

# INPLASY PROTOCOL

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## INTRODUCTION

**Review question / Objective:** The present systematic review aims to provide an updated overview of the available evidence on the putative action of antipsychotics on

## Schizophrenia synaptic pathology and antipsychotic treatment in the framework of oxidative and mitochondrial dysfunction: translational highlights for the clinics and treatment

De Simone, G<sup>1</sup>; Mazza, B<sup>2</sup>; Vellucci, L<sup>3</sup>; Barone, A<sup>4</sup>; Ciccarelli, M<sup>5</sup>; de Bartolomeis, A<sup>6</sup>.

**Review question / Objective:** The present systematic review aims to provide an updated overview of the available evidence on the putative action of antipsychotics on mitochondrial function in the setting of schizophrenia and their potential antioxidant/oxidant role.

**Information sources:** EMBASE, Scopus, and Medline/PubMed databases were queried on 18 January 2023. The latest update was conducted on 15 February 2023. The search string adopted for the Medline/Pubmed database is reported as follows: (((("schizophre-nia"[Title/Abstract]) OR ("schizophrenia spectrum and other psychotic disorders"[MeSH Terms])) OR ("psychosis"[Title/Abstract]) OR ("psychotic disorder"[Title/Abstract]) OR ("antipsychotic"[Title/Abstract])) AND (((("mitochondria"[Title/Abstract]) OR (mitochon-drion[Title/Abstract]) OR ("mitochondria"[MeSH Terms])) OR ("free radi-cal"[Title/Abstract])) OR ("antioxidant"[Title/Abstract])).

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 February 2023 and was last updated on 23 February 2023 (registration number INPLASY202320106).

mitochondrial function in the setting of schizophrenia and their potential antioxidant/oxidant role.

**Condition being studied:** We dwelled on oxidant/antioxidant and mitochondrial

pathway in psychotic disorders, especially schizophrenia and treatment-resistant schizophrenia.

## METHODS

**Participant or population:** We included studies conducted on patients affected by psychotic disorders as well as animal and in vitro models evaluating antipsychotic effects on mitochondria and antioxidant pathway.

**Intervention:** We analyzed the impact of antipsychotics on antioxidant/oxidant pathway and mitochondria function.

**Comparator:** Healthy control population or individuals administered with placebo and animal or cell models treated with vehicle.

**Study designs to be included:** Randomized clinical trials, preclinical studies as well as in vitro and ex vivo models.

**Eligibility criteria:** No time constraints were applied, and original clinical, and preclinical research studies and reviews were included. Conference abstracts, and commentaries were excluded. We deemed eligible English-written articles, published in peer-reviewed journals, related to the topic.

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**Main outcome(s):** We included all the information on mitochondria function,

including protein levels, gene expression, or enzymatic activity and oxidant/antioxidant pathways.

**Quality assessment / Risk of bias analysis:** Not applicable.

**Strategy of data synthesis:** Not applicable.

**Subgroup analysis:** Not applicable.

**Sensitivity analysis:** Not applicable.

**Country(ies) involved:** Italy.

**Keywords:** antipsychotics; mitochondria; antioxidants; dopamine; synapse; treatment resistant; schizophrenia; glutamate; postsynaptic density; glutathione.

### Contributions of each author:

Author 1 - Giuseppe De Simone.

Author 2 - Benedetta Mazza.

Author 3 - Licia Vellucci.

Author 4 - Annarita Barone.

Author 5 - Mariateresa Ciccarelli.

Author 6 - Andrea de Bartolomeis.

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