

The Urgent Need to Assess and Prevent the Deposits of Microplastics and Nanoplastics in Our Brain

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The exponential use of plastics at a world scale is causing a global accumulation of both microplastics (MP: size between 1 micron and 5 mm) and nanoplastics (NP: size below 1 micron) in the environment, disseminating in the ecosystems and impacting the planet [1]. Their production has exploded since the 1960s [2]. For example, 400.3 million metric tons of plastics have been produced in 2023, and there are numerous industrial applications [2]. The global plastic production has reached growth rates up to 4% per year [3]. Plastics include, in particular, acrylics, polyesters, silicones, polyethylenes, polypropylenes, and halogenated plastics on the basis of the chemical structure of the primary polymer and side chains [2–6]. Plastic particles are produced especially following the deterioration and peeling of numerous plastic wastes [3]. MP/NP have a very long-standing presence in the environment [3]. MP/NP pollute oceans and rivers, with about 8 million metric tons of plastic waste mixing with the marine ecosystem every year [3]. MP/NP enter the food chain and contaminate numerous species, including humans [5,6].

MP/NP may enter the human host through the digestive tract, respiratory tract, or via dermal exposure [2]. The gastrointestinal tract is likely the main point of entry, in particular following ingestion of contaminated seafood and via bottled water [2]. NP may enter the lung tissue through the respiratory epithelium, whose alveolar surface is about 150 m². The use of MP/NP in cosmetics and textiles is associated with prolonged skin exposure. Plastic size, intake rates, and exposure frequency are likely important factors for human contamination [2].

Major concerns are raised in terms of potential impacts on human health as MP/NP have been identified in several body fluids (blood, sputum, saliva, urine, breast milk) and organs including the placenta (cumulative mass of 400–500 mg of MP/NP for a human placental weight of about 500

gr), kidney, liver and gut [1,5,7]. MP/NP likely accumulate in specific organs [1]. In the brain, high concentrations have been found, with higher levels in the brain than in the liver or kidneys [6]. The predominant polymer and related fragments/fibers identified in the brain are polyethylenes, and their relative proportion is greater in the brain. The significant increases in concentrations in the brain in cadavers over a period of 8 years represent a genuine alarm signal for the scientific community [6]. In a group of 27 cadavers from 2016 (mean age: 50 ± 11.4 years), the mean concentrations of MP/NP extracted from the frontal cortex were 3057 microgr/gr, whereas in a group of 24 cadavers from 2024 (mean age: 52.3 ± 16.8 years) the mean concentration rose to 4806 microgr/gr. Electron microscopy showed numerous shard-like particles with a size below 200 nm for the majority of deposits. A contamination through masks during the Coronavirus Disease 2019 (COVID-19) pandemic is not excluded [4].

It remains unclear whether MP/NP induce a direct toxic effect or represent rather a vehicle for harmful molecules such as phthalates, which are known to be endocrine disruptors. Increased inflammation might be triggered by MP/NP in carotid atheromas, as shown in a recent study [8]. Patients showing MP/NP in carotid artery plaques have a greater risk of myocardial infarction or stroke. The exposure of the respiratory epithelium to NP triggers an inflammatory reaction, and a related decrease in the transepithelial electrical resistance [9]. Plastics might trigger protein aggregation [10]. NP internalize in neurons and impair the metabolism of alpha-synuclein, raising the possibility that they might contribute to the pathogenesis of Parkinson's disease [10]. It has also been suggested that MP/NP might cause apoptosis, oxidative stress, genotoxicity, and might disturb the gut-brain axis [2,11]. These mechanisms are known to be involved in neurode-

velopmental disorders and neurodegeneration [11]. MP/NP might either worsen a pre-existing pathological process or even directly generate it [11].

So far, studies have used mainly visualization (microscopy) and tools based on spectroscopy to identify the MP, but NP are often missed by these methods [6]. Recent analytical techniques to assess MP/NP in human tissues include Raman or Fourier-transform infrared (FTIR) spectral techniques and pyrolysis-based gas chromatography and mass spectrometry (Py-GC-MS), following KOH saponification and ultracentrifugation [6]. There is a need to standardize these techniques, in particular through multidisciplinary collaboration, especially between physicians and chemists, and to develop methods to avoid contamination via the nearly ubiquitous plastic tools used in numerous laboratories and in clinical settings.

The rising concentrations of MP/NP in the environment represent a major concern worldwide. There is an urgent need to identify the mechanisms of penetration of MP/NP through the human blood-brain barrier in the central nervous system and to develop innovative strategies for preventing their bioaccumulation in the human brain. Experiments addressing the clearance of plastics from the human brain are currently missing. It remains unclear whether the glymphatic system/Pacchioni granulations, the microglia, and the blood-brain-barrier (efflux) participate or not in a cleaning mechanism in the brain. The lipophilic feature of plastics and the very high concentrations of lipids in the brain should be considered.

Public awareness campaigns are considered vital to minimize the contamination of ecosystems and to plan efficient strategies of removal [2]. The accumulation of debris requires integrated national and international initiatives to move towards a circular economy, which appears as a long-term solution [12–14]. Given the major challenge at a world scale, the effort must be continuous for governmental/non governmental organizations and must involve techniques easily accessible including manual removal of debris from coastal areas, but also more sophisticated techniques such as biosorption, magnetic extraction, ultrafiltration and nanofiltration to reach meaningful removal rates [3,13,14]. The scientific community has a major role to play in this endeavor. Biodegradable plastics are being developed and will likely be associated with reduced exposure if habits of life change drastically [12]. This will contribute to the reduction of the burden of MP/NP.

Availability of Data and Materials

Not applicable.

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MM, JL. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest. Mario Manto serves as one of the editorial board members of this journal. We declare that Mario Manto had no involvement in the review of this article and has no access to information regarding its review.

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