

INPLASY

INPLASY2026100070

doi: 10.37766/inplasy2026.10.0070

Received: 14 October 2026

Published: 14 October 2026

Corresponding author:

Shih-Ping Liu

spliu@mail.cmu.edu.tw

Author Affiliation:

Translational Medicine Research
Center, China Medical University
Hospital.

hESC- and hiPSC-derived dopaminergic cell products for Parkinson's disease in rodent models: a systematic review and network meta-analysis protocol

Ting, B; Kuo, CL; Tseng, RJH; Liu, SP.

ADMINISTRATIVE INFORMATION**Support** - National Science and Technology Council, Taiwan.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY2026100070

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 October 2026 and was last updated on 14 October 2026.

INTRODUCTION

Review question / Objective To compare the effects of hESC- and hiPSC-derived dopaminergic grafts, with and without sorting or enrichment, on drug-induced rotation behavior in rodent models of Parkinson's disease using systematic review and network meta-analysis.

Rationale Dopaminergic graft studies vary in pluripotent stem-cell source and sorting or enrichment strategy, but direct comparisons are limited. A network meta-analysis can compare these broad product categories using a commonly reported functional outcome.

Condition being studied Parkinson's disease is characterized by progressive loss of nigrostriatal dopaminergic neurons. The review evaluated preclinical rodent models of Parkinsonian dopaminergic lesions used to test human pluripotent stem-cell-derived dopaminergic grafts.

METHODS

Search strategy PubMed, Embase, CENTRAL, and Web of Science were searched on 21 June 2026. Boolean combinations covered Parkinson's disease; human pluripotent stem cells (iPSC, hiPSC, hPSC, and hESC); dopaminergic progenitors or neurons; transplantation or grafting; and rodent models including 6-OHDA and MPTP. Database-specific strategies are reported in Supplementary Table S2.

Participant or population Rodent models of Parkinson's disease, including rats and mice with experimentally induced dopaminergic lesions.

Intervention hESC- or hiPSC-derived dopaminergic grafts were classified as hiPSC_SORT, hiPSC_UNSORT, hESC_SORT, or hESC_UNSORT. SORT denoted a reported sorting or enrichment procedure for the intended graft population; UNSORT denoted no such enrichment in the analysis classification.

Comparator Eligible comparators were another active graft node or V_CTRL, a pooled non-cell Parkinsonian control comprising vehicle, culture medium, saline, artificial cerebrospinal fluid, sham, or lesion-only controls. Intact animals and marker-negative cellular fractions were not classified as V_CTRL.

Study designs to be included Original full-text in vivo rodent studies evaluating pluripotent-stem-cell-derived neural or dopaminergic grafts and drug-induced rotation behavior were eligible. Network meta-analysis additionally required an eligible node comparison and sufficient quantitative data for effect-size estimation.

Eligibility criteria Human or non-rodent studies, unrelated diseases, out-of-scope cell sources, and non-original reports were excluded. Publications meeting the systematic-review criteria remained in the narrative review when their arms could not be assigned to an eligible NMA node or lacked an estimable eligible comparison.

Information sources PubMed, Embase, CENTRAL, and Web of Science were searched on 21 June 2026. Full-text reports and available supplementary information were used for eligibility, data extraction, and risk-of-bias assessment.

Main outcome(s) The primary outcome was change from baseline in drug-induced rotation behavior at the 16-week landmark, with assessments at 16–18 weeks eligible. Effects were expressed as standardized mean differences (SMDs) with 95% confidence intervals.

Additional outcome(s) The same outcome was assessed at an early landmark (6–12 weeks) and a durability landmark using the earliest eligible observation at or beyond 24 weeks. The three landmark networks were analyzed separately and were not interpreted as longitudinal within-product comparisons.

Data management Two reviewers (Ting and Tseng) independently screened records and full-text reports, with disagreements resolved by discussion or consultation with Liu. Data were extracted at the experiment-arm level by Ting and verified by a second reviewer. Landmark-specific datasets were prepared for the early, primary, and durability analyses.

Quality assessment / Risk of bias analysis Risk of bias was assessed at the publication level using the 10-domain SYRCLE tool, with domains rated as low, high, or unclear risk. Confidence in network

estimates was assessed using the CINeMA framework.

Strategy of data synthesis Separate frequentist random-effects network meta-analyses were performed for the three landmarks using MetaInsight 7.1.1 with its netmeta-based implementation. Effects were expressed as SMDs with 95% confidence intervals, heterogeneity was summarized by τ^2 , and multi-arm studies were handled within the network model. Transitivity was considered based on the comparability of relevant study characteristics, local inconsistency was assessed by direct–indirect evidence splitting, and treatment ordering was interpreted descriptively.

Subgroup analysis No subgroup analyses were reported. Separate networks were fitted for the early, primary, and durability landmarks.

Sensitivity analysis Leave-one-publication-out analyses were performed separately for each landmark. The networks were also reanalyzed using an assumed pre–post correlation of 0.5 instead of 0.8 for change-score standard deviations.

Language restriction No language restriction was applied.

Country(ies) involved Taiwan.

Other relevant information This review was retrospectively registered after completion of the principal analyses but before publication. Registration was completed at this stage to provide a transparent public record of the review methods.

Keywords Parkinson’s disease; human pluripotent stem cells; dopaminergic grafts; cell sorting/enrichment; network meta-analysis; rodent models.

Dissemination plans The completed review will be submitted for publication in a peer-reviewed journal.

Contributions of each author

Author 1 - Berne Ting - Conceptualization; Methodology; Validation; Formal analysis; Data curation; Writing – original draft.

Email: berne.ting@gmail.com

Author 2 - Chien-Liang Kuo - Methodology; Validation; Writing – review and editing.

Email: u109048001@cmu.edu.tw

Author 3 - Ray Jui-Hung Tseng - Investigation;
Data curation.
Email: i54131046@gs.ncku.edu.tw
Author 4 - Shih-Ping Liu - Conceptualization;
Writing – review and editing; Supervision; Funding
acquisition.
Email: spliu@mail.cmu.edu.tw