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EXPOSURE TO MICROPLASTICS, NANOPLASTICS, AND PLASTIC-ASSOCIATED CHEMICALS: MENTAL HEALTH OUTCOMES AND PSYCHONEUROIMMUNOENDOCRINE MECHANISMS — A SYSTEMATIZED LITERATURE REVIEW (2000–2025)

EXPOSIÇÃO A MICROPLÁSTICOS, NANOPLÁSTICOS E SUBSTÂNCIAS QUÍMICAS ASSOCIADAS A PLÁSTICOS: DESFECHOS EM SAÚDE MENTAL E MECANISMOS PSICONEUROIMUNOENDÓCRINOS — UMA REVISÃO SISTEMATIZADA DA LITERATURA (2000–2025)

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ABSTRACT

Global plastic production exceeds 400 million metric tons annually, contributing to the widespread occurrence of microplastics and nanoplastics in the environment, as well as exposure to plastic-associated chemicals, including bisphenols, phthalates, and per- and polyfluoroalkyl substances (PFAS). These contaminants have raised growing concerns regarding their potential effects on the nervous, endocrine, and immune systems. This study aimed to critically examine the available scientific evidence on the associations between exposure to plastic particles and associated chemicals, mental disorders, and psychoneuroimmunoendocrine mechanisms. A systematized literature review was conducted using PubMed/MEDLINE, Scopus, Web of Science, and ScienceDirect, covering

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publications from 2000 to 2025. Twenty-five studies were included, comprising human epidemiological investigations and *in vivo* and *in vitro* experimental studies. The reviewed evidence suggests several potential mechanisms underlying the neurobiological effects of these contaminants, including alterations in hypothalamic–pituitary–adrenal (HPA) axis regulation, neuroinflammation, oxidative stress, changes in gut microbiota composition and gut–brain axis communication, and disturbances in neurotransmission. Epidemiological studies reported positive associations between urinary phthalate metabolites and depressive symptoms, with odds ratios (ORs) ranging from 1.24 to 1.44. A cross-sectional study involving university students identified an association between higher estimated microplastic exposure and increased odds of depressive symptoms (OR = 1.38). Experimental studies also reported anxiety-like and depressive-like behaviors, as well as neurobehavioral alterations resembling features associated with neurodevelopmental disorders. Furthermore, investigations of human brain tissue have identified the presence of microplastic and nanoplastic particles. However, methodological heterogeneity, differences in exposure conditions, and limitations inherent to observational and experimental studies constrain the extrapolation of these findings and the establishment of causal relationships. Overall, the available evidence supports the biological plausibility of associations between exposure to plastic-related contaminants and neurobehavioral and psychoneuroimmunoendocrine alterations. Nevertheless, longitudinal studies and experimental investigations using environmentally relevant exposure conditions are needed to clarify the potential risks to human mental health.

Keywords: Plastics; Endocrine Disruptors; Mental Disorders; Psychoneuroimmunology; Microplastics; Depression.

RESUMO

A produção global de plásticos ultrapassa 400 milhões de toneladas anuais, contribuindo para a disseminação de microplásticos e nanoplásticos no ambiente, além da exposição a substâncias químicas associadas aos materiais plásticos, como bisfenóis, ftalatos e substâncias per- e polifluoroalquiladas (PFAS). Esses contaminantes têm despertado crescente preocupação devido aos seus potenciais efeitos sobre os sistemas nervoso, endócrino e imunológico. O presente estudo teve como objetivo analisar criticamente as evidências científicas disponíveis sobre as associações entre a exposição a partículas plásticas e substâncias químicas associadas, os transtornos mentais e os mecanismos psiconeuroimunoendócrinos. Foi realizada uma revisão sistematizada da literatura, com buscas nas bases PubMed/MEDLINE, Scopus, Web of Science e ScienceDirect, abrangendo publicações de 2000 a 2025. Foram incluídos 25 estudos, compreendendo investigações epidemiológicas em humanos e estudos experimentais *in vivo* e *in vitro*. As evidências analisadas apontam possíveis mecanismos envolvidos nos efeitos neurobiológicos desses contaminantes, incluindo alterações na regulação do eixo hipotálamo-hipófise-adrenal (HPA), neuroinflamação, estresse oxidativo, alterações na microbiota intestinal e na comunicação do eixo intestino–cérebro, além de modificações na neurotransmissão. Estudos epidemiológicos identificaram associações positivas entre metabólitos urinários de ftalatos e sintomas depressivos, com razões de chances (OR) variando de 1,24 a 1,44. Um estudo transversal com universitários identificou associação entre maior exposição estimada a microplásticos e maior chance de sintomas depressivos (OR = 1,38). Estudos experimentais também relataram alterações neurocomportamentais semelhantes à ansiedade, depressão e manifestações relacionadas a transtornos do neurodesenvolvimento, enquanto investigações em tecidos humanos identificaram a presença de partículas microplásticas e nanoplásticas no encéfalo.

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Entretanto, a heterogeneidade metodológica, as diferenças nas condições de exposição e as limitações dos estudos observacionais e experimentais restringem a extrapolação dos resultados e o estabelecimento de relações causais. Conclui-se que as evidências disponíveis sustentam a plausibilidade biológica de associações entre a exposição a contaminantes relacionados aos plásticos e alterações neurocomportamentais e psiconeuroimunoendócrinas, embora sejam necessários estudos longitudinais e investigações experimentais com condições de exposição ambientalmente relevantes para esclarecer os riscos à saúde mental humana.

Palavras-chave: Plásticos; Disruptores Endócrinos; Transtornos Mentais; Psiconeuroimunologia; Microplásticos; Depressão.

INTRODUCTION

Mental disorders, including major depressive disorder, anxiety disorders, attention-deficit/hyperactivity disorder (ADHD), and autism spectrum disorder (ASD), represent a substantial global public health burden. Neurodegenerative diseases may also involve psychiatric and neurobehavioral manifestations, although they constitute distinct clinical categories. The etiology and progression of these conditions involve complex interactions among genetic, environmental, developmental, and biological factors (GRANDJEAN; LANDRIGAN, 2006; WHO, 2013).

Within this context, the psychoneuroimmunoendocrine (PNIE) framework provides an integrative perspective for understanding the bidirectional interactions among the nervous, endocrine, and immune systems and their potential contributions to neurobehavioral alterations. Particular attention has been directed toward the hypothalamic–pituitary–adrenal (HPA) axis, which plays a central role in neuroendocrine stress responses through the regulation of glucocorticoid secretion and feedback mechanisms (GRANDJEAN; LANDRIGAN, 2006; WHO, 2013; HANSEL-MARTINS et al., 2023).

Environmental exposure to plastic particles and plastic-associated chemicals has emerged as an area of growing concern due to their widespread occurrence and potential biological effects. Bisphenol A (BPA), phthalates, and certain per- and polyfluoroalkyl substances (PFAS) have been investigated for their endocrine-disrupting and neurotoxic potential (NIHART et al., 2025; FANG et al., 2025).

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Microplastics (MPs), commonly defined as plastic particles smaller than 5 mm, and nanoplastics (NPs), frequently characterized as particles smaller than 1 μm, may originate from the fragmentation of larger plastic materials or be released during manufacturing, use, and disposal. These particles have been reported in environmental compartments, including water, air, and food, as well as in human biological samples and tissues. Recent investigations have also reported the presence of microplastic and nanoplastic particles in human brain tissue, raising questions about their potential distribution within the central nervous system and their biological implications (NIHART et al., 2025; FANG et al., 2025).

Experimental investigations have suggested that exposure to microplastics, nanoplastics, and certain plastic-associated chemicals may influence biological pathways involved in neurological and behavioral regulation. Proposed mechanisms include oxidative stress, mitochondrial dysfunction, neuroinflammatory responses, endocrine signaling alterations, changes in neurotransmitter regulation, and disturbances in gut microbiota composition and gut–brain axis communication. These pathways are particularly relevant from a PNIE perspective because they involve interconnected physiological systems that may contribute to neurobehavioral dysfunction. Nevertheless, the magnitude and biological significance of these effects depend on several factors, including the chemical or particulate nature of the contaminant, particle size and composition, exposure concentration and duration, developmental stage, and characteristics of the experimental model (NIHART et al., 2025; FANG et al., 2025).

Although epidemiological and experimental studies have reported associations between plastic-related contaminants and neurobehavioral outcomes, important uncertainties remain regarding the consistency of these findings and their relevance to human mental health. Human observational studies may be affected by exposure assessment limitations, residual confounding, and difficulties in establishing temporal relationships. Furthermore, experimental investigations frequently employ exposure conditions that differ from those encountered in everyday environments, limiting direct extrapolation to human populations. Distinguishing associations observed in epidemiological studies from mechanistic evidence

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obtained in experimental models is therefore essential for a balanced interpretation of the available literature (NIHART et al., 2025; FANG et al., 2025).

In this context, integrating epidemiological findings with experimental evidence may contribute to a more comprehensive understanding of the potential relationships between plastic-related environmental contaminants, mental health outcomes, and psychoneuroimmunoendocrine alterations. Accordingly, this systematized literature review aims to critically examine scientific evidence published between 2000 and 2025 concerning exposure to microplastics, nanoplastics, and plastic-associated chemicals, with particular emphasis on mental and neurobehavioral outcomes, underlying PNIE mechanisms, methodological limitations, and remaining research gaps.

METHODOLOGY

Study design and literature search

This study was conducted as a systematized literature review aimed at synthesizing scientific evidence on the associations between exposure to plastic particles and plastic-associated chemicals, mental and neurobehavioral outcomes, and psychoneuroimmunoendocrine mechanisms. The review covered publications from January 2000 to October 2025 and included searches conducted in PubMed/MEDLINE, Scopus, Web of Science, and ScienceDirect.

The methodological approach comprised four main stages: (i) formulation of the research question and development of database-specific search strategies; (ii) identification of potentially relevant publications; (iii) selection of studies according to predefined eligibility criteria; and (iv) extraction, organization, and narrative synthesis of the available evidence.

Eligibility criteria

Eligible publications included original epidemiological investigations involving human populations, experimental studies using animal models, *in vitro* investigations, and

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scoping reviews addressing associations between exposure to plastic particles or plastic-associated chemicals and psychiatric, neurobehavioral, or psychoneuroimmunoendocrine outcomes.

Studies were considered relevant when they investigated mental health outcomes, neurobehavioral alterations, or biological mechanisms potentially associated with nervous, endocrine, and immune system interactions.

Publications outside the defined period and studies that did not address relevant neurobehavioral outcomes or associated biological mechanisms were excluded.

Search strategy

The search strategies combined terms related to plastic exposure with terms associated with mental health, neurobehavioral alterations, and psychoneuroimmunoendocrine mechanisms.

Boolean operators (AND and OR), truncation symbols (*), and quotation marks were employed according to the search functionalities of each database. Database-specific search expressions and applied filters are presented in Quadre 1.

Quadre 1: Databases, Boolean search strategies and applied filters.

Data-base	Boolean search strategy	Applied filters
PubMed/ MEDLINE	("plastic*"[Title/Abstract] OR "microplastic*"[Title/Abstract] OR "nanoplastic*"[Title/Abstract] OR "bisphenol A"[Title/Abstract] OR "phthalate*"[Title/Abstract] OR "PFAS"[Title/Abstract] OR "endocrine disrupt*"[Title/Abstract]) AND ("mental disorder*"[MeSH Terms] OR "depress*"[Title/Abstract] OR "anxiet*"[Title/Abstract] OR "psychiatric"[Title/Abstract] OR "psychoneuroimmun*"[Title/Abstract] OR "neurobehavioral"[Title/Abstract] OR "HPA axis"[Title/Abstract]) AND ("2000/01/01"[Date - Publication] : "2025/10/31"[Date - Publication])	Humanes and animals; English; 2000–2025
Scopus	TITLE-ABS-KEY(plastic* OR microplastic* OR nanoplastic* OR "bisphenol A" OR phthalate* OR pfas OR "endocrine disrupt*") AND TITLE-ABS-KEY("mental disorder*" OR depress* OR anxiet* OR psychiatric OR psychoneuroimmun* OR neurobehavioral OR "hpa axis") AND PUBYEAR > 1999 AND PUBYEAR < 2026	Articles and reviews; 2000–2025
Web of Science	TS=((plastic* OR microplastic* OR nanoplastic* OR "bisphenol A" OR phthalate* OR PFAS OR "endocrine disrupt*") AND ("mental disorder*" OR depress* OR anxiet* OR psychiatric OR psychoneuroimmun* OR neurobehavioral OR "HPA axis")) AND PY=(2000–2025)	Science Citation Index Expanded

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ScienceDirect	("plastic" OR "microplastic" OR "bisphenol A" OR "phthalate") AND ("depression" OR "anxiety" OR "mental health" OR "psychiatric")	Toxicology and environmental health journals

Source: Prepared by the authors. Search expressions reproduced from the original manuscript, with formatting adjustments; database execution has not yet been independently verified.

Evidence synthesis

The review included 25 publications addressing human epidemiological associations, experimental neurobehavioral alterations, and potential biological mechanisms related to exposure to plastic particles and plastic-associated chemicals.

The evidence was organized according to study design, exposure characteristics, investigated outcomes, and reported findings. The results were presented through descriptive tables, figures, and narrative synthesis, emphasizing similarities and differences between epidemiological and experimental evidence.

Bibliographic citations and references were formatted according to the Brazilian Association of Technical Standards (ABNT), specifically NBR 10520:2023.

RESULTS

Epidemiological evidence in humans: Bisphenol A, phthalates, PFAS and microplastics

Epidemiological investigations have reported associations between exposure to plastic-associated chemicals and mental or neurobehavioral outcomes, although the direction and magnitude of these associations vary according to the contaminant, study population, exposure assessment, and outcome evaluated.

Birth cohort studies have investigated the potential neurobehavioral effects of prenatal bisphenol A (BPA) exposure, reporting sex-specific associations during childhood. Braun et al. (2009) observed an association between higher prenatal BPA exposure and externalizing behaviors among two-year-old girls. Subsequently, Braun et al. (2011) reported associations with anxiety, depressive symptoms, and hyperactivity among girls at three years of age. Other prospective investigations reported associations between prenatal BPA exposure and

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emotional or behavioral alterations in children, with differences according to sex and developmental stage (HARLEY et al., 2013; PERERA et al., 2016). These findings suggest that prenatal exposure may be associated with neurobehavioral outcomes; however, the observed differences across studies warrant cautious interpretation.

Regarding phthalates, a cross-sectional analysis involving 2.030 participants from the National Health and Nutrition Examination Survey (NHANES, 2005–2012) reported positive associations between urinary phthalate metabolites and depressive symptoms, including mono (3-carboxypropyl) phthalate (MCPP; OR = 1.24) and mono (carboxynonyl) phthalate (MCNP; OR = 1.42) (KIM et al., 2016).

Similarly, an analysis involving 7.340 NHANES participants (2005–2018) identified associations between urinary phthalate metabolites and depressive symptoms, including metabolites associated with di(2-ethylhexyl) phthalate (DEHP; OR = 1.30), mono (2-ethyl-5-hydroxyhexyl) phthalate (MEHHP; OR = 1.43), and mono (2-ethyl-5-carboxypentyl) phthalate (MECPP; OR = 1.44) (WANG et al., 2023). These findings indicate positive associations in the investigated populations, although the cross-sectional designs do not establish temporal or causal relationships.

Evidence concerning per- and polyfluoroalkyl substances (PFAS) remains heterogeneous. A prospective cohort study involving 1.499 Black women of reproductive age reported no appreciable association between the investigated PFAS mixture and depressive symptoms (SCHILDROTH et al., 2024). Other publications have discussed potential associations between PFAS exposure and neurological or neurobehavioral outcomes, although the available findings remain insufficient to establish a consistent relationship with depressive disorders.

For microplastics, a cross-sectional study involving 1.420 Chinese university students reported that participants in the highest category of estimated microplastic exposure had higher odds of depressive symptoms than those in the reference category (OR = 1.38; 95% CI: 1.21–1.57). The reported exposure assessment considered environmental exposure pathways, with inhalation identified as a relevant contributor (LUO; LIN, 2025). Nevertheless, the

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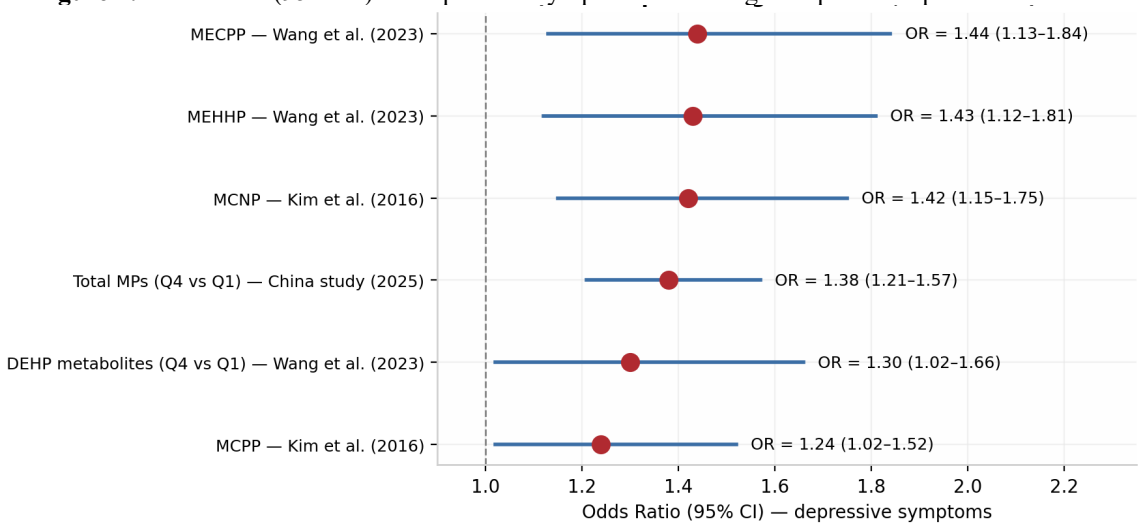
observational design and uncertainties associated with exposure estimation limit causal interpretation.

In addition to epidemiological investigations, Nihart et al. (2025) reported the presence of microplastic and nanoplastic particles in post-mortem human brain tissue, with differences in measured concentrations across investigated samples. Although these findings provide evidence of the presence of plastic particles in human neural tissue, they do not establish that such particles cause psychiatric or neurodegenerative disorders.

Figure 1 presents selected odds ratios reported in studies investigating associations between plastic-related contaminants and depressive symptoms.

Figure 1: Odds ratios (95% CI) for depressive symptoms according to exposure to plastic contaminants.



Source: Prepared by the authors, with data from Kim et al. (2016), Wang et al. (2023) and Association between microplastics exposure (2025).

Table 2 summarizes the main human studies included in this section.

Table 2: Human epidemiological and observational studies investigating plastic-related contaminants and neurobehavioral or neurological outcomes.

Study (author, year)	Design	Sample	Exposure	Outcome	Main result
Braun et al. (2009)	Birth cohort	249 children (2 years)	Maternal urinary BPA	Behavior (BASC-2)	Externalizing behavior in girls
Braun et al. (2011)	Birth cohort	240 children (3 years)	Maternal urinary BPA	Anxiety, depression, hyperactivity	Significant association in girls
Harley et al. (2013)	Birth cohort	198 children (3–5	Prenatal urinary	CBCL	Sex-specific effects:

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		years)	BPA		emotional reactivity/aggressiveness in boys
Perera et al. (2016)	Prospective cohort	241 children (10–12 years)	Prenatal urinary BPA	Anxiety and depression	More symptoms in boys with higher exposure
Kim et al. (2016)	Cross-sectional (NHANES 2005–2012)	2.030 older adults	Urinary phthalate metabolites	Depression (PHQ-9)	MCPP OR = 1.24; MCNP OR = 1.42
Wang et al. (2023)	Cross-sectional (NHANES 2005–2018)	7.340 adults	11 phthalate metabolites	Depression (PHQ-9)	DEHP OR = 1.30; MEHHP OR = 1.43; MECPP OR = 1.44
Schildroth et al. (2024)	Prospective (SELF cohort)	1.499 women (23–35 years)	9 plasma PFAS	Depression (CES-D) and perceived stress	Null association for PFAS mixture
Association between microplastics exposure (2025)	Cross-sectional	1.420 college students	Daily MP exposure (air and water)	Depression (PHQ-2)	OR = 1.38 (Q4); inhalation route predominant
Nihart et al. (2025)	Post-mortem case-control	Brains of deceased individuals	MP/NP bioaccumulation	Brain plastic burden	MPs detected in 100% of samples; higher concentration in brains of dementia patients

Source: Prepared by the authors (2025).

Psychoneuroimmunoendocrine mechanisms

Experimental investigations have identified several biological pathways potentially involved in the neurotoxic effects of microplastics, nanoplastics, and plastic-associated chemicals. From a psychoneuroimmunoendocrine perspective, these mechanisms involve interactions among neuroendocrine regulation, inflammatory responses, oxidative balance, neurotransmission, and intestinal microbiota. Endocrine-related mechanisms include potential alterations in hypothalamic–pituitary–adrenal (HPA) axis signaling and stress-response regulation. Certain plastic-associated chemicals have been investigated for their capacity to interfere with endocrine signaling pathways, although the specific mechanisms and their relevance to psychiatric outcomes vary among compounds and experimental models (BROWN-LEUNG; CANNON, 2022).

Neuroinflammatory responses represent another proposed mechanism. Experimental studies and mechanistic reviews have described microglial and astrocytic activation, accompanied by alterations in inflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6). Signaling pathways involving Toll-like receptors, nuclear factor kappa B (NF-κB), and the NLRP3 inflammasome have also

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been implicated in experimental models of plastic particle-associated neurotoxicity (FANG et al., 2025).

Oxidative stress and mitochondrial dysfunction have likewise been associated with experimental exposure to plastic particles. Reported alterations include increased oxidative damage, disturbances in cellular redox homeostasis, and activation of pathways associated with neuronal injury and cell death (YIN et al., 2022).

Changes in neurotransmitter signaling and synaptic regulation have also been investigated, including pathways involving dopamine, serotonin, glutamate, and gamma-aminobutyric acid (GABA). Experimental evidence suggests that alterations in glutamate transport, neurotrophic signaling, and synaptic homeostasis may contribute to observed neurobehavioral effects, although these mechanisms should not be generalized across all plastic-related contaminants (LIU et al., 2024; SU et al., 2025).

The microbiota–gut–brain axis constitutes an additional potential pathway linking intestinal exposure to neurological alterations. Experimental investigations have reported changes in gut microbial composition, intestinal inflammatory signaling, and neurobehavioral responses following exposure to microplastic or nanoplastic particles (TENG et al., 2022; YANG et al., 2023; SHI et al., 2024; WANG et al., 2024a). These findings suggest possible interactions among intestinal homeostasis, immune signaling, and central nervous system function, although the relative contribution of individual pathways remains incompletely understood.

The potential distribution of plastic particles within the central nervous system has also received increasing attention. Experimental studies have investigated particle translocation and neurodevelopmental alterations following exposure during pregnancy and lactation (TIAN et al., 2024). In humans, microplastic and nanoplastic particles have been reported in cerebrospinal fluid and post-mortem brain tissue, raising questions about blood–brain barrier integrity, particle transport, and tissue accumulation (XIE et al., 2024; NIHART et al., 2025). However, the detection of particles in neural compartments should not be interpreted as direct evidence of neurotoxicity or psychiatric disease causation.

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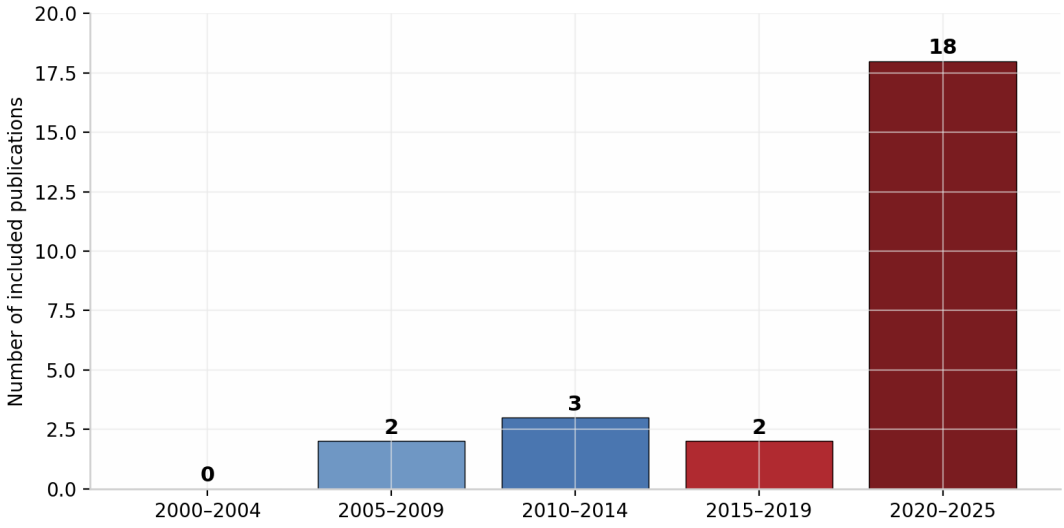
At the behavioral level, Su et al. (2025) reported anxiety-like and depressive-like behaviors in mice exposed to polystyrene nanoplastics, accompanied by reduced expression of excitatory amino acid transporter 2 (EAAT2). Vignon et al. (2025) described ADHD-like behavioral alterations following lifelong nanoplastic exposure in mice, whereas Zaheer et al. (2022) investigated neurodevelopmental alterations potentially relevant to autism-related behavioral phenotypes. Other experimental investigations have reported reduced social behavior and altered oxytocin signaling (WANG et al., 2024a), as well as interactions between anionic nanoplastics and α-synuclein aggregation, a molecular process relevant to Parkinson's disease (LIU et al., 2023). Collectively, these studies support the investigation of multiple interconnected biological mechanisms. Nevertheless, differences in particle characteristics, exposure concentrations, experimental duration, and biological models limit direct comparisons and extrapolation to human mental health outcomes.

Figure 2 presents the temporal distribution of publications included in the review.

Figure 2: Temporal distribution of the publications included in the corpus (n = 25), 2000–2025.



Source: Prepared by the authors.

Table 3 presents the main experimental and human tissue investigations addressing neurobehavioral outcomes and associated mechanisms.

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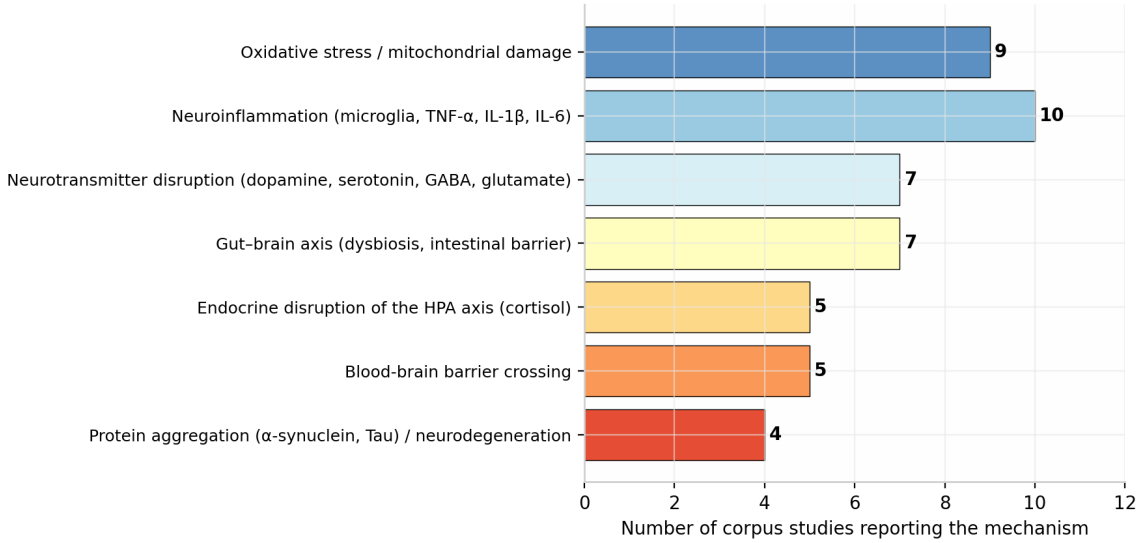
Table 3: Experimental and human tissue studies investigating plastic particle exposure, neurobehavioral outcomes, and associated biological mechanisms.

Study (author, year)	Model	Exposure	Behavioral outcome	Main mechanism
Su et al. (2025)	Mice	PS nanoplastics	Anxiety and depressive-like behavior	↓ EAAT2; neuroinflammation
Vignon et al. (2025)	Mice (lifelong)	PS nanoplastics	ADHD-like phenotype; brain aging	Dopaminergic dysfunction
Zaheer et al. (2022)	Mice	Pre/post-natal microplastics	ASD-like behaviors	Neuroinflammation; corticosterone
Tian et al. (2024)	Pregnant/lactating rats	Nanoplastics	Neurodevelopmental deficits in offspring	Fetal bioaccumulation in the brain
Wang et al. (2024a)	Mice	PS microplastics	↓ sociability	↓ oxytocin in prefrontal cortex via gut–brain axis
Yang et al. (2023)	Mice	Nanoplastics (oral route)	Brain dysfunction	Intestinal IL-1 signal in macrophages
Liu et al. (2023)	In vitro/in vivo models	Anionic nanoplastics	—	α-synuclein aggregation
Xie et al. (2024)	Humans (CSF, 28 patients)	MPs/NPs in cerebrospinal fluid	—	Selective BBB passage; PP/PE × permeability correlation
Nihart et al. (2025)	Humans (brains)	Brain MPs/NPs	—	Bioaccumulation; higher burden in dementias

Source: Prepared by the authors.

Figure 3 summarizes the biological mechanisms identified in the selected literature.

Figure 3: Psychoneuroimmunoendocrine mechanisms reported in the reviewed corpus.



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Comparative analysis of the evidence

The reviewed literature indicates that the nature and strength of the available evidence differ considerably across plastic-related contaminants and investigated outcomes.

For phthalates, population-based epidemiological studies have reported positive associations between urinary metabolites and depressive symptoms. However, the predominance of cross-sectional designs, potential confounding factors, and variability in exposure assessment limit causal inference.

For BPA, prospective birth cohort investigations provide evidence of associations between prenatal exposure and childhood behavioral outcomes, although the findings vary according to sex, developmental stage, and behavioral domains.

For PFAS, the available evidence regarding depressive symptoms remains limited and heterogeneous, with some investigations reporting no appreciable associations. Consequently, the findings do not support a uniform interpretation across different PFAS compounds, mixtures, and populations.

For microplastics and nanoplastics, human epidemiological evidence remains preliminary. Experimental investigations provide mechanistic insights into neuroinflammation, oxidative stress, endocrine signaling, gut–brain axis alterations, and neurobehavioral responses. Nevertheless, exposure conditions used in experimental models may differ substantially from those encountered in human environments, limiting their direct translational relevance (FANG et al., 2025).

The detection of plastic particles in human brain tissue (NIHART et al., 2025), together with reported epidemiological associations between estimated microplastic exposure and depressive symptoms (LUO; LIN, 2025), highlights the importance of further investigation. However, these findings represent distinct types of evidence and cannot independently establish a causal relationship between plastic particle accumulation and psychiatric disorders.

Overall, the available literature supports the biological plausibility of neurobehavioral and psychoneuroimmunoendocrine alterations associated with exposure to certain plastic-

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related contaminants. Further longitudinal investigations, improved exposure characterization, and experimental studies employing environmentally relevant conditions are necessary to clarify the consistency, magnitude, and potential clinical significance of these associations.

CONCLUSION

As final considerations, the scientific literature published between 2000 and 2025 provides evidence of associations between exposure to certain plastic-associated chemicals and mental or neurobehavioral outcomes, alongside experimental findings suggesting potential neurobiological effects of microplastics and nanoplastics. The proposed mechanisms involve interconnected psychoneuroimmunoendocrine pathways, including alterations in hypothalamic–pituitary–adrenal (HPA) axis regulation, neuroinflammatory responses, oxidative stress, intestinal microbiota composition, gut–brain axis communication, and neurotransmitter signaling.

Human epidemiological studies have reported associations between phthalate exposure and depressive symptoms, while prospective investigations of prenatal bisphenol A (BPA) exposure have identified potential associations with childhood behavioral alterations. Evidence concerning per- and polyfluoroalkyl substances (PFAS) remains heterogeneous, whereas human studies investigating microplastic and nanoplastic exposure and mental health outcomes are still limited. Although experimental investigations provide biological plausibility for neurobehavioral effects, differences in exposure conditions, study designs, and biological models restrict direct extrapolation to human populations and prevent definitive causal conclusions.

Future research should prioritize longitudinal epidemiological studies incorporating validated exposure biomarkers, standardized experimental protocols using environmentally relevant concentrations, and investigations addressing combined exposures and critical developmental windows, particularly pregnancy and early childhood. Furthermore, improved characterization of plastic particles and associated chemicals, together with integrated assessments of neuroendocrine, immune, neurological responses, and neurotransmitters in

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psychiatric disorders may contribute to a more comprehensive understanding of their potential health implications.

These advances are essential to support evidence-based environmental health strategies and inform preventive measures aimed at reducing potentially harmful exposures, particularly among vulnerable populations.

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