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Efficacy of engineered exosomes in the treatment of Alzheimer's disease: A systematic review and meta-analysis of preclinical animal models

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 August 2025 and was last updated on 21 August 2025.

INTRODUCTION

Review question / Objective Our primary objectives are to: (1) systematically assess the therapeutic effects of engineered exosomes compared to control groups across multiple outcome domains including cognitive function, pathological markers, and neuroinflammation; (2) quantitatively compare the efficacy of engineered exosomes versus natural exosomes to determine the added therapeutic value of engineering modifications; (3) identify sources of heterogeneity in treatment effects through subgroup analyses of animal model types, administration routes, and treatment protocols; and (4) evaluate the methodological quality of existing preclinical evidence using established assessment tools. This comprehensive meta-analysis will provide evidence-based guidance for optimizing engineered exosome therapies and inform the design of future clinical trials, ultimately advancing the translation of this promising therapeutic approach from bench to bedside.

Condition being studied Alzheimer's disease is a progressive neurodegenerative disorder characterised by β-amyloid protein deposits, tau protein neurofibrillary tangles, and chronic neuroinflammation. Its pathogenesis is complex and involves multiple intertwined factors, leading to limited efficacy of traditional single-target therapies. Innovative treatment strategies that can simultaneously intervene in multiple pathological processes are urgently needed.
Engineered exosomes, as nanoscale extracellular vesicles, possess excellent biocompatibility and the ability to cross the blood-brain barrier. Through surface modification, drug loading, and genetic engineering techniques, their targeting specificity and drug delivery efficiency can be enhanced. Preclinical studies have shown that engineered exosomes functionalised with peptides, loaded with drugs, or carrying therapeutic microRNAs demonstrate potential for anti-neuroinflammatory effects, promotion of neural regeneration, and improvement of cognitive function in AD models.

However, significant knowledge gaps remain in this field: substantial heterogeneity exists among preclinical studies, making it challenging to uniformly assess efficacy; the advantages of engineered exosomes over natural exosomes have not been systematically quantified; and optimal engineering strategies, administration routes, and treatment regimens remain undefined. The absence of a systematic quality assessment of existing evidence also limits the deep understanding of mechanisms and the optimisation of clinical translation pathways.

METHODS

Participant or population AD animal models.

Intervention Engineered exosome therapy.

Comparator No treatment or treatment with natural exosomes only.

Study designs to be included Preclinical animal testing.

Eligibility criteria Exclusion criteria: (1) Do not use engineered exosomes; (2) Study subjects are humans animals; (3)The study does not report the required outcome data; (4) Non-original publications lacking raw data, such as review articles, organisational guidelines, expert opinions, conference abstracts. (5)Study datas are missing and not available in full.

Information sources PubMed, EMBASE, and Web of Science databases.

Main outcome(s) Morris water maze test (MWM), Aβ peptide or Aβ plaque levels, tau protein phosphorylation levels, inflammatory marker levels.

Quality assessment / Risk of bias analysis We will Use SYRCLE, CAMARADES, and ARRIVE to assess bias risk, methodological quality, and reporting completeness.

Strategy of data synthesis If an outcome measure involves at least three studies, we use Stata 17 software to perform a meta-analysis. In the analysis, we collecte the sample size, mean, and standard deviation (SD) of each study, and use the standardised mean difference (SMD) to calculate the effect size, p-value, and 95% confidence interval (CI). In the meta-analysis, we calculate the weights for each study using the inverse variance method, prioritise the fixed-effects model, and estimate the effect size using the Mantel-Haenszel method. When the pooled heterogeneity exceeds 50%, we switch to the random-effects model and estimate the effect size using the DerSimonian-Laird method.

Subgroup analysis If the I^2 value remains above 50%, subgroup analysis is conducted to explore the sources of heterogeneity. We conduct subgroup analyses based on animal species, gender, model group category, whether the exosomes are from the same species, administration method, and administration time (0–1 week, 1–2 weeks, or more than 2 weeks) to investigate the sources of heterogeneity.

Sensitivity analysis We perform a leave-one-out sensitivity analysis on all data and observe the differences between the results after sequentially excluding each study. If there are significant differences, the study is excluded.

Language restriction English.

Country(ies) involved China.

Keywords Alzheimer's disease; engineered exosomes; preclinical animal models; cognitive function.

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