# Placeholder ’cause old one was too cringey

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# Abstract

*Keywords*: microplastics, immunity, neuroinflammation

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# Introduction

First named by ([Thompson et al., 2004](#ref-thompsonLostSeaWhere2004)), microplastics are defined as particles with diameters from to , while nanoplastics have diameters smaller than .

# MP Transport and Crossing the Blood-Brain Barrier (BBB)

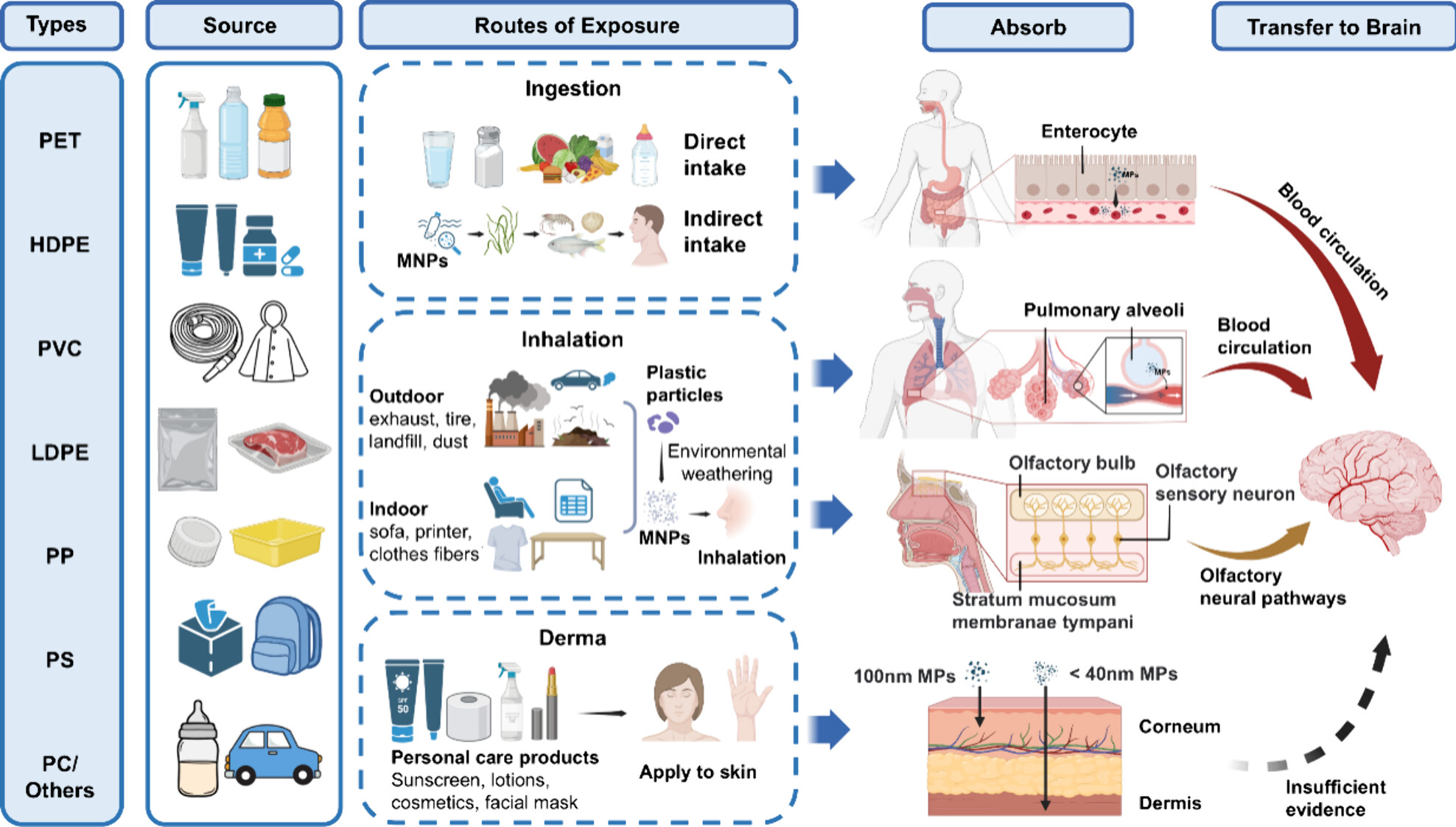
Lorem ipsum…

## Routes of Entry

Micro- and nanoplastics (MPs/NPs) enter the body via several primary routes of entry. The most prevalent pathways are ingestion—mainly from contaminated food and drinking water, which are almost everywhere in modern times—and inhalation—often from airborne particles such as indoor dust and synthetic clothing fibers. While dermal absorption remains a possibility, it is generally considered a less significant route. [Figure 1](#fig-entry-routes) depicts in detail how MNPs travel to the brain from outside. Recent research discovered that nanoplastics appear to be the most dangerous in terms of systemic effects, as their diminutive size facilitates rapid entrance into the bloodstream and distribution throughout the body ([Kopatz et al., 2023](#ref-kopatzMicroNanoplasticsBreach2023)).

Figure 1

Environmental Sources and MNPs’ Pathways to the Brain



*Note*. This diagram showcases the types of plastics, where they come from, and how they enter the body. The American Plastics Industry Association created the SPI code (SPI-Code) to provide a standard method for classifying plastics. Nanoplastics are best at traversing through the BBB into the brain due to their diminutive size. Reprinted from Ma, Q., Lei, J., Pang, Y., Shen, Y., & Zhang, T. (2025). Neurotoxicity of Micro- and Nanoplastics: A Comprehensive Review of Central Nervous System Impacts. Environment & Health. https://doi.org/10.1021/envhealth.5c00087.

## Blood-Brain Barrier Structure

The central nervous system (CNS) has a sophisticated shield called the Blood-Brain Barrier (BBB) that separates brain matter from the rest of the body. This structure is formed by specialized cerebral endothelial cells connected by tight junctions, along with pericytes and astrocytes ([McConnell & Mishra, 2022](#ref-mcconnellCellsBloodbrainBarrier2022)). The BBB effectively limits the passage of foreign substances, pathogens, and large molecules from the circulatory system past the outer brain layer, which helps maintain the neural microenvironment’s homeostasis.

## Translocation Hypotheses

There are many hypotheses regarding the MNPs’ route through the BBB. One such route is paracellular diffusion, which in theory could allow even smallest nanoplastic particles to pass, although this pathway is heavily restricted ([Campbell et al., 2012](#X004f712ec1095099a0c1c2348f1de96e549812f); [Winiarska et al., 2024](#ref-winiarskaPotentialImpactNano2024)). A more probable mechanism is endocytosis—where NPs are internalized by the brain endothelial cells and subsequently exocytosed into the brain interstitial fluid ([Hamed et al., 2022](#ref-hamedNeurotoxicEffectsDifferent2022)). A third, highly discussed hypothesis is the “Trojan Horse effect”. This scenario presumes that MNPs are first phagocytized by circulating immune cells, which then act as vectors to carry them across the BBB ([Li et al., 2025](#ref-liNewEvidenceMechanisms2025)).

## Associated Toxicants

A critical factor that exacerbates MNP-related neurotoxicity is associated toxicants. MNPs, due to their high surface-to-volume ratio, readily absorb chemical additives and environmental pollutants, (e.g., benzo[a]pyrene, okadaic acid) ([Yan et al., 2023](#Xe629b25df5763d94ad90b0417c5c121df366051)). These chemicals also have the capability to disrupt the BBB and impair tight junction integrity, thereby allowing the plastic particles easier access to the brain tissue and synergizing the overall neurotoxic effect. ([Cheng et al., 2023](#ref-chengEffectsAdsorbedBenzoapyrene2023))

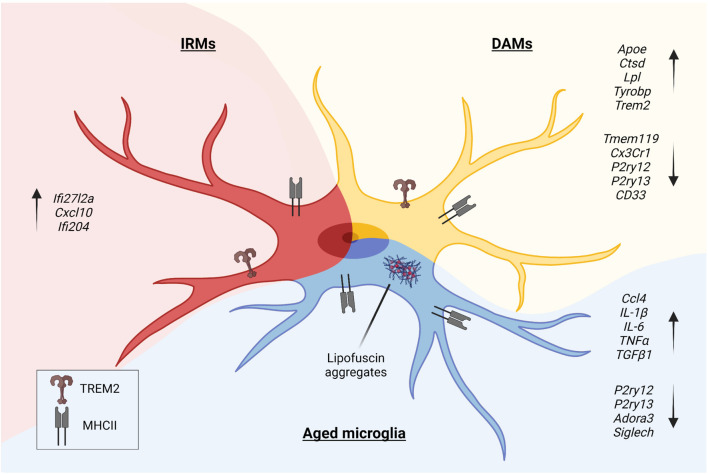
# Microglial Activation and Neuroinflammation

## The Role of Microglia

Microglial cells are the brain’s resident macrophages and the primary immune cells of the CNS. In their resting state, microglia adopt a branched morphology, actively surveying the microenvironment for pathogens, damaged cells, or misfolded proteins ([Wake et al., 2011](#ref-wakeFunctionsMicrogliaCentral2011)). When activated, these cells will rapidly undergo functional and morphological transformation, proliferate, migrate to the injury site, and engage in immunological activies—i.e., phagocytosis, antigen presentation, and the release of signaling molecules ([Yang et al., 2010](#ref-yangRoleMicrogliaCentral2010)). The neuroinflammation is marked by thechronic, uncontrolled activation of cells like microglia, which leads to persistent neurotoxicity and neuronal damage ([Muzio et al., 2021](#X8c4db74612eb4359854825ace8f5a75bc5d1444)).’

Figure 1

Different Activation States of Microglia



*Note*. Microglia experience morphologic and phenotypic/functional changes upon activation. Shown in this drawing are Disease-Associated Microglia (DAMs), Injury-Responsive Microglia (IRMs), and aged microglia, each representing a distinct activation state. Reprinted from Muzio, L., Viotti, A., & Martino, G. (2021). Microglia in Neuroinflammation and Neurodegeneration: From Understanding to Therapy. Frontiers in Neuroscience, 15, 742065. https://doi.org/10.3389/fnins.2021.742065.

## Direct Activation Mechanism

One primary hypothesized mechanism involves the direct interaction of ultra-fine plastic particles (nanoplastics) with microglia. As discussed in the above section, NPs are believed capable of crossing the BBB and be taken up via phagocytosis by nearby microglial cells. Being non-degradable, these particles persist within the microglial lysosome, which leads to a phenomenon coined “frustrated phagocytosis.” The inability to clear the foreign material results in chronic lysosomal stress and damage—akin to choking themselves to death ([Mularski et al., 2018](#Xc075ecd0603de099cd0d3801a41cc8bb5d7a187)). Persistent internal stress like this drives a sustained microglial activation state that remains even in the absence of a live pathogen.

# Consequences and Future Directions

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