Supplementary Materials

Exercise under Particulate Matter Exposure: Neurotrophic Responses and Functional Brain Outcomes

Supplementary Methods S1

Database search strategies

The search strategy combined pollution, exercise or physical activity, and brain-related outcome b locks using AND; alternatives within each block were linked by OR. Both databases were searche d on 13 October 2026 without publication-year, language or document-type filters.

S1.1 PubMed

The following search expression was used in PubMed. The exported result set contained 412 records. [Mesh] denotes Medical Subject Headings and [tiab] denotes title/abstract fields.

("Air Pollution"[Mesh] OR "Particulate Matter"[Mesh] OR "Vehicle Emissions"[Mesh] OR "particulate matter"[tia b] OR PM2.5[tiab] OR "PM 2.5"[tiab] OR PM10[tiab] OR "PM 10"[tiab] OR PM1[tiab] OR "PM 1"[tiab] OR "ultrafine par ticle*"[tiab] OR "traffic-related air pollution"[tiab] OR "traffic related air pollution"[tiab] OR "diesel exhaust"[tiab] OR "black carbon"[tiab] OR "air pollution"[tiab])

AND

("Exercise"[Mesh] OR "Motor Activity"[Mesh] OR exercis*[tiab] OR "physical activ*"[tiab] OR "aerobic training"[ti ab] OR "endurance training"[tiab] OR "resistance training"[tiab] OR "interval training"[tiab] OR HIIT[tiab] OR wa lking[tiab] OR cycling[tiab] OR running[tiab] OR treadmill[tiab])

AND

("Brain"[Mesh] OR "Cognition"[Mesh] OR "Memory"[Mesh] OR "Dementia"[Mesh] OR "Blood-Brain Barrier"[Mes h] OR brain[tiab] OR neuro*[tiab] OR cognit*[tiab] OR hippocamp*[tiab] OR memor*[tiab] OR dement*[tiab] OR BDNF[tiab] OR "brain-derived neurotrophic factor"[tiab] OR VEGF[tiab] OR "vascular endothelial growth factor" [tiab] OR IGF1[tiab] OR "IGF-1"[tiab] OR "insulin-like growth factor*"[tiab] OR BBB[tiab] OR "blood-brain barrier "[tiab] OR cerebrovascular[tiab] OR "cerebral blood flow"[tiab] OR "cerebral oxygenation"[tiab] OR "executive fu nction*"[tiab] OR attention[tiab] OR "reaction time"[tiab] OR fNIRS[tiab] OR "near-infrared spectroscopy"[tiab])

S1.2 Web of Science Core Collection

Query entered in the Topic field across the editions available through the institutional interface. The export ed result set contained 1,386 records.

("particulate matter" OR PM2.5 OR "PM 2.5" OR PM10 OR "PM 10" OR PM1 OR "PM 1" OR "ultrafine particle*" OR "tr affic-related air pollution" OR "traffic related air pollution" OR "diesel exhaust" OR "black carbon" OR "air polluti on")

AND

(exercis* OR "physical activ*" OR "aerobic training" OR "endurance training" OR "resistance training" OR "interva l training" OR HIIT OR walking OR cycling OR running OR treadmill)

AND

(brain OR neuro* OR cognit* OR hippocamp* OR memor* OR dement* OR BDNF OR "brain-derived neurotrophi c factor" OR VEGF OR "vascular endothelial growth factor" OR IGF1 OR "IGF-1" OR "insulin-like growth factor*" OR BBB OR "blood-brain barrier" OR cerebrovascular OR "cerebral blood flow" OR "cerebral oxygenation" OR "e xecutive function*" OR attention OR "reaction time" OR fNIRS OR "near-infrared spectroscopy")

After removal of 265 duplicates from the 1,798 exported records, 1,533 records remained.

Supplementary Table S1. Detailed study characteristics and findings

Detailed records for the 33 main and four indirect reports summarised in Table 2 of the main manuscript. Reference numbers follow the main manuscript.

Study	Design and sample	Exposure and activity	Main finding	Interpretation
A Human exercise studies · 8 reports				
Molina-Sotomayor et al. (2019) [28]	Two-city, two-year training comparison; 181 older women; active and sedentary groups in each city.	Ambient $PM_{2.5}$: 28.0 versus 12.8 μg/m³; progressive walking.	MMSE improved in both active groups (+4.7%); post-training MMSE did not differ significantly between them. Estimated VO_2 max gains were smaller in the more polluted city.	Retained cognitive improvement with smaller cardiorespiratory gains. No factorial interaction was established; city-level confounding remains.
Liu et al. (2023) [29]	Randomised parallel trial; 93 participants; three activity conditions and air filtration.	Two-hour filtered/unfiltered-air exposure; 20-min HIIT or MICT versus stretching.	$PM_{2.5}$ × HIIT coefficients for congruent/incongruent Stroop reaction time were 2.231/3.305 ms per μg/m³, with both confidence intervals above zero; MICT intervals included zero. Prefrontal haemodynamic findings were channel- and task-specific.	Supports attenuation of the HIIT contrast. The approximately 33 μg/m³ split was sample-based, not a reversal threshold; a difference between HIIT and MICT interaction coefficients was not established.
Molina-Sotomayor et al. (2020) [30]	Two-city training comparison; 157 older women with MMSE scores of 13–24 at recruitment.	Ambient $PM_{2.5}$: 29.2 versus 12.8 μg/m³; 24-month progressive resistance training, twice weekly.	MMSE improved in both active groups, more in the lower-pollution setting. IGF-1 increased within both active groups, although the post-test omnibus group comparison was non-significant ($p = 0.322$).	Within-group changes and post-test group comparisons address different contrasts. No factorial interaction was reported; city-level confounding and attrition limit interpretation.
Cassilhas et al. (2022) [31]	Randomised four-group trial; 48 adults aged ≥60 years; 12 weeks.	Indoor treadmill or outdoor park exercise, three times weekly at 60–70% heart-rate reserve; stretching controls. Monitored particle concentrations were higher outdoors.	Exercise × site interactions favoured indoor exercise for serum BDNF and Trail Making A/B and forward/backward digit span (all $p < 0.001$).	Peripheral and cognitive outcomes were concordant, but site and exercise modality co-varied; these comparisons do not isolate PM effects or establish BDNF-mediated cognitive change.
Bos et al. (2013) [20]	Non-randomised urban/rural training comparison; 34 enrolled, 24 analysed.	Twelve weeks of walking/running, three times weekly; urban/rural particle counts averaged 7,244/5,625 particles/cm³.	Stroop reaction time improved in the rural group, with a time × site interaction ($p = 0.04$). Serum BDNF changes were non-significant in both groups; working-memory and vigilance tasks showed no clear effects.	The cognitive interaction was not accompanied by a statistically significant serum BDNF change. Age imbalance, attrition and other site differences qualify the comparison.

Study	Design and sample	Exposure and activity	Main finding	Interpretation
Silveira et al. (2022) [18]	Crossover chamber study; ten recreationally trained male cyclists; blood analyses in nine.	Self-paced 50-km cycling time trial under traffic-related air pollution or filtered air.	Plasma BDNF post/pre-exercise ratios were greater under polluted air (3.3 versus 1.3; paired comparison, p = 0.048). Endurance-performance measures did not differ significantly between conditions.	Enhanced peripheral BDNF response; cognition was not assessed. Adaptation to repeated pollution exposure was not established.
Bos et al. (2011) [17]	Within-person cycling comparison; 38 recruited, 35 analysed.	Approximately 20-min cycling at 74% maximal heart rate; roadside versus filtered-room $PM_{2.5}$: 24.6 versus 2.0 μg/m^3.	Serum BDNF increased under filtered air (+14.4%, p = 0.02) but not roadside (+0.5%, p = 0.42); post-exercise concentrations did not differ between conditions (p = 0.74).	Suggestive response pattern, without a reported between-condition change contrast or condition × time test.
Pasqua et al. (2020) [19]	Crossover chamber study; ten healthy men.	Ninety minutes of moderate cycling under polluted urban air or filtered air; blood sampling at rest and 30, 60 and 90 min.	Serum VEGF was higher under polluted air at 90 min (p = 0.026), alongside higher IL-6 and post-exercise blood pressure.	A time-point contrast in a peripheral vascular marker does not establish a condition × time interaction. Cognition was not assessed.
B Observational human studies · 21 reports				
Zhang et al. (2022) [32]	Repeated panel of 90 young adults in Beijing; four one-week assessments.	Personal $PM_{2.5}$ (mean 26.3 μg/m^3); accelerometer-measured MVPA.	MVPA was associated with faster Stroop responses. Associations were numerically stronger at higher pollution, but the formal linear $PM_{2.5}$ × MVPA interaction was not significant.	Activity-related benefit was observed, but amplification and a compensatory exercise dose were not established.
Zhang and Xu (2026) [33]	UK Biobank cohort; 96,661 participants; 235 AD and 112 vascular dementia events.	Residential PM and nitrogen oxides; seven-day wrist accelerometry (PA IQR 10.13 milli-gravity units).	Selected interactions suggested attenuation: for AD, the PA × $PM_{2.5}$ interaction HR comparing Q4 with Q1 was 1.97 (95% CI 1.17–3.32). Most interactions were not significant.	The interaction HR does not indicate harm from PA itself. Unadjusted multiple comparisons make these attenuation signals exploratory.
Das and Ayalon (2026) [34]	LASI Wave 1; cross-sectional analysis of 31,902 adults aged ≥60 years.	Composite household-combustion proxy; self-reported moderate/vigorous activity or yoga-based practices.	Overall PA × pollution interaction: β −0.29 (95% CI −0.78 to 0.20). The PA × pollution × female interaction was −1.19 (−2.11 to −0.26), suggesting sex differences.	The three-way interaction is not a women-only two-way test. The exposure proxy and mixed activity measure do not quantify inhaled PM or exercise dose.

Study	Design and sample	Exposure and activity	Main finding	Interpretation
Furlong et al. (2022) [22]	UK Biobank; cross-sectional MRI analysis of 8,600 participants.	Residential NO_2, $PM_{2.5}$ absorbance and PM mass; wrist-accelerometer vigorous PA.	NO_2 and $PM_{2.5}$ absorbance interacted with vigorous PA on white matter hyperintensity volume (FDR-adjusted p = 0.037). The favourable PA association was attenuated at higher exposure.	Findings were specific to the pollutant and MRI outcome. $PM_{2.5}$ absorbance is not interchangeable with $PM_{2.5}$ mass; cross-sectional associations do not establish changes over time.
Gui et al. (2020) [35]	Guangzhou children aged 6–12 years; cross-sectional parent ratings (n = 5,028) and computerised testing (n = 522).	Estimated annual residential $PM_{2.5}$/PM_{10}; reported MVPA, compared at <60 versus ≥60 min/day.	Higher PM exposure was associated with poorer working memory or inhibitory control. The main text reported no significant effect modification by MVPA.	Reported activity and residential exposure limit individual-dose inference; non-significance does not establish equivalent associations.
Li et al. (2024) [36]	Fuyang community sample; cross-sectional analysis of 3,937 adults aged ≥ 60 years.	Three-year residential PM_1/$PM_{2.5}$/PM_{10}; self-reported activity volume (MET-h/week).	MMSE associations suggested attenuation of PA benefits at higher PM. Interaction p-values were 0.066, 0.178 and 0.112 for PM_1, $PM_{2.5}$ and PM_{10}, respectively.	All exceeded 0.05; findings used an exploratory p < 0.20 criterion. Concentrations where significance disappeared were not validated benefit-to-harm thresholds or safe limits.
Hong et al. (2025) [37]	Kidney-transplant evaluation cohort, age ≥50 years; baseline cognition in 2,073 patients; dementia follow-up in 1,683.	Annual residential ZIP-code $PM_{2.5}$ (>9 μg/m³); self-reported leisure PA.	High-exposure associations with 3MS scores were stronger at low PA (−4.84 points) than high PA (−1.61 points; interaction p < 0.001).	The cognitive-score analysis supports activity-related modification in a clinical population. Dementia effect modification was not tested because only 29 events occurred.
Zhu and Zou (2025) [38]	CHARLS 2018; cross-sectional analysis of middle-aged and older adults.	Prior-year regional PM_1/$PM_{2.5}$/PM_{10} and gaseous pollutants; self-reported PA split at 69.3 MET-h/week.	The adverse $PM_{2.5}$ association with cognitive scores was weaker at higher PA in the instrumental-variable model (interaction p = 0.006).	Association directions differed between ordinary least-squares and instrumental-variable models; instrument assumptions constrain causal interpretation.
Liu et al. (2023b) [23]	CFPS 2010/2014/2018; 108,099 repeated observations, not unique participants.	Annual residential $PM_{2.5}$/components; self-reported leisure PA frequency and hours/week.	Activity associations with combined verbal/mathematics scores persisted but weakened at higher $PM_{2.5}$. $PM_{2.5}$ × PA frequency: β −0.005 (95% CI −0.006 to −0.003), per μg/m³ and occasion/week.	Frequency and duration do not measure intensity; component coefficients cannot establish universal toxicity ratios.
Yu et al. (2026) [39]	CHARLS 2011–2020; five-wave mixed-effects analysis; 12,196 participants and 32,477 person-waves.	Prior-year city $PM_{2.5}$/components; log-transformed self-reported weekly PA volume.	Table S3 of the original study showed a buffering interaction for mental status (β 0.000630; 95% CI 0.0002–0.0010; p = 0.0021), but not overall cognition (p = 0.07) or episodic memory (p = 0.59).	Abstract and supplementary interaction estimates disagree. The signal is outcome-specific and does not validate a compensatory exercise prescription.

Study	Design and sample	Exposure and activity	Main finding	Interpretation
Tuffier et al. (2024) [40]	Danish Nurse Cohort; prospective follow-up of female nurses; 1,409 incident dementia cases.	Long-term residential $PM_{2.5}$ and NO_2; self-reported leisure activity classified as low, moderate or high.	Associations of $PM_{2.5}$ and NO_2 with incident dementia were weaker at higher activity levels; likelihood-ratio interaction tests supported effect modification.	Consistent with activity-related buffering of pollution associations. Adjustment included road traffic noise; applicability is limited by the female occupational cohort and self-reported activity.
Zhang et al. (2024) [41]	UK Biobank prospective study; 155,828 adults aged ≥60 years.	Modelled residential pollution; self-reported activity volume, <600 versus ≥600 MET-min/week in interaction analyses.	For AD, $PM_{2.5}$ × low activity showed additive interaction: RERI 0.330 (95% CI 0.012–0.648); multiplicative interaction p = 0.067. Neither scale supported interaction for all-cause or vascular dementia.	The $PM_{2.5}$ result supports outcome-specific additive effect modification; multiplicative modification remains uncertain.
Ran et al. (2021) [42]	Hong Kong Elderly Health Centres cohort; 57,775 adults aged ≥65 years; 1,157 incident dementia cases.	Modelled annual residential $PM_{2.5}$; self-reported activity volume and type.	Higher activity was associated with lower dementia risk: high versus inactive HR 0.59 (95% CI 0.47–0.75). No clear additive or multiplicative interaction; activity-volume interaction p = 0.569 for all-cause dementia.	Consistent with retained activity-related benefit across exposure levels, without establishing equivalent effects.
Küçükali et al. (2025) [43]	Northern Ireland NICOLA longitudinal cohort; 2,836 participants; 137 cases of ≥3-point MMSE decline.	Residential $PM_{2.5}$ divided at 6.6 $\mu g/m^3$; self-reported recreational MVPA, <10 versus ≥10 min/week.	High $PM_{2.5}$ × low MVPA: multiplicative interaction estimate 1.76 (95% CI 0.84–3.72); additive RERI 0.63 (−0.98–2.24).	Both intervals include their null values, leaving effect modification uncertain. Estimates were sensitive to exposure/activity cut-points; positive point estimates alone do not establish synergy.
Song et al. (2022) [44]	Repeated panel of 34 healthy retirees in Xinxiang, China; five visits per participant.	Fixed-site $PM_{2.5}$ and constituents; higher (n = 24) versus lower (n = 10) reported activity volume.	The $PM_{2.5}$–serum NfL association was stronger in the lower-activity group, with a significant between-group contrast indicated. No significant activity-group contrast was indicated for BDNF.	A potential buffering signal specific to NfL; small, unequal activity strata and the unclear between-group test method constrain interpretation.
Raichlen et al. (2022) [45]	UK Biobank prospective cohort; 35,562 adults aged ≥60 years; incident all-cause dementia.	Modelled residential $PM_{2.5}$ and $PM_{2.5}$ absorbance; wrist-accelerometer average acceleration.	Inverse activity–dementia associations weakened at higher pollution levels; multiplicative interactions were reported for $PM_{2.5}$ and absorbance. Activity HRs in the highest exposure tertiles remained below 1, with CIs including 1.	Attenuation, without demonstrated reversal to harm. Exposure concentration thresholds cannot be inferred from these contrasts.

Study	Design and sample	Exposure and activity	Main finding	Interpretation
Lee et al. (2022) [46]	KoGES Ansan–Ansung cohort data; cross-sectional cognitive assessment of 4,175 adults aged >50 years.	Long-term $PM_{2.5}$ and PM_{10}; self-reported regular exercise causing sweating at least once weekly.	Adverse associations between long-term PM exposure and K-MMSE scores were stronger in non-exercisers; activity-related effect modification was reported from interaction analyses.	Consistent with a potentially buffering association. The cognitive assessment does not estimate longitudinal decline, and the exercise classification cannot resolve intensity-specific effects.
Tan et al. (2021) [47]	Chinese Veteran Clinical Research Platform; cross-sectional study of 7,040 male veterans.	Three-year $PM_{2.5}$ and PM_{10}; daily activity of at least walking intensity for ≥30 min.	Per 10 μg/m³ higher $PM_{2.5}$, dementia ORs were 1.37 (95% CI 1.17–1.61) in active and 0.91 (0.70–1.18) in inactive participants; between-stratum difference $p < 0.01$.	A stronger pollution association among active participants for prevalent dementia. This outcome-specific contrast should not be generalised to MCI or other pollutants.
Zhang et al. (2023) [48]	CLHLS 2018 cross-sectional analysis; 9,839 adults aged ≥65 years.	Self-reported major-road distance in five bands as a traffic-pollution proxy; regular exercise, yes/no.	Selected exercise–distance joint categories showed lower cognitive-impairment odds than non-exercise/<50 m, after adjustment for the other five lifestyle behaviours and covariates.	Common-reference joint categories do not establish exercise-by-distance interaction or isolate particle effects. Road distance also represents other environmental attributes.
Fu et al. (2025) [49]	Zhejiang prospective cohort; 10,055 adults aged ≥60 years; 879 incident AD cases.	Joint score for $PM_{2.5}$, PM_{10}, NO_2, SO_2 and O_3; leisure exercise, yes/no.	Pollution-score–AD associations were stronger among exercisers; multiplicative score-by-exercise interaction HR 1.65 (95% CI 1.13–2.40), $p = 0.009$.	The mixture score cannot define a $PM_{2.5}$ concentration threshold. A stronger pollution association within exercisers does not itself establish that exercise increased AD risk.
Deng et al. (2021) [50]	CLHLS prospective study, 2011–2018; 4,161 adults aged ≥65 years without baseline cognitive impairment.	Self-reported biomass versus cleaner cooking fuels; regular exercise, yes/no.	Biomass–cognitive-decline HRs were 0.99 (95% CI 0.80–1.23) in exercisers and 1.31 (1.13–1.53) in non-exercisers; interaction $p = 0.04$. For cognitive impairment, interaction $p = 0.19$.	Potential buffering for decline, with uncertain modification for impairment. Fuel type is a household-pollution proxy.
C Animal experiments · 4 reports				
Cho and Roh (2025) [25]	Randomised four-group experiment; 40 male C57BL/6 mice.	Intravenous PM_{10}-like ERM-CZ120, 0.5 μg/g three times weekly; eight-week treadmill training, five times weekly.	PM-plus-exercise increased serum IGF-1, BDNF and VEGF versus PM alone (all $p < 0.05$); S100B and NSE remained elevated versus control ($p < 0.05$).	One-way ANOVA and pairwise comparisons were reported, without a factorial PM × exercise test. These peripheral biomarker findings neither directly measure BBB permeability nor establish responses to inhaled particles.

Study	Design and sample	Exposure and activity	Main finding	Interpretation
Bos et al. (2012) [21]	Randomised 2 × 2 experiment; 24 male Wistar rats, six per group.	Soot UFP inhalation for 90 min (approximately 1.2 × 10^7 particles/cm^3), with forced treadmill running or rest.	At 24 h, hippocampal BDNF mRNA was 1.543-fold higher after ambient-air exercise than ambient-air rest (p = 0.034); UFP-plus-exercise did not differ significantly from ambient-air rest.	Suggestive attenuation at a molecular endpoint; no factorial interaction was reported. Different comparison-wise significance does not establish effect modification.
Cho and Roh (2026) [26]	Four-group experiment; 48 male mice; normal-diet and high-fat-diet conditions.	Intravenous PM_{10}-like material three times weekly; eight weeks of ladder-climbing resistance training in the exposed high-fat-diet condition.	Versus exposed sedentary HFD mice, training increased serum BDNF (p = 0.001) and VEGF (p = 0.027) and reduced S100B (p = 0.001); the NSE contrast was non-significant.	The exposed-group exercise contrast is informative, but no PM-free exercise group was included to estimate a full PM × exercise interaction. Outcomes were peripheral.
Sun et al. (2025) [24]	Six-group experiment in male C57BL/6J mice; endpoint-specific samples commonly 3–5.	Intratracheal particles (reported 5.45 mg/kg), followed by cerebral ischaemia/reperfusion; voluntary wheel exercise for 4, 6 or 8 weeks before exposure.	Selected behavioural, brain-injury and tight-junction-protein outcomes improved in exercised exposed mice, with the strongest pattern after six weeks.	Preventive exercise in an instillation/disease model; no PM-free exercised ischaemia/reperfusion group or full interaction estimate. Brain barrier-associated proteins were measured, rather than direct BBB tracer permeability.
D Indirect evidence · 4 reports				
Han (2021) [51]	Four-group environment/activity comparison; 116 university students.	Fifteen-minute walking or jogging in natural or built environments; monitoring-station $PM_{2.5}$ and PM_{10} entered regression models alongside other environmental variables.	PM measures showed no clear associations with spatial/digit-span attention outcomes; no PM × activity coefficient was reported.	Indirect multifactor environmental comparison; route effects cannot be attributed specifically to particles.
Sun et al. (2023) [52]	Shanghai–Minhang Birth Cohort; 512 mother–child pairs; activity-stratified analyses in 503.	Modelled prenatal $PM_{2.5}$ and constituents; outdoor activity at age six, ≤2 versus >2 h/week.	$PM_{2.5}$ × activity interaction p-values were 0.16, 0.20 and 0.10 for full-scale IQ, verbal comprehension and perceptual reasoning; selected constituent interactions for verbal comprehension were significant.	Indirect life-course evidence: exposure and activity were non-concurrent, and activity intensity was unmeasured. $PM_{2.5}$-specific protective effect modification was not established.
Deng et al. (2025) [53]	Shenzhen Birth Cohort; 1,547 mother–child pairs; repeated developmental assessments through 24 months.	Modelled prenatal/postnatal $PM_{2.5}$ and components; outdoor time, split at the median, served as an activity proxy.	No significant activity-proxy interaction was found across five ASQ-3 domains; postnatal $PM_{2.5}$ interaction p-values ranged from 0.177 to 0.310. Component interactions were also non-significant.	Indirect developmental evidence: outdoor time does not quantify infant exercise intensity or dose.

Study	Design and sample	Exposure and activity	Main finding	Interpretation
Roe et al. (2020) [54]	Counterbalanced crossover walking pilot; 11 older adults recruited, with one second-walk observation missing.	Twenty-minute walks along green and built-up routes; portable $PM_{2.5}$ monitoring.	Simple reaction time did not differ clearly between routes ($p = 0.403$). PM × environment models concerned heart-rate variability, not the cognitive outcome.	Indirect evidence from a small, multifactor environmental comparison. The green route did not consistently provide lower PM exposure; route labels therefore cannot serve as a clean-versus-polluted contrast.

Note: A–C comprise 33 reports in the main synthesis; D comprises four indirect reports. Counts refer to reports, not independent cohorts. Reports from shared cohorts may overlap and are not independent replications. Confidence intervals are 95%. Observational associations do not establish causality. Different within-group significance levels do not establish an interaction; non-significance does not demonstrate equivalence. Additive and multiplicative interaction scales are distinct. Retained responses indicate that a favourable association or response was observed under pollution exposure, without establishing equivalence to cleaner conditions. Circulating biomarkers do not establish central neural effects, direct BBB permeability or cognitive mediation. Intravenous and instillation models are not equivalent to ambient inhalation. 3MS, Modified Mini-Mental State Examination; AD, Alzheimer's disease; ANOVA, analysis of variance; ASQ-3, Ages and Stages Questionnaires, third edition; BBB, blood–brain barrier; BDNF, brain-derived neurotrophic factor; CFPS, China Family Panel Studies; CHARLS, China Health and Retirement Longitudinal Study; CI, confidence interval; CLHLS, Chinese Longitudinal Healthy Longevity Survey; FDR, false discovery rate; HFD, high-fat diet; HIIT, high-intensity interval training; HR, hazard ratio; IGF-1, insulin-like growth factor 1; IL-6, interleukin-6; IQ, intelligence quotient; IQR, interquartile range; K-MMSE, Korean Mini-Mental State Examination; KoGES, Korean Genome and Epidemiology Study; LASI, Longitudinal Ageing Study in India; MCI, mild cognitive impairment; MET, metabolic equivalent; MICT, moderate-intensity continuous training; MMSE, Mini-Mental State Examination; MRI, magnetic resonance imaging; mRNA, messenger RNA; MVPA, moderate-to-vigorous physical activity; NfL, neurofilament light chain; NICOLA, Northern Ireland Cohort for the Longitudinal Study of Ageing; NO_2, nitrogen dioxide; NSE, neuron-specific enolase; O_3, ozone; OR, odds ratio; PA, physical activity; PM, particulate matter; Q1/Q4, lowest/highest quartile; RERI, relative excess risk due to interaction; S100B, S100 calcium-binding protein B; SO_2, sulfur dioxide; UFP, ultrafine particles; VEGF, vascular endothelial growth factor; VO_2max, maximal oxygen uptake; β, regression coefficient.