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Fetal Alcohol Syndrome and its Effects on Brain Development

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Abstract

Birth defects caused by maternal alcohol use during pregnancy, such as Fetal Alcohol Syndrome (FAS), are well-documented and preventable. The etiology, clinical characteristics, diagnosis, prevalence, and long-term effects of FAS are all covered in this paper's thorough evaluation of the current state of knowledge. The teratogenic effects of alcohol on the growing fetus, as well as genetic, environmental, and maternal variables, all play a role in the complex etiology of FAS. A wide spectrum of physical, mental, and behavioral problems resulting from prenatal alcohol exposure on fetal development are discussed. FAS is characterized clinically by facial dysmorphology, growth retardation, central nervous system dysfunction, and neurodevelopmental abnormalities. A multidisciplinary approach incorporating clinical assessments, maternal history, and objective testing methods is necessary for the accurate diagnosis of FAS. Diagnostic criteria have been devised to assist doctors in identifying affected individuals and offering the proper interventions, Additionally, FAS has long-term effects that go beyond early life and infancy. Learning deficiencies, attention deficits, executive dysfunction, and mental health problems are just a few of the difficulties that people with FAS deal with throughout their lives. These unfavorable results impose a heavy weight on those who are afflicted, their families, and society at large. The best way to lessen the effects of FAS is still to prevent it. Public health initiatives should include spreading knowledge about the dangers of alcohol use during pregnancy, encouraging early detection and intervention, and offering assistance and resources to those who are affected and their families.

Introduction

Fetal alcohol syndrome affects children born to mothers who consumed alcohol during pregnancy. Alcohol consumption while pregnant is quite risky, especially during the first trimester. This could be harmful to the fetus since the most important parts of the brain are developing in the first trimester. It can happen before the mother even recognizes that she's pregnant. This could be harmful to the developing fetus. Particular developmental difficulties for kids born with Fetal Alcohol Syndrome (FAS) include memory and cognitive deficits, attention deficit disorder, mental retardation, or learning difficulties. Diagnostic standards generally used for alcohol-related illnesses are used to make the diagnosis of FAS. This paper will provide a detailed discussion of the numerous impacts that alcohol has on the growing fetal brain.

Methods

The following research is based on the analysis of numerous articles from various databases, that include but are not limited to The Touro College Library online, ProQuest, EBSCO, Pubmed, and Google searches.

Discussion

Four different groups make up the broad diagnosis known as fetal alcohol spectrum disorder. The most serious of them all, fetal alcohol syndrome (FAS), requires the fulfillment of every diagnostic requirement. This consists of a pattern of minute facial deviations including a thin upper lip, a smooth philtrum, or short palpebral fissures, the region between the eyelids. Prenatal and/or postnatal growth insufficiency is another requirement for the diagnosis of FAS. In addition, a child born with FAS will have anatomical abnormalities of the brain, such as semilobar holoprosencephaly or agenesis of the corpus callosum, and will have small head circumference (Burd, 2022). Semilobar holoprosencephaly is characterized by the presence of the cerebral lobes' fusion, most frequently anteriorly and at the thalami, the brain's primary relay stations (Glick, 2022). The child will also experience neurobehavioral deficits, which are labels for the behavioral issues that come along with both brain disease and brain injury. Agenesis of the corpus callosum (ACC) is a condition in which there is partial or complete absence of the tissue that links the right and left hemispheres of the brain. This is brought on by a disturbance in the migration of brain cells during embryonic development (NIH, 2023a).

The less severe Fetal Alcohol Spectrum Disorders are partial fetal alcohol syndrome (PFAS), alcohol related neurodevelopmental disorder (ARND), and alcohol related birth defects (ARBD). Similar to FAS, PFAS occurs when a child is born with mild facial defects. Additionally, they will suffer from neurobehavioral disorders such as autism spectrum disorder (ASD) or attention deficit/hyperactivity disorder (ADHD). An alcohol related neurodevelopmental disorder diagnosis cannot be made with certainty on children younger than three years old. This diagnosis calls for proof of prenatal alcohol exposure, and the child's neurodevelopmental problems will be how it manifests. Finally, confirmed prenatal alcohol exposure and one or more specified significant malformations in the eyes, ears, cardiac, renal, or skeletal systems are required for the diagnosis of alcohol related birth defects (Gill, 2022).

The most critical period for embryonic brain development is the first trimester, which starts as soon as conception. The neural plate, the structure that will eventually become the baby's brain and spinal cord, develops four weeks after conception. It folds in on itself as it lengthens until the fold eventually turns into a groove. That groove will eventually develop into the neural tube. Around week six or week seven, the anterior and posterior ends of the tube close, at which point the front brain, midbrain,

and hindbrain separate from one another. The region that will eventually develop into the baby's spinal cord is located directly behind the hindbrain. These regions of the brain will soon divide into the cerebrum, cerebellum, brain stem, pituitary gland, and hypothalamus, constituting the five distinct divisions of the brain. The foundation of the brain is building throughout these critical first several months. It is crucial that this area grows properly so that the rest of the body forms normally (Targonskaya, 2019).

Early gestational alcohol exposure impairs the development of brain regions linked to motor function. We are able to walk, breathe, move smoothly, and maintain equilibrium thanks to the brainstem and cerebellum. The brain's volume is reduced when there aren't enough neurons in a certain region. This may make it difficult to think clearly, remember things, and carry out daily chores. The smaller the volume, the greater the impairment. Balance problems may occur in people with smaller brainstem and cerebellar volumes. The infant will eventually struggle to coordinate multiple muscles at once, and they might find it difficult to balance while walking, climbing stairs, or getting in and out of a car. Additionally, the Central Nervous System's white matter tracts are regions with myelinated axons. By assisting in the distribution of action potentials to various brain regions, these tracts have an impact on learning and mental processes. Alcohol drinking reduces the water's ability to reach these tracts.. The MRI of the fetus's brain at gestation day 135 revealed structural abnormalities that were functionally significant. Itrevealed diffusion of water to white matter tracts and dramatically reduced brainstem and cerebellar volumes (O'Neil, 2010).

More than any other species, rhesus macaque monkeys' early prenatal neurodevelopment is most similar to that of humans. Both a control group and a group of pregnant monkeys were treated to ethanol. They were watched over at various stages of the pregnancy. A pattern of decreased brainstem and cerebellum volume in the ethanol-exposed babies at about gestation day 135 was noted. At various gestational ages, there was no difference in total brain volume between the alcohol-exposed and the control groups. Unfortunately, because the cerebellum and brainstem volume differences are so minute, they can only be found at a much later stage of pregnancy. As a result, the brain shows greater sensitivity to early gestation alcohol on gestation day 135 than at other times. The most sensitive time to look for aberrant fetal brain growth brought on by alcohol will be in the third trimester of pregnancy (Wang et. al., 2020).

The hippocampus is a tiny but intricate brain region that is crucial to learning and the creation of new memories. The limbic system, which controls how we feel and act, includes the hippocampus. The hypothalamus and amygdala are also part of the limbic system, which is situated on the cortex's periphery. These organs aid in the regulation of several body processes, including the endocrine system and the "fight or flight" reaction. Declarative memories and spatial associations are two types of memory that the hippocampus aids in processing and retrieving. Declarative memories are tied to specific events and facts. Memorizing facts for a test is an illustration of this. Pathways or routes play a role in spatial connection memories. For instance, bus drivers employ spatial memory when learning a new route. In the hippocampus, short-term memories are transformed into long-term ones. Then, the brain stores these memories in a distinct region.

The two main gyri in the hippocampus, the Cornus Ammonis and the dentate, each go through waves of neurogenesis, neuronal migration, and neuronal maturation separately during hippocampal formation. The process by which new neurons develop in the brain is known as neurogenesis. When an embryo is growing, neurogenesis is essential. Neurogenesis also continues in the brain region during adulthood. Millions of neurons migrate when they move from their area of origin to the central nervous system, where they remain permanently. It is well recognized that this stage is sensitive to environmental stimuli, although it is unknown what causes this. The expression of genes that control the destiny, survival, migration, and differentiation of pyramidal and granule cells has been demonstrated to be altered by alcohol exposure. Pyramidal cells are common in the motor and premotor parts of the brain. Granule cells play a role in memory and learning. The hippocampus development that underlies the learning and memory problems associated with fetal alcohol syndrome may be compromised by undermining this process.

Inhibiting epigenetic activity while also mimicking alcohol-induced growth retardation in multiple organs, including the brain and heart, has recently been discovered to actively modify epigenetic programming during neural tube development. Instead of changing the gene itself, epigenetics focuses on how the gene is expressed. Epigenetics refers to modifications in the way the body "reads" DNA. Alcohol has been found to change gene expression by interfering with DNA methylation during the early stages of hippocampus formation. The process of adding methyl groups to the DNA molecule is known as DNA methylation. Methylation can alter a DNA segment's activity without even altering the sequence. The expression of particular genes is frequently suppressed by DNA

methylation. This can alter how the body works and have a variety of health effects on the fetus. Negative health effects have been linked to changes in DNA methylation. As a result, drinking alcohol while pregnant may alter how some genes are expressed, which could have harmful effects on the unborn baby's health (Chen et. al., 2013).

Atypical thyroid levels throughout the development of the alcohol-exposed fetus may contribute to some of the severe FAS symptoms, such as learning and memory problems. The thyroid gland produces and secretes thyroid hormones. Specific hormones released by the thyroid gland move throughout the body and control essential processes. Breathing, heart rate, metabolism, and body temperature are all influenced by thyroid hormones. Thyroid hormone levels must be adequate for the brain to develop appropriately. Many target tissues, especially the brain and skeleton, depend on thyroid hormones for growth and maturation. Maternal thyroxine, which provides thyroid hormone-dependent tissues, is crucial for fetal development during key times in the first trimester of pregnancy. The mother's thyroid glands are necessary for the fetus until It's glands are fully developed. The minimal amount of alcohol-induced thyroid hormone that is now reaching the fetus's brain and neurons will have an impact on the neurodevelopmental genes. Studies of alcohol consumption during pregnancy have demonstrated significant alterations in thyroid function, and excessive drinking lowers thyroxine levels (Tunc-Ozcanet. al., 2018).

Another thing to consider is that oxygen deprivation might cause a condition called hypoxia. Body tissues begin to function poorly when they don't receive adequate oxygen. The brain is the organ that is most in danger. When the brain is depleted of oxygen, it affects one's capacity to make important judgments, hinders their ability to move, and can even make them pass out. Confusion, agitation, difficulty breathing, a quick heartbeat, and bluish skin are all signs of hypoxia. To produce energy and support the function of our organs and tissues, our cells require oxygen. While some of our tissues are able to adapt to brief drops in oxygen levels, persistent hypoxia can harm organs. Damage to the heart and brain is highly hazardous and fatal (Cleveland, 2022a).

Alcohol consumption and hypoxia are connected, and hypoxia is a major factor in cellular deterioration. The amount of oxygen in the blood would dramatically drop if the mother drinks alcohol and the alcohol is processed in the liver. The liver excretes a substance known as bile and controls the majority of blood chemical levels. This aids in removing waste from the liver. The liver receives all the blood that exits the intestines and stomach. The liver processes this blood, metabolizes medications and other poisons, and also breaks down, balances, and produces nutrients. As a result, the liver's role is to digest alcohol. It can suffer severe damage if excess alcohol is consumed (Hopkins, 2023). As a result, hypoxia may influence fetal development-related cell damage. Particularly, it may have an impact on parts of the developing brain that are sensitive to hypoxia and alcohol exposure, such as the hippocampus and cerebellum (Hur et. al., 2022).

Alcohol can change how the brain functions and looks by interfering with the brain's communication networks. Alcohol impairs the function of the parts of the brain that control balance, memory, speech, and judgment, increasing the risk of accidents and other unfavorable outcomes. Alcohol is a cytotoxic substance that can cause changes in the neurons over time, including shrinkage of their size. (NIH, 2023). Both the developing and adult brains are affected in diverse ways by neuronal damage brought on by alcohol. It has been suggested that alcohol reduces the amount of neurons by increasing cell death and decreasing cell division. Neurogenesis is the process by which neural stem cells (NSCs) develop into neurons. The subventricular zone and the dentate gyrus of the hippocampus are where this happens most frequently in the brain. Recent research has started to point to decreased neurogenesis as the cause of particular illnesses and symptoms associated with drinking, such as depression and cognitive decline. Heavy drinking reduced neurogenesis, according to an animal study, while in-vitro investigations revealed that the hippocampus produced less new neurons following alcohol exposure. Additionally, MRI analyses of alcoholics showed diminished brain sizes, particularly in the hippocampus. There is evidence linking this volume deficit to a decline in hippocampal neurons (Tateno and Saito, 2008).

Fetal Alcohol Spectrum Disorders are a group of developmental abnormalities and growth retardation that are caused by maternal alcohol consumption during pregnancy and affect the growing baby negatively. The brain impairment and accompanying cognitive and neurobehavioral dysfunction, which frequently lasts into adulthood, are among the most severe and defining outcomes. One of the most important brain areas for these tasks and one of the most vulnerable to ethanol-induced neurotoxicity is the hippocampus. Memory impairment, learning difficulties, and mood issues are all symptoms of FAS in children. (Mayo, 2018).

The most recognizable and severe effects of prenatal alcohol exposure include craniofacial malformations, growth deficiency, microcephaly and mental retardation characteristic of Fetal Alcohol Syndrome. The baby's skull is made up of bone plates connected by soft regions known as sutures. The skull unites and the sutures fuse

during the first six to eighteen months of life. The infant's skull fuses together abnormally or prematurely, resulting in craniosynostosis and other craniofacial abnormalities. The child may experience neurological issues as a result of the brain's inability to properly develop as it grows when the bones fuse too soon. To give the brain more room to expand, surgery may be required to alter the shape of the face and skull. Additionally, children born with FAS are very prone to have growth deficiencies. Lack of growth hormone is the cause of growth deficit. The child could be little and appear younger than other kids his age. Children with this disorder grow very slowly. Their growth charts may appear slow or flat at two or three years old. Sometimes kids will be chubby and preserve a youthful body shape as they become older due to their inability to eliminate baby fat. Their bones may look younger than their actual age. Additionally, they might exhibit delayed tooth emergence and puberty (Cleveland, 2022). Microcephaly is defined as having a small head relative to body size. It is based on the ratio of height or weight to head circumference. Microcephaly occurs when there is a problem with brain development. It may lead to neurological abnormalities, learning difficulties, delayed cognition, or even mental retardation. Currently, the most prevalent known cause of mental impairment is fetal alcohol syndrome. Development is disturbed in mentally retarded children, resulting in deficient adaptive and cognitive abilities. Although they are able to learn new things, they do so very slowly. Intellectual functioning and adaptive behaviors are two areas where people with mental impairment are restricted. The term "intellectual functioning," usually referred to as "IQ," describes a person's capacity for learning, problem-solving, and decision-making. The ability to take care of oneself, engage with others, and communicate successfully are examples of adaptive behaviors. (NIH, 2023).

The most frequently mentioned issues with Fetal Alcohol Spectrum Disorders' are various neurodevelopmental and cognitive consequences, including anxiety disorders, depressive disorders, social challenges, and issues with attention and hyperactivity, are connected to learning and memory. Due to their anxiety symptoms, people with anxiety disorders will find it difficult to go about their regular lives. There are numerous varieties of anxiety disorders, including phobia-related disorders, social anxiety disorder, and panic disorder. These condtions might take the form of panic attacks, intense social anxiety, or excessive, unreasonable worry about particular things or circumstances. People who have depressive illnesses may frequently feel exceedingly depressed and uninterested. Depression can cause emotional and physical issues as well as cognitive impairment. Even worse, they can think life isn't worth living. Additionally, FAS patients have a tougher time recognizing social signs. This can lead to incorrect actions in social contexts. As the youngster grows older and social expectations rise, the situation simply gets worse. A child born with fetal alcohol syndrome may experience attention impairment and hyperactivity. These kids could struggle mightily to maintain organization and their attention on the work at hand. Impulsivity may also be a sign. A person might behave without contemplation or restraint. This can also seem as a desire for quick outcomes and fast fulfillment. A person with impulsivity may constantly interrupt others or make snap judgments without taking potential implications into account. Similarly, hyperactivity occurs when a person moves about a lot, fidgets, taps, and talks—sometimes even at inappropriate times. These issues, which are not the result of ignorance or resistance, can be quite aggravating for those who experience them.

The most frequent effects of fetal alcohol syndrome are issues with learning and memory. When compared to something that happened lately, which might not be as challenging, children may find it difficult to recall specific events or information from the past. It can be even harder to recall a specific incident, like what was for lunch today at school. Memory issues in people with FAS may persist from childhood to throughout adulthood. These issues are a result of alcohol exposure during pregnancy, which harms several parts of the brain, including the hippocampus which is responsible for memory functions. When a person with FAS seems to have problems remembering verbal knowledge, it can actually be because the individual has trouble learning the material in the first place. What appears to be a memory issue may actually be a learning issue. When appropriately learnt, the information may be retained by the individual in this situation. Since verbal memory formation heavily depends on language ability, language comprehension issues may worsen memory issues. Once more, this might be due to a problem with information encoding rather than a problem with information retention (Edmonton, 2021).

Clinical research consistently demonstrates a high correlation between maternal alcohol use and the child's learning and memory problems. Some studies indicate that these deficiencies can persist into adulthood, while others indicate that these issues most frequently arise in school, these kids demonstrate extremely poor academic performance, which is frequently connected to a decreased propensity for learning as well as issues with memory retention. The hippocampus, a portion of the brain that has been proven to be particularly susceptible

to the teratogenic effects of alcohol, is primarily responsible for controlling learning and memory function. It has been established that the CA1 and CA3 areas of the hippocampus have fewer pyramidal cells after extensive alcohol exposure during development. Additionally, it has been demonstrated that drinking alcohol causes significant changes in the cytoarchitecture of the dendrites of pyramidal cells in the hippocampus and impairs the induction of long-term potentiation (LTP) in CA1 pyramidal cells. There is some proof that the hippocampus's pyramidal cell synapses operate less effectively after being exposed to relatively tiny amounts of alcohol.

Anxiety-like phenotypes can be induced in adult rats by exposure to low doses of ethanol, The first two trimesters of a human pregnancy were used as the gestational period for this investigation. They looked at how mouse models' spatial memories worked using a Y-shaped maze. The study's findings indicate that neither persistent low-dose prenatal alcohol exposure nor aging of the rats' spatial working memory had any negative effects. The CA1 and CA3 areas of the hippocampus did not experience changes in pyramidal cell number or density in the chronic low dose model of prenatal ethanol exposure. Deficits in hippocampal-dependent learning and memory function cannot be brought about by this alone. This implies that exposure to low doses of ethanol during pregnancy may not alter basic spatial learning and memory function, but may affect more complicated learning and memory processes. (Cullen and Burne, 2014).

Conclusion

Researchers have come to the conclusion that there is no known safe trimester or safe level of alcohol use during pregnancy. Pregnant women frequently drink excessively in the early stages of pregnancy while fully ignorant that they are expecting, endangering the brain development of their unborn child. The formation of the five different parts of the fetal brain, including the cerebrum, cerebellum, brain stem, pituitary gland, and hypothalamus occurs during the first trimester which is the most critical period for brain development. The remainder of the body develops after those areas of the brain. Awareness of pregnancy is crucial from the very beginning for this reason. Fetal alcohol syndrome is a serious public health issue with lasting effects on those affected and their families. Educating people about the risks of drinking while pregnant, promoting early identification, and providing support and resources to those who are impacted are all important aspects of limiting the frequency of this disorder.

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