporal lobe that is situated somewhat above the external ear.
References


Particulate Matter: Its Detrimental Effects on the Brain

Kathyayini Mendu

Abstract

80% of the population is living in areas where the air quality levels are unsafe. Breathing in polluted air can be severely detrimental to one's health, making it a significant problem that needs to be addressed. The following research describes the adverse impacts of particulate matter pollution on the brain in order to spread awareness about the effects of particulate matter air pollution on the brain. It was found that generally a significant increase in particulate matter pollutants can deteriorate brain matter, impair cognitive function and brain development, and increase the risk of developing neurological disorders. The synthesis paper describes each of these effects in detail. An interview was conducted with a professional in addition to documents being analyzed in order to further understand the topic. The secondary research supported the hypothesis that a significant increase in particulate matter will hinder the brain and can produce many adverse side effects and neurological development disorders.

Introduction

Oftentimes in the media, environmental concerns are dismissed. Many people believe that economic benefits outweigh the impacts of pollution, but air pollution can significantly damage one's health. Pollutants can have numerous near-fatal consequences and have led to the deaths of millions worldwide. New research has even found that air pollution can even harm one of the body’s most sheltered organs: the brain. A significant increase in particulate matter will hinder the brain’s ability to function by causing deterioration of the brain, slow
development in fetal life, and increase the risk of developing neurodegenerative disorders.

**Cognitive Decline**

A substantial increase in the concentration of particulate matter can harm the brain's ability to function. Particulate matter pollution can deteriorate brain matter, which impairs one's ability to do tasks they normally would not have trouble with. Studies have determined that particulate matter has a great impact on certain regions of the brain, including the olfactory bulb, cerebral cortex, striatum, hippocampus, and cerebellum\[6\]. Each of these structures is vital to our daily functioning: the olfactory bulb is related to the sense of smell; the cerebral cortex is the largest part of the brain and carries out most functions; the hippocampus is the seat of memory, and the cerebellum is related to tasks that involve motor coordination\[4\]. Impairing these places will not only affect the brain but the parts of the body they correspond to. It can also degrade white matter: one of the two types of matter in the brain. White matter is essential for communication between neurons as they send electrical signals from one cell to another\[11\]. According to Xin Zhang, a researcher at Beijing Normal University's school of statistics, men have less white matter in the brain on average \[8\]. They were particularly impacted and had lower verbal and math test scores\[8\]. In addition, the outer layer of the brain, also known as the blood-brain barrier, which is important in keeping unwanted elements out of the brain, is damaged. This can have a myriad of consequences, such as decreasing cognitive functioning or increasing the risk of neurodegenerative disorders. Breathing in pollutants for extensive periods of time can speed up the aging process\[8\]. Cognitive functioning is the means or ability to acquire any information\[8\]. A decrease in the ability to learn can severely hinder the lives of others and their ability to perform certain tasks. A study published in the Proceedings for the National Academy of Sciences found that long-term exposure to particulate matter contributed to cognitive decline in patients as they aged \[8\].

**Hindrance of Early Development**

Particulate matter pollution has many other harmful effects, like hindering development in a fetus. The brain of a fetus is especially susceptible to external influences. Particulate matter impacts children more than adults as developing brains are more susceptible to pollutants\[18\]. Having a properly developed brain is important for carrying out many tasks\[15\]. A study regarding pollutants from traffic observed trends of decreasing birth weight across increasing pollutant concentrations. Particulate matter less than 2.5 micrometers in length was consistently associated with an increased risk of low birth weight\[14\]. It was estimated that about 3% of term low birth weight cases in London were directly attributable to exposure to particulate matter\[14\]. An increase in pollutants was found to be associated with behavioral problems, an increase in inattentiveness, and a decrease in the volume of the brain, specifically the caudate region\[14\]. The caudate specializes in motor planning as well as processing memories and learning\[13\]. A growing body of evidence begets the conclusion that air pollution might be associated with neurobehavioral outcomes in young children. Pollution affects the brain by causing neuroinflammation\[13\]. Exposure to fine particles during fetal life was associated with a thinner cortex or outer layer of the brain\[13\]. The study showed that these brain abnormalities increase the difficulty to establish self-control over impulsive behavior. It found that
an increase in pollutants is associated with poorer cognitive development in young children, neuroinflammation, and an alteration of the brain’s immune responses. Diesel exhaust is one of the biggest contributors to air pollution[18]. Pollutants can be linked with neurotoxicity, behavioral abnormalities, neuroinflammation, and they can also hinder the development of the brain [9].

The particles lodge themselves on the placenta. A recent observational study that examined the placenta of five pregnant women discovered soot in their placenta[17]. Even though the particles were not in the baby’s body, they can degrade the placenta which will directly impact the fetus[17]. A different experiment showed that maternal exposure to particulate matter during pregnancy caused mitochondrial dysfunction and the destruction of nerve cells in the cerebral cortex of mice offspring [17].

Neurodegenerative and Psychological Disorders

Particulate matter pollution can cause certain neurological disorders as well, such as Alzheimer’s disease[5]. Air pollution has been found to damage the blood-brain barrier, which can lead to conditions like Alzheimer’s and Parkinson’s disease in later life. Some particles like magnetite can also enter the body through the olfactory nerve and the gut. Magnetite’s magnetic charge makes the substance very toxic to the brain[5].

There is growing evidence of a link between pollution and dementia. Many studies, including one that found areas with unsafe levels of air quality doubled the risk of dementia in women, have added to the growing body of research that demonstrates air pollution’s adverse impacts on the brain[16]. This theory was first researched in the 2000s when dogs living in polluted cities in Mexico developed symptoms similar to those of dementia [16]. These dogs were found to have plaques in their neurons, a symptom associated with

Figure 2. Path of particulate matter and potential effects on the body [20]
Alzheimer's [16]. An experiment analyzing mice that were exposed to pollutants found plaques in the neurons of the mice [16].

This long-term exposure can also increase the risk of developing schizophrenia, as described by a recent study by the University of Rochester Medical Center[7]. Air pollution is known to have disastrous effects on the body. A study that was a time-series analysis done in Beijing, China, investigated the effects of particulate matter on hospital admissions for mental disorders[3]. The authors reported that elevated levels of particulate matter were significantly associated with a slight increase in hospital admissions for schizophrenia [5].

Another harmful effect of particulate matter is that it can lead to autism. One recent study of children living in California reported that those exposed to the highest levels of traffic-related air pollution during pregnancy and in the first year of life were twice as likely to be on the autism spectrum than those who were breathing in clean air[7]. Two studies by Volk et al. found that the proximity of crowded highways and roads and exposure to the pollution that resulted from the exhaust was associated with autism [9]. This was confirmed by another recent study in which exposure was significantly associated with autism spectrum disorders, particularly in boys[9]. Children with autism have been noted to have higher levels of neuroinflammation, which are also the typical effects found in individuals exposed to severe air pollution [9].

Conclusion

Particulate matter is a harmful substance that can deteriorate certain regions of the brain such as white matter and the outer layer, hinder development in a fetus by causing neuroinflammation and lodging themselves in the placenta, and can increase the risk of neurological disorders such as Alzheimer's, schizophrenia, and autism through neuroinflammation. Particles can implant themselves inside the brain and then irritate it, leading to a slightly higher risk of these disorders. If this problem continues to be ignored, it can have catastrophic events. If more awareness and attention is brought to this issue, residents of deeply polluted cities can try to avoid this pollution or contact those who shape public policy in order to help solve this issue.

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