

Endocrine Disruptive Effects of Bisphenol A on Human

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Abstract. Given its widespread use in food packaging and other types of plastic packaging, bisphenol A is a common toxin that people come into contact with on a daily basis. Since it was first discovered to be a prevalent toxin many years ago, bisphenol A has been shown to be present in more than 90% of people. This review's primary goal is to draw the conclusion that BPA, one of the endocrine disruptors, negatively affects human neurological, reproductive, and growth systems. BPA exposure has also been linked to memory loss, impaired reproductive function, and permanent impacts on fetal growth. Further study is required to determine whether BPA has detrimental effects on the development and growth of humans. This study focuses on the three primary effects BPA has on people, suggests caution when using products containing BPA, especially for expectant mothers, and calls for more BPA research to determine the full extent of the risks BPA poses to people and to develop healthier products designs.

Keywords: Bisphenol-A, endocrine disruptor, neurotransmitter signaling, reproductive disorders.

1. Introduction

More than 92 percent of Americans have Bisphenol A (BPA) in their bodies, according to researchers from the Centers for Disease Control and Prevention (CDC), with children frequently having the highest percentages. The primary source of BPA exposure in humans is the migration of BPA from plastic packaging into foods and beverages. 2,2-Bis(4-hydroxyphenyl) propane, commonly known as bisphenol A (BPA), is a common ingredient with a molecular weight of 228,29 that is extensively used in the creation of food as well as residential items such as plastic bottles, dental sealants, and packaging materials [1]. BPA is categorized as an ecological proteus molecule since this exhibit estrogenic effects in a significant number of studies, which indicate that it may impair the normal operation of the endocrine system. Chemicals classified as endocrine disruptors can affect an organism's hormonal system by imitating, blocking, or altering how hormones typically operate. They can be present in a variety of goods, including plastics, cosmetics, insecticides, and medications, and they can reach the environment through several different channels. Endocrine disruptors may have a large negative impact on living things. Some of these consequences include reproductive abnormalities, which can result from lower fertility, aberrant sexual development, and a rise in the prevalence of reproductive malignancies. Developmental diseases, such as birth deformities, cognitive and behavioral deficiencies, and immune system malfunction, can be brought on by exposure to endocrine disruptors during crucial stages of fetal and juvenile development. It has been demonstrated that BPA mimics estrogen, a hormone essential to the growth and operation of the brain. When BPA attaches to estrogen receptors, it can stimulate or inhibit the endocrine system's normal operation and interfere with the body's capacity to regulate hormones. Negative neurological repercussions from this disturbance might include behavioral problems, poor learning and memory, and developmental delays. Exposure to BPA during fundamental developmental stages, such as the prenatal and early postnatal stages, can have long-lasting effects on brain function and behavior.

Endocrine disruptors known as xenoestrogens act in the body similarly to estrogen. These are artificial substances that don't exist in nature and can infiltrate the environment from a variety of sources, including pesticides, plastics, and personal care items. BPA can be considered a xenoestrogen as plastics are one of its sources that harms living organisms and causes genotoxicity and cytotoxicity, mutagenicity, and carcinogenic effects [2]. BPA has both anti-hormonal and hormonal properties, causing damage to physiological tissues and organs, including those involved in reproduction, immune function, and neurohormonal regulation [3]. Besides, In the body,

xenoestrogens can adhere to sex hormones and either promote or inhibit estrogen's typical hormonal function. BPA appears to have a significant influence on the human endocrine system, based on a compilation of prior studies. Almost a billion worth of BPA are thought to leak into the environment every year, and more than 90% of people who have been tested have measurable levels of BPA in their systems, in accordance with a report on BPA from the United States government, with infants and children having the highest levels. The basic intention of this paper is to provide an explanation of the three main effects of BPA on the human endocrine system in light of this horrible scenario, including effects on neuronal function, sexual function, and growth. This will help with upcoming BPA research and the creation of better safeguards against BPA's harmful effects on the human body.

2. Neuronal Function

BPA has a variety of methods through which it might impact neuronal function. BPA has the capacity to influence the production and release of neurotransmitters like both serotonin and dopamine, along with the transcription factors that those same neurotransmitters engage. Changes in behavior and cognition may result from this because it can affect synaptic transmission and hinder neural communication. BPA can also alter gene expression which means that BPA can modulate the expression of genes involved in neuronal development and function, leading to changes in synaptic plasticity, neuronal connectivity, and neural circuitry. As a concrete instance, it has been shown that contact with BPA modifies the transcription of genes involved in brain development, cell signaling, and axonal growth. Gentilcore et al. examined BPA use male rats that were orally administered different doses of BPA and a control vehicle for 14 days. After 14 days, the rats were sacrificed, and their thyroid glands were removed and analyzed for changes in gene expression. The findings indicate that thyroid-specific genes, particularly those associated in the manufacture of thyroid hormone and maintenance, were drastically less expressed after the administration of BPA. The amount of the drug reduction in gene expression had been seen, with larger doses of BPA generating more pronounced alterations in cell proliferation. BPA exposure can interfere with the functioning of the thyroid gland, potentially leading to disruptions in thyroid hormone synthesis and metabolism. This experiment demonstrates that BPA would alter the gene expression in the human body [4]. The capacity of the junctions to alter their amplitude in relation to action potentials, or synaptic plasticity, is further compromised by BPA. This can alter the structure and function of neural circuits and affect learning and memory processes. Throughout the trial, Kawato et al. used two groups of pregnant female rats—one receiving BPA and one receiving a placebo—were randomly assigned. Throughout pregnancy and breastfeeding, the BPA group got 50 g/kg/day of BPA orally, whereas the control group received the same amount of a vehicle. The male and female young were separated after weaning and kept in groups of three or four per cage until they reached maturity. The adult rats were transcranially perfused with a fixative solution after being asleep for 12 weeks. The hippocampi were then separated and prepared for Golgi-Cox staining after the brains had been removed. Afterward, a confocal microscope and a computer-aided image analysis system were used to evaluate dendritic spines. The number and morphology of dendritic spines in the CA1 and CA3 regions of the hippocampus were evaluated. The research reveals that male and female rats' dendritic spines responded differently to prenatal BPA exposure. Males' dendritic spine density and length in the CA1 and CA3 areas of the hippocampus were decreased after exposure to BPA. Females exposed to BPA experienced an increase in dendritic spine length in the CA1 area but no discernible change in dendritic spine density. According to sequencing research, BPA exposure caused altered gene expression in men and females, especially in genes involved in estrogen signaling, cytoskeleton control, and synaptic plasticity. These results demonstrate that BPA exposure can modify gene expression associated with synaptic plasticity and cytoskeleton control, which can disrupt dendritic spine formation in a sex-specific way [5]. In conclusion, BPA can have an impact on neuronal function in a variety of ways, including by affecting neurotransmitter signaling, changing gene expression, and reducing synaptic plasticity. Many

neurological conditions, including as anxiety, depression, autism, and cognitive deficits, have been related to these BPA-induced changes in neuronal function.

3. Sexual Dysfunction

BPA can disrupt normal hormonal signaling, particularly the actions of estrogen and androgen hormones, which play key roles in sexual development and function. BPA has also been linked to reproductive disorders in humans, including decreased sperm quality and fertility, early puberty in girls, and altered menstrual cycles. Zahra et al. exposed normal human ovarian cells to environmentally relevant concentrations of BPA for 24 hours. The concentrations of BPA used in the study ranged from 10^{-8} M to 10^{-6} M, which is equivalent to the concentrations of BPA found in the serum of humans who have come into contact with the substance through occupational or environmental sources. The researcher obtained the ovarian cells after the treatment period of 24 hours and used microarray analysis to identify any modifications in the expression of genes [6]. Consumption to BPA has been found to alter the regulation of genes involved in the formation of follicles, which may result in modifications to ovarian function and fertility. In addition, the researchers discovered polymorphisms in the transcription of genes involved in the production of steroid synthesis, including those involved in the synthesis and metabolism of female hormones and progesterone [7]. The gene transcription involved in cellular signaling pathways also changed as a result of BPA exposure, which might have an impact on cell proliferation, differentiation, and survival. So, it states that BPA exposure has a significant impact on females. BPA has been shown to interfere with the normal functioning of hormones, particularly androgenic steroids such as testosterone, which play an essential function in the development as well as the progression of prostate cancer. Colorectal risk of lung cancer has been linked to BPA exposure, as have changes in bladder cancer cell growth and proliferation. Furthermore, BPA may cause modifications to the manifestation of genes that are important in germ cell differentiation and proliferation by interfering with the expression and function of FXR in the testes. This can cause alterations in gene expression. This may result in an imbalance in the ratio of the various kinds of germ cells, in addition to aberrant sperm shape and motility [8,9]. Di Donato et al. reviewed a previous study that examined the impact of BPA and other EDCs on cellular metabolism, proliferation, and androgen receptor signaling using human prostate carcinoma cell lines. These experiments revealed that BPA exposure can disrupt the regulation of genes involved in androgen signaling, resulting in a rise in prostate cancer cell growth and proliferation [10]. Overall, the potential impact of BPA on sexual organs highlights the need for continued research into the effects of this chemical on human health, as well as efforts to reduce exposure to BPA and identify safer alternatives for use in consumer products.

4. Growth Inhibition

BPA has been shown to have endocrine-disrupting properties, which means that it can interfere with hormone levels and potentially impact growth and development. White Leghorn chicken fertilized eggs were obtained by Harnett et al. and maintained at 37.5 °C with 60% humidity. The eggs were split into six groups after 72 hours of incubation: a control group, a group that had been exposed to TMBPF, a group that had been exposed to BPA, a group that had been exposed to BPS, a group that had been exposed to BPAF, and a group that had been exposed to a combination of BPA, BPS, and BPAF. The eggs were subsequently retrieved for study after an additional 96 hours of incubation. The growth of the embryos was evaluated based on a number of factors, including body weight, body length, and the weight of various organs, as well as their examination for anomalies under a stereomicroscope. The embryos exposed to BPA clearly showed a decrease in body weight and length when examined specifically in the BPA treatment group. It was shown through research on animals that exposure to BPA during crucial developmental times, including pregnancy or early infancy, can alter hormone levels and impair healthy growth and development [11]. Dirkes et al.

exposed pregnant mice to either a control, BPA, or BPS-containing diet, and their offspring were exposed to the same diets during lactation. The researchers then examined the bone mass, structure, and strength of the female offspring when they reached adulthood. The research indicates that early-life contact with BPA had not any impact on the skeletal development of adult female rodents. Bone mass, microarchitecture, and strength were not significantly distinct between the control and BPA or BPS-exposed groups. The study found very few differences in bone microarchitecture between the BPA exposed groups and the unexposed group. According to the research, BPA or BPS exposure during pregnancy and breastfeeding may not have any appreciable long-term effects on the health of mice's skeletons. The study stresses the need for more research into these chemicals' impact on human health, as human exposure levels to them may vary from the ones utilized in the study. BPA's effects on growth and development are a complicated subject that still needs further research. Human research has had inconsistent outcomes, despite evidence from animal studies that BPA exposure may alter hormone levels and impair healthy growth and development. While other studies have not identified any conclusive connections, some have linked BPA exposure to stunted development in newborns and children. Several experts advise reducing exposure to BPA, particularly for pregnant women and young children, due to the possible health hazards linked with it. This includes avoiding goods marketed as BPA-free and avoiding plastic food and drink containers with recycling codes 3 or 7, which may contain BPA.

5. Conclusion

It has been established that BPA may pass the blood-brain barrier, allowing it to enter the brain and have a direct impact on brain cells. The brain's neurotransmitter signaling can be disrupted by BPA, which may have an impact on cognition, behavior, and mood. It has been demonstrated that BPA interferes with the proper operation of neurotransmitter receptors. This may result in altered behavior, such as heightened anxiety, reduced motor coordination, and memory and learning impairments. BPA has been demonstrated to modify the regulation of several genes, including the thyroid gland gene. In investigations involving animals, BPA modifies brain function by reducing synaptic plasticity. Prenatal contact with BPA in humans has been associated with a higher probability of behavioral and cognitive problems in children, such as hyperactivity, aggression, and concentration and memory difficulties.

Consequently, BPA has been connected with a higher occurrence of neurological diseases such as Parkinson's and Alzheimer's. It is possible that BPA exposure contributed to the emergence of anxiety and depressive disorders. BPA has demonstrated that it has a detrimental effect on sexual function, including interference with hormone signaling pathways, alteration of gene regulation, and modifications in the structure and function of reproductive tissue, based on the conclusion that it alters gene expression. BPA exposure in females has been linked to changed hormone levels, decreased fertility, and alterations in menstrual cyclicality. A higher risk of reproductive issues in female children, such as early puberty and reduced ovarian function, has also been associated with maternal BPA exposure. BPA exposure has been linked to lower testosterone levels, altered testicular function, and worse sperm quality in males. BPA exposure during pregnancy has also been associated with an increased chance of male children developing reproductive issues, such as reduced sperm production and malformed testicles. According to recent experimental investigations, exposure to BPA during pregnancy only causes animals to have extremely severe effects on their embryo weight and size as well as embryonic bone formation. This is true even though BPA has a significant impact on the human brain and reproductive system. There is valid research that can definitively demonstrate that BPA has a deleterious effect on human embryonic growth, but still, the quantity of BPA utilized in these animal experiments is larger than the limit authorized by the FDA department. Although more research is required to determine whether BPA has a negative impact on human fetal growth, this review only covers a few recent experiments and only highlights the three main effects of BPA on humans. Nevertheless, pregnant women should exercise caution when using products that contain

BPA despite the lack of conclusive evidence. To corroborate the effects of BPA on human fetuses, additional research is required, and manufacturers of BPA-containing products must adhere more strictly to FDA regulations.

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