

Neurobehavioral Effects of Diesel Exhaust Exposure in Mice: A Systematic Review

Dr. S. Yamona Nidhya¹, Dr. Sowjanya Bandlamudi², Dr. A. Kafeel Hussain³,
Dr. M. Mahima sophia⁴

¹ Tutor, (Ph.D Part time Internal Scholar), Department of Anatomy, Shri Sathya Sai Medical College and Research Institute (SSSMCRI), SBV Chennai Campus, Sri Balaji Vidyapeeth (Deemed-to-be University), Shri Sathya Sai Nagar, Ammapettai, Thiruporur, Chengalpattu, Tamil Nadu-603108, India; Sri Balaji Vidyapeeth (Deemed-to-be University), Pondicherry-607402, India.

Email: yamonanidhya@gmail.com | ORCID: 0000-0002-4166-4650

² Professor and Head, Department of Anatomy, Shri Sathya Sai Medical College and Research Institute (SSSMCRI), SBV Chennai Campus, Sri Balaji Vidyapeeth (Deemed-to-be University), Shri Sathya Sai Nagar, Ammapettai, Thiruporur, Chengalpattu, Tamil Nadu-603108, India; Sri Balaji Vidyapeeth (Deemed-to-be University), Pondicherry-607402, India.

Email: sowjanya.vneni@gmail.com

³MD. Ph. D, Professor and HOD, Department of Anatomy, Bhaarith Medical College & Hospital, Bharath Institute of Higher Education & Research, Tamil Nadu, India,

Akafeelhussain@gmail.com

⁴MBBS, MD (Anatomy), Professor and Head, Department of Anatomy, Panimalar medical College Hospital and Research Institute, Chennai, India, Mahimasophia1982@gmail.com

Corresponding Author: Dr. S. Yamona Nidhya, Tutor (Ph.D Part time Internal Scholar), Department of Anatomy, Shri Sathya Sai Medical College and Research Institute (SSSMCRI), SBV Chennai Campus, Sri Balaji Vidyapeeth (Deemed-to-be University), Shri Sathya Sai Nagar, Ammapettai, Thiruporur, Chengalpattu, Tamil Nadu-603108, India; Sri Balaji Vidyapeeth (Deemed-to-be University), Pondicherry-607402, India.

Email: yamonanidhya@gmail.com

HOW TO CITE: ABSTRACT:

S. Yamona Nidhya, Sowjanya
Bandlamudi, A. Kafeel Hussain, M.
Mahima sophia (2026).
Neurobehavioral Effects of Diesel
Exhaust Exposure in Mice: A
Systematic Review.
International Journal of Special
Education, 41(25s), 705 - 727

Background: Diesel exhaust (DE) is a major source of urban fine and ultrafine particulate matter and a classified human carcinogen, yet its effects on the brain and behaviour are far less characterised than its respiratory and cardiovascular effects. Mouse models allow exposure, developmental timing and genotype to be controlled, but the neurobehavioural literature on DE has not been systematically synthesised.

Objectives: To systematically review controlled studies of DE, diesel exhaust particles (DEP) and DE-derived secondary organic aerosol (DE-SOA) in mice that measured at least one neurobehavioural outcome, and to describe exposure paradigms, behavioural domains affected, sex- and window-specific effects, and methodological quality.

Methods: The review followed PRISMA 2020. Studies were identified through structured web searching and citation chasing conducted over a three-month period (May–July 2026), without

bibliographic-database exports. Eligible studies were in vivo experiments in mice comparing diesel exhaust (DE), diesel exhaust particulate (DEP), or diesel exhaust–secondary organic aerosol (DE-SOA) exposure with clean-air or vehicle controls and reporting behavioural endpoints. Studies involving other species, non-diesel particulate matter, single chemical constituents, in vitro systems, and conference abstracts were excluded. Reporting of randomisation and blinding was appraised narratively against SYRCLE domains. Findings were synthesised narratively by behavioural domain, with vote counting by direction of effect.

Results: Twenty-eight studies published between 2008 and 2025 were included: 15 used developmental (prenatal, perinatal or neonatal) exposure and 13 used adult exposure; 22 used whole-body inhalation, 2 parenteral and 2 airway instillation or aspiration (intranasal, oropharyngeal), with route not stated for 2. Where reported, particle concentrations ranged from about 50 $\mu\text{g}/\text{m}^3$ to 19 mg/m^3 . Adverse effects on learning and memory were reported in 14 of 18 studies that tested it, anxiety-like behaviour in 4 of 5, depression-like behaviour in 4 of 4, and social, repetitive or aggressive behaviour in all 4 studies that tested these domains. Locomotor and motor effects were inconsistent in direction. Null or slight findings came mainly from neonatal, acute and resuspended-DEP designs. Roughly two-thirds of studies originated from three research groups, most tested males only (at least 13 of 28), and exposure characterisation and blinding were reported unevenly.

Conclusions: Preclinical evidence supports a neurobehavioural signal for DE exposure, most consistently for hippocampus-dependent cognition, mood-like behaviour and developmental social and repetitive phenotypes. Heterogeneity in exposure type, route and timing, limited female data, clustering within a few laboratories and incomplete reporting limit confidence. Standardised exposure reporting, inclusion of both sexes, blinded and pre-registered designs, and independent replication are priorities.

Keywords: diesel exhaust; diesel exhaust particles; air pollution; neurotoxicity; neurobehaviour; cognition; anxiety; autism; mice.

COPYRIGHT STATEMENT:

Copyright: © 2026 Authors.
Open access publication under the
terms and conditions
of the Creative Commons Attribution
(CC BY)
license (<http://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Diesel engine exhaust is a dominant contributor to the ultrafine fraction of traffic-related air pollution and was classified as carcinogenic to humans (IARC Group 1) in 2012 [1]. Diesel exhaust (DE) is a complex mixture of a carbonaceous particle core carrying polycyclic aromatic hydrocarbons, metals and oxidised

organics, together with gases such as nitrogen oxides and carbon monoxide. Its health burden has traditionally been framed around the lungs and cardiovascular system, but a growing literature links traffic-related air pollution to cognitive decline, depression and neurodevelopmental disorders [2–4].

Several routes could carry DE-related insults to the brain: direct translocation of ultrafine particles along the olfactory nerve, passage across a compromised blood–brain barrier [5], and indirect signalling through lung and systemic inflammation. In mice, subchronic DE inhalation increases microglial activation, cytokine expression and early markers of Alzheimer-type and Parkinson-type pathology in a concentration-dependent manner [6]. Whether such cellular changes translate into measurable behavioural phenotypes, and under which exposure conditions, is less clear.

Mice are the most widely used model for this question because exposure can be tightly controlled, developmental windows can be targeted, and transgenic lines can test susceptibility. However, published mouse studies differ in what they call "diesel exhaust" (whole DE, filtered DE, engine-derived DEP, standard reference DEP, or atmospherically aged DE-SOA), in route (whole-body inhalation versus injection), in age at exposure (gestational, neonatal or adult), and in the behavioural tests used. Single studies report impaired spatial learning, anxiety- and depression-like behaviour, autism-like phenotypes, altered locomotion and increased aggression, while others, particularly those using neonatal or acute exposure, report no behavioural effect [27, 32].

A recent systematic review addressed air pollution in general and internalising outcomes

(anxiety and depression) across animal and human studies [7]. To our knowledge, no systematic review has focused specifically on diesel exhaust and the full range of neurobehavioural outcomes in mice. A diesel-specific synthesis is useful because DE is a regulated, identifiable source, because its composition differs from ambient PM_{2.5}, and because the mouse literature is large enough to ask which behavioural domains and exposure windows are supported.

Objectives. We aimed to (i) identify and describe controlled mouse studies of DE, DEP or DE-SOA that measured neurobehavioural outcomes; (ii) summarise exposure paradigms and test batteries; (iii) synthesise the direction of effect by behavioural domain, developmental window and sex; and (iv) appraise methodological quality and identify gaps for future work.

2. Methods

2.1 Protocol and reporting

The review was designed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [8]. Reporting of the included animal studies was assessed with reference to the ARRIVE 2.0 essential items [10], while the SYRCLE risk-of-bias domains [9] were used to structure the appraisal of methodological quality and reporting.

2.2 Eligibility criteria (PICOS)

Element	Inclusion	Exclusion
Population	Laboratory mice (<i>Mus musculus</i>), any strain, sex or age, including prenatal or neonatal exposure and transgenic models	Rats, other species, humans, in vitro or ex vivo systems only
Exposure	Whole or filtered diesel exhaust, engine-derived or standard-reference DEP, or DE-derived secondary organic aerosol, by inhalation, intranasal, intratracheal or parenteral routes	Ambient or concentrated ambient PM, carbon black, single constituents (for example 1-nitropyrene), non-diesel combustion sources

Element	Inclusion	Exclusion
Comparator	Clean or filtered air, or vehicle control	No concurrent control
Outcomes	At least one behavioural endpoint: cognition (learning, memory), anxiety-like, depression-like, locomotor and motor, social, repetitive, aggressive, sensory or olfactory behaviour. Neurobiological outcomes extracted as secondary data	No behavioural outcome (histology, MRI or molecular endpoints only)
Design	Controlled in vivo experiments published as full peer-reviewed articles in English	Reviews, conference abstracts and proceedings, preprints, commentaries

2.3 Information sources and search strategy

Studies were identified by structured web-based searching and citation chasing up to 6 October 2026. The strategy below, which combines three concept blocks with an animal filter [11], is provided so that the search can be reproduced in PubMed/MEDLINE, Scopus, Web of Science and Embase (Supplementary S1):

("diesel exhaust"[tiab] OR "diesel engine exhaust"[tiab] OR "diesel exhaust particle"[tiab]
OR "diesel particulate"[tiab] OR "diesel emission"[tiab] OR DEP[tiab]

OR "secondary organic aerosol"[tiab])

AND (mice[tiab] OR mouse[tiab] OR murine[tiab] OR "Mice"[MeSH])

AND (behavio*[tiab] OR neurobehavio*[tiab] OR cognit*[tiab] OR memory[tiab] OR learning[tiab]

OR anxiety[tiab] OR depress*[tiab] OR locomotor[tiab] OR "open field"[tiab]

OR "water maze"[tiab] OR "elevated plus maze"[tiab] OR social[tiab] OR autis*[tiab]

OR "forced swim"[tiab] OR "tail suspension"[tiab] OR rotarod[tiab] OR aggress*[tiab])

Equivalent search strings for Scopus, Web of Science, and Embase are provided in Supplementary S1. Reference lists of included

studies and relevant reviews were hand-searched. The study set was assembled through targeted web-based searches and citation chasing over a three-month period from May to July 2026. Twenty topic-specific queries were used, covering anxiety and depression, learning and memory, prenatal and developmental exposure, social and autism-like behaviour, neurodegeneration models, adult and aged exposure, intranasal and intratracheal DEP exposure, and recent reports published during 2023–2026. No bibliographic-database exports were used, and this was acknowledged as a methodological limitation in Section 4.5.

2.4 Selection and data extraction

Reports were screened against the PICOS criteria by a single reviewer, using titles, abstracts and, where openly accessible, full texts; no independent second reviewer was involved. Extracted items were: study identifiers; strain, sex, age and group size; exposure agent, generation system, route, concentration, daily duration, schedule and developmental window; control condition; behavioural tests and outcomes; direction and significance of effect; and secondary neurobiological findings. Where several exposure groups existed, the DE or DEP group closest to environmental relevance and its matched control were used for direction-of-effect coding.

2.5 Risk of bias

The ten SYRCLE domains were considered: sequence generation, baseline characteristics, allocation concealment, random housing, blinding of caregivers, random outcome assessment, blinding of outcome assessors, incomplete outcome data, selective outcome reporting and other sources of bias. Because full texts were openly accessible for only a minority of studies, formal domain-by-domain scoring was not completed; reporting of randomisation, blinding and unit of analysis is described narratively (section 3.6), and a scoring template is provided in Supplementary S4.

2.6 Synthesis

Because tests, endpoints, exposures and reporting differed widely, results were

synthesised narratively by behavioural domain. For each domain we counted studies reporting an adverse effect of exposure on the primary task and studies reporting no effect. No quantitative meta-analysis was undertaken, because group means, variances and sample sizes could not be extracted consistently across studies, and small-study effects could not be assessed. Vote counting ignores effect size and precision and is presented descriptively.

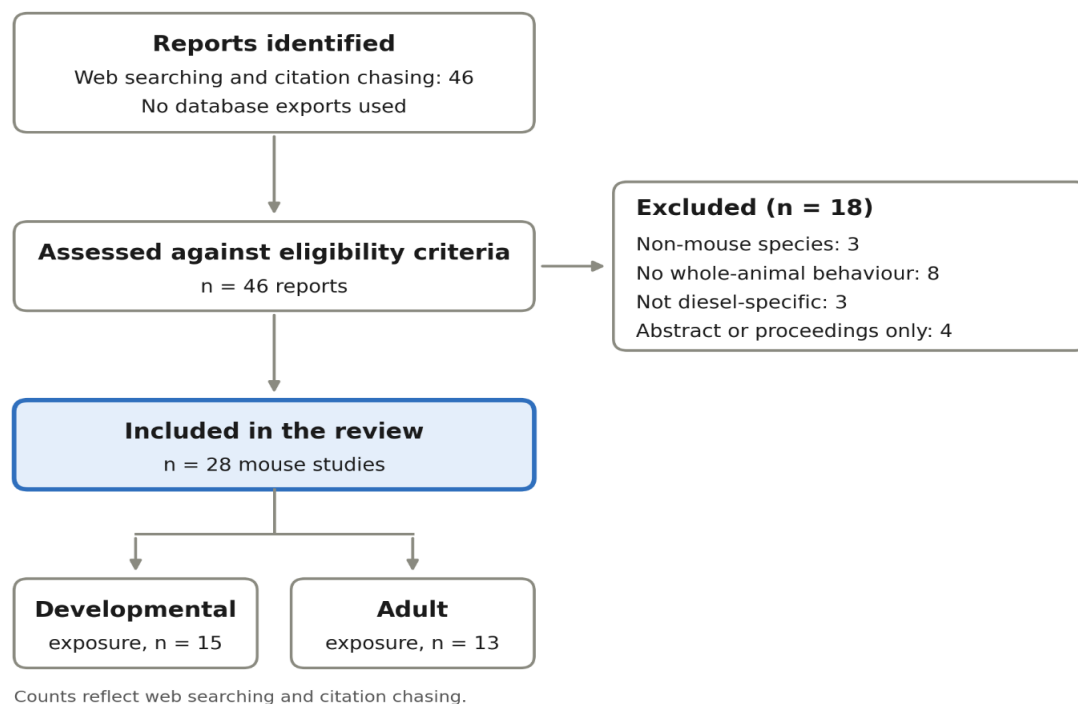
3. Results

3.1 Study selection

Forty-six unique reports were assessed against the eligibility criteria; 28 were included and 18 excluded (Table 1). No bibliographic-database totals are reported because database exports were not used.

Table 1. Study selection (PRISMA flow).

Stage	Reports (n)	Reason
Unique reports assessed for eligibility	46	
Excluded: non-mouse species	3	Rat studies (2021, 2023); Drosophila study (2025)
Excluded: no whole-animal behaviour	8	In vitro microglia preprint; histology- or gene-expression-only studies [6]; MRI and single-cell preprints
Excluded: not diesel-specific	3	Single constituent (1-nitropyrene); ultrafine carbon particles; prenatal urban air nanoparticles
Excluded: abstract or proceedings only	4	Three conference abstracts; one proceedings paper
Included	28	

Figure 1. Flow of studies through the review (PRISMA 2020 format)**Figure 1. Flow of studies through the review (PRISMA 2020 format).**

Reports were identified by structured web searching and citation chasing; no bibliographic-database exports were used.

3.2 Characteristics of included studies

Included studies were published between 2008 and 2025. Fifteen used developmental exposure (gestation, lactation or neonatal period) and thirteen used adult exposure. Twenty-two used whole-body inhalation in an exposure chamber or cage-rack system, two administered DEP parenterally to pregnant dams (subcutaneous or intravenous) [18, 31], two used airway instillation

or aspiration in adult mice (intranasal [35], oropharyngeal [32]), and two did not state the route in the accessible sources [17, 39]. Where particle mass was reported, concentrations spanned roughly 50 $\mu\text{g}/\text{m}^3$ to 19 mg/m^3 , with most chamber studies at 100 to 1,000 $\mu\text{g}/\text{m}^3$. At least 13 studies tested males only, three tested females only [15, 22, 38], and three tested both sexes [23, 24, 28]. Studies clustered within a few groups: an Iranian group (about six studies), a Japanese group at the National Institute for Environmental Studies (seven) and a group at Tokyo University of Science (five).

Table 2. Characteristics and behavioural findings of included studies.

Ref	Model	Exposure	Behavioural endpoints	Main behavioural finding
[12] Hougaard 2008	C57BL/6 BomTac, prenatal	Resuspended NIST 2975 DEP, 19 mg/m^3 , 1	Activity, learning, memory	Only slight, non-significant tendencies in female offspring (faster platform finding, more open-field activity); most outcomes similar to controls;

Ref	Model	Exposure	Behavioural endpoints	Main behavioural finding
		h/day, GD 9–19, inhalation		reduced weight gain during lactation
[13] Win-Shwe 2008	Male BALB/c, adult	Nanoparticle-rich DE (≈ 149 vs ≈ 4.6 $\mu\text{g}/\text{m}^3$ clean air), inhalation, $\pm$ LTA	Morris water maze	Longer latency only with DE plus LTA; DE alone no effect
[14] Suzuki 2010	Male offspring, prenatal	DE at 0.171 mg DEP/ m^3 , maternal inhalation, 8 h/day; offspring tested at 4 weeks	Spontaneous locomotor activity	Reduced activity; altered monoamines
[15] Win-Shwe 2012	Female BALB/c, adult	Mid- or high-dose nanoparticle-rich DE, or filtered DE, 3 months	Morris water maze	High dose: longer latency to platform
[16] Yokota 2013	Male offspring, prenatal	Maternal DE inhalation	Rotarod, cliff avoidance	Reduced rotarod time; more falls and corner time
[17] Thirtamara Rajamani 2013	Adult male offspring	High-level DEP in pregnancy and nursing	Locomotion, three-chamber social test, grooming, rearing	More locomotion, grooming and rearing; sociability and novelty preference normal
[18] Yokota 2015	Male offspring ICR	DEP 200 $\mu\text{g}/\text{kg}$ s.c. to dams, GD 6, 9, 12, 15, 18	Water maze, passive avoidance	Water maze deficits; passive avoidance unchanged; lower hippocampal NR2A
[19] Win-Shwe 2015	BALB/c pups, PND 11	DE or DE-SOA, GD 14–PND 10, chamber	Olfactory-based spatial learning	Longer time to target with DE and DE-SOA
[20] Win-Shwe 2016	BALB/c, tested adult	Clean air, DE, DE-SOA or gas only, GD 14–PND 21	Sociability, social novelty	Impaired social behaviour in males; altered hypothalamic genes
[21] Aggression study 2016	Male offspring, prenatal	Low-dose maternal DE	Resident–intruder test, locomotion	More territorial aggression; locomotion unchanged

Ref	Model	Exposure	Behavioural endpoints	Main behavioural finding
[22] Hullmann 2017	Female 5XFAD and wild-type	Diluted DE 0.95 mg/m ³ , 6 h/day, 5 days/week, 3 or 13 weeks	String suspension (grip, coordination)	Poorer motor performance in 13-week 5XFAD mice; plaque acceleration not sustained at 13 weeks
[23] Nway 2017	Neonatal C3H/HeN and C3H/HeJ (TLR4-mutated) mice, both sexes	DE or DE-SOA, GD 14–PND 10, 5 h/day for 5 days, chamber	Olfactory-based spatial learning	Poorer test-phase performance after DE and DE-SOA, more marked in TLR4-mutated mice
[24] Chang 2018	C57BL/6J, both sexes	DE 250–300 µg/m ³ , 6 h/day, 5 days/week, E0– PND 21	Open field, three-chamber, reciprocal interaction, USV, olfactory habituation, T- maze, marble burying	Deficits across social, communication and repetitive domains, partly sex-specific; open field unchanged
[25] Ehsanifar 2019 (adult)	Male NMRI, n = 48	Nanoscale DEP (<200 nm), locked whole-body system, 3, 6 or 8 h/day, 5 days/week, 12 weeks; n = 12 per group	Physical ability, anxiety and depression tests	Worse performance; more oxidative stress and inflammation in olfactory bulb and hippocampus
[26] Ehsanifar 2019 (prenatal)	Male NMRI offspring	350–400 µg DEP/m ³ , 2, 4 or 6 h/day to dams	Elevated plus maze, water maze	Deficits on both; lower NR2A and NR3B
[27] Morris- Schaffer 2019	C57BL/6J pups	Aerosolised SRM 1650b, 4 h/day, PND 4–7 and 10– 13	Fixed-interval temporal control learning	No protracted behavioural deficit; transient GFAP rise
[28] Ehsanifar 2020 (male and female)	Male and female mice	DEP 350–400 µg/m ³ , 6 h/day, 5 days/week, 8 weeks, closed chamber	Anxiety and depression tests	More anxiety- and depression- like behaviour; sex modulation proposed

Ref	Model	Exposure	Behavioural endpoints	Main behavioural finding
[29] Ehsanifar 2021	Male mice	DEP 2, 5 or 7 h/day, 12 weeks	Water maze, elevated plus maze	Impaired acquisition and retention; more hippocampal inflammation
[30] Ehsanifar 2023	Male mice	DEP for 6 or 12 weeks	Depressive-like tests, water maze	More depressive-like behaviour; impaired spatial learning; more hippocampal microglia
[31] Yu 2024	Male C57BL/6 offspring	DEP i.v. to dams every other day, 10 injections	Water maze	Longer latency, fewer platform crossings; NMDAR/PKA/CREB and CPEB3 signalling implicated
[32] Chuang 2025	Adult female C57BL/6NCrl mice	SRM 1650b DEP, 50 µg/mouse by oropharyngeal aspiration, twice weekly for 3 weeks; tested at weeks 4 and 15	Passive avoidance, water maze	No group differences in either phase; acute rise in lipid peroxidation (cerebellum, hippocampus) and cortical Tau/p-Tau

Table 2 (continued). Studies added in the second search round.

Ref	Model	Exposure	Behavioural endpoints	Main behavioural finding
[33] Yokota 2009	Mice, prenatal	Prenatal DE, 1.0 mg DEP/m ³	Spontaneous locomotor activity	Reduced locomotor activity; lower striatal dopamine turnover
[34] Win-Shwe 2014	Male BALB/c, adult	Clean air, DE or DE-SOA, 5 h/day, 5 days/week, 1 or 3 months	Novel object recognition; maternal behaviour in females (1 month)	Impaired object recognition and altered hippocampal NMDA receptor expression in DE-SOA males
[35] NLRP3 study	Male C57BL/6 and Nlrp3-knockout, adult	Intranasal DEP instillation	Hippocampus-dependent learning and memory	Impaired learning and memory; knockout mice resistant; taurine rescued deficits
[36] Liu 2024	Mice, adult (sex not stated in)	Inhaled DEPM at several doses	Open field, novel object recognition, Y-maze	Dose-related hyperactivity; trend toward memory

Ref	Model	Exposure	Behavioural endpoints	Main behavioural finding
	accessible sources)			decline; Purkinje cell, BDNF and fecal SCFA changes
[37] Garrick 2023	Mice exposed perinatally, tested at 6 and 20 months	DE 250–300 $\mu\text{g}/\text{m}^3$, E0–PND 21	T-maze alternation, object recognition	Modest reduction in T-maze alternation; no object-recognition effect; oxidative stress; effects less marked than in younger animals

Table 2 (continued, second round). Two further studies identified while verifying references.

Ref	Model	Exposure	Behavioural endpoints	Main behavioural finding
[38] Win-Shwe 2012 (object recognition)	Female BALB/c, adult	Clean air, mid-dose nanoparticle-rich DE (47 $\mu\text{g}/\text{m}^3$), high-dose (129 $\mu\text{g}/\text{m}^3$) or filtered high-dose DE, 3 months	Novel object recognition	High-dose and filtered DE groups could not discriminate novel from familiar objects; altered glutamate-related hippocampal genes
[39] Ehsanifar 2022	Mice, adult (sex not stated in accessible sources)	DEP (route not stated in accessible sources)	Spatial learning and memory, depressive-like tests	Impaired spatial learning and memory; depressive-like responses; hippocampal inflammation

3.3 Exposure paradigms

Whole DE from engines, standard-reference DEP (NIST SRM 1650b and 2975), nanoparticle-rich DE with gases retained or filtered, and DE-SOA formed by ozone ageing were all used. Studies differed in whether gases co-occurred with particles. Only the Win-Shwe group included filtered or gas-only atmospheres [15, 20], and few studies characterised particle size or gas composition in the exposure atmosphere (Chang et al. is a detailed example [24]). Two studies delivered DEP by injection to dams, so fetal exposure reflects systemic DEP rather than inhaled exhaust [18, 31]. Reported daily exposure ranged from about 2 to 8 h in chamber studies; adult exposure windows ranged from 3 to 13 weeks, and developmental windows spanned E0

to PND 21 or shorter gestational or neonatal periods.

3.4 Behavioural outcomes by domain

Spatial learning and memory. Eighteen studies tested a learning or memory task. Fourteen reported impairment on at least one task: water maze deficits in adult males [29, 30], adult females [15], prenatally exposed male offspring [18, 26, 31], and olfactory-based spatial learning deficits in preweaning pups [19]. Novel object recognition was impaired after DE-SOA exposure in adult males [34]; intranasal DEP impaired hippocampus-dependent learning and memory, and this depended on microglial NLRP3 [35]; inhaled DEPM produced dose-related hyperactivity with a trend toward memory

decline [36]; and perinatal DE modestly reduced T-maze spontaneous alternation in aged mice without affecting object recognition [37]. Novel object recognition was also impaired in adult females after high-dose nanoparticle-rich or filtered DE [38]; neonatal mice of both TLR4-intact and TLR4-mutated strains performed worse in an olfactory-based spatial learning test after DE or DE-SOA, more markedly in the TLR4-mutated strain [23]; and spatial learning deficits were reported after DEP exposure in a further study from the Iranian group [39]. Four found no effect, or only slight effects: adult males exposed to DE without a co-stressor [13], neonatally exposed mice tested on temporal control learning [27], acute plus recovery exposure [32], and prenatal inhalation of resuspended DEP, where only slight effects appeared in female offspring [12]. Passive avoidance was unaffected where measured [18, 32]. Hippocampal NMDA receptor subunit changes (NR2A, NR2B, NR3B) and cytokine changes accompanied behavioural impairment in several studies [13, 15, 18, 19, 26].

Anxiety-like behaviour. Four of five studies reported increased anxiety-like behaviour, all from the Iranian group using the elevated plus maze and related tests [25, 26, 28, 29]. The one developmental study with an open-field readout

found no difference in thigmotaxis or locomotion [24].

Depression-like behaviour. All four studies that tested depression-like behaviour reported more immobility-type responses after DEP exposure [25, 28, 30, 39]; all are from the same group, and neurobiological correlates included hippocampal and olfactory bulb inflammation and oxidative stress.

Social, repetitive and aggressive behaviour. All four studies in this domain reported an adverse effect. Developmental DE produced reduced social interaction, altered ultrasonic vocalisations, failure to habituate to social odours and increased repetitive behaviour in both sexes [24]; DE-SOA impaired social behaviour in adult male offspring [20]; high-level DEP increased repetitive behaviour but spared sociability [17]; and prenatal DE increased territorial aggression [21].

Locomotor and motor function. Results were inconsistent in direction: prenatal DE reduced spontaneous locomotion [14, 33] and rotarod performance [16], high-level developmental DEP and inhaled DEPM in adults increased locomotion [17, 36], and 13-week exposure worsened motor performance in 5XFAD mice [22]. Four studies found no change in locomotion [12, 21, 24, 27].

Table 3. Vote counting of behavioural findings by domain.

Domain	Studies testing (n)	Adverse effect reported (n)	No effect (n)	Notes
Spatial learning and memory	18	14	4	Nulls in neonatal, acute and DE-alone designs
Anxiety-like behaviour	5	4	1	Positives from one group
Depression-like behaviour	4	4	0	All one group
Social, repetitive, aggressive	4	4	0	Sex-specific patterns [24]; sociability spared in [17]

Domain	Studies testing (n)	Adverse effect reported (n)	No effect (n)	Notes
Locomotor and motor	10	6	4	Direction mixed (reduced and increased)

Study [12] is counted as no effect because only slight cognitive effects appeared, in female offspring. Studies can contribute to more than one domain. Study [36] is counted as adverse on the basis of a trend toward memory decline, and [37] for reduced T-maze alternation despite no object-recognition effect.

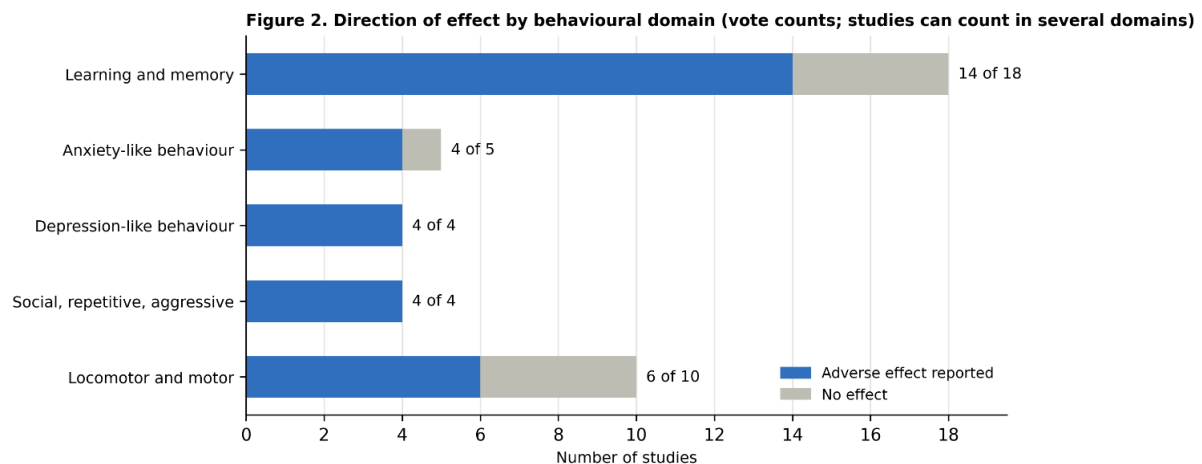


Figure 2. Direction of effect by behavioural domain. Locomotor and motor results were the least consistent (6 adverse, 4 no effect) and also differed in direction (reduced activity in some studies, increased in others).

Table 4. Evidence map: direction of effect by study and behavioural domain. Adv = adverse effect reported; Nil = no effect; – = not tested (all results extracted). D = developmental exposure, A = adult exposure.

Ref	Study	Stage	Learning and memory	Anxiety-like	Depression-like	Social, repetitive, aggressive	Locomotor and motor
[12]	Hougaard 2008	D	Nil	–	–	–	Nil
[13]	Win-Shwe 2008	A	Nil*	–	–	–	–
[14]	Suzuki 2010	D	–	–	–	–	Adv
[15]	Win-Shwe 2012	A	Adv	–	–	–	–
[16]	Yokota 2013	D	–	–	–	–	Adv

Ref	Study	Stage	Learning and memory	Anxiety-like	Depression-like	Social, repetitive, aggressive	Locomotor and motor
[17]	Thirtamara Rajamani 2013	D	–	–	–	Adv†	Adv
[18]	Yokota 2015	D	Adv	–	–	–	–
[19]	Win-Shwe 2015	D	Adv	–	–	–	–
[20]	Win-Shwe 2016	D	–	–	–	Adv	–
[21]	Aggression study 2016	D	–	–	–	Adv	Nil
[22]	Hullmann 2017	A	–	–	–	–	Adv
[23]	Nway 2017	D	Adv	–	–	–	–
[24]	Chang 2018	D	–	Nil	–	Adv	Nil
[25]	Ehsanifar 2019 (adult)	A	–	Adv	Adv	–	–
[26]	Ehsanifar 2019 (prenatal)	D	Adv	Adv	–	–	–
[27]	Morris-Schaffer 2019	D	Nil	–	–	–	Nil
[28]	Ehsanifar 2020 (male, female)	A	–	Adv	Adv	–	–
[29]	Ehsanifar 2021	A	Adv	Adv	–	–	–
[30]	Ehsanifar 2023	A	Adv	–	Adv	–	–
[31]	Yu 2024	D	Adv	–	–	–	–
[32]	Chuang 2025	A	Nil	–	–	–	–
[33]	Yokota 2009	D	–	–	–	–	Adv

Ref	Study	Stage	Learning and memory	Anxiety-like	Depression-like	Social, repetitive, aggressive	Locomotor and motor
[34]	Win-Shwe 2014	A	Adv	–	–	–	–
[35]	NLRP3 study	A	Adv	–	–	–	–
[36]	Liu 2024	A	Adv‡	–	–	–	Adv
[37]	Garrick 2023	D	Adv§	–	–	–	–

* DE alone had no effect; impairment appeared only with an inflammatory co-stressor. † Repetitive behaviour increased; sociability preserved. ‡ Trend toward memory decline. § T-maze alternation reduced; object recognition unaffected.

Table 4 (continued).

Ref	Study	Stage	Learning and memory	Anxiety-like	Depression-like	Social, repetitive, aggressive	Locomotor and motor
[38]	Win-Shwe 2012 (object recognition)	A	Adv	–	–	–	–
[39]	Ehsanifar 2022	A	Adv	–	Adv	–	–

Table 5. Neurobiological correlates reported alongside behaviour.

Pathway	Findings in exposed mice	Refs
Glutamatergic signalling	Altered hippocampal NMDA receptor subunits (NR1, NR2A, NR2B, NR3B); NMDAR/PKA/CREB and CPEB3 signalling after prenatal DEP	[13, 15, 18, 19, 26, 31, 34, 38]
Neuroinflammation and glia	Higher hippocampal and olfactory bulb cytokines and microglial markers; NLRP3 inflammasome required for learning impairment	[13, 19, 25, 29, 30, 35]
Oxidative stress	Higher oxidative stress markers in olfactory bulb and hippocampus	[25]
Neurotrophic and barrier genes	Higher hippocampal BDNF mRNA in exposed females; lower BDNF and blood–brain barrier gene expression after DEPM inhalation	[15, 36]

Pathway	Findings in exposed mice	Refs
Monoamines	Altered dopamine, noradrenaline and serotonin turnover in several regions	[14, 16, 33]
Innate immune receptors and social circuitry	TLR4 involvement in neonatal DE-SOA effects; altered hypothalamic social-behaviour genes	[20, 23]
Neurodegeneration	Accelerated amyloid plaque formation in 5XFAD mice, not sustained at 13 weeks	[22]
Cerebellum and gut	Purkinje cell disruption, reduced frontal cortex neurotransmitters, higher fecal short-chain fatty acids	[36]

Table 6. Summary of findings by domain (author judgement; not a formal GRADE rating).

Domain	Studies (n)	Pattern	Independent groups (approx.)	Main concerns	Confidence
Learning and memory	18	14 adverse, 4 no effect	10	Heterogeneous tests and exposures; nulls in neonatal, acute and DE-alone designs; incomplete blinding reports	Low to moderate
Anxiety-like behaviour	5	4 adverse, 1 no effect	2 (adverse findings from 1)	Positive results from a single group; few tests	Low
Depression-like behaviour	4	4 adverse	1	Single group; immobility-type tests only	Low
Social, repetitive, aggressive	4	4 adverse (one partial)	4	Mostly developmental exposure; sex-specific patterns; small samples	Low to moderate
Locomotor and motor	10	6 adverse, 4 no effect; direction mixed	6	Inconsistent direction; different tests and ages	Very low

3.5 Sex and developmental window

Few studies reported sex-specific analyses; the clearest examples are [24] and [28]. In the most detailed of these, social novelty preference was lost in exposed females whereas reduced reciprocal sniffing and fewer ultrasonic calls were clearer in males [24]. Developmental exposure

produced behavioural effects in 13 of the 15 developmental studies (modest in [37]); the exceptions were a neonatal inhalation study of standard-reference DEP given over eight exposure days [27] and a prenatal study of resuspended DEP with only slight effects in female offspring [12]. The other null result came from an acute adult design [32].

3.6 Risk of bias

Formal SYRCLE scoring was not completed (section 2.5). From the full texts that could be read, randomisation of litters and blinded scoring of behaviour are explicitly reported in some studies [24] but are not consistently described across the set, so these domains would be judged "unclear" for most studies. In developmental studies the dam or litter is the unit of exposure; whether litter or pup was the unit of analysis was not consistently reported.

4. Discussion

4.1 Principal findings

Across 28 mouse studies, DE, DEP and DE-SOA exposure was most often followed by impaired spatial learning and memory, anxiety- and depression-like behaviour, and altered social, repetitive or aggressive behaviour. Developmental exposure produced behavioural effects in nearly every developmental study with extracted results [14, 16–21, 23, 24, 26, 31, 33, 37], whereas the null findings came from a prenatal study of resuspended DEP with only slight effects in female offspring [12], a neonatal inhalation study of standard-reference DEP [27], an acute adult design [32], and an adult design in which DE alone did not impair learning unless combined with an inflammatory co-stressor [13]. Motor and locomotor outcomes pointed in different directions, with reduced activity after low-level prenatal DE [14] but increased activity after high-level developmental DEP [17] and adult DEPM inhalation [36], which argues against a single "hypo-" or "hyperactivity" phenotype.

4.2 Possible mechanisms

The neurobiological endpoints collected alongside behaviour converge on a few pathways. First, hippocampal glutamatergic signalling: changes in NMDA receptor subunit expression accompanied learning deficits in adult, female and developmentally exposed mice [13, 15, 18, 19, 26], and a recent study implicated NMDAR/PKA/CREB and CPEB3 signalling in prenatal DEP effects [31]. Hippocampal brain-derived neurotrophic factor expression was also altered in DE-exposed females [15]. Second,

neuroinflammation and oxidative stress, including raised hippocampal and olfactory bulb inflammatory markers and microglial activation [25, 29, 30], including NLRP3 inflammasome activation that was required for DEP-induced learning impairment in knockout mice [35], consistent with the dose-dependent neuroinflammatory and early neurodegenerative changes seen after subchronic DE inhalation [6]. Third, innate immune signalling: a role for TLR4 was described in DE-SOA effects in neonatal mice [23], and Chang et al. proposed overlap with maternal immune activation pathways [24]. Fourth, monoaminergic and endocrine changes were reported after prenatal DE [14, 16, 21]. These mechanisms are mostly correlative; few studies used genetic or pharmacological manipulation to test necessity.

4.3 Why results differ between studies

Exposure type. Whole DE, filtered DE, standard-reference DEP and DE-SOA differ in particle size, organic carbon content and gas fraction. Only a minority of studies separated particle from gas effects [15, 20]. Because nitrogen oxides and other gases co-occur with particles in whole DE, attributing effects to the particulate fraction remains an assumption [24].

Route and dose. Two studies delivered DEP to dams by injection [18, 31] and two instilled or aspirated DEP into the airways of adults [32, 35]. Subcutaneous or intravenous DEP bypasses the nasal and pulmonary routes by which inhaled ultrafine particles reach the brain, so these findings speak to fetal susceptibility to systemic DEP rather than to inhaled exhaust. Exposure concentrations (roughly 50 µg/m³ to 19 mg/m³ where reported; the highest, resuspended DEP at 19 mg/m³ for 1 h/day, produced only slight cognitive effects [12]) exceed typical ambient levels in most settings, although they approximate peak levels in some highly polluted cities [24].

Timing. Exposure windows ranged from a few postnatal days to 13 weeks in adults to E0–PND 21. The one neonatal inhalation study with null behavioural findings used eight exposure days [27], suggesting that duration and window, not

only dose, matter; this cannot be resolved without dose–duration–window comparisons within the same laboratory. Follow-up of perinatally exposed mice to 20 months found only modest deficits, suggesting that some early effects attenuate with age [37].

Sex, strain and co-stressors. Strains (BALB/c, NMRI, ICR, C57BL/6J, 5XFAD) differ in baseline anxiety and learning. Sex-specific effects were seen where both sexes were tested [24], yet most studies used males only. In a transgenic Alzheimer model, DE accelerated plaque formation early without a sustained difference at 13 weeks [22], and an inflammatory co-stressor was required for learning impairment in one study [13], indicating that baseline susceptibility modifies outcomes.

Research-group clustering and reporting. Roughly two-thirds of included studies came from three groups, so the apparent consistency of positive findings partly reflects shared protocols, equipment and exposure systems rather than independent replication. All anxiety- and depression-like findings originated from a single group, and independent confirmation is lacking. Negative results appear less often than positive ones, and publication bias cannot be excluded.

4.4 Interpretation and translational relevance

Behavioural labels such as "autism-like" or "depression-like" describe performance on specific mouse tests rather than diagnoses. Findings are strongest where the same construct is supported by more than one test, as in the three-domain autism-related battery in [24], and weakest where conclusions rest on one test, such as immobility or a single maze. The developmental findings align with epidemiological associations between traffic-related air pollution and autism risk [4], but mouse–human extrapolation of exposure window, dose and outcome is uncertain.

4.5 Strengths and limitations

Strengths include a diesel-specific scope, coverage of both adult and developmental exposure, and explicit extraction of exposure

type, route and window. Limitations include: (i) the study set was assembled by web-based searching and citation chasing without bibliographic-database exports, so eligible studies are likely to have been missed; (ii) screening and extraction were done by a single reviewer with AI assistance and without independent verification, and some details could not be confirmed from accessible sources; (iii) vote counting disregards effect size and precision, and no pooled estimates were possible; (iv) formal risk-of-bias scoring was not completed and reporting was often incomplete; (v) English-only inclusion; and (vi) the small number of independent groups limits generalisability.

4.6 Recommendations for future research

Report exposure fully: particle mass, number and size distribution, PAH and organic carbon content, gas concentrations, generation system, daily duration and chamber conditions.

Include both sexes and analyse sex as a factor; use the litter as the unit of analysis in developmental designs.

Randomise, conceal allocation and blind outcome assessment; pre-register protocols and report ARRIVE 2.0 items.

Separate particle, gas and combined effects with filtered and gas-only arms, and run dose–duration–window designs in the same laboratory.

Use test batteries that probe each construct with more than one assay, and report effect sizes with confidence intervals and raw data.

Pursue independent replication of the anxiety- and depression-like findings, and test mechanisms with intervention studies.

5. Conclusions

Mouse studies provide consistent but not independently replicated evidence that diesel exhaust exposure can impair hippocampus-dependent cognition and alter mood-like, social, repetitive and motor behaviour, with developmental exposure the most reliably affected window. Confidence is limited by heterogeneous exposure paradigms, limited testing of females, clustering within a few

laboratories, incomplete reporting of randomisation and blinding, and a small number of null studies that point to roles for exposure duration, window and route. Standardised exposure reporting, sex-balanced and blinded designs, particle-versus-gas comparisons, and independent replication are needed before these findings can inform human risk assessment.

Declarations

Funding: This review received no external funding.

Competing interests: None declared.

Author contributions (CRediT): Conceptualization, methodology, investigation, literature search, data curation, formal analysis, risk-of-bias assessment, visualization, writing—original draft, writing—review and editing, and project administration were undertaken by the

author(s). Study selection and methodological appraisal were performed using predefined eligibility criteria and the SYRCLE risk-of-bias domains. Data were organised using spreadsheet-based tools, and the review was reported according to PRISMA 2020. The author(s) approved the final manuscript and accept responsibility for the accuracy, integrity, and transparency of the work.

Data availability: All data supporting this review (search strategies, screening log, data-extraction sheet, risk-of-bias worksheet, excluded-studies list and PRISMA 2020 checklist) are provided in the Supplementary Data workbook accompanying this article. No new primary data were generated.

Ethics: Not applicable; this review used published data only.

References

- Benbrahim-Tallaa L, Baan RA, Grosse Y, et al. Carcinogenicity of diesel-engine and gasoline-engine exhausts and some nitroarenes. *Lancet Oncol.* 2012;13:663–664.
- Block ML, Calderón-Garcidueñas L. Air pollution: mechanisms of neuroinflammation and CNS disease. *Trends Neurosci.* 2009;32:506–516.
- Costa LG, Cole TB, Coburn J, Chang Y-C, Dao K, Roqué PJ. Neurotoxicity of traffic-related air pollution. *Neurotoxicology.* 2017;59:133–139.
- Volk HE, Lurmann F, Penfold B, Hertz-Picciotto I, McConnell R. Traffic-related air pollution, particulate matter, and autism. *JAMA Psychiatry.* 2013;70:71–77.
- Hartz AMS, Bauer B, Block ML, Hong J-S, Miller DS. Diesel exhaust particles induce oxidative stress, proinflammatory signaling, and P-glycoprotein up-regulation at the blood–brain barrier. *FASEB J.* 2008;22:2723–2733.
- Levesque S, Surace MJ, McDonald J, Block ML. Air pollution & the brain: subchronic diesel exhaust exposure causes neuroinflammation and elevates early markers of neurodegenerative disease. *J Neuroinflammation.* 2011;8:105.
- Zundel CG, Ryan P, Brokamp C, Heeter A, Huang Y, Strawn JR, Marusak HA. Air pollution, depressive and anxiety disorders, and brain effects: a systematic review. *Neurotoxicology.* 2022;93:272–300.
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71.
- Hooijmans CR, Rovers MM, de Vries RBM, Leenaars M, Ritskes-Hoitinga M, Langendam MW. SYRCLE's risk of bias tool for animal studies. *BMC Med Res Methodol.* 2014;14:43.
- Percie du Sert N, Hurst V, Ahluwalia A, et al. The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. *PLoS Biol.* 2020;18:e3000410.
- Hooijmans CR, Tillema A, Leenaars M, Ritskes-Hoitinga M. Enhancing search efficiency by means of a search filter for finding all studies on animal experimentation in PubMed. *Lab Anim.* 2010;44:170–175.
- Hougaard KS, Jensen KA, Nordly P, et al. Effects of prenatal exposure to diesel exhaust particles on postnatal development, behavior, genotoxicity and inflammation in mice. *Part Fibre Toxicol.* 2008;5:3.

- Win-Shwe T-T, Yamamoto S, Fujitani Y, Hirano S, Fujimaki H. Spatial learning and memory function-related gene expression in the hippocampus of mouse exposed to nanoparticle-rich diesel exhaust. *Neurotoxicology*. 2008;29:940–947.
- Suzuki T, Oshio S, Iwata M, et al. In utero exposure to a low concentration of diesel exhaust affects spontaneous locomotor activity and monoaminergic system in male mice. *Part Fibre Toxicol*. 2010;7:7.
- Win-Shwe T-T, Yamamoto S, Fujitani Y, Hirano S, Fujimaki H. Nanoparticle-rich diesel exhaust affects hippocampal-dependent spatial learning and NMDA receptor subunit expression in female mice. *Nanotoxicology*. 2012;6:543–553.
- Yokota S, Moriya N, Iwata M, Umezawa M, Oshio S, Takeda K. Exposure to diesel exhaust during fetal period affects behavior and neurotransmitters in male offspring mice. *J Toxicol Sci*. 2013;38:13–23.
- Thirtamara Rajamani K, Doherty-Lyons S, Bolden C, et al. Prenatal and early-life exposure to high-level diesel exhaust particles leads to increased locomotor activity and repetitive behaviors in mice. *Autism Res*. 2013;6:248–257.
- Yokota S, Sato A, Umezawa M, Oshio S, Takeda K. In utero exposure of mice to diesel exhaust particles affects spatial learning and memory with reduced N-methyl-D-aspartate receptor expression in the hippocampus of male offspring. *Neurotoxicology*. 2015;50:108–115.
- Win-Shwe T-T, Kyi-Tha-Thu C, Moe Y, Maekawa F, Yanagisawa R, Furuyama A, Tsukahara S, Fujitani Y, Hirano S. Nano-sized secondary organic aerosol of diesel engine exhaust origin impairs olfactory-based spatial learning performance in preweaning mice. *Nanomaterials*. 2015;5(3):1147–1162.
- Win-Shwe T-T, Kyi-Tha-Thu C, Moe Y, Fujitani Y, Tsukahara S, Hirano S. Exposure of BALB/c mice to diesel engine exhaust origin secondary organic aerosol (DE-SOA) during the developmental stages impairs the social behavior in adult life of the males. *Front Neurosci*. 2016;9:524.
- Yokota S, Oshio S, Moriya N, Takeda K. Social isolation-induced territorial aggression in male offspring is enhanced by exposure to diesel exhaust during pregnancy. *PLoS One*. 2016;11:e0149737.
- Hullmann M, Albrecht C, van Berlo D, et al. Diesel engine exhaust accelerates plaque formation in a mouse model of Alzheimer's disease. *Part Fibre Toxicol*. 2017;14:35.
- Nway NC, Fujitani Y, Hirano S, Mar O, Win-Shwe T-T. Role of TLR4 in olfactory-based spatial learning activity of neonatal mice after developmental exposure to diesel exhaust origin secondary organic aerosol. *Neurotoxicology*. 2017;63:155–165.
- Chang Y-C, Cole TB, Costa LG. Prenatal and early-life diesel exhaust exposure causes autism-like behavioral changes in mice. *Part Fibre Toxicol*. 2018;15:18.
- Ehsanifar M, Tameh AA, Farzadkia M, Kalantari RR, Zavareh MS, Nikzaad H, Jafari AJ. Exposure to nanoscale diesel exhaust particles: oxidative stress, neuroinflammation, anxiety and depression on adult male mice. *Ecotoxicol Environ Saf*. 2019;168:338–347.
- Ehsanifar M, Jafari AJ, Nikzad H, Zavareh MS, Atlasi MA, Mohammadi H, Tameh AA. Prenatal exposure to diesel exhaust particles causes anxiety, spatial memory disorders with alters expression of hippocampal pro-inflammatory cytokines and NMDA receptor subunits in adult male mice offspring. *Ecotoxicol Environ Saf*. 2019;176:34–41.
- Morris-Schaffer K, Merrill AK, Wong C, Jew K, Sobolewski M, Cory-Slechta DA. Limited developmental neurotoxicity from neonatal inhalation exposure to diesel exhaust particles in C57BL/6 mice. *Part Fibre Toxicol*. 2019;16:1.
- Ehsanifar M, Yavari Z, Karimian M, Behdarvandi M. Anxiety and depression following diesel exhaust nano-particles exposure in male and female mice. *J Neurophysiol Neurol Disord*. 2020;6(101):1–8.
- Ehsanifar M, Jafari AJ, Montazeri Z, Kalantari RR, Gholami M, Ashtarinezhad A. Learning and memory disorders related to hippocampal inflammation following exposure to air pollution. *J Environ Health Sci Eng*. 2021;19(1):261–272.
- Ehsanifar M, Montazeri Z, Zavareh MS, Rafati M, Wang J. Cognitive impairment, depressive-like behaviors and hippocampal microglia activation following exposure to air pollution nanoparticles. *Environ Sci Pollut Res Int*. 2023;30(9):23527–23537.

- Yu S, Zhang Z, Qin Z, et al. Prenatal diesel exhaust exposure alters hippocampal synaptic plasticity in offspring. *Aging* (Albany NY). 2024;16(5):4348–4362. DOI: 10.18632/aging.205592.
- Chuang H-C, Chen H-C, Lee L-Y, et al. Acute and recovery phase effects of diesel exhaust particles on lung and brain in mice. *Aerosol Air Qual Res*. 2025;25(7):38. DOI: 10.1007/s44408-025-00033-x.
- Yokota S, Mizuo K, Moriya N, Oshio S, Sugawara I, Takeda K. Effect of prenatal exposure to diesel exhaust on dopaminergic system in mice. *Neurosci Lett*. 2009;449:38–41.
- Win-Shwe T-T, Fujitani Y, Kyi-Tha-Thu C, Furuyama A, Michikawa T, Tsukahara S, Nitta H, Hirano S. Effects of diesel engine exhaust origin secondary organic aerosols on novel object recognition ability and maternal behavior in BALB/c mice. *Int J Environ Res Public Health*. 2014;11(11):11286–11307. DOI: 10.3390/ijerph111111286.
- Li X, Zhang Y, Li B, et al. Activation of NLRP3 in microglia exacerbates diesel exhaust particles-induced impairment in learning and memory in mice. *Environ Int*. 2020;136:105487.
- Liu H, Wang G, Zhang J, Lu B, Li D, Chen J. Inhalation of diesel exhaust particulate matter induces locomotor hyperactivity and its relationship with brain and gut metabolism. *Environ Int*. 2024;183:108359.
- Garrick JM, Cole TB, Dao K, Phillips A, Costa LG. Perinatal diesel exhaust exposure causes persistent changes in the brains of aged mice: an assessment of behavioral and biochemical endpoints related to neurodegenerative disease. *Environ Toxicol*. 2023;38(4):899–913.
- Win-Shwe T-T, Fujimaki H, Fujitani Y, Hirano S. Novel object recognition ability in female mice following exposure to nanoparticle-rich diesel exhaust. *Toxicol Appl Pharmacol*. 2012;262(3):355–362.
- Ehsanifar M, Yavari Z, Rafati M. Exposure to urban air pollution particulate matter: neurobehavioral alteration and hippocampal inflammation. *Environ Sci Pollut Res Int*. 2022;29:50856–50866.

Supplementary material

S1. Search strategies

Limits: English language. Strings are provided for reproducibility; the study set was assembled by web searching and citation chasing (section 2.3). The PubMed string is in section 2.3.

Scopus

TITLE-ABS-KEY (("diesel exhaust" OR "diesel engine exhaust" OR "diesel exhaust particle*" OR "diesel particulate*" OR "diesel emission*" OR "secondary organic aerosol*") AND (mice OR mouse OR murine) AND (behavio* OR neurobehavio* OR cognit* OR memory OR learning OR anxiety OR depress* OR locomotor OR "open field" OR "water maze" OR "elevated plus maze" OR social OR autis* OR "forced swim" OR "tail suspension" OR rotarod OR aggress*)) AND (LIMIT-TO (LANGUAGE , "English"))

Web of Science Core Collection

TS = (("diesel exhaust" OR "diesel engine exhaust" OR "diesel exhaust particle*" OR "diesel particulate*" OR "diesel emission*" OR "secondary organic aerosol*") AND (mice OR

mouse OR murine) AND (behavio* OR neurobehavio* OR cognit* OR memory OR learning OR anxiety OR depress* OR locomotor OR "open field" OR "water maze" OR "elevated plus maze" OR social OR autis* OR "forced swim" OR "tail suspension" OR rotarod OR aggress*))

Embase

('diesel exhaust'/exp OR 'diesel exhaust':ti,ab OR 'diesel engine exhaust':ti,ab OR 'diesel exhaust particle*':ti,ab OR 'diesel particulate*':ti,ab OR 'diesel emission*':ti,ab OR 'secondary organic aerosol*':ti,ab)

AND ('mouse'/exp OR mice:ti,ab OR mouse:ti,ab OR murine:ti,ab)

AND ('behavior'/exp OR behavio*:ti,ab OR neurobehavio*:ti,ab OR cognit*:ti,ab OR memory:ti,ab OR learning:ti,ab OR anxiety:ti,ab OR depress*:ti,ab OR locomotor:ti,ab OR 'open field':ti,ab OR 'water maze':ti,ab OR social:ti,ab OR autis*:ti,ab OR 'forced swim':ti,ab OR 'tail suspension':ti,ab OR rotarod:ti,ab OR aggress*:ti,ab)

AND [english]/lim

S2. Excluded reports and reasons

#	Report	Reason for exclusion
1	Perinatal DE-SOA and autism-like behaviour in rats (Int J Mol Sci 2021;22:538)	Non-mouse species
2	Early-life traffic-related air pollutants and anxiety-like behaviour in rats (Int J Mol Sci 2023;24:586)	Non-mouse species
3	Diesel exhaust particles and brain damage in Drosophila (bioRxiv 2025)	Non-mouse species
4	Levesque et al., subchronic DE, neuroinflammation and neurodegeneration markers (J Neuroinflammation 2011;8:105)	No behavioural outcome
5	Cole et al., sex and genetic differences in acute DE effects on brain inflammation (Toxicology 2016;374:1–9)	No behavioural outcome
6	DE impairs TREM2 and dysregulates neuroinflammation (J Neuroinflammation 2020)	No behavioural outcome
7	Olfactory bulb gene expression and rearing environment after DE (PLoS One 2013)	No behavioural outcome
8	DE inhalation and olfactory bulb toxicity through glial activation (Environ Occup Med 2023)	No behavioural outcome
9	DEP and iPSC-derived microglia in Alzheimer models (bioRxiv 2026)	In vitro; preprint
10	MRI of white matter response to DEP (preprint 2023)	No behavioural outcome; preprint
11	Single-cell profiling of DEP-induced inflammation and neurogenesis (bioRxiv 2026)	No behavioural outcome; preprint
12	Prenatal 1-nitropyrene and autism-like behaviour (2024)	Single constituent, not diesel exhaust
13	Neonatal ultrafine carbon particles (Part Fibre Toxicol 2019)	Not diesel-specific
14	Prenatal urban air nanoparticles and depression-like responses (PLoS One 2013;8:e64128)	Ambient urban nanoparticles, not diesel-specific
15	Short-term DE, neuroinflammation and white matter injury (conference abstract, 2021)	Abstract only
16	Short-term DEP neurotoxicity mediated by TLR4 across age and sex (conference abstract, 2022)	Abstract only

#	Report	Reason for exclusion
17	DE and glymphatic clearance of amyloid beta (Alzheimer's & Dementia abstract, 2021)	Abstract only
18	Ehsanifar and Rafati, DE nanoparticles and depression-like behaviour (conference proceedings, 2025)	Proceedings only

S3. PRISMA 2020 checklist

Item	Topic	Location	Status
1	Title	Title	Reported
2	Structured abstract	Abstract	Reported
3–4	Rationale, objectives	Section 1	Reported
5	Eligibility criteria	Section 2.2	Reported
6–7	Sources, search strategy	Section 2.3, S1	Reported (web-based search; strings provided for reproduction)
8–9	Selection, data collection	Section 2.4	Reported (single reviewer)
10	Data items	Section 2.4	Reported
11	Risk of bias methods	Section 2.5	Reported (formal scoring not completed)
12–13	Effect measures, synthesis	Section 2.6	Reported (narrative; no pooling)
14	Reporting bias methods	Section 2.6	Narrative only
15	Certainty methods	Table 6	Author judgement, not formal GRADE
16	Study selection	Section 3.1, Figure 1	Reported
17, 19	Study characteristics, individual results	Tables 2, 4	Reported
18	Risk of bias results	Section 3.6	Not completed (section 2.5)
20	Synthesis results	Section 3.4, Figure 2, Table 3	Reported
21	Reporting biases	Section 4.3	Narrative only

Item	Topic	Location	Status
22	Certainty of evidence	Table 6	Author judgement
23	Discussion	Section 4	Reported
24	Registration and protocol	Section 2.1, Declarations	Not registered
25– 27	Support, competing interests, data availability	Declarations	Reported

S4. SYRCLE risk-of-bias template

Item	Signalling question	Scoring in this version
1. Sequence generation	Was the allocation sequence adequately generated and applied?	Not scored
2. Baseline characteristics	Were groups similar at baseline or adjusted for confounders?	Not scored
3. Allocation concealment	Was allocation adequately concealed?	Not scored
4. Random housing	Were animals randomly housed during the experiment?	Not scored
5. Blinding of caregivers	Were caregivers and investigators blinded to exposure?	Not scored
6. Random outcome assessment	Were animals selected at random for outcome assessment?	Not scored
7. Blinding of outcome assessors	Was the outcome assessor blinded?	Not scored
8. Incomplete outcome data	Were incomplete data adequately addressed?	Not scored
9. Selective outcome reporting	Are reports free of selective outcome reporting?	Not scored
10. Other bias	Is the study free of other problems, for example unit-of-analysis errors or contamination?	Not scored