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### **Supplemental Material**

#### **Evaluation of Neurotoxicity in BALB/c Mice following Chronic Exposure to Polystyrene Microplastics**

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#### **Table of Contents**

**Table S1.** Primer sequences used for qRT-PCR.

**Table S2.** Detailed information of primary antibodies.

**Table S3.** The mean and SD summary data for quantification.

**Table S4.** *P*-values for non-statistically and statistically significant results.

**Table S5.** Thigmotaxis of mice in Morris water maze test. Thigmotaxis is defined as mice were swimming in the outer 10% close to walls, which means mice swim almost exclusively in the periphery. The rate of thigmotaxis was expressed as the ratio of the number of mice showing thigmotaxis to the total number of mice according to the swim path trajectories.

**Figure S1.** Biodistribution of various diameters of polystyrene MPs (PS-MPs) in different tissues of mice. Mice were provided drinking water containing three sizes of fluorescent PS-MPs for 180 consecutive days. Fluorescence pictures of excised brain tissues and gastric tissues were detected. The colors in pictures indicated that fluorescence PS-MPs in tissues.

**Figure S2.** BBB integrity was detected by biotin tracer experiments. The sections were stained with biotin (red) and DAPI (blue). The existence of biotin in brain tissues was examined by immunofluorescence microscopy. The biotin signal of the liver parenchyma was used as a positive control (scale bar = 20  $\mu$ m).

**Figure S3.** Ultrastructure of BBB in PS-MP-exposed and unexposed mice as detected by an electron microscope. Upper images displayed the ultrastructure of BBB. Lower images referred to magnified boxed areas.

**Figure S4.** The average swim speed of mice on days 1-5 in Morris water maze test is shown. Circle (Control), square (100 µg/L), triangle (1000 µg/L). (A) Control and 0.5 µm PS-MPs exposure groups. (B) Control and 4 µm PS-MPs exposure groups. (C) Control and 10 µm PS-MPs exposure groups. The results are expressed as means ± SD (n = 10 mice/per group). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. Data were detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.

**Figure S5.** The total path length to find the hidden platform of mice on days 1-5 in Morris water maze test are shown. Circle (Control), square (100 µg/L), triangle (1000 µg/L). (A) Control and 0.5 µm PS-MPs exposure groups. (B) Control and 4 µm PS-MPs exposure groups. (C) Control and 10 µm PS-MPs exposure groups. The results are expressed as means ± SD (n = 10 mice/per group). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \**P* < 0.05 vs. control, as detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.

**Figure S6.** The recognition scores (time spent (s) investigating one object/time spent (s) investigating both objects in total) of mice on day 1 (A) and day 2 (B) of novel object recognition (NOR) experiment were examined (n = 10 mice/per group). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4.

**Figure S7.** The total distance moved (A) and average movement speed (B) of mice in testing day (day 3) of the novel object recognition test are shown. The results are expressed as means ± SD (n = 10 mice/per group). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \**P* < 0.05 vs. control, as detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.

**Figure S8.** The numbers of neurons in the hippocampal cornu ammonis 1 (CA1), cornu ammonis 3 (CA3), and dentate gyrus (DG) sections were counted (n = 3 mice/group, n = 3 slides/mice). Data are shown as mean ± SD. The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \**P* < 0.05 compared with control, as detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.

**Figure S9.** The mRNA levels of *caspase 3* (A), the *Bax/Bcl-2* mRNA ratio (B) in the hippocampus were tested with quantitative real-time PCR (qRT-PCR) by normalizing to *Gapdh*. The results are expressed as means ± SD (n = 3, N = 3 mice/group). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \**P* < 0.05 and \*\**P* < 0.01 compared with the control, as detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.

**Figure S10.** The expression of synapsin 1, synaptophysin, and PSD 95 protein in the hippocampus was measured via western blotting. The western blotting results were quantified and statistically analyzed, as shown in (Figure 7C) as mean ± SD (n = 3, N = 3 mice/group). The mean and SD summary data for quantification of western blotting are shown in Table S3. *P*-Values for all comparisons are reported in Table S4.

**Figure S11.** The mRNA expression levels of *Gap43*(A), *Syt 4* (B), and *Ncam*(C) were detected by qRT-PCR in the hippocampus of mice exposed to PS-MPs and control mice. Data are shown as mean  $\pm$  SD (n = 3). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \*\**P* < 0.01 compared with control, as detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.

**Figure S12.** (A) A confocal fluorescence microscope was used to detect colocalization of Alexa Fluor 594-labeled MCP-1 (red)/TNF- $\alpha$  (red) and DAPI (blue) (scale bar = 20  $\mu$ m, n = 3) in the hippocampus of mice exposed to PS-MPs and control mice. (B) Percent of positivity was calculated based on the percentage of MCP-1 positive cells out of the total number of cells in an image. (C) Percent of positivity was calculated based on the percentage of TNF- $\alpha$  positive cells out of the total number of cells in an image. Data are shown as mean  $\pm$  SD (n = 3). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \**P* < 0.05, \*\**P* < 0.01 compared with control, as detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.

**Table S1.** Primer sequences used for qRT-PCR.

Accession number	Gene	Primer	Sequence 5' → 3'	Product size (base pairs)
NM_001289726.1	<i>Gapdh</i>	Forward	AGGTCGGTGTGAACGGATTTG	178
		Reverse	TGTAGACCATGTAGTTGAGTCA	
NM_001048139.1	<i>Bdnf</i>	Forward	TCATACTTCGGTTGCATGAAGG	137
		Reverse	AGACCTCTCGAACCTGCCC	
NM_001252341.1	<i>Syt 1</i>	Forward	CTGTCACCACTGTTGCGAC	130
		Reverse	GGCAATGGGATTTTATGCAGTTC	
NM_009308.3	<i>Syt 4</i>	Forward	TGCTTTTGGCCTCGTCTTCA	192
		Reverse	GCGGTTTTACCCTTCACTTCAC	
NM_001081445.1	<i>Ncam</i>	Forward	GACAGAACCCGAAAAGGGC	94
		Reverse	GTTGGGGACCGTCTTGACTT	
NM_008083.2	<i>Gap43</i>	Forward	TGGTGTCAAGCCGGAAGATAA	114
		Reverse	GCTGGTGCATCACCTTCT	
NM_001278601.1	<i>Tnf-α</i>	Forward	TCCCAGGTTCTCTTCAAGGGA	51
		Reverse	GGTGAGGAGCACGTAGTCGG	
NM_011333.3	<i>Mcp-1</i>	Forward	TTAAAAACCTGGATCGGAACCAA	121
		Reverse	GCATTAGCTTCAGATTTACGGGT	
NM_021274.2	<i>Cxcl10</i>	Forward	CCAAGTGCTGCCGTCATTTTC	157
		Reverse	GGCTCGCAGGGATGATTTCAA	
NM_031168.2	<i>Il-6</i>	Forward	TAGTCCTTCCTACCCCAATTTCC	76
		Reverse	TTGGTCCTTAGCCACTCCTTC	
NM_008361.4	<i>Il-1β</i>	Forward	GCAACTGTTCTGAACTCAACT	89
		Reverse	ATCTTTTGGGGTCCGTCAACT	
NM_009810.3	<i>Caspase 3</i>	Forward	ATGGAGAACAACAAAACCTCAGT	74
		Reverse	TTGCTCCCATGTATGGTCTTTAC	
NM_007527.3	<i>Bax</i>	Forward	TGAAGACAGGGGCCTTTTTG	140
		Reverse	AATTCGCCGGAGACTCG	
NM_009741.5	<i>Bcl-2</i>	Forward	ATGCCTTTGTGGA ACTATATGGC	120
		Reverse	GGTATGCACCCAGAGTGATGC	

**Table S2.** Detailed information of primary antibodies.

antibody	species	company	catalog	dilution
Anti-GAPDH	mouse mAb	Proteintech	60004-1-Ig	1:1000 (WB)
Anti-PSD95	rabbit polyclonal Ab	Proteintech	20665-1-AP	1:1000 (WB)
Anti-synaptophysin	rabbit polyclonal Ab	Proteintech	17785-1-AP	1:1000 (WB)
Anti-synapsin 1	rabbit polyclonal Ab	Proteintech	20258-1-AP	1:1000 (WB)

**Table S3.** The mean and SD summary data for quantification.

<b>Figure 1C: zeta potential</b>	mean	SD		
(mV)				
0.5 $\mu\text{m}$	-31.10	0.64		
4 $\mu\text{m}$	-37.53	0.75		
10 $\mu\text{m}$	-29.97	0.50		
<b>Figure 4B: Time for mice (exposed or not to PS-MPs) to find the platform during learning trials (seconds)</b>				
	mean	SD	mean	SD
	Day 1		Day2	
Control	78.53	19.19	52.01	30.15
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	71.82	28.44	52.08	30.15
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	65.94	32.08	63.7	25.88
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	71.16	20.79	63.585	25.60
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	82.21	13.72	69.28	21.20
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	75.25	27.71	64.13	28.17
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	67.46	25.12	66.57	31.26
	Day 3		Day 4	
Control	55.31	31.10	39.63	29.75
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	50.02	31.28	50.37	24.42
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	54.72	30.66	51.54	27.95
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	61.33	24.31	48.52	28.35

4 µm 1000 µg/L	65.79	29.00	60.03	28.57
10 µm 100 µg/L	47.87	28.94	48.52	31.71
10 µm 1000 µg/L	70.06	26.77	67.43	29.61
	Day 5			
Control	25.40	13.85		
0.5 µm 100 µg/L	33.04	24.52		
0.5 µm 1000 µg/L	40.34	30.64		
4 µm 100 µg/L	37.59	24.74		
4 µm 1000 µg/L	46.81	21.80		
10 µm 100 µg/L	38.39	32.72		
10 µm 1000 µg/L	54.72	26.76		
<b>Figure 4D: Number of times mice (exposed or not to PS-MPs) crossed the target platform on sixth day</b>				
	mean	SD		
Control	3.75	1.85		
0.5 µm 100 µg/L	1.25	0.97		
0.5 µm 1000 µg/L	0.875	1.05		
4 µm 100 µg/L	1.00	1.00		
4 µm 1000 µg/L	0.625	0.70		
10 µm 100 µg/L	1.25	0.83		
10 µm 1000 µg/L	0.75	0.83		

**Figure 4E: Percentage of time mice (exposed or not to PS-MPs) took in the quadrant of the target platform (sixth day)**

	mean	SD		
Control	44.37	12.80		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	25.72	17.17		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	24.03	19.16		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	32.40	15.68		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	16.87	15.47		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	22.44	12.93		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	20.06	9.77		

**Figure 5C: Novelty scores (time spent (s) investigating novel object/time spent (s) investigating both objects in total for mice exposed or not to PS-MPs)**

	mean	SD		
Control	0.46	0.07		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	0.26	0.13		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	0.24	0.13		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	0.27	0.13		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	0.26	0.07		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	0.26	0.13		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	0.22	0.09		

<b>Figure 7B: Number of dendritic spines in hippocampus of mice exposed or not to PS-MPs</b>				
	mean	SD		
Control	12.25	0.83		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	6.50	0.50		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	4.50	0.50		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	5.25	1.09		
<b>Figure 7C: Protein expression of synapsin 1 in the hippocampus of mice exposed or not to PS-MPs</b>				
<b>Synapsin/GAPDH ratio</b>	mean	SD		
Control	1.0222	0.0299		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	0.7478	0.0935		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	0.4472	0.0523		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	0.7969	0.0932		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	0.5002	0.0585		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	0.8760	0.1095		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	0.6659	0.0778		
<b>Figure 7C: Protein expression of synaptophysin in the hippocampus of mice exposed or not to PS-MPs</b>				
<b>Synaptophysin/GAPDH ratio</b>	mean	SD		
Control	1.0039	0.0236		



0.5 µm 100 µg/L	0.7508	0.0576		
0.5 µm 1000 µg/L	0.3228	0.1531		
4 µm 100 µg/L	0.5738	0.0705		
4 µm 1000 µg/L	0.3609	0.0616		
10 µm 100 µg/L	0.5631	0.0672		
10 µm 1000 µg/L	0.2965	0.1265		

**Figure 7C: Protein expression of PSD95 in the hippocampus of mice exposed or not to PS-MPs**

<b>PSD95/GAPDH ratio</b>	mean	SD		
Control	1.0097	0.0159		
0.5 µm 100 µg/L	0.7614	0.0743		
0.5 µm 1000 µg/L	0.4557	0.0828		
4 µm 100 µg/L	0.7880	0.0754		
4 µm 1000 µg/L	0.4572	0.0446		
10 µm 100 µg/L	0.8130	0.1168		
10 µm 1000 µg/L	0.8368	0.0817		

**Figure 7D: mRNA expression of *Bdnf* in the hippocampus of mice exposed or not to PS-MPs**

<b><i>Bdnf</i>/Gapdh ratio</b>	mean	SD		
Control	1.0015	0.0397		
0.5 µm 100 µg/L	0.6347	0.0382		
0.5 µm 1000 µg/L	0.7628	0.0121		

4 µm 100 µg/L	0.7141	0.0634		
4 µm 1000 µg/L	0.7258	0.0457		
10 µm 100 µg/L	0.6733	0.0411		
10 µm 1000 µg/L	0.6889	0.0312		

**Figure 7E: mRNA expression of *syt1* in the hippocampus of mice exposed or not to PS-MPs**

<i>syt1/Gapdh</i> ratio	mean	SD		
Control	1.0009	0.0275		
0.5 µm 100 µg/L	0.7317	0.0592		
0.5 µm 1000 µg/L	0.8920	0.0336		
4 µm 100 µg/L	0.9568	0.0192		
4 µm 1000 µg/L	0.8523	0.0023		
10 µm 100 µg/L	0.8485	0.0230		
10 µm 1000 µg/L	0.8965	0.0141		

**Figure 8: Expression various inflammation-related mRNAs in the hippocampus of mice exposed or not to PS-MPs**

<i>Tnf-α/Gapdh</i> ratio	mean	SD		
Control	1.0004	0.0344		
0.5 µm 100 µg/L	2.2895	0.3995		
0.5 µm 1000 µg/L	4.5516	0.5359		
4 µm 100 µg/L	5.4554	0.7650		
4 µm 1000 µg/L	14.0082	1.4922		

10 µm 100 µg/L	3.3178	0.5503		
10 µm 1000 µg/L	4.5896	0.0068		
<b><i>Mcp-1/Gapdh ratio</i></b>	mean	SD		
Control	1.0162	0.1777		
0.5 µm 100 µg/L	2.1331	0.3062		
0.5 µm 1000 µg/L	7.2351	2.2340		
4 µm 100 µg/L	4.5054	0.8103		
4 µm 1000 µg/L	10.8836	2.9398		
10 µm 100 µg/L	7.2899	1.8559		
10 µm 1000 µg/L	12.4737	1.7237		
<b><i>Il-6/Gapdh ratio</i></b>	mean	SD		
Control	1.0261	0.2181		
0.5 µm 100 µg/L	1.1366	0.0387		
0.5 µm 1000 µg/L	1.2323	0.0274		
4 µm 100 µg/L	1.3007	0.0333		
4 µm 1000 µg/L	1.1565	0.0153		
10 µm 100 µg/L	1.0271	0.0076		
10 µm 1000 µg/L	1.0865	0.0667		
<b><i>Il-1β/Gapdh ratio</i></b>	mean	SD		

Control	1.0066	0.1162		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.6457	0.0567		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	1.8675	0.3591		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.9543	0.3027		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	3.1457	0.6149		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	2.8568	0.6061		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	3.8213	0.5092		
<b><i>Cxcl10/Gapdh</i> ratio</b>	mean	SD		
Control	1.0086	0.1404		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	3.9309	0.5711		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	3.1314	0.7554		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	5.3048	0.1642		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	4.4966	0.8317		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	4.1451	0.5905		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	6.1071	1.5465		
<b>Figure S4: Average swim speed (mm/s) on days 1-5 in the Morris water maze test for mice exposed or not to PS-MPs</b>				
	mean	SD	mean	SD
	Day 1		Day 2	
Control	7.23	3.47	9.07	3.06
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	10.63	3.39	10.63	3.37

0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	10.51	2.13	9.93	2.43
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	9.70	1.63	11.41	3.14
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	9.72	2.89	11.57	2.61
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	10.69	2.78	10.20	3.69
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	7.00	3.39	8.01	3.08
	Day 3		Day 4	
Control	9.60	2.40	8.94	4.48
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	6.15	4.31	8.90	3.38
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	8.13	4.14	6.99	4.12
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	10.37	2.76	8.19	2.65
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	10.64	3.59	6.70	3.85
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	12.04	3.15	8.47	1.91
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	7.19	3.74	5.65	3.53
	Day 5			
Control	6.99	3.41		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	8.95	4.36		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	7.53	2.92		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	8.46	3.27		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	8.70	3.32		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	10.11	2.88		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	5.79	3.98		

**Figure S5: Total path length to find the hidden platform (mm) of mice exposed or not to PS-MPs on days 1-5 in Morris water maze test**

	mean	SD	mean	SD
	Day 1		Day 2	
Control	605.28	302.50	484.55	328.86
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	751.98	403.53	462.85	177.71
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	661.03	326.06	607.90	270.06
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	699.20	218.69	668.47	382.04
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	807.78	297.77	817.31	330.70
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	770.91	268.20	601.62	293.47
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	561.54	291.52	551.15	306.82
	Day 3		Day 4	
Control	546.82	376.23	347.48	290.25
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	259.47	339.36	487.42	313.87
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	440.49	419.87	395.86	296.70
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	608.05	258.77	382.22	245.75
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	643.65	318.67	407.91	311.49
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	747.16	339.14	394.88	220.00
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	440.00	313.13	348.95	308.49
	Day 5			
Control	184.70	129.15		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	318.53	313.21		

0.5 µm 1000 µg/L	251.68	234.49		
4 µm 100 µg/L	324.23	248.26		
4 µm 1000 µg/L	377.74	187.09		
10 µm 100 µg/L	442.81	414.12		
10 µm 1000 µg/L	230.22	115.40		

**Figure S6A: The recognition scores (time spent (s) investigating one object/time spent (s) investigating both objects in total) of mice exposed or not to PS-MPs on day 1**

	mean	SD		
Control	0.50	0.01		
0.5 µm 100 µg/L	0.50	0.01		
0.5 µm 1000 µg/L	0.50	0.01		
4 µm 100 µg/L	0.50	0.01		
4 µm 1000 µg/L	0.49	0.01		
10 µm 100 µg/L	0.49	0.01		
10 µm 1000 µg/L	0.50	0.01		

**Figure S6B: The recognition scores (time spent (s) investigating one object/time spent (s) investigating both objects in total) of mice exposed or not to PS-MPs on day 2**

	mean	SD		
Control	0.50	0.01		
0.5 µm 100 µg/L	0.50	0.01		
0.5 µm 1000 µg/L	0.51	0.01		
4 µm 100 µg/L	0.50	0.01		

4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	0.50	0.01		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	0.50	0.01		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	0.49	0.01		
<b>Figure S7A: The total distance moved (m) for mice (exposed or not to PS-MPs) in the novel object recognition testing day (day 3)</b>				
	mean	SD		
Control	4.10	0.80		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	4.04	1.05		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	3.63	0.97		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	3.95	1.32		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	3.37	1.29		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	3.63	1.21		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	2.73	1.11		
<b>Figure S7B: The average movement speed (mm/s) for mice (exposed or not to PS-MPs) in the novel object recognition testing day (day 3)</b>				
	mean	SD		
Control	34.19	6.63		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	33.66	8.75		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	30.23	8.06		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	32.90	11.03		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	28.06	10.79		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	30.23	10.08		



10 µm 1000 µg/L	22.73	9.29		
<b>Figure S8A: Number of neurons in the hippocampal CA1 for mice exposed or not to PS-MPs</b>				
	mean	SD		
Control	1.01	0.02		
0.5 µm 100 µg/L	1.00	0.03		
0.5 µm 1000 µg/L	0.98	0.04		
4 µm 100 µg/L	0.97	0.04		
4 µm 1000 µg/L	0.97	0.04		
10 µm 100 µg/L	0.99	0.03		
10 µm 1000 µg/L	0.99	0.05		
<b>Figure S8B: Number of neurons in the hippocampal CA3 for mice exposed or not to PS-MPs</b>				
	mean	SD		
Control	1.02	0.03		
0.5 µm 100 µg/L	0.98	0.03		
0.5 µm 1000 µg/L	0.98	0.03		
4 µm 100 µg/L	0.95	0.06		
4 µm 1000 µg/L	0.98	0.06		
10 µm 100 µg/L	0.98	0.05		
10 µm 1000 µg/L	0.96	0.06		

**Figure S8C: Number of neurons in the dentate gyrus for mice exposed or not to PS-MPs**

	mean	SD		
Control	1.01	0.02		
0.5 µm 100 µg/L	0.96	0.04		
0.5 µm 1000 µg/L	0.97	0.03		
4 µm 100 µg/L	0.93	0.05		
4 µm 1000 µg/L	0.94	0.06		
10 µm 100 µg/L	0.97	0.04		
10 µm 1000 µg/L	0.99	0.05		

**Figure S9A: mRNA level of *caspase-3* in the hippocampus of mice exposed or not to PS-MPs**

<b><i>Caspase-3/Gapdh</i> ratio</b>	mean	SD		
Control	0.9999	0.0171		
0.5 µm 100 µg/L	1.1327	0.0559		
0.5 µm 1000 µg/L	1.2987	0.1153		
4 µm 100 µg/L	1.1491	0.0267		
4 µm 1000 µg/L	1.3089	0.0838		
10 µm 100 µg/L	1.1281	0.0304		
10 µm 1000 µg/L	1.1773	0.0354		

**Figure S9B: *Bax/Bcl-2* mRNA ratio in the hippocampus of mice exposed or not to PS-MPs**

<b><i>Bax/Bcl-2</i> ratio</b>	mean	SD		
Control	1.0003	0.0372		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.8476	0.1304		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	1.6885	0.1353		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.8125	0.2710		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	1.6351	0.0880		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.6239	0.0967		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	1.6136	0.0880		

**Figure S11A: Expression of *Gap43* mRNA in hippocampus of mice exposed or not to PS-MPs**

<b><i>Gap43/Gapdh</i> ratio</b>	mean	SD		
Control	1.0013	0.0408		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.2930	0.2807		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	1.1059	0.0664		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.3914	0.2779		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	1.2130	0.2703		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.3225	0.3283		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	1.3995	0.2376		

**Figure S11B: Expression of *syt4* mRNA in hippocampus of mice exposed or not to PS-MPs**

<b><i>syt4/Gapdh</i> ratio</b>	mean	SD		
Control	1.0013	0.0361		

0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.3104	0.1811		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	1.1961	0.1022		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.1193	0.0650		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	1.1186	0.0825		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.0513	0.0765		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	1.0575	0.0550		

**Figure S11C: Expression of *Ncam* mRNA in hippocampus of mice exposed or not to PS-MPs**

<i>Ncam/Gapdh</i> ratio	mean	SD		
Control	1.0007	0.0156		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.2054	0.1273		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	1.0183	0.0461		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	1.1795	0.1093		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	0.8776	0.1129		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	0.9086	0.0136		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	0.9664	0.0340		

**Figure S12B: Percent of total cells in view that were *Mcp-1* positive in the hippocampus of mice exposed or not to PS-MPs**

	mean	SD		
Control	5.50	1.08		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	14.67	2.75		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	15.30	2.79		

4 $\mu\text{m}$ 100 $\mu\text{g/L}$	15.33	1.45		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	13.43	2.66		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	14.57	2.65		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	18.43	1.72		
<b>Figure S12C: Percent of total cells in view that were TNF-<math>\alpha</math> positive in the hippocampus of mice exposed or not to PS-MPs</b>				
<b>Figure S12C</b>	mean	SD		
Control	4.90	1.14		
0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$	14.83	2.13		
0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$	15.70	1.80		
4 $\mu\text{m}$ 100 $\mu\text{g/L}$	21.20	3.24		
4 $\mu\text{m}$ 1000 $\mu\text{g/L}$	20.03	2.42		
10 $\mu\text{m}$ 100 $\mu\text{g/L}$	20.87	2.27		
10 $\mu\text{m}$ 1000 $\mu\text{g/L}$	15.40	1.61		

**Table S4.** *P*-values for non-statistically and statistically significant results.

<b>Figure 4B: Time for mice (exposed or not to PS-MPs) to find the platform during learning trials (seconds)</b>				
	P value	Summary	P value	Summary
	Day1		Day 2	
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.6127	ns	0.9986	ns
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.3880	ns	0.4518	ns

Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.5606	ns	0.4541	ns
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.6864	ns	0.2371	ns
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.8004	ns	0.4523	ns
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.3697	ns	0.3920	ns
	Day 3		Day 4	
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.7560	ns	0.4728	ns
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.9719	ns	0.4530	ns
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.6928	ns	0.5764	ns
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.5247	ns	0.2119	ns
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.6502	ns	0.5973	ns
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.3577	ns	0.1016	ns
	Day 5			
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.4846	ns		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.2593	ns		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.2743	ns		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0457	*		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.3500	ns		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0254	*		
<b>Figure 4D: Number of times mice (exposed or not to PS-MPs) crossed the target platform on sixth day</b>				
	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0069	**		

Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0031	**		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0039	**		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0009	**		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0057	**		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0016	**		

**Figure 4E: Percentage of time mice (exposed or not to PS-MPs) took in the quadrant of the target platform (sixth day)**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0071	**		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0035	**		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0352	*		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0028	**		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0066	**		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0013	**		

**Figure 5C: Novelty scores (time spent (s) investigating novel object/time spent (s) investigating both objects in total for mice exposed or not to PS-MPs)**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0026	**		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0011	**		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0046	**		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0000	**		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0021	**		

Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0001	**		
<b>Figure 7B: Number of dendritic spines in hippocampus of mice exposed or not to PS-MPs</b>				
	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0001	**		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0000	**		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0001	**		
<b>Figure 7C: Protein expression of synapsin 1 in the hippocampus of mice exposed or not to PS-MPs</b>				
	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0168	*		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0002	**		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0312	*		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0004	**		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.1427	ns		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0038	**		
<b>Figure 7C: Protein expression of synaptophysin in the hippocampus of mice exposed or not to PS-MPs</b>				
	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0045	**		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0034	**		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0012	**		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0002	**		



Control vs 10 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0009	**		
Control vs 10 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0015	**		
<b>Figure 7C: Protein expression of PSD95 in the hippocampus of mice exposed or not to PS-MPs</b>				
	P value	Summary		
Control vs 0.5 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0099	**		
Control vs 0.5 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0007	**		
Control vs 4 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0152	*		
Control vs 4 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0001	**		
Control vs 10 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0777	ns		
Control vs 10 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0425	*		
<b>Figure 7D: mRNA expression of <i>Bdnf</i> in the hippocampus of mice exposed or not to PS-MPs</b>				
	P value	Summary		
Control vs 0.5 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0007	**		
Control vs 0.5 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0012	**		
Control vs 4 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0056	**		
Control vs 4 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0030	**		
Control vs 10 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0013	**		
Control vs 10 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0009	**		
<b>Figure 7E: mRNA expression of <i>syt1</i> in the hippocampus of mice exposed or not to PS-MPs</b>				

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0043	**		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0238	*		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.1363	ns		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0016	**		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0038	**		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0087	**		

**Figure 8: Expression various inflammation-related mRNAs in the hippocampus of mice exposed or not to PS-MPs**

<i>Tnf-<math>\alpha</math></i>	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0104	*		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0007	**		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0012	**		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0002	**		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0040	**		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0000	**		

<i>Mcp-1</i>	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0111	*		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0172	*		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0040	**		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0091	**		

Control vs 10 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0089	**		
Control vs 10 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0007	**		
<b><i>Il-6</i></b>	P value	Summary		
Control vs 0.5 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0179	*		
Control vs 0.5 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0015	**		
Control vs 4 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0012	**		
Control vs 4 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0008	**		
Control vs 10 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0173	*		
Control vs 10 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.1801	ns		
<b><i>Il-1<math>\beta</math></i></b>	P value	Summary		
Control vs 0.5 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0022	**		
Control vs 0.5 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0321	*		
Control vs 4 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0144	*		
Control vs 4 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0084	**		
Control vs 10 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0133	*		
Control vs 10 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0016	**		
<b><i>Cxcl10</i></b>	P value	Summary		
Control vs 0.5 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0022	**		
Control vs 0.5 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0174	*		

Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0000	**		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0043	**		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0019	**		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0097	**		
<b>Figure S4: Average swim speed (mm/s) on days 1-5 in the Morris water maze test for mice exposed or not to PS-MPs</b>				
	P value	Summary	P value	Summary
	Day 1		Day 2	
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0853	ns	0.3790	ns
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0512	ns	0.5696	ns
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.1107	ns	0.1967	ns
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.1674	ns	0.1223	ns
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0584	ns	0.5439	ns
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.9004	ns	0.5270	ns
	Day 3		Day 4	
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0858	ns	0.9848	ns
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.4306	ns	0.4103	ns
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.5860	ns	0.7105	ns
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.5346	ns	0.3320	ns
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.1255	ns	0.8036	ns
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.1734	ns	0.1491	ns
	Day 5			

Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.3632	ns		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.7552	ns		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.4222	ns		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.3570	ns		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0851	ns		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.5563	ns		
<b>Figure S5: Total path length to find the hidden platform (mm) of mice exposed or not to PS-MPs on days 1-5 in Morris water maze test</b>				
	P value	Summary	P value	Summary
<b>Figure S5</b>	Day 1		Day 2	
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.4543	ns	0.8801	ns
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.7451	ns	0.4559	ns
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.5164	ns	0.3508	ns
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.2275	ns	0.0780	ns
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.2967	ns	0.4938	ns
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.7869	ns	0.7011	ns
	Day 3		Day 4	
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.1557	ns	0.4011	ns
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.6255	ns	0.7623	ns
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.7281	ns	0.8126	ns
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.6115	ns	0.7129	ns
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.3131	ns	0.7357	ns

Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.5729	ns	0.9928	ns
	Day 5			
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.3137	ns		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.5187	ns		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.2083	ns		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0413	*		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.1378	ns		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.4982	ns		

**Figure S6A: The recognition scores (time spent (s) investigating one object/time spent (s) investigating both objects in total) of mice exposed or not to PS-MPs on day 1**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.3473	ns		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.9779	ns		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.5071	ns		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.2017	ns		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.1485	ns		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.4350	ns		

**Figure S6B: The recognition scores (time spent (s) investigating one object/time spent (s) investigating both objects in total) of mice exposed or not to PS-MPs on day 2**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.5867	ns		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.4449	ns		

Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.5676	ns		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.9157	ns		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.9893	ns		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.3454	ns		

**Figure S7A: The total distance moved (m) for mice (exposed or not to PS-MPs) in the novel object recognition testing day (day 3)**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.6502	ns		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.8094	ns		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.8052	ns		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.2210	ns		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.4001	ns		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0188	*		

**Figure S7B: The average movement speed (mm/s) for mice (exposed or not to PS-MPs) in the novel object recognition testing day (day 3)**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.6505	ns		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.8090	ns		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.9811	ns		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.8047	ns		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.8165	ns		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0188	*		

**Figure S8A: Number of neurons in the hippocampal CA1 for mice exposed or not to PS-MPs**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.5243	ns		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.1837	ns		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0810	ns		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.1404	ns		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.3345	ns		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.5133	ns		

**Figure S8B: Number of neurons in the hippocampal CA3 for mice exposed or not to PS-MPs**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.1137	ns		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.1109	ns		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0887	ns		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.3072	ns		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.1756	ns		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.1308	ns		

**Figure S8C: Number of neurons in the dentate gyrus for mice exposed or not to PS-MPs**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0527	ns		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0461	*		



Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0313	*		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0819	ns		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.1050	ns		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.5691	ns		

**Figure S9A: mRNA level of *caspase-3* in the hippocampus of mice exposed or not to PS-MPs**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0326	*		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0223	*		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0027	**		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0069	**		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0065	**		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0031	**		

**Figure S9B: *Bax/Bcl-2* mRNA ratio in the hippocampus of mice exposed or not to PS-MPs**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0009	**		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0023	**		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0137	*		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0007	**		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0010	**		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0008	**		

**Figure S11A: Expression of *Gap43* mRNA in hippocampus of mice exposed or not to PS-MPs**

	P value	Summary		
Control vs 0.5 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.2195	ns		
Control vs 0.5 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.1306	ns		
Control vs 4 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.1210	ns		
Control vs 4 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.3349	ns		
Control vs 10 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.2416	ns		
Control vs 10 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0798	ns		

**Figure S11B: Expression of *syt4* mRNA in hippocampus of mice exposed or not to PS-MPs**

	P value	Summary		
Control vs 0.5 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0770	ns		
Control vs 0.5 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.0638	ns		
Control vs 4 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0882	ns		
Control vs 4 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.1392	ns		
Control vs 10 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.4501	ns		
Control vs 10 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.2932	ns		

**Figure S11C: Expression of *Ncam* mRNA in hippocampus of mice exposed or not to PS-MPs**

	P value	Summary		
Control vs 0.5 $\mu$ m 100 $\mu$ g/L PS-MPs group	0.0869	ns		
Control vs 0.5 $\mu$ m 1000 $\mu$ g/L PS-MPs group	0.6351	ns		

Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0839	ns		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.2013	ns		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0033	**		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.2646	ns		

**Figure S12B: Percent of total cells in view that were *Mcp-1* positive in the hippocampus of mice exposed or not to PS-MPs**

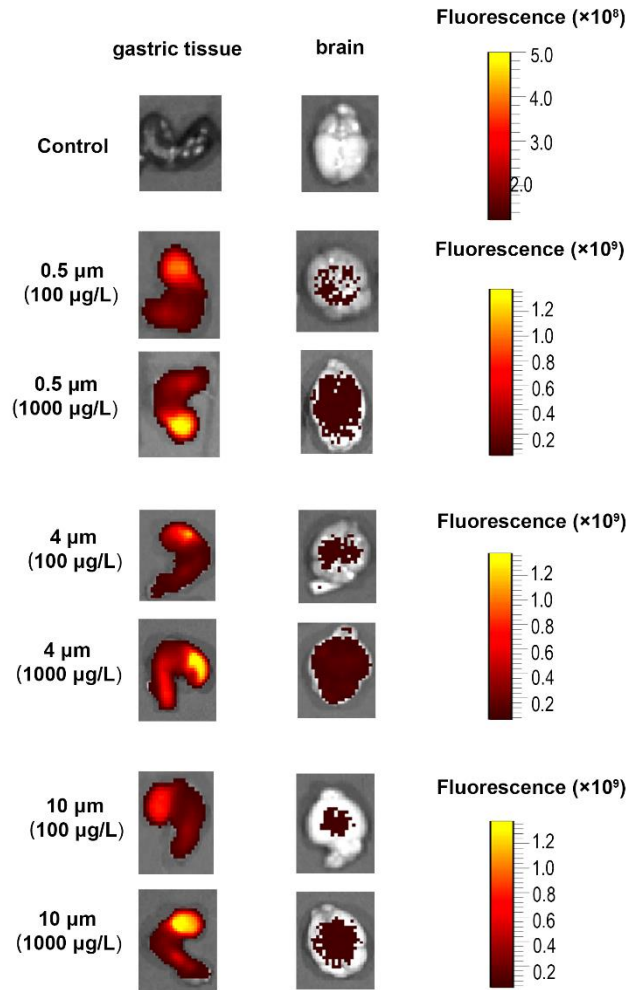
	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0118	*		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0098	**		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0015	**		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0174	*		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0110	*		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0008	**		

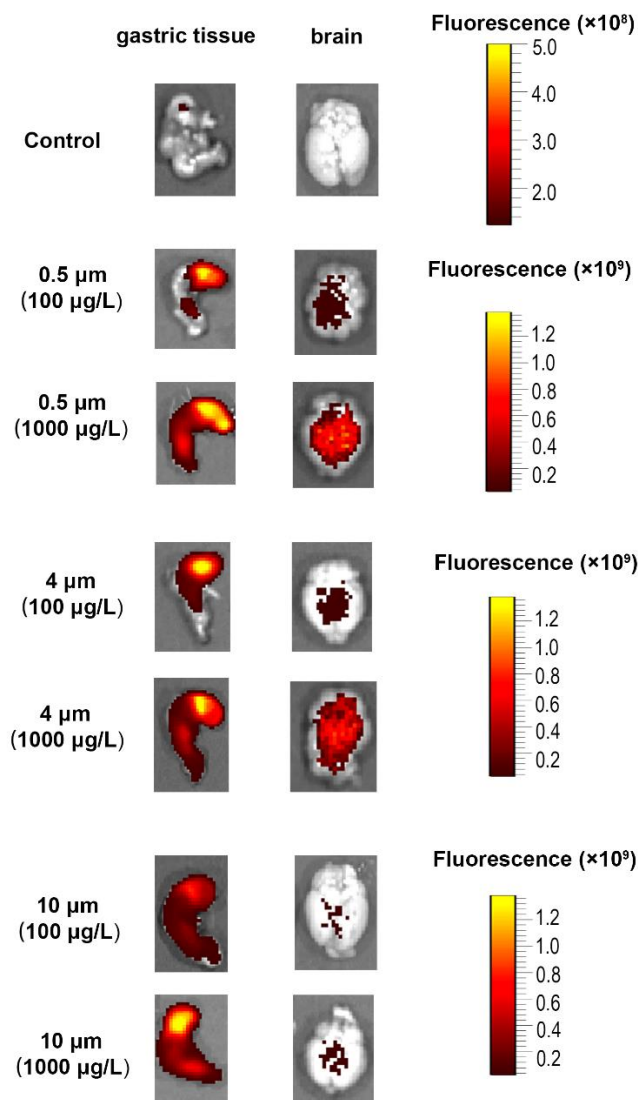
**Figure S12C: Percent of total cells in view that were *TNF- $\alpha$*  positive in the hippocampus of mice exposed or not to PS-MPs**

	P value	Summary		
Control vs 0.5 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0044	**		
Control vs 0.5 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0020	**		
Control vs 4 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0026	**		
Control vs 4 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0013	**		
Control vs 10 $\mu\text{m}$ 100 $\mu\text{g/L}$ PS-MPs group	0.0009	**		
Control vs 10 $\mu\text{m}$ 1000 $\mu\text{g/L}$ PS-MPs group	0.0017	**		

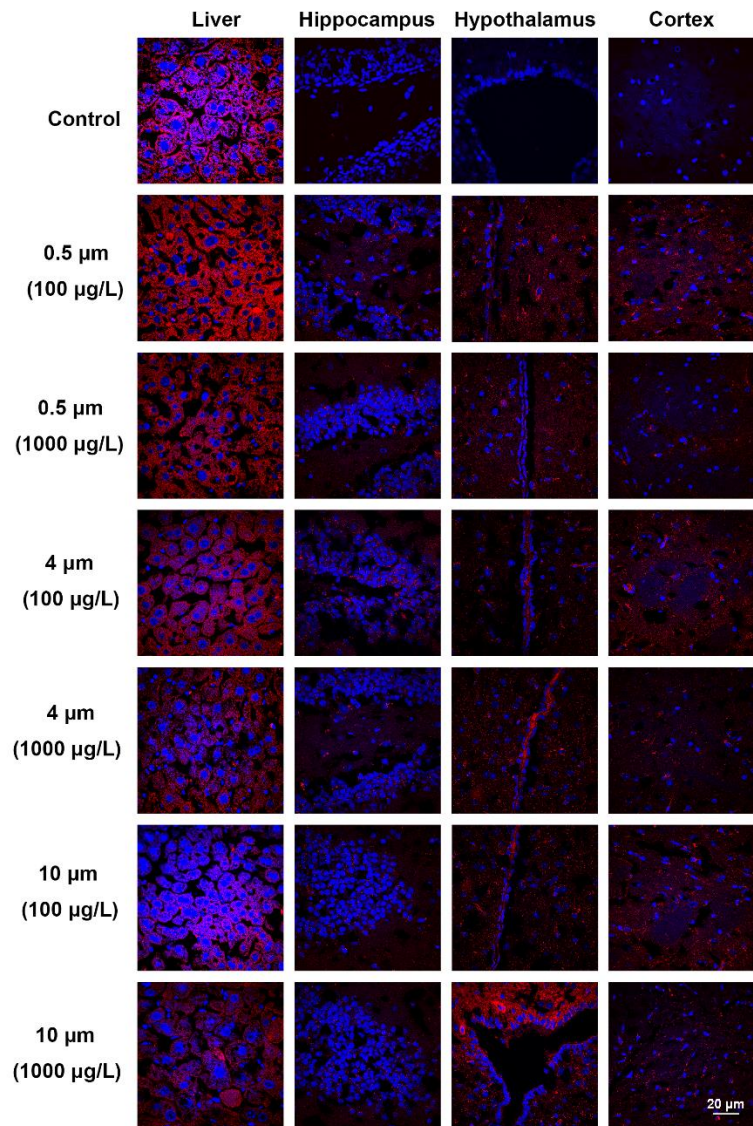
**Table S5.** Thigmotaxis of mice in Morris water maze test. Thigmotaxis is defined as mice were swimming in the outer 10% close to walls, which means mice swim almost exclusively in the periphery. The rate of thigmotaxis was expressed as the ratio of the number of mice showing thigmotaxis to the total number of mice according to the swim path trajectories.

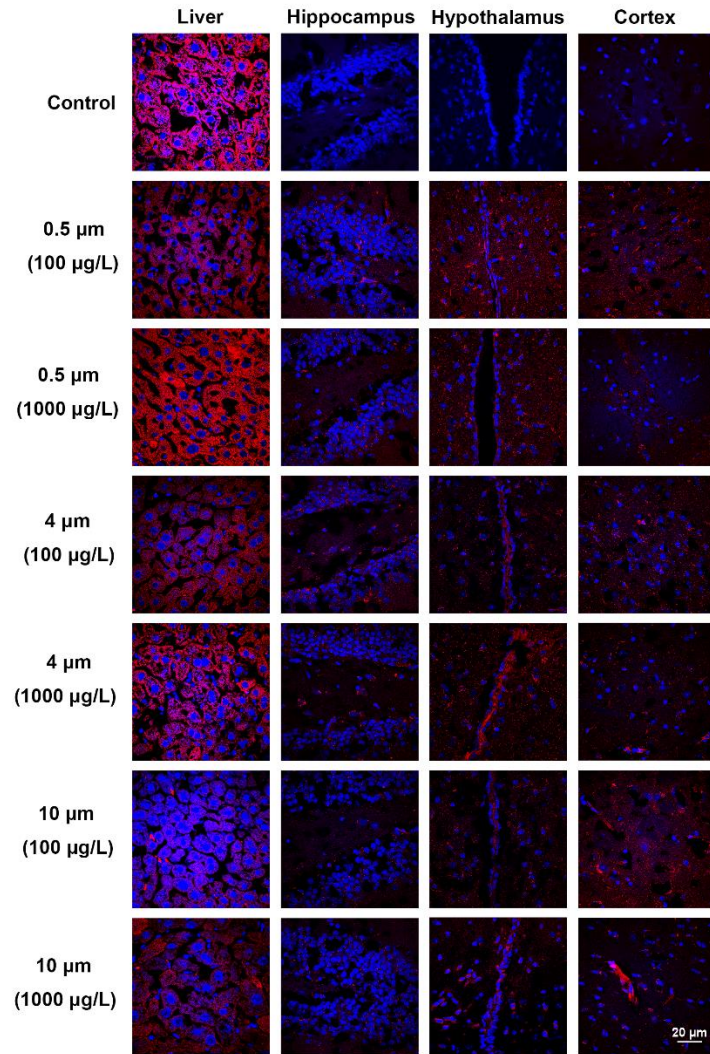
	Trials	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Control	40	9 (22.5%)	8 (20%)	7 (17.5%)	5 (12.5%)	4 (10%)	4 (10%)
100 µg/L 0.5 µm	40	8 (20%)	7 (17.5%)	7 (17.5%)	6 (15%)	4 (10%)	4 (10%)
1000 µg/L 0.5 µm	40	9 (22.5%)	8 (20%)	8 (20%)	6 (15%)	5 (12.5%)	3 (7.5%)
100 µg/L 4 µm	40	8 (20%)	8 (20%)	7 (17.5%)	5 (12.5%)	5 (12.5%)	4 (10%)
1000 µg/L 4 µm	40	8 (20%)	8 (20%)	6 (15%)	6 (15%)	4 (10%)	4 (10%)
100 µg/L 10 µm	40	8 (20%)	8 (20%)	7 (17.5%)	7 (17.5%)	6 (15%)	3 (7.5%)
1000 µg/L 10 µm	40	9 (22.5%)	8 (20%)	7 (17.5%)	7 (17.5%)	6 (15%)	4 (10%)





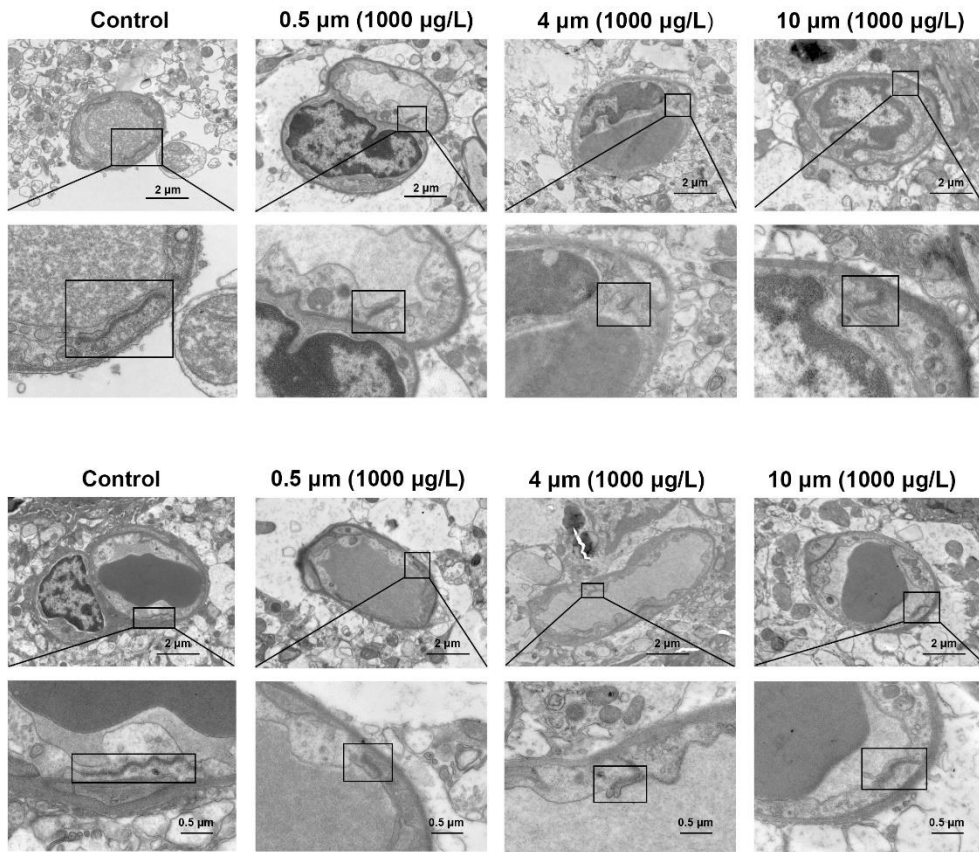
**Figure S1.** Biodistribution of various diameters of polystyrene MPs (PS-MPs) in different tissues of mice. Mice were provided drinking water containing three sizes of fluorescent PS-MPs for 180 consecutive days. Fluorescence pictures of excised brain tissues and gastric tissues were detected. The colors in pictures indicated that fluorescence PS-MPs in tissues.



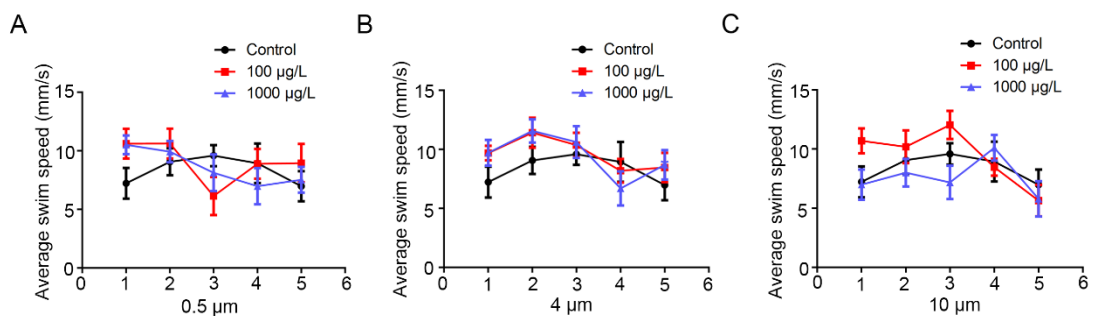


**Figure S2.** BBB integrity was detected by biotin tracer experiments. The sections were stained with biotin (red) and DAPI (blue). The existence of biotin in brain tissues was examined by immunofluorescence microscopy. The biotin signal of the liver parenchyma was used as a positive control (scale bar = 20  $\mu\text{m}$ ).



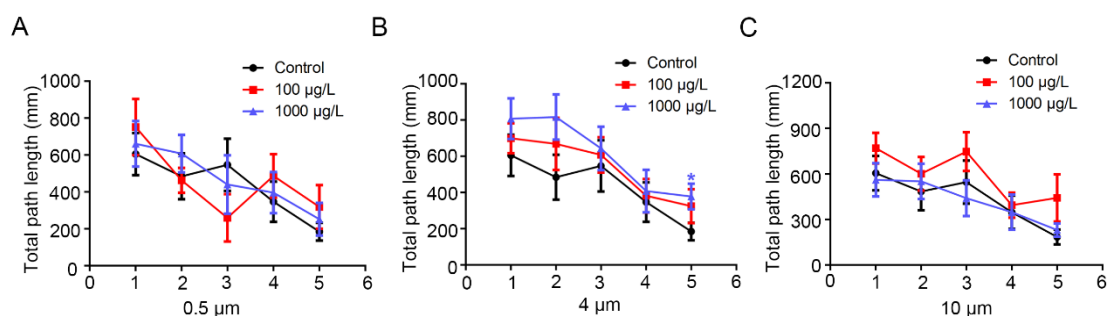


**Figure S3.** Ultrastructure of BBB in PS-MP-exposed and unexposed mice as detected by an electron microscope. Upper images displayed the ultrastructure of BBB. Lower images referred to magnified boxed areas.

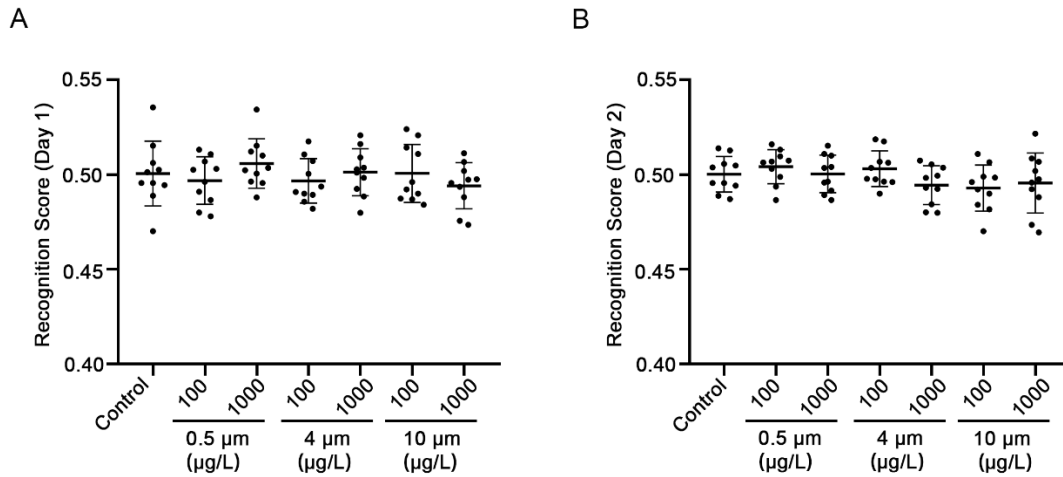


**Figure S4.** The average swim speed of mice on days 1-5 in Morris water maze test is shown. Circle (Control), square (100 μg/L), triangle (1000 μg/L). (A) Control and 0.5 μm PS-MPs exposure groups. (B) Control and 4 μm PS-MPs exposure groups. (C) Control and 10 μm PS-

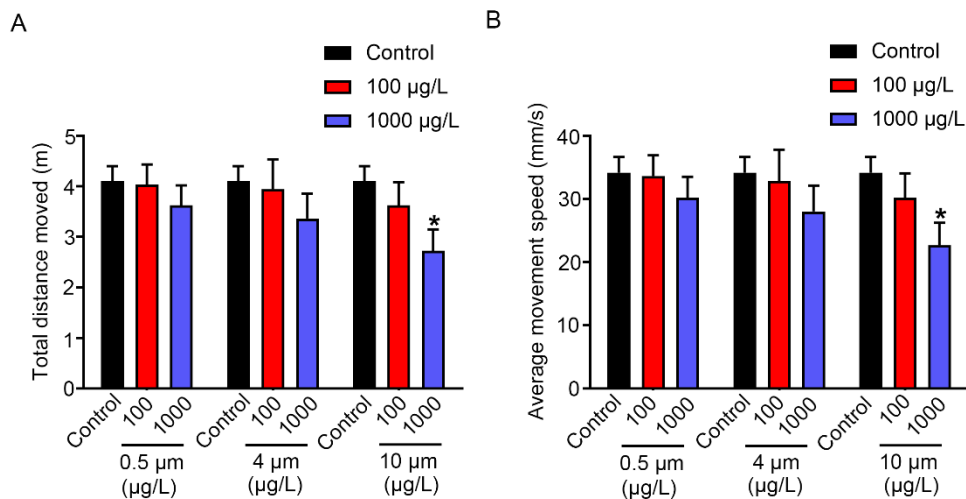
MPs exposure groups. The results are expressed as means  $\pm$  SD (n = 10 mice/per group). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. Data were detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.



**Figure S5.** The total path length to find the hidden platform of mice on days 1-5 in Morris water maze test are shown. Circle (Control), square (100  $\mu$ g/L), triangle (1000  $\mu$ g/L). (A) Control and 0.5  $\mu$ m PS-MPs exposure groups. (B) Control and 4  $\mu$ m PS-MPs exposure groups. (C) Control and 10  $\mu$ m PS-MPs exposure groups. The results are expressed as means  $\pm$  SD (n = 10 mice/per group). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \**P* < 0.05 vs. control, as detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.

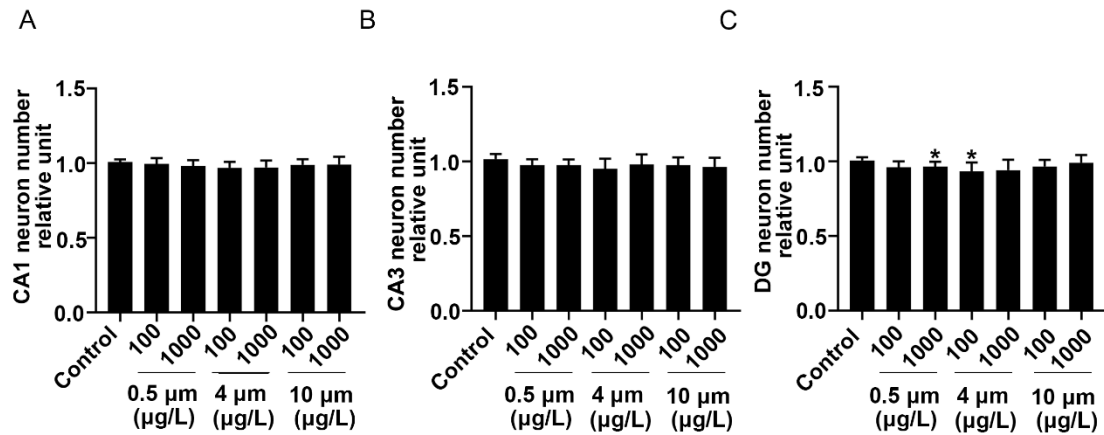


**Figure S6.** The recognition scores (time spent (s) investigating one object/time spent (s) investigating both objects in total) of mice on day 1 (A) and day 2 (B) of novel object recognition (NOR) experiment were examined (n = 10 mice/per group). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4.

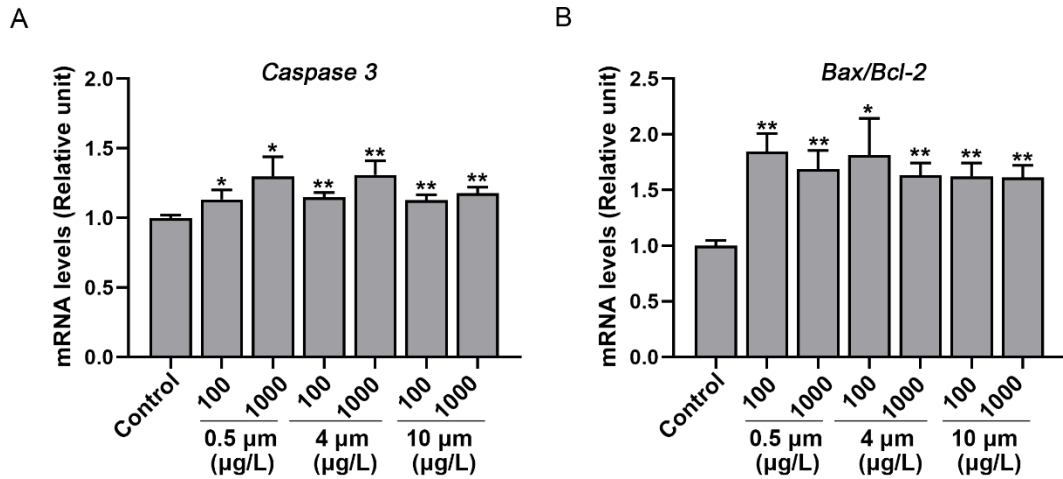


**Figure S7.** The total distance moved (A) and average movement speed (B) of mice in testing day (day 3) of the novel object recognition test are shown. The results are expressed as means  $\pm$  SD (n = 10 mice/per group). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \**P* < 0.05 vs. control, as

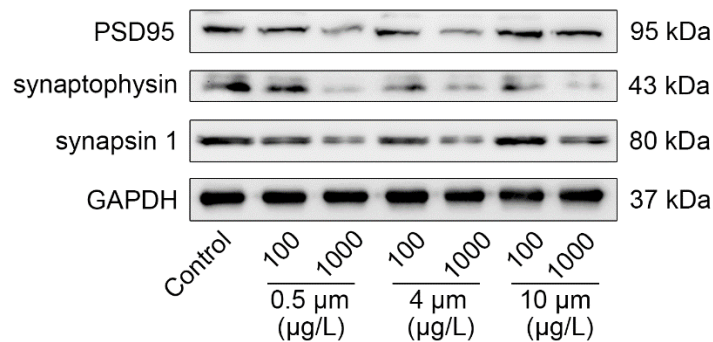
detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.



**Figure S8.** The numbers of neurons in the hippocampal cornu ammonis 1 (CA1), cornu ammonis 3 (CA3), and dentate gyrus (DG) sections were counted (n = 3 mice/group, n = 3 slides/mice). Data are shown as mean  $\pm$  SD. The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \**P* < 0.05 compared with control, as detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.

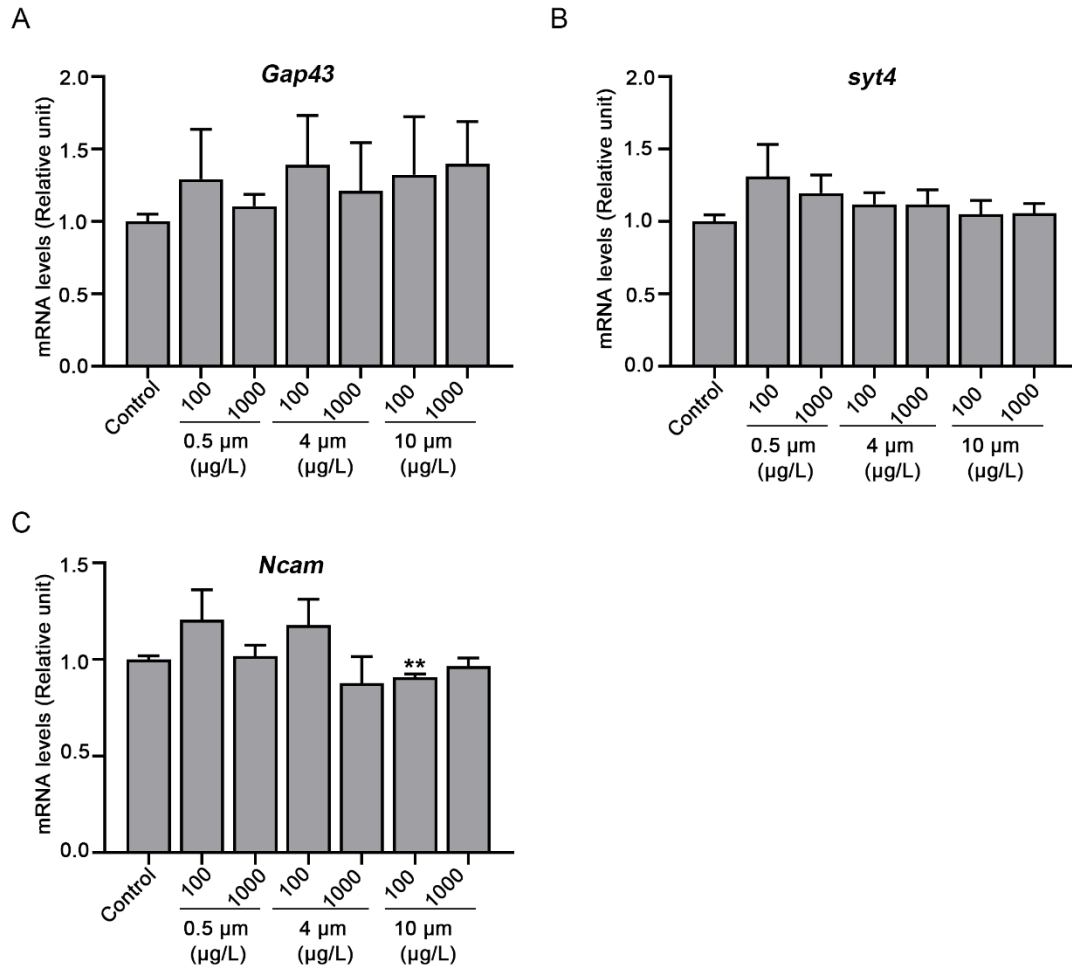


**Figure S9.** The mRNA levels of *caspase 3* (A), the *Bax/Bcl-2* mRNA ratio (B) in the hippocampus were tested with quantitative real-time PCR (qRT-PCR) by normalizing to *Gapdh*. The results are expressed as means  $\pm$  SD (n = 3, N = 3 mice/group). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \**P* < 0.05 and \*\**P* < 0.01 compared with the control, as detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.

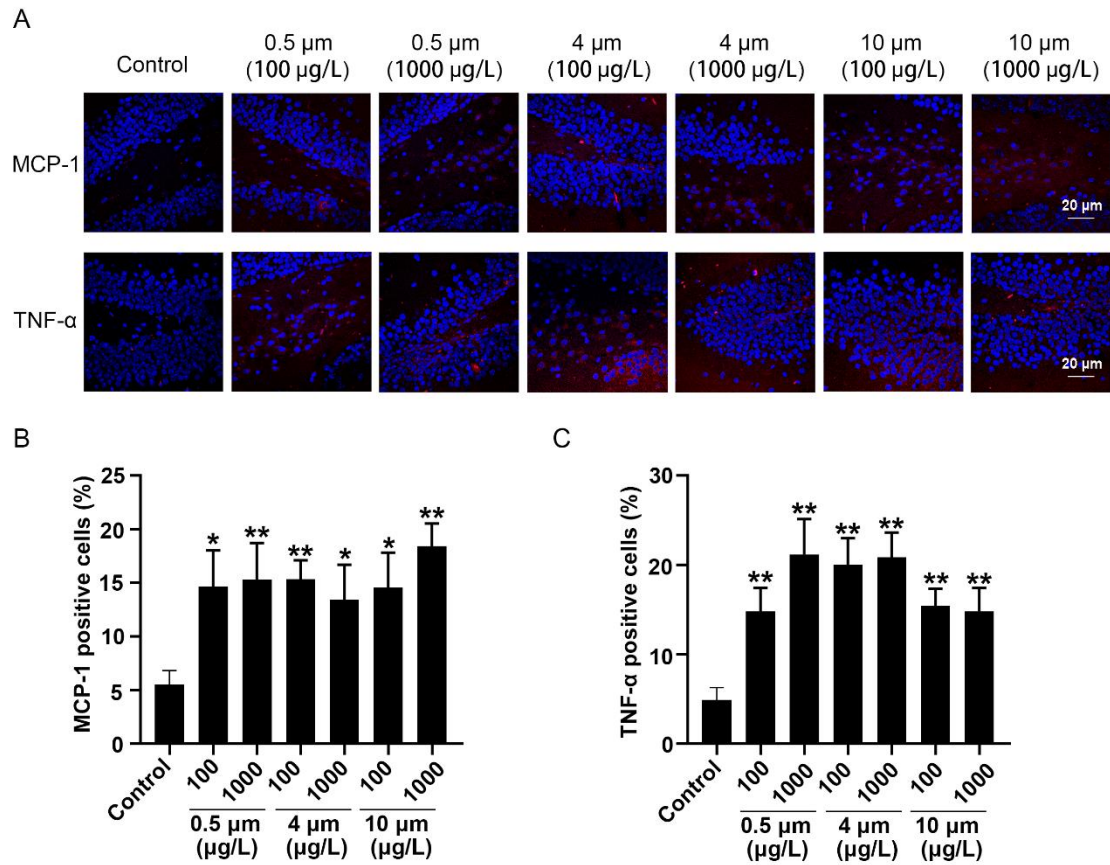


**Figure S10.** The expression of synapsin 1, synaptophysin, and PSD 95 protein in the hippocampus was measured via western blotting. The western blotting results were quantified and statistically analyzed, as shown in (Figure 7C) as mean  $\pm$  SD (n = 3, N = 3 mice/group). The mean and SD summary data for quantification of western blotting are shown in Table S3.

*P*-Values for all comparisons are reported in Table S4.



**Figure S11.** The mRNA expression levels of *Gap43*(A), *Syt 4* (B), and *Ncam*(C) were detected by qRT-PCR in the hippocampus of mice exposed to PS-MPs and control mice. Data are shown as mean  $\pm$  SD ( $n = 3$ ). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \*\* $P < 0.01$  compared with control, as detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.



**Figure S12.** (A) A confocal fluorescence microscope was used to detect colocalization of Alexa Fluor 594-labeled MCP-1 (red)/TNF- $\alpha$  (red) and DAPI (blue) (scale bar = 20  $\mu$ m, n = 3) in the hippocampus of mice exposed to PS-MPs and control mice. (B) Percent of positivity was calculated based on the percentage of MCP-1 positive cells out of the total number of cells in an image. (C) Percent of positivity was calculated based on the percentage of TNF- $\alpha$  positive cells out of the total number of cells in an image. Data are shown as mean  $\pm$  SD (n = 3). The mean and SD summary data for quantification are shown in Table S3. *P*-Values for all comparisons are reported in Table S4. \**P* < 0.05, \*\**P* < 0.01 compared with control, as detected by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests.