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Review

Mental Health Disorders Following Exposure to Endocrine Disruptor Chemicals

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Abstract

There is growing scientific concern regarding how endocrine-disrupting chemicals (EDCs) impact central nervous system (CNS) disorders. Both anecdotal and preclinical studies suggest a link between EDC exposure and major depressive disorder (MDD), potentially leading to neurodegenerative outcomes. EDCs primarily exhibit their biological effects by interacting with hormone receptors. Nonetheless, there is scientific evidence pointing to dysfunction in the hypothalamic-pituitary-gonadal-adrenal axis, which is linked to neuropsychiatric conditions. Additionally, the global incidence of MDD has risen. Various factors like gender, genetic components, age, hormonal balance, and cultural influences may explain differences in MDD prevalence. Recently, environmental pollutants such as industrial chemicals, emollients, plastics, fungicides, and pesticides have emerged as critical factors influencing this disorder. This review delves into the influence of key phthalate and bisphenol compounds on chronic inflammation and MDD.

Keywords
Major depression; neuroinflammation; environmental exposure; endocrine-disrupting chemicals; indoor pollution; phthalates; bisphenols

1. Introduction

Major Depressive Disorder (MDD), a complex mood disorder, is recognized as a significant global health issue due to the burden it places on public health systems and its prevalence worldwide [1-3]. Characterized by enduring low mood, loss of interest in activities, fatigue, and low energy, MDD is one of the most common mental health conditions [4]. It is linked to a lower quality of life, reduced productivity at work, and a heightened risk of mortality from any cause [5]. The inhalation of environmental pollutants contributes to oxidative stress and neuroinflammation, which may trigger MDD [6]. The incidence of MDD is rising, and access to effective treatments is often insufficient [7], making the identification of risk factors and the development of preventive strategies crucial for public health. Research has shown that breathing in pollutants from the air can provoke oxidative stress and inflammation in the brain, potentially causing neurotoxicity that affects dopamine [8]. Evidence links exposure to air pollution with reduced satisfaction with one's living conditions and self-assessed health, both associated with mental health [9]. This suggests a plausible theory that air pollution could play a role in the development of MDD. Research has explored various aspects, including hormonal changes, genetic predisposition, neurochemicals, and inflammation in the nervous system [10]. Despite significant investment in developing pharmaceuticals for MDD, no truly effective treatments exist, and adherence to treatments is poor, leading to higher rates of treatment failure. Studies, although limited, suggest environmental contaminants such as DEP, DBP, BBP, DEHP, and BPA may be involved in the onset and worsening of MDD symptoms. These findings have led to an examination of such environmental exposures in properly diagnosed patients to understand the underlying mechanisms and factors that contribute to the large patient population [11-13]. As bisphenols, phthalates, and other endocrine-disrupting chemicals (EDCs) imitate hormonal actions, this review will delve into how exposure to the principal components of phthalates and bisphenols, commonly found in everyday products, affects men and women diagnosed with depression.

2. Methodology

A systematic search was conducted across multiple databases, including PubMed, Scopus, and Web of Science, using keywords such as Mental Health Disorders, Environmental exposure, Endocrine Disruptor Compounds (EDCs), and neuroinflammation. The review includes studies published between 2010 and 2023, ensuring that the most current findings are represented. The inclusion criteria were focused on peer-reviewed articles that involved both animal and human models and specifically examined EDCs' effects on MDD and endocrine functions. Studies not related to EDCs, those involving other pollutants, or those that lacked MDD insights were excluded. The selected studies were synthesized to assess consistent findings on EDCs' ability to induce

oxidative stress, including the production of reactive oxygen species (ROS) and inflammation, as well as their endocrine-disrupting effects and MDD.

3. **Neuroinflammation and MDD**

Inflammation and neuropsychiatric disorders, including MDD, are closely connected. MDD can trigger inflammatory responses, while inflammation can exacerbate MDD and other similar disorders. Patients with MDD show diagnostic markers of inflammation, such as activated sensors and elevated circulating inflammatory signals targeting multiple tissues [4, 14]. Inflammation can drive the clinical advancement and pathology of these conditions. Proinflammatory cytokines can alter mood, behavior, and cognition by reducing the availability of brain monoamines, initiating neuroendocrine reactions, impairing brain plasticity, and promoting excitotoxicity (increasing glutamate levels). Studies indicate that the source of ongoing inflammation often involves environmental EDC exposures that promote inflammation. Additionally, changes in neuroendocrine regulation, metabolism, diet/microbiota, and unhealthy behaviors contribute to inflammation [15, 16]. The four elements central to an inflammatory reaction include: (1) Inflammatory inducers or pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs); (2) Sensory receptors in immune cells that detect these inducers; (3) Inflammatory mediators prompted by these sensors (like reactive oxygen species, cytokines, chemokines, and prostaglandins); (4) Target tissues affected by these mediators. Individuals with mood disorders and MDD present numerous indicators of immune dysfunction across cellular, molecular, and tissue levels. Environmental stressors are tied to higher circulating inflammatory triggers, notably DAMPs, which are endogenous molecules that amplify following cellular oxidative stress and damage. These molecules, when present outside of cells due to stress or necrosis, act as DAMPs [17]. DAMPs include circulating uric acid, extracellular ATP, heat shock proteins (HSPs), and oxidized molecules. Research demonstrates that environmental and psychological stresses can elevate these DAMPs, catalyzing nervous and peripheral system inflammatory responses [18]. Beyond tissue harm, stress-induced DAMPs can incite systemic inflammation. There is documented evidence of heightened circulating DAMPs in neurological and psychiatric conditions, with particularly elevated serum uric acid and HSP70 levels in MDD and Bipolar Disorder (BD) [19, 20]. MDD patients have immune cells with heightened activation in response to DAMPs or PAMPs. Individuals with BD often show increased TLR receptor presence in peripheral monocytes and lymphocytes, as well as heightened TLR-mediated intracellular signaling [21]. Furthermore, elevated serum interleukin (IL)-1 and IL-18 levels have been detected in MDD patients [22]. Studies have found a positive correlation between oxidative stress and inflammatory markers and MDD symptoms [23]. Patients with MDD also exhibit higher levels of inflammatory mediators. Research has found that proinflammatory cytokines and their receptors, along with acute phase reactants like CRP, chemokines, and soluble adhesive molecules, are highly present in plasma and peripheral blood of those with BD, MDD, and schizophrenia [24-26]. The increase of innate immune cells, such as activated T cells, monocytes, and neutrophils, correlates with cell activation and growth [27, 28]. Greater inflammation levels are linked to the progression or intensity of MDD symptoms. Indeed, heightened CRP and IL-6 levels can provoke depressive episodes in MDD patients [29], while remission is linked to reduced inflammatory markers [30]. It is notable that both the number and intensity of inflammatory disorders influence depression severity [31].

4. Influence of Environmental Pollutants on MDD Patients

EDCs do not directly cause neuronal tissue damage or cell death. However, they can indirectly disrupt the structure and function of the nervous system through neuroendocrine-related mechanisms [32]. EDCs may affect the brain through two main pathways: disrupting neuroendocrine processes originating in the hypothalamus and affecting steroid hormone receptors and signaling pathways throughout the brain [33]. Studies have highlighted that various factors, including genetics, age, hormonal conditions, and socio-cultural elements, contribute to the differing prevalence of MDD [34]. According to the World Health Organization (WHO), MDD is a mood disorder involving neurochemical, hormonal, and inflammatory alterations [35, 36]. It is also noted that the incidence of MDD is twice as high in women compared to men [37]. Environmental pollutants, such as plastics, industrial chemicals, emollients, fungicides, and pesticides, have emerged as significant contributors to this disorder [34]. The exposure to these pollutants, particularly EDCs, has been linked with various neurological conditions like autism spectrum disorder and attention-deficit/hyperactivity disorder [38, 39]. Some EDCs, including the additive DEHP, regulate the hypothalamic-pituitary-adrenal axis, which plays a crucial role in neurological and reproductive functions [40]. Bisphenols and phthalates, common ambient pollutants, disrupt homeostasis across different bodily systems. Predominantly found in dairy products, these compounds have permeated diverse sources such as air, food, and water globally, posing significant health risks [41, 42]. Being lipophilic, they are readily absorbed through the skin and can leach from plastics with changes in temperature or pH, entering the body through ingestion. Once inside, bisphenols and phthalates antagonize steroid receptors, altering signaling pathways typically activated by natural ligands [43, 44]. Notably, exposure to emollients, phthalates, and bisphenols during crucial life stages can detrimentally impact health [45]. This indicates that pathways involving maternal-infant interactions, perinatal exposure, and adulthood could be linked to heightened susceptibility to MDD.

5. Gender-Specific Effects of Pollutant Exposure in MDD

MDD is linked with changes in neurotransmitter systems, including serotonergic, noradrenergic, dopaminergic, and cholinergic pathways. Estrogens such as estradiol (E2) enhance serotonergic system efficiency through transcriptional regulation of TPH-2, 5-HT (SERT or 5-HTT), and monoamine oxidase A and B (MAO). Hence, E2 is attributed to significant antidepressant functions [46, 47]. The combination of serotonin reuptake inhibitors, sertraline and fluoxetine, with E2, has shown promising outcomes in treating depression among older women [48]. It is crucial to note that malfunctions in MAOs are significant in sustaining and developing MDD [49]. Additionally, MDD occurrence often corresponds with hormonal disturbances in women [50, 51]. EDCs interrupt regular hormonal functions and can impair hormone-sensitive organ systems such as the brain. In animal studies, EDC exposure resulted in inadequate methylation of genes in the brain, hampering neuronal development and function across generations [52, 53]; possibly influencing depression development. Estrogen receptors, which are present in immune cells, may exhibit either pro- or anti-inflammatory effects based on the tissue type of the cell. Estradiol contributes to Th1 and Th2 response modulation [54], where an imbalance in Th2 response is clinically associated with MDD [55]. The influence of varying EDCs in modulating Th1 and Th2 responses remains underexplored. Exposure to BPA in early life stages corresponded with a shift towards Th2 response in female mice

[56]. BBP, an asymmetric high molecular weight phthalate used to plasticize PVC products, has been found in higher serum concentrations in women than men, existing in dual forms [11]. As the most active estrogenic phthalate, BBP can adjust several genes dependent on hormonal cues [57]. Its linkage to endometriosis is significant due to direct associations with high blood concentrations of this contaminant [12]. Various phthalates also reduce E2 levels by repressing gene expression of aromatase, the enzyme responsible for E2 production, thereby extending the estrous cycle and hindering mouse ovulation [58]. Given E2's pivotal role in managing multiple systems and its essential antidepressant capability, it's crucial to concurrently evaluate EDC and E2 levels in MDD patients to recalibrate hormonal balance. Moreover, numerous unknown pleiotropic impacts of phthalates on neural functions are recognized [59]. Research measuring BBP metabolite concentrations demonstrated larger quantities in women's serum in contrast to men's [60]. The higher BBP serum levels observed in women are likely linked to more frequent use of cosmetics and medications, as phthalates are present in pharmaceutical capsules and packaging materials [61].

6. Exposure to Phthalates and Bisphenols Effects in MDD Patients

Studies suggest that phthalates may encourage Th2 differentiation, as observed in vitro, in vivo, and through epidemiological research on asthma [62]. Research has evaluated serum E2 levels in MDD patients, identifying them to be around 175-85 pg/ml in males and 55 pg/ml in females [63, 64]. Several investigations have sought to measure bisphenols and phthalates in different biological fluids [65, 66], but there is still no data on their serum levels in MDD patients. Among phthalates, two are characterized by high molecular weight, primarily found in plastic products, while another two are low molecular weight compounds, often located in cosmetics and personal care items [65, 67]. It is presumed that following BPA exposure and its absorption, it is quickly metabolized into an inactive form (glucuronic acid) and excreted with a half-life of about 5 hours [68]. The half-life of phthalates varies with molecular weight. Low molecular weight phthalates, like DBP and DEP, are quickly hydrolyzed to monoesters and excreted, while high molecular weight phthalates, like BBP and DEHP, undergo hydrolysis followed by multi-step oxidative metabolism [59, 65]. Evidence exists that the enzyme β-glucuronidase, found in multiple tissues, can generate and release the active BPA form within the body [69]. Since BPA is lipophilic, it can potentially migrate and accumulate in tissues, fostering bioaccumulation concerns. Some argue against this notion, pointing out that animals and humans frequently encounter BPA and similar substances. Given BPA’s ability to revert to its active form, is it feasible to measure unconjugated parent metabolites? Should we assess various contaminants in the blood and tissues to gauge potential bodily effects? [68]. The lipophilicity of BBP [70] may aid in its central nervous system transport and storage, potentially leading to MDD. BBP exposure also reduces serotonin (5-HT) levels, affecting adenylyl cyclase activation via G protein-coupled receptors (GPCRs). This enzyme, by using ATP, converts it into cAMP through an energy-reliant process, potentially disrupting protein kinase A activation and eventually lowering CREB phosphorylation levels. These sequences might result in behavioral dysfunction, oxidative harm, or pathological brain changes, as noted in mouse studies [71]. Regarding phthalates' cellular impacts, DBP seems to augment reactive oxygen levels [72], which may significantly damage neurons. Reports indicate that different phthalates alter sex enzymes and hormone processes in male and female animal models [73]. In vivo models suggest that these hormonal disruptions might lead to conditions analogous to human MDD, evidenced by cognitive

decline and impaired learning and memory. Perinatal phthalate exposure notably affects mouse hippocampal impairment. It downregulates androgen receptor and expression, indicating potential placental and brain barrier crossings [74, 75], Previous research on air pollutant transmission across the blood-brain barrier (BBB), brain inflammation including hippocampal cytokine gene expression and behavioral modifications [76-78] implies that phthalates might contribute to air pollutant BBB crossing and memory, learning, anxiety, [79] and depression in mice [80] Prenatal phthalate exposure is linked to hippocampal disruption, demonstrated by reduced androgen and estrogen receptor expression in mice [74] and placental barrier crossings [75], hinting at possible BBB penetration. Furthermore, early life phthalate and other EDCs exposure might impair neuronal function through brain methylation profile alteration [81], increasing the risk of neurological disorders such as adult MDD. Postnatal DEHP exposure reportedly impacts male mice's hippocampal growth but spares females [82]. DEHP may alter the female hippocampal lipid profile, raising sphingomyelin and phosphatidylcholine levels, with no such effects found in males, suggesting potential female protective neuro-properties [83]. Bisphenol research revealed no significant BPA and BPS disparities between depressed and healthy individuals [84]. Possibly due to limited depressed patient studies. There’s growing biological evidence of environmental pollutant roles in disorders like MDD, though strong clinical data supporting this link is still missing [85].

7. Conclusions

Research indicates that chronic inflammation plays a mediating role in the link between exposure to EDCs and symptoms of MDD. The variance in MDD prevalence across different studies may stem from using diverse measurement scales for MDD, population composition variations, and sample size discrepancies. Studies consistently demonstrate a robust association between elevated concentrations of phthalates found in urine and MDD symptoms, although the precise mechanism by which phthalate exposure leads to MDD remains unclear. This review highlights the pivotal role of EDCs, particularly benzyl butyl phthalate (BBP), in potentially causing or exacerbating mental disorders such as MDD and other psychiatric issues. Nonetheless, a definitive conclusion requires further investigation involving a broader population, including comprehensive surveys of EDC exposure and assessments of their serum concentrations alongside measurements of metabolites, neurotransmitters, serum levels of E2, other hormone concentrations, lipid and methylation profiles, and varied cytokines. These evaluations will crucially offer a global perspective on the impact of EDCs in a significant subset of MDD patients. Elevated EDC levels correlate with an increased risk of MDD, and chronic inflammation is identified as a risk factor. Findings indicate that general inflammatory factors partly mediate the relationship between EDC exposure and heightened MDD risk. This new analytical framework is a valuable tool to understand the effects of exposure to EDCs, including phthalates, on MDD.

Abbreviations

EDCs	Endocrine-disrupting chemicals
PM	particulate matter
MDD	Major depressive disorder
BD	bipolar disorder
E2	estradiol

TLR	Toll-Like Receptor
CRP	C-reactive protein
CSF	cerebrospinal fluid
HSPs	heat shock proteins
DEP	di-ethyl phthalate
DBP	di-n-butyl phthalate
BPA	bisphenol A
BBP	butyl-benzyl phthalate
DEHP	di-ethylhexyl-phthalate
TPH-2	tryptophan hydroxylase-2
MAO	monoamine oxidase
SERT	serotonin transporter (5-HT or 5-HTT)
SSRIs	Serotonin reuptake inhibitors
FLX	such as sertraline and fluoxetine
ERs	estrogen receptors
CNS	central nervous system
GPCRs	G protein-coupled receptors
BBB	blood–brain barrier

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Competing Interests

The authors declare that they have no competing interests.

References

1. Vogelzangs N, Duivis HE, Beekman AT, Kluft C, Neuteboom J, Hoogendijk W, et al. Association of depressive disorders, depression characteristics and antidepressant medication with inflammation. Transl Psychiatry. 2012; 2: e79.
2. Ehsanifar M, Montazeri Z, Zavareh MS, Rafati M, Wang J. Cognitive impairment, depressive-like behaviors and hippocampal microglia activation following exposure to air pollution nanoparticles. Environ Sci Pollut Res. 2023; 30: 23527-23537.

3. Ehsanifar M, Yavari Z, Rafati M. Exposure to urban air pollution particulate matter: Neurobehavioral alteration and hippocampal inflammation. Environ Sci Pollut Res. 2022; 29: 50856-50866.
4. Puentes-Orozco M, Albarracin SL, Velásquez MM. Neuroinflammation and major depressive disorder: Astrocytes at the crossroads. Front Cell Neurosci. 2024; 18: 1504555.
5. Ferenchick EK, Ramanuj P, Pincus HA. Depression in primary care: Part 1—Screening and diagnosis. BMJ. 2019; 365: l794.
6. Wu A, Zhang J. Neuroinflammation, memory, and depression: New approaches to hippocampal neurogenesis. J Neuroinflammation. 2023; 20: 283.
7. Ramanuj P, Ferenchick EK, Pincus HA. Depression in primary care: Part 2—Management. BMJ. 2019; 365: l835.
8. Vásquez-Pérez JM, González-Guevara E, Gutiérrez-Buenabad D, Martínez-Gopar PE, Martinez-Lazcano JC, Cárdenas G. Is nasal dysbiosis a required component for neuroinflammation in major depressive disorder? Mol Neurobiol. 2025; 62: 2459-2469.
9. Von Lindern E, Hartig T, Lercher P. Traffic-related exposures, constrained restoration, and health in the residential context. Health Place. 2016; 39: 92-100.
10. Jazvinšćak Jembrek M, Oršolić N, Karlović D, Peitl V. Flavonols in action: Targeting oxidative stress and neuroinflammation in major depressive disorder. Int J Mol Sci. 2023; 24: 6888.
11. Lyche JL, Gutleb AC, Bergman Å, Eriksen GS, Murk AJ, Ropstad E, et al. Reproductive and developmental toxicity of phthalates. J Toxicol Environ Health B. 2009; 12: 225-249.
12. Reddy BS, Rozati R, Reddy BV, Raman NV. General gynaecology: Association of phthalate esters with endometriosis in Indian women. BJOG Int J Obstet Gynaecol. 2006; 113: 515-520.
13. Hassamal S. Chronic stress, neuroinflammation, and depression: An overview of pathophysiological mechanisms and emerging anti-inflammatories. Front Psychiatry. 2023; 14: 1130989.
14. Medzhitov R. Inflammation 2010: New adventures of an old flame. Cell. 2010; 140: 771-776.
15. Troubat R, Barone P, Leman S, Desmidt T, Cressant A, Atanasova B, et al. Neuroinflammation and depression: A review. Eur J Neurosci. 2021; 53: 151-171.
16. Ehsanifar M, Yavari Z. Neurotoxicity following exposure to micro and nanoplastics. OBM Neurobiol. 2025; 9: 277.
17. Fleshner M, Frank M, Maier SF. Danger signals and inflammasomes: Stress-evoked sterile inflammation in mood disorders. Neuropsychopharmacology. 2017; 42: 36-45.
18. Cox SS, Speaker KJ, Beninson LA, Craig WC, Paton MM, Fleshner M. Adrenergic and glucocorticoid modulation of the sterile inflammatory response. Brain Behav Immun. 2014; 36: 183-192.
19. Bartoli F, Crocamo C, Mazza MG, Clerici M, Carra G. Uric acid levels in subjects with bipolar disorder: A comparative meta-analysis. J Psychiatr Res. 2016; 81: 133-139.
20. Tao R, Li H. High serum uric acid level in adolescent depressive patients. J Affect Disord. 2015; 174: 464-466.
21. Wieck A, Grassi-Oliveira R, do Prado CH, Viola TW, Petersen LE, Porto B, et al. Toll-like receptor expression and function in type I bipolar disorder. Brain Behav Immun. 2016; 54: 110-121.
22. Kim HK, Chen W, Andreazza AC. The potential role of the NLRP3 inflammasome as a link between mitochondrial complex I dysfunction and inflammation in bipolar disorder. Neural Plast. 2015; 2015: 408136.

23. Carr AL, Sluiman AJ, Grecian SM, Forster R, McLachlan S, Strachan MW, et al. Depression as a risk factor for dementia in older people with type 2 diabetes and the mediating effect of inflammation. Diabetologia. 2021; 64: 448-457.
24. Köhler CA, Freitas TH, Maes MD, De Andrade NQ, Liu CS, Fernandes BS, et al. Peripheral cytokine and chemokine alterations in depression: A meta-analysis of 82 studies. Acta Psychiatr Scand. 2017; 135: 373-387.
25. Inoshita M, Numata S, Tajima A, Kinoshita M, Umehara H, Nakataki M, et al. A significant causal association between C-reactive protein levels and schizophrenia. Sci Rep. 2016; 6: 26105.
26. Goldsmith DR, Rapaport MH, Miller BJ. A meta-analysis of blood cytokine network alterations in psychiatric patients: Comparisons between schizophrenia, bipolar disorder and depression. Mol Psychiatry. 2016; 21: 1696-1709.
27. Do Prado CH, Rizzo LB, Wieck A, Lopes RP, Teixeira AL, Grassi-Oliveira R, et al. Reduced regulatory T cells are associated with higher levels of Th1/TH17 cytokines and activated MAPK in type 1 bipolar disorder. Psychoneuroendocrinology. 2013; 38: 667-676.
28. Barbosa IG, Rocha NP, Assis F, Vieira ÉL, Soares JC, Bauer ME, et al. Monocyte and lymphocyte activation in bipolar disorder: A new piece in the puzzle of immune dysfunction in mood disorders. Int J Neuropsychopharmacol. 2015; 18: pyu021.
29. Valkanova V, Ebmeier KP, Allan CL. CRP, IL-6 and depression: A systematic review and meta-analysis of longitudinal studies. J Affect Disord. 2013; 150: 736-744.
30. Cattaneo A, Gennarelli M, Uher R, Breen G, Farmer A, Aitchison KJ, et al. Candidate genes expression profile associated with antidepressants response in the GENDEP study: Differentiating between baseline 'predictors' and longitudinal 'targets'. Neuropsychopharmacology. 2013; 38: 377-385.
31. Kiecolt-Glaser JK, Derry HM, Fagundes CP. Inflammation: Depression fans the flames and feasts on the heat. Am J Psychiatry. 2015; 172: 1075-1091.
32. Patisaul HB, Belcher SM. Endocrine disruptors, brain, and behavior. New York: Oxford University Press; 2017.
33. Gore AC, Chappell VA, Fenton SE, Flaws JA, Nadal A, Prins GS, et al. EDC-2: The endocrine society's second scientific statement on endocrine-disrupting chemicals. Endocr Rev. 2015; 36: E1-E150.
34. National Research Council, Board on Children, Youth, Committee on Depression, Parenting Practices, the Healthy Development of Children. Depression in parents, parenting, and children: Opportunities to improve identification, treatment, and prevention. Washington, D.C.: The National Academies Press; 2009.
35. Pochigaeva K, Druzhkova T, Yakovlev A, Onufriev M, Grishkina M, Chepelev A, et al. Hair cortisol as a marker of hypothalamic-pituitary-adrenal Axis activity in female patients with major depressive disorder. Metab Brain Dis. 2017; 32: 577-583.
36. Gabra RH, Ebrahim OS, Osman DM, Al-Attar GS. Knowledge, attitude and health-seeking behavior among family caregivers of mentally ill patients at Assiut University Hospitals: A cross-sectional study. Middle East Curr Psychiatry. 2020; 27: 10.
37. James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018; 392: 1789-1858.

38. Shoaff JR, Coull B, Weuve J, Bellinger DC, Calafat AM, Schantz SL, et al. Association of exposure to endocrine-disrupting chemicals during adolescence with attention-deficit/hyperactivity disorder–Related behaviors. JAMA Netw Open. 2020; 3: e2015041.
39. Ehsanifar M, Rajati R, Gholami A, Reiss JP. Mold and mycotoxin exposure and brain disorders. J Integr Neurosci. 2023; 22: 137.
40. Liu T, Jia Y, Zhou L, Wang Q, Sun D, Xu J, et al. Effects of di-(2-ethylhexyl) phthalate on the hypothalamus–uterus in pubertal female rats. Int J Environ Res Public Health. 2016; 13: 1130.
41. Geens T, Goeyens L, Covaci A. Are potential sources for human exposure to bisphenol-A overlooked? Int J Hyg Environ Health. 2011; 214: 339-347.
42. Koniecki D, Wang R, Moody RP, Zhu J. Phthalates in cosmetic and personal care products: Concentrations and possible dermal exposure. Environ Res. 2011; 111: 329-336.
43. Acconcia F, Pallottini V, Marino M. Molecular mechanisms of action of BPA. Dose-Response. 2015; 13. doi: 10.1177/1559325815610582.
44. Balaguer P, Delfosse V, Grimaldi M, Bourguet W. Structural and functional evidences for the interactions between nuclear hormone receptors and endocrine disruptors at low doses. C R Biol. 2017; 340: 414-420.
45. Thoene M, Dzika E, Gonkowski S, Wojtkiewicz J. Bisphenol S in food causes hormonal and obesogenic effects comparable to or worse than bisphenol A: A literature review. Nutrients. 2020; 12: 532.
46. Hernández-Hernández OT, Martínez-Mota L, Herrera-Pérez JJ, Jiménez-Rubio G. Role of estradiol in the expression of genes involved in serotonin neurotransmission: Implications for female depression. Curr Neuropharmacol. 2019; 17: 459-471.
47. Hiroi R, Handa RJ. Estrogen receptor-β regulates human tryptophan hydroxylase-2 through an estrogen response element in the 5’ untranslated region. J Neurochem. 2013; 127: 487-495.
48. Schneider LS, Small GW, Clary CM. Estrogen replacement therapy and antidepressant response to sertraline in older depressed women. Am J Geriatr Psychiatry. 2001; 9: 393-399.
49. Yeung AW, Georgieva MG, Atanasov AG, Tzvetkov NT. Monoamine oxidases (MAOs) as privileged molecular targets in neuroscience: Research literature analysis. Front Mol Neurosci. 2019; 12: 143.
50. Maki PM, Kornstein SG, Joffe H, Bromberger JT, Freeman EW, Athappilly G, et al. Guidelines for the evaluation and treatment of perimenopausal depression: Summary and recommendations. J Womens Health. 2019; 28: 117-134.
51. Gordon JL, Girdler SS, Meltzer-Brody SE, Stika CS, Thurston RC, Clark CT, et al. Ovarian hormone fluctuation, neurosteroids, and HPA axis dysregulation in perimenopausal depression: A novel heuristic model. Am J Psychiatry. 2015; 172: 227-236.
52. Shutoh Y, Takeda M, Ohtsuka R, Haishima A, Yamaguchi S, Fujie H, et al. Low dose effects of dichlorodiphenyltrichloroethane (DDT) on gene transcription and DNA methylation in the hypothalamus of young male rats: Implication of hormesis-like effects. J Toxicol Sci. 2009; 34: 469-482.
53. Yaoi T, Itoh K, Nakamura K, Ogi H, Fujiwara Y, Fushiki S. Genome-wide analysis of epigenomic alterations in fetal mouse forebrain after exposure to low doses of bisphenol A. Biochem Biophys Res Commun. 2008; 376: 563-567.
54. Bereshchenko O, Bruscoli S, Riccardi C. Glucocorticoids, sex hormones, and immunity. Front Immunol. 2018; 9: 1332.

55. Pavón L, Sandoval-López G, Hernández ME, Loría F, Estrada I, Pérez M, et al. Th2 cytokine response in major depressive disorder patients before treatment. J Neuroimmunol. 2006; 172: 156-165.
56. Nava-Castro KE, Togno-Peirce C, Palacios-Arreola MI, Del Rio-Araiza VH, Hernandez-Bello R, Morales Montor J. Bisphenol A induces protection through modulation of the immune response against the helminth parasite Taenia Crassiceps. Parasite Immunol. 2020; 42: e12733.
57. Tyl RW, Myers CB, Marr MC, Fail PA, Seely JC, Brine DR, et al. Reproductive toxicity evaluation of dietary butyl benzyl phthalate (BBP) in rats. Reprod Toxicol. 2004; 18: 241-264.
58. Lovekamp-Swan T, Davis BJ. Mechanisms of phthalate ester toxicity in the female reproductive system. Environ Health Perspect. 2003; 111: 139-145.
59. Dutta S, Haggerty DK, Rappolee DA, Ruden DM. Phthalate exposure and long-term epigenomic consequences: A review. Front Genet. 2020; 11: 405.
60. Frederiksen H, Jørgensen N, Andersson AM. Correlations between phthalate metabolites in urine, serum, and seminal plasma from young Danish men determined by isotope dilution liquid chromatography tandem mass spectrometry. J Anal Toxicol. 2010; 34: 400-410.
61. Wittassek M, Koch HM, Angerer J, Brüning T. Assessing exposure to phthalates–the human biomonitoring approach. Mol Nutr Food Res. 2011; 55: 7-31.
62. Hansen JF, Nielsen CH, Brorson MM, Frederiksen H, Hartoft-Nielsen ML, Rasmussen ÅK, et al. Influence of phthalates on in vitro innate and adaptive immune responses. PloS One. 2015; 10: e0131168.
63. Flores-Ramos M, Burrola-Suárez MA, Guiza-Zayas R, Enciso-Araujo JM, Islas-Preciado D, Estrada Camarena E. Evaluation of hormonal and metabolic factors related to depression in reproductive age women. Salud Ment. 2020; 43: 35-41.
64. Findikli E, Kurutas EB, Camkurt MA, Karaaslan MF, Izci F, Fındıklı HA, et al. Increased serum G protein-coupled estrogen receptor 1 levels and its diagnostic value in drug naïve patients with major depressive disorder. Clin Psychopharmacol Neurosci. 2017; 15: 337.
65. Wang Y, Zhu H, Kannan K. A review of biomonitoring of phthalate exposures. Toxics. 2019; 7: 21.
66. Corrales J, Kristofco LA, Steele WB, Yates BS, Breed CS, Williams ES, et al. Global assessment of bisphenol A in the environment: Review and analysis of its occurrence and bioaccumulation. Dose-Response. 2015; 13. doi: 10.1177/1559325815598308.
67. Inoue H, Yuki G, Yokota H, Kato S. Bisphenol A glucuronidation and absorption in rat intestine. Drug Metab Dispos. 2003; 31: 140-144.
68. Genuis SJ, Beesoon S, Birkholz D, Lobo RA. Human excretion of bisphenol A: Blood, urine, and sweat (BUS) study. J Environ Public Health. 2012; 2012: 185731.
69. Ginsberg G, Rice DC. Does rapid metabolism ensure negligible risk from bisphenol A? Environ Health Perspect. 2009; 117: 1639-1643.
70. Domínguez-Romero E, Scheringer M. A review of phthalate pharmacokinetics in human and rat: What factors drive phthalate distribution and partitioning? Drug Metab Rev. 2019; 51: 314-329.
71. Min A, Liu F, Yang X, Chen M. Benzyl butyl phthalate exposure impairs learning and memory and attenuates neurotransmission and CREB phosphorylation in mice. Food Chem Toxicol. 2014; 71: 81-89.
72. Sicińska P, Kik K, Bukowska B. Human erythrocytes exposed to phthalates and their metabolites alter antioxidant enzyme activity and hemoglobin oxidation. Int J Mol Sci. 2020; 21: 4480.

73. Hlisníková H, Petrovičová I, Kolena B, Šidlovská M, Sirotkin A. Effects and mechanisms of phthalates' action on reproductive processes and reproductive health: A literature review. Int J Environ Res Public Health. 2020; 17: 6811.
74. Xu X, Yang Y, Wang R, Wang Y, Ruan Q, Lu Y. Perinatal exposure to di-(2-ethylhexyl) phthalate affects anxiety-and depression-like behaviors in mice. Chemosphere. 2015; 124: 22-31.
75. Lin H, Yuan K, Li L, Liu S, Li S, Hu G, et al. In utero exposure to diethylhexyl phthalate affects rat brain development: A behavioral and genomic approach. Int J Environ Res Public Health. 2015; 12: 13696-13710.
76. Ehsanifar M, Tameh AA, Farzadkia M, Kalantari RR, Zavareh MS, Nikzaad H, et al. Exposure to nanoscale diesel exhaust particles: Oxidative stress, neuroinflammation, anxiety and depression on adult male mice. Ecotoxicol Environ Saf. 2019; 168: 338-347.
77. Ehsanifar M, Jafari AJ, Nikzad H, Zavareh MS, Atlasi MA, Mohammadi H, et al. Prenatal exposure to diesel exhaust particles causes anxiety, spatial memory disorders with alters expression of hippocampal pro-inflammatory cytokines and NMDA receptor subunits in adult male mice offspring. Ecotoxicol Environ Saf. 2019; 176: 34-41.
78. Ehsanifar M, Montazeri Z, Taheri MA, Rafati M, Behjati M, Karimian M. Hippocampal inflammation and oxidative stress following exposure to diesel exhaust nanoparticles in male and female mice. Neurochem Int. 2021; 145: 104989.
79. Ehsanifar M, Jafari AJ, Montazeri Z, Kalantari RR, Gholami M, Ashtarinezhad A. Learning and memory disorders related to hippocampal inflammation following exposure to air pollution. J Environ Health Sci Eng. 2021; 19: 261-272.
80. Ehsanifar M, Karimian M, Behdarvandi M. Anxiety and depression following diesel exhaust nano-particles exposure in male and female mice. J Neurophysiol Neurol Disord. 2020; 8: 1-8.
81. Kajta M, Wójtowicz AK. Impact of endocrine-disrupting chemicals on neural development and the onset of neurological disorders. Pharmacol Rep. 2013; 65: 1632-1639.
82. Smith CA, Holahan MR. Reduced hippocampal dendritic spine density and BDNF expression following acute postnatal exposure to di (2-ethylhexyl) phthalate in male Long Evans rats. PloS One. 2014; 9: e109522.
83. Smith CA, Farmer K, Lee H, Holahan MR, Smith JC. Altered hippocampal lipid profile following acute postnatal exposure to Di (2-Ethylhexyl) phthalate in rats. Int J Environ Res Public Health. 2015; 12: 13542-13559.
84. Parada Jr H, Gammon MD, Ettore HL, Chen J, Calafat AM, Neugut AI, et al. Urinary concentrations of environmental phenols and their associations with breast cancer incidence and mortality following breast cancer. Environ Int. 2019; 130: 104890.
85. van den Bosch M, Meyer-Lindenberg A. Environmental exposures and depression: Biological mechanisms and epidemiological evidence. Annu Rev Public Health. 2019; 40: 239-259.