INPLASY PROTOCOL

To cite: Cataford et al. Cognitive and motor function effects of antipsychotics in traumatic brain injury: a systematic review of preclinical studies. Inplasy protocol 202310034. doi: 10.37766/inplasy2023.1.0034

Received: 12 January 2023

Published: 12 January 2023

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Support: **Fonds de Recherche en Santé - Québec.**

Review Stage at time of this submission: **Data extraction.**

Conflicts of interest:
None declared.

Cognitive and motor function effects of antipsychotics in traumatic brain injury: a systematic review of preclinical studies

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Review question / Objective: **The objective is to systematically review and summarize the literature addressing the effect of typical and atypical antipsychotics following a TBI, on cognitive and motor function in animal models.**
Condition being studied: **Pre-clinical animal studies evaluating the effects of antipsychotics on cognitive and motor functions in models of traumatic brain injury.**
Main outcome(s): **Motor (such as beam-balance task, beam-walk time, rotarod time, foot faults, neuroscore) and cognitive functions (such as the Morris Water Maze).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 January 2023 and was last updated on 12 January 2023 (registration number INPLASY202310034).

INTRODUCTION

Review question / Objective: **The objective is to systematically review and summarize the literature addressing the effect of typical and atypical antipsychotics following a TBI, on cognitive and motor function in animal models.**

Rationale: **During hospital stay, patients who experience a TBI are often treated with antipsychotics to treat the symptoms of agitation, aggression or other behaviors. Despite their frequent use, there have been no randomized controlled studies of antipsychotics for the management of agitation in TBI patients. By interfering with dopaminergic circuits, antipsychotics may impede neuronal plasticity processes important to cognitive recovery. Observational studies in TBI patients have also suggested longer posttraumatic**

amnesia duration with typical antipsychotics. Studies demonstrating the potential of amantadine, a dopamine agonist, to improve functional outcomes in TBI further supports the hypothesis of harm of dopamine receptor blockade. Based on this data, some TBI rehabilitation guidelines have advised against the use of antipsychotics, while others suggested short term use only. Preclinical data has demonstrated variable effects of pharmacological treatment on cognitive and motor recovery post-TBI. To date, there has been no systematic evaluation of the pre-clinical literature summarizing the effects of antipsychotics on cognitive and motor function following experimental TBI

Condition being studied: Pre-clinical animal studies evaluating the effects of antipsychotics on cognitive and motor functions in models of traumatic brain injury.

METHODS

Search strategy: MedLine and Embase databases were searched from inception to November 23rd 2022 with the help of a health sciences librarian with expertise in systematic reviews.

Participant or population: All types of mammalians reproducing any form of traumatic brain injury including focal, diffuse and complex TBIs induced by blast injury, penetrating injury, repetitive injury or others types of models.

Intervention: All pre-clinical animal studies evaluating the effects of antipsychotics on cognitive and motor functions are considered for inclusion.

Comparator: Placebo, an active treatment or a non-pharmacological intervention.

Study designs to be included: Randomized and non-randomized experiments.

Eligibility criteria: No restrictions with respect to sex, age or mammalian species.

Information sources: Medline and Embase.

Main outcome(s): Motor (such as beam-balance task, beam-walk time, rotarod time, foot faults, neuroscore) and cognitive functions (such as the Morris Water Maze).

Data management: Data from all included studies will be independently extracted in duplicate using a pre-tested data extraction form by the authors. The following variables were recorded for each study: the study title, the name of the first author, the year of publication, the country of origin, language of publication, source of funding, preclinical animal model, experimental TBI method, outcome measures for cognitive, functional, behavioral and motor evaluation, pharmacological intervention including dose and timing of medication administration, type of comparator, and timing of evaluations.

Quality assessment / Risk of bias analysis: Two reviewers will independently evaluate each included study with the SYRCLE's risk of bias tool for animal studies.

Strategy of data synthesis: The results of the systematic review will be presented as both a descriptive overview and meta-analysis. To enable meta-analysis, we will graphically extrapolate repeated data measures and standard errors of the mean using WebPlotDigitizer 4.3. If the statistical heterogeneity is acceptable, we will proceed to a meta-analysis of the data using Review Manager (RevMan 5.4) software (Nordic Cochrane Center, Cochrane Collaboration).

Subgroup analysis: Will stratify the analysis by type of antipsychotic.

Sensitivity analysis: No sensitivity analyses are planned.

Language restriction: English and French.

Country(ies) involved: Canada.

Keywords: Traumatic brain injury, antipsychotics, animal models, cognitive.

Contributions of each author:

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