# INPLASY PROTOCOL

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Conflicts of interest: None declared.

#### **INTRODUCTION**

Review question / Objective: To study the relationship between environmental enrichment and cognitive function through a meta-analysis of the literature, analyze its effects on the improvement of cognitive function in patients and animals, and evaluate the effects of different

Improvement of Environmental enrichment on Cognitive Functions in Patients and animals : A systematic review and meta-analysis

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**Review question / Objective:** To study the relationship between environmental enrichment and cognitive function through a meta-analysis of the literature, analyze its effects on the improvement of cognitive function in patients and animals, and evaluate the effects of different environmental enrichment measures on cognitive function improvement.

Condition being studied: Cognitive decline refers to an individual's memory, language, reasoning and other aspects of cognitive function showing obvious, measurable decline or abnormal. The causes of cognitive decline are various, including neurodegeneration, cerebrovascular disease, infection, trauma, and depression. Alzheimer's disease and stroke are the most common.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 December 2022 and was last updated on 04 December 2022 (registration number INPLASY2022120014).

## environmental enrichment measures on cognitive function improvement.

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### **METHODS**

Search strategy: We searched PubMed, Embase and Cochrane Library until November 30, 2022. In the retrieval strategy, we use "cognition" and"Environemntal Enrichment"keywords and other free words together with Boolean operators (OR,AND) to combine the search. In the search, we do not apply language or publication type restrictions. EndNote20 is used to store and sort retrieved literature. and to automatically and manually delete duplicate files through the software. Two people independently screen titles and abstracts based on predefined inclusion criteria. Inconsistent results are determined by additional discussion or by a third examiner. In addition, we searched references to other studies to ensure that our search strategy found all relevant studies. Subsequently, we determined the final inclusion by reviewing the full text of the remaining studies.

Participant or population: Patients and animals with cognitive decline or impairment.Patients: Mainly stroke patients and Alzheimer's patientsAnimals: intracerebral hemorrhage perfusion models and Alzheimer's disease and model animals.

Intervention: Intervention group received environmental enrichment treatment.

**Comparator:** Patients and animals in the control group received routine care.

Study designs to be included: The s study was designed as a randomized controlled trial (RCT).

Eligibility criteria: All studies included in the initial search strictly met the criteria of the Population, Intervention, Comparison, Results and Research Design (PICOS) framework. Human: (1) Adult age ≥18 years.

(2) Patients with cognitive decline or cognitive dysfunction Intervention group received environmental enrichment treatment.Comparator: Patients in the control group received routine care.At least one cognitive function outcome was measured.The s study was designed as a randomized controlled trial (RCT).Animals: (1) The subjects were female and male rodents with cognitive impairment.(2) environmental enrichment therapy.(4) Cognitive function results were measured by at least one test method.(5) The study design was a randomized controlled trial.

**Information sources:** We searched PubMed, Embase and Cochrane Library.

Main outcome(s): cognitive function evaluation. Patient: Cognitive functions were assessed by the Simple Mental State Scale (MMSE), the Montreal Cognitive Test (MoCA), the Montreal Cognitive Assessment (MoCA), the Simple Intelligent Mental State Examination Scale (MMSE), the Elderly Cognitive Function Screening Measure (CASI), the Intelligent Test Score (MTS), or the General Practitioner Cognitive Function Assessment Scale (GPCOG) Scale evaluation

In animals, the Morris Water Maze (MWM) test, Y maze test, new object recognition test (ORT) and passive avoidance test (PAT) were used to assess cognitive function.

Quality assessment / Risk of bias analysis:

The Cochrane tool will be used to assess the risk of bias through random sequence generation, assignment concealment, participant/person blinding, outcome variable assessment blinding, outcome data integrity, selective reporting of study results, and other biases.

Animals: STAIR list combined with Camarades list will be used to assess bias in the following areas: Sample size calculation, inclusion and exclusion criteria, random-sequence generation, hidden animal grouping protocol, blind ischemia induction, appropriate application of animal models, anesthetics with no apparent intrinsic neuroprotective activity, descriptions with temperature control, reporting of reasons for animal exclusion analysis, blind evaluation of outcomes, stating potential conflicts of interest and research funding and other bias, etc.

Strategy of data synthesis: The Cochrane system software Revman version 5.4 was used for statistical analysis. Aggregated SMD (standard mean difference) values and 95%CI reports are used for impact sizes, and forest maps are used to present the results.

Subgroup analysis: The subgroup analysis method and meta-regression analysis were used to investigate the source of heterogeneity. If the source of heterogeneity could not be determined, we used a general description.

Sensitivity analysis: Heterogeneity using Cochran's Q test and I2 statistics. I2 values of 25%-50%, 50%-75%, and  $\geq$ 75% indicate low, medium, and high heterogeneity, respectively. When the heterogeneity p value is less than 0.1, heterogeneity is considered. When the heterogeneity is low, the fixed effects model is used, and when the heterogeneity is high, the random effects model is used. In order to find the possible sources of heterogeneity, we will conduct a sensitivity analysis.

Language restriction: English.

Country(ies) involved: China.

**Keywords:** Environmental Enrichment Cognitive Function Therapy.

Contributions of each author:

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