



Human Health Effects of Environmental Micro and Nanoplastic (MNP) Exposure: Linking Hippocampal Memory and Neurodegenerative Mechanisms

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Abstract

Microplastics and nanoplastics (MNPs) have become a serious matter because of their widespread prevalence in the environment and accumulation in human tissues, including the brain. Animal studies indicated that MNP exposure impaired hippocampal learning and memory through oxidative stress, neuroinflammation, mitochondrial dysfunction, and blood-brain barrier (BBB) disruption, but evidence in humans remains inadequate. This proposed study will investigate the relationship among MNP exposure, hippocampal memory, and potential neurodegenerative mechanisms using complementary behavioral and cellular approaches. A cross-sectional behavioral study will compare hippocampus-dependent memory between plastic factory workers with high occupational MNP exposure and matched workers with lower exposure using the Mnemonic Similarity Task (MST). The Montreal Cognitive Assessment (MoCA) will be used as a measure of cognitive function. A human induced pluripotent stem cell (iPSC)-derived BBB model containing brain microvascular endothelial cells, astrocytes, pericytes, and hippocampal neurons will be exposed to MNPs to evaluate oxidative stress, mitochondrial dysfunction, neuroinflammation, synaptic impairment, apoptosis, and neuronal viability. The behavioral arm is expected to determine whether occupational exposure is associated with differences in hippocampus-dependent memory, while the cell culture arm is expected to characterize cellular responses to controlled MNP exposure. We expect highly exposed workers to demonstrate lower memory performance than matched controls. We also expect MNP-treated cell cultures to show changes consistent with cellular stress, impaired neuronal function, and neurodegenerative processes. Because the two study arms use different samples, their findings will be interpreted as complementary evidence rather than as a direct individual-level relationship between cellular changes and memory performance. By combining human behavioral assessment with evidence from human-derived cell culture models, this study aims to reduce the gap between existing animal research and human health. The findings may contribute to understanding the potential neurological effects of chronic MNP exposure and provide a basis for future studies of exposure reduction and neurological health.

Keywords

Micro- and Nanoplastic (MNPs); Neurodegenerative Diseases; Hippocampal Memory; Mnemonic Similarity Task; Human iPSC-Derived Neurons

Introduction

The practicality of plastic has led to an annual global production of over 390 million tons (Zuri et al., 2023). Although it leads to serious environmental issues, plastic is still commonly used. Disposed plastic waste accumulates in environments and gradually fragments into microplastics and nanoplastics (MNPs). Microplastics are plastic particles ranging from 1 μm to 5 mm, which can further degrade into nanoplastics, which are smaller than 1 μm (Gao et al., 2025).

More attention has shifted from environmental impacts toward understanding the consequences of chronic MNP exposure on human health, as plastic contamination continues to increase. In addition, many studies emphasize the urgency to study the molecular mechanisms of how the accumulation of MNPs contributes to the progression of neurodegenerative diseases (Lee et al., 2022). Understanding these potential mechanisms is important because MNP exposure can occur through food, water, and air.

Humans can be exposed to MNPs through ingestion of contaminated food and water and inhalation of particles from indoor and outdoor air (Figure 1) (Zuri et al., 2023). An average adult is estimated to take in tens of thousands of plastic particles a year from diet alone, and more once inhaled particles are included (Cox et al., 2019).

After ingestion, MNPs disrupt the intestinal barrier and enter the bloodstream. Smaller particles penetrate the blood-brain barrier (BBB) through diffusion, endothelial uptake, or transcytosis. They also enter the brain through the olfactory nerve. In the brain, they mostly accumulate in different regions, including the hippocampus and cerebral cortex, as proven in animal studies (Gao et al., 2025).

Figure 1. Major Routes of Human Exposure to Micro- and Nanoplastics (MNPs).

Humans are exposed to micro- and nanoplastics through ingestion of contaminated food and water, inhalation of particles, and infant feeding. These can result in lifelong exposure. Adapted from Zuri et al. (2023).

Some groups of people may experience substantially greater occupational exposure to MNPs due to their work environment. For example, workers in plastic manufacturing and recycling environments may experience higher exposure than individuals without occupational contact with plastic materials. Previous studies have found a significant amount of MNPs on and in plastic factory workers' bodies, indicating occupational exposure to MNPs in these settings (Shahsavari et al., 2023). However, even in the same factory, the exposure is not spread evenly. Studies have also concluded that cutting and shredding plastics throws more microparticles into the air, exposing these specific workers to higher airborne particle concentrations than the surrounding background (Swinerton et al., 2024).

Previous studies have already detected MNPs in various biological samples, including human stool, blood, and brain tissue after death (Leslie et al., 2022; Nihart et al., 2025; Schwabl et al., 2019). These findings demonstrate that human exposure can result in internal exposure, although the extent to which MNPs reach specific brain regions remains uncertain.

Previous research also showed that some MNPs particles can reach the human brain. Specifically, more MNPs had been detected in the brain than in the liver or kidney (Nihart et al., 2025). However, this research focused on the frontal cortex, not the hippocampus. Therefore, although MNPs have been detected in human brain tissue, whether they reach the human hippocampus remains uncertain.

Evidence concerning hippocampal effects currently comes primarily from animal studies. When mice were exposed to polystyrene MNPs over several weeks to months, particles accumulated in the brain, including the hippocampus, and exposed mice performed worse on learning and memory tasks (Jin et al., 2022; Lee et al., 2022). These studies also reported BBB disruption, neuroinflammation, and altered memory-related signaling in exposed animals (Jin et al., 2022; Lee et al., 2022). These findings provide biological motivation for investigating whether a similar association can be observed in humans, although animal findings cannot be assumed to translate directly to human health.

The hippocampus is relevant for one of its important functions of pattern separation. It is the ability to distinguish between similar memories so that they remain distinct (Stark et al., 2019). Since this ability depends on the hippocampus, it is one of the first to weaken when the hippocampus is damaged, and it can be used as an indicator of hippocampal damage. To date, no study has yet tested whether real-world MNP exposure is linked to hippocampus-dependent memory in humans.

Environmental agents such as pesticides and industrial solvents can increase neurological risk through mechanisms involving oxidative stress and neuroinflammation. Oxidative stress can contribute to mitochondrial dysfunction, neuronal injury, and synaptic dysfunction (Ma et al., 2025). Animal studies of MNP exposure have similarly demonstrated hippocampus-dependent learning and memory impairment (Jin et al., 2022; Lee et al., 2022).

These mechanisms have been associated with neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, multiple sclerosis, and amyotrophic lateral sclerosis (Cannon & Greenamyre, 2011). Recent research has also reported greater concentrations of plastic particles in the brains of individuals with dementia than in those without dementia, although these observations do not establish that MNP exposure caused dementia (Nihart et al., 2025).

The present proposal therefore addresses two related but distinct questions. First, is occupational MNP exposure associated with hippocampus-dependent memory performance in humans? Second, can MNP exposure produce cellular responses relevant to neuronal dysfunction in a human-derived BBB model?

Our study will investigate the relationship between occupational MNP exposure and human learning and memory through the MST. We will also examine human-derived neuronal cells exposed to MNPs to study neurodegeneration-related changes, mitochondrial dysfunction, oxidative stress, neuroinflammation, and neuronal damage. This study will combine two complementary approaches. A behavioral study will evaluate hippocampus-dependent memory in workers with different occupational exposure levels. A human-derived BBB cell culture model will examine potential mechanisms of MNP-induced neurotoxicity at a cellular level. Because these two arms involve different samples, the study is designed to provide complementary evidence rather than directly connect a cellular measurement to memory performance within the same individual.

We hypothesize that individuals with higher occupational MNP exposure will demonstrate lower hippocampus-dependent memory performance on the MST, while human-derived BBB cultures exposed to MNPs will exhibit increased oxidative stress, neuroinflammation, mitochondrial dysfunction, apoptosis, and impaired synaptic function.

Methods

Behavioral Test

Experimental Design

This study will use a cross-sectional research design to compare hippocampus-dependent memory between workers with high and low occupational MNP exposure. Within a single plastic manufacturing or recycling facility, workers will be divided into two groups according to their primary daily task. The high-exposure group will consist of workers whose primary responsibilities involve cutting or shredding plastics. Cutting and shredding can release substantial quantities of airborne plastic particles (Swinerton et al., 2024). The low-exposure group will consist of workers whose primary responsibilities do not involve mechanically breaking plastics, such as packaging, inspection, or warehouse work.

These groups will be matched by age, sex, education, and job tenure to reduce differences in major background characteristics. Workers with diagnosed neurological or psychiatric conditions, a significant history of head injury, uncorrected visual impairment, or heavy alcohol use will be excluded.

The behavioral study will aim to recruit 128 participants, with 64 participants in each exposure group. This target is based on an a priori two-group comparison designed to provide approximately 80% statistical power to detect a moderate standardized difference in LDI between exposure groups at a two-sided $\alpha = 0.05$ significance level. The final sample-size calculation will be refined using pilot data if available before recruitment begins.

In addition to the categorical exposure groups, each participant will receive an occupational exposure score from 0 to 3 based on their primary task: 0 for non-cutting office or inspection work, 1 for packaging or plastic handling, 2 for occasional cutting or shredding, and 3 for cutting or shredding as the primary job. This score represents an occupational exposure proxy rather than a direct measurement of each participant's internal MNP burden. The exposure contrast will be informed by previous measurements of airborne particle release during plastic cutting and shredding (Swinerton et al., 2024).

Because workers performing different tasks may also experience different levels of dust, heat, noise, fumes, or other occupational exposures, these factors represent potential confounders. Where feasible, information about major occupational co-exposures will be collected and considered in sensitivity analyses.

Ethical Considerations

Before recruitment, the behavioral study will obtain approval from the appropriate institutional review board or research ethics committee. All participants will provide informed consent after receiving an explanation of the study procedures, risks, benefits, confidentiality protections, and their right to withdraw without penalty. Participant data will be coded and analyzed without directly identifying information.

MST and MoCA results will be coded before statistical analysis, and the personnel responsible for scoring or analyzing the cognitive outcomes will be masked to occupational exposure groups whenever feasible.

Survey and Visual Screening

Participants will also complete a visual screening procedure to confirm that they can clearly see the digital MST stimuli and do not have an uncorrected visual impairment that could interfere with performance.

Montreal Cognitive Assessment

Each participant will complete one session of the Montreal Cognitive Assessment (MoCA), a brief screening test of general cognitive function (Nasreddine et al., 2005). The five-point delayed-recall component will be removed from the total score and analyzed separately as MoCA-without-memory. This measure will be included as a covariate to account for differences in general cognitive ability that could influence MST performance.

The MoCA will be administered by trained personnel following standardized administration procedures.

Mnemonic Similarity Task

Each participant will complete the optimized MST for efficient administration (Stark et al., 2023). The MST consists of two phases. During the first phase, participants will view images of everyday objects and make a simple indoor/outdoor judgment. They will not be explicitly instructed to memorize the images.

During the second phase, participants will view a new set of images and classify each image as "new," "old," or "similar." The test includes exact repetitions, completely new images, and visually similar images.

Two primary outcomes will be obtained. The Lure Discrimination Index (LDI) measures the ability to distinguish similar images from previously viewed images and serves as a hippocampus-sensitive measure of pattern separation. The Recognition Index (REC) measures the ability to distinguish repeated images from new images and serves as a control measure of general recognition memory.

A trained study administrator will provide standardized instructions and a brief practice session before the scored MST. MST scoring will be automated or performed according to the standardized scoring procedure, with exposure-group information unavailable to the analyst.

Behavioral Testing Procedure

Each participant will be tested individually in a quiet room under standardized conditions. The session will begin with the survey and visual screening, followed by the MoCA. Participants will then complete a brief MST practice session before completing the scored MST. Testing order, instructions, environmental conditions, and testing equipment will be standardized across participants.

Data Quality and Exclusion

Participants with an REC score below 0.5 will be excluded from the primary analysis because this score may indicate inadequate understanding of the recognition component of the task. Additional exclusions will be applied only according to predefined criteria established before data analysis, such as incomplete testing or technical failure.

Behavioral Statistical Analysis

The primary behavioral outcome will be the difference in LDI between the high- and low-exposure groups. An independent-samples t-test will be used for the primary comparison if the assumptions of the test are met. If normality or variance assumptions are substantially violated, an appropriate nonparametric alternative will be used.

REC scores will be compared between the two groups using the same approach to determine whether group differences are specific to hippocampus-sensitive pattern separation rather than general recognition memory.

An analysis of covariance (ANCOVA) will additionally be used to compare LDI between exposure groups while adjusting for MoCA-without-memory and other prespecified covariates such as age, sex, education, and job tenure if necessary after matching.

The occupational exposure score will be analyzed as an ordinal exposure measure. Spearman rank correlation will be used to assess the association between exposure score and LDI because the exposure score consists of four ordered categories. A linear regression model may additionally be used to estimate the change in LDI associated with increasing exposure score while adjusting for relevant covariates.

Sex will not be analyzed as completely separate samples for the primary analysis because doing so would substantially reduce statistical power. Instead, sex will be included as a covariate, and an exposure-by-sex interaction will be examined as an exploratory analysis to determine whether the association differs by sex.

Statistical significance will be set at $p < 0.05$, with effect sizes and confidence intervals reported where appropriate.

Cell Culture Study

Human iPSC-Derived BBB Model

A human iPSC-derived BBB model will be used to simulate key components of the human neurovascular unit and investigate cellular responses to MNP exposure. The model will include iPSC-derived brain microvascular endothelial cells (BMECs), astrocytes, pericytes, and hippocampal neurons (Figure 2).

BMECs form the BBB and its tight junctions, which regulate molecular permeability. Astrocytes support BBB formation and maintenance. Pericytes contribute to vascular stability and endothelial cell support. Hippocampal neurons will provide a human-derived neuronal component through which potential effects on neuronal function can be evaluated (Naik & Cucullo, 2013).

The planned model does not include microglia or other immune cells. Therefore, although inflammatory responses can be measured in the model, it will not fully reproduce the immune-cell-mediated component of neuroinflammation in the human brain.

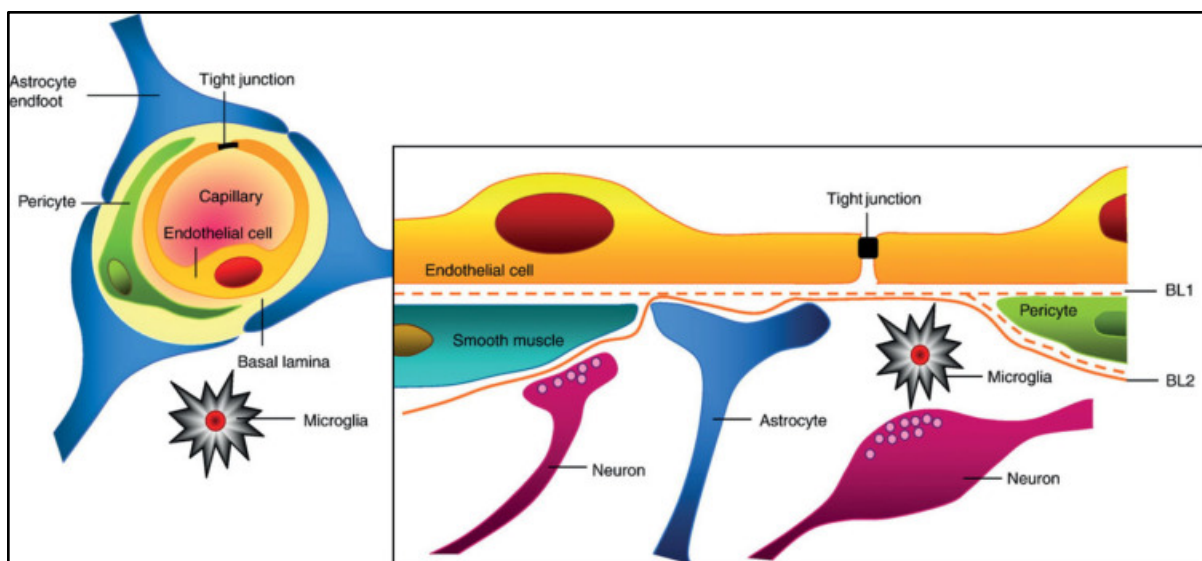


Figure 2. Human iPSC-Derived Blood–Brain Barrier (BBB) Model. Schematic representation of the planned model containing iPSC-derived brain microvascular endothelial cells, astrocytes, pericytes, and hippocampal neurons. Microglia are not included in the proposed model.

Cell Culture Conditions

The four cell types will be maintained using appropriate culture media and supplements under standardized cell culture conditions. Cultures will be maintained in a humidified CO₂ incubator under manufacturer- and protocol-recommended temperature, pH, and CO₂ conditions.

Cell density, number of cells seeded, culture medium and supplements, temperature, CO₂ concentration, humidity, pH, plate format, and handling procedures will be standardized across treatment groups.

Experimental Design and MNP Exposure

BBB cultures will be randomly assigned to a control group or one of three MNP exposure groups.

Table 1. Study Design for Control and Experimental Groups with MNP Exposure Conditions

Group	MNP Concentration
Negative control	0 mg/g
Low exposure	0.010 mg/g
Medium exposure	0.015 mg/g
High exposure	0.025 mg/g

Each treatment condition will contain at least three independent biological replicates.

The MNP treatment used in this proposal will consist of polystyrene particles with a nominal diameter of 1 µm. Because particles at this size are classified as microplastics rather than nanoplastics, this experimental arm specifically evaluates microplastic exposure; effects of particles in the nanoscale range will require a separate experiment.

The particles will be applied to the vascular side of the BBB model to simulate exposure from the bloodstream. The control group will undergo the same handling procedures without MNP addition.

Three exposure durations will be evaluated: 24, 48, and 72 hours. Separate culture wells will be allocated to each time point so that destructive assays do not affect measurements at later time points.

Outcome Measurements

Cell cultures will be evaluated at baseline and after 24, 48, and 72 hours of exposure.

Cell viability and metabolic activity will be assessed using an MTT assay. MTT reduction to formazan will be quantified by measuring absorbance at 570 nm using a microplate reader. Cellular morphology and growth will also be monitored using phase-contrast microscopy.

Reactive oxygen species (ROS) production will be assessed using a DCFH-DA fluorescence assay. Fluorescence intensity will be measured and reported as relative fluorescence units (RFU) after normalization to appropriate controls.

Cellular ATP production will be measured using an ATP assay to evaluate changes associated with mitochondrial function.

Changes in neuronal function and synaptic plasticity will be assessed through gene-expression analysis using reverse transcription quantitative polymerase chain reaction (RT-qPCR). Relative expression will be calculated in comparison with the control group.

Changes associated with neuroinflammation will be assessed through gene-expression analysis and, where feasible, protein-level analysis using appropriate immunoassays.

Neurodegeneration-related cellular changes will be assessed using immunocytochemistry and fluorescence microscopy.

Apoptotic cell changes will be evaluated using immunocytochemistry, with the proportion of apoptotic cells quantified through microscopy.

Cell Culture Statistical Analysis

Data from biological replicates will be summarized as mean $\pm$ standard deviation.

Because the cell culture experiment contains two independent experimental factors—MNP concentration (control, low, medium, and high) and exposure duration (24, 48, and 72 hours)—a two-way ANOVA will be used to evaluate the main effects of concentration, duration, and their interaction.

An appropriate post hoc multiple-comparison test will be performed when significant effects are detected.

The concentration $\times$ duration interaction will determine whether the effect of MNP concentration changes depending on exposure duration. This will allow the study to distinguish concentration-dependent effects from time-dependent effects.

The relationship between MNP concentration and each measured biological outcome will additionally be examined using scatterplots and dose-response curves. Because concentration is an experimentally controlled continuous variable, Pearson correlation or regression analysis will be used where assumptions are satisfied to assess linear associations between concentration and cellular outcomes.

Statistical significance will be set at $p < 0.05$.

Results and Discussion

Expected Outcome

Because this manuscript describes a proposed investigation, no empirical results have yet been collected. The following outcomes represent the study's prespecified hypotheses rather than observed findings.

Behavioral Test

The primary prediction is that the high-exposure group will demonstrate a lower LDI score than the low-exposure group, indicating poorer hippocampus-sensitive pattern separation among workers with greater occupational exposure. This prediction is informed by animal studies reporting impaired hippocampus-dependent learning and memory following MNP exposure (Lee et al., 2022; Jin et al., 2022), human studies detecting MNPs in brain tissue (Nihart et al., 2025), and research associating plastic exposure with poorer cognitive function (Zhu et al., 2024).

The two groups are expected to show relatively similar REC scores. If LDI differs between groups while REC does not, this pattern would be consistent with a more selective difference in hippocampus-sensitive memory rather than a broad impairment in recognition performance. However, such a pattern would not by itself establish that MNPs specifically caused hippocampal dysfunction.

The study also predicts a graded relationship between occupational exposure score and LDI. As exposure score increases from 0 to 3, LDI is expected to decrease. Because the exposure score is an occupational proxy rather than a direct measurement of individual MNP burden, any dose-response pattern would be interpreted as an association with occupational exposure intensity rather than a direct biological dose-response relationship.

The study will also explore whether the exposure-memory association differs by sex. Based on previous human and animal studies suggesting possible sex-related differences in the cognitive effects of plastic exposure (Lee et al., 2022; Zhu et al., 2024), an exposure-by-sex interaction may be observed; however, this will be considered exploratory rather than a primary hypothesis.

Because no prior research has measured MST performance in humans according to occupational MNP exposure, these predictions describe expected directions and trends rather than specific numerical values.

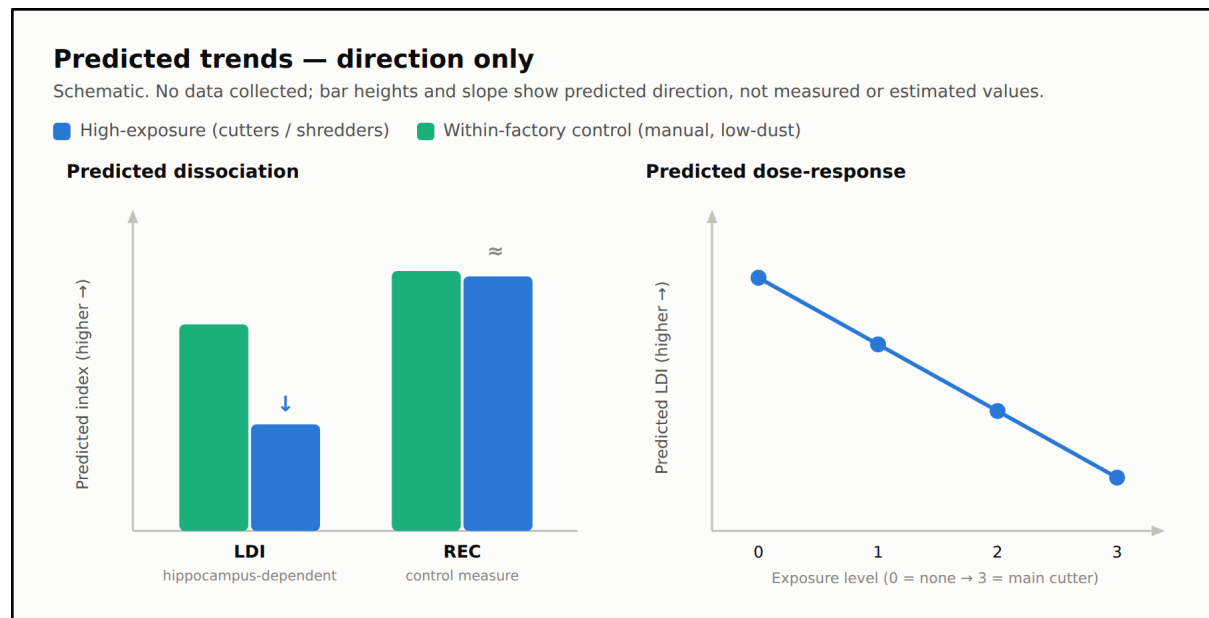


Figure 3. Predicted direction of the behavioral results. LDI is expected to be lower in the high-exposure group while REC remains approximately similar between groups (left), and LDI is expected to decrease as occupational exposure score increases from 0 to 3 (right). These are hypothetical predictions and do not represent observed data.

Cell Culture Study

We expect MNP exposure to produce concentration- and time-dependent effects in the human-derived BBB model. Compared with negative controls, cultures exposed to higher MNP concentrations or longer exposure durations are expected to show reduced cell viability, metabolic activity, and growth. These changes may be reflected by lower MTT absorbance and altered cellular morphology.

MNP-exposed cultures are also expected to demonstrate increased intracellular ROS levels, indicating greater oxidative stress, and reduced ATP production, indicating impaired mitochondrial function. RT-qPCR is expected to reveal changes in the expression of genes associated with synaptic function. Neuroinflammation-related and neurodegeneration-related cellular responses are also expected to change following MNP exposure, consistent with reported activation and stress responses in human astrocytes exposed to polystyrene MNPs (Kiran et al., 2025). Immunocytochemistry is expected to demonstrate a higher proportion of apoptotic cells in MNP-treated cultures than in controls.

If these outcomes are observed, they would provide evidence that MNP exposure can induce cellular responses associated with oxidative stress, mitochondrial dysfunction, neuroinflammation, altered synaptic function, and apoptosis in the human-derived model. However, these cellular findings would not independently demonstrate that MNP exposure causes hippocampal memory impairment or neurodegenerative disease in humans.

Discussion

Mice are valuable models for studying human disease because some aspects of brain structure, cellular organization, and disease-related pathways are evolutionarily conserved. Mice and humans share several neuronal and non-neuronal cell classes, including excitatory neurons, inhibitory neurons, astrocytes, microglia, oligodendrocytes, endothelial cells, and pericytes. The organization of some cortical cell types is conserved despite species-specific differences in gene expression (Hodge et al., 2019).

The hippocampus also has conserved anatomical organization between mice and humans, including the dentate gyrus, CA3, and CA1 regions. The BBB, which regulates molecular transport between the bloodstream and brain, also shares important structural features across species. However, these similarities do not eliminate important differences in gene expression, cellular physiology, and disease susceptibility. Many genes involved in neuronal signaling, neurotransmitter receptors, ion channels, and cell adhesion exhibit species-specific expression patterns that can influence neurological disease mechanisms (Perlman, 2016).

With observational studies still unable to determine whether MNP accumulation causes neurological disease, human-based research is needed (Nihart et al., 2025). The proposed study addresses this gap through two complementary approaches: behavioral assessment in occupationally exposed humans and mechanistic testing in a human iPSC-derived BBB model.

The two experiments test different aspects of the research question, and neither can answer the entire question independently. The behavioral arm tests whether occupational MNP exposure is associated with weaker hippocampus-sensitive memory in humans, but it cannot determine the biological mechanisms responsible for any observed association. The cell culture arm tests whether MNP exposure can produce cellular changes relevant to neuronal dysfunction in a human-derived model, but it cannot demonstrate an effect on memory in living humans.

Accordingly, the findings from the two arms should be interpreted as complementary rather than as evidence of a direct biological link between cellular changes and memory performance. If both arms produce results consistent with the hypotheses, the findings would strengthen the overall evidence that MNP exposure warrants further investigation as a potential neurological risk factor. However, concordant findings would not establish that the cellular changes observed *in vitro* are the mechanism responsible for any memory differences observed in the behavioral study because the two experiments involve different samples and experimental conditions.

The behavioral study has several important limitations. Cutting and shredding plastics do not only produce MNPs; these activities may also involve increased dust, heat, noise, and fumes that could affect cognitive performance independently. Therefore, a lower LDI among cutting and shredding workers could reflect a combination of occupational exposures rather than MNP exposure alone. Furthermore, because participants are classified according to job tasks rather than individual measurements of airborne MNP concentration or internal MNP burden, exposure misclassification is possible. Individual exposure may vary within each occupational group.

Because the behavioral study is cross-sectional, it can identify associations but cannot establish temporal sequence or causation. Longitudinal studies with direct measurements of personal MNP exposure would be needed to determine whether chronic MNP exposure predicts subsequent changes in hippocampus-dependent memory.

The cell culture model also has limitations. The BBB model is a simplified representation of the human neurovascular system and cannot reproduce the complete process of MNP ingestion, absorption, metabolism, circulation, excretion, and brain accumulation. Although the model includes multiple human-derived cell types, it cannot reproduce the full complexity of the living human brain or interactions among multiple brain regions.

The absence of microglia and other immune-cell populations is another limitation. Consequently, inflammatory responses observed in the model may not fully represent neuroinflammation in the human brain. In addition, the proposed exposure duration of 24–72 hours is substantially shorter than the years or decades of exposure experienced by humans. Therefore, acute or subacute cellular responses may not accurately predict long-term effects.

Another limitation is that the proposed cell culture experiment uses 1 μm polystyrene particles, which represent microplastics rather than nanoplastics. Therefore, the cellular findings should not automatically be generalized to all MNPs or to nanoscale particles. Future experiments should examine multiple polymer types, particle sizes, shapes, surface properties, and environmentally relevant concentrations.

Most importantly, although human-derived cell models provide greater human relevance than animal models, findings should be validated through additional experimental and clinical research before conclusions about human neurodegenerative disease can be made.

Future studies should develop methods to determine whether MNPs are present specifically in the human hippocampus. Current research has detected MNPs in human brain tissue, including the frontal cortex, but direct evidence concerning hippocampal accumulation remains limited. Direct measurement of hippocampal MNP burden, where ethically and technically feasible, would help clarify whether exposure is associated with particle accumulation in the brain region underlying the memory process examined in this study.

Future research should also use longitudinal human studies, direct personal exposure measurements, and more physiologically complex human neural models containing immune cells. Such approaches could help determine whether the cellular mechanisms identified *in vitro* are relevant to long-term neurological outcomes.

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