INPLASY PROTOCOL

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None declared.

Antipsychotics-induced changes in synaptic architecture and functional connectivity. Translational implications for treatment response and resistance

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Review question / Objective: **We aimed at investigating the impact of antipsychotics on synaptic architecture, immediate early gene expression, and functional connectivity, with emphasis on different topographical patterns of action and clinical implications.**
Condition being studied: **We have included all preclinical studies, such as those conducted in animal species, especially rodents, and in vitro, exploring antipsychotic-induced changes in synaptic architecture, immediate gene expression, and functional connectivity, focusing on clinical translatability in psychotic disorders.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 November 2022 and was last updated on 21 November 2022 (registration number INPLASY2022110107).

INTRODUCTION

Review question / Objective: **We aimed at investigating the impact of antipsychotics on synaptic architecture, immediate early gene expression, and functional connectivity, with emphasis on different topographical patterns of action and clinical implications.**

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METHODS

Search strategy: We performed a systematic search of the literature available on Medline/Pubmed and Embase in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria by combining the following keywords in a search string: antipsychotic, chlorpromazine, haloperidol, paliperidone, risperidone, asenapine, olanzapine, clozapine, quetiapine, amisulpride, aripiprazole, brexpiprazole, cariprazine, lurasidone, lumateperone, xanomeline, Arc/Arg, BDNF, c-fos, fos, c-Jun, Jun, Egr1, Delta, Narp1, NPAS-4, Homer, Nor1, Nurr1, NGFI-B/Nur77, Nerve Growth Factor Inducible-B, ISH, fMRI, EEG, functional connectivity, connectome, network.

Participant or population: Animal species, especially rodents.

Intervention: Administration of antipsychotics, including any type of compound, in animals with or without pretreatment with other drugs.

Comparator: Vehicle-treated control animals.

Study designs to be included: Preclinical intervention studies.

Eligibility criteria: We deemed eligible English-written preclinical studies published in peer-reviewed journals that were pertinent to the topic, i.e., investigating the antipsychotic effects on synaptic architecture, IEGs expression, and, on a larger scale, anatomical and functional brain connectivity, without time or design methodology constraints.

Information sources: The screening, data extraction, and eligibility of included studies were independently performed by three investigators (MT, LV, GDS). Any disagreements were solved by consensus. Two investigators made the final decision when a consensus could not be reached (AdB, AB). The PubMed/MEDLINE and Scopus databases were systematically searched for references indexed from inception until September 10th, 2022. In addition, relevant cross-references, textbooks, and other materials were hand-searched to identify potential additional references not captured in the original searches.

Main outcome(s): Any outcome related to antipsychotics' modification in synaptic architecture, functional connectivity (fMRI, EEG, ISH), and immediate early gene (Homer1a, c-fos, arc, BDNF, zif-268, etc.) expression in preclinical studies was considered for inclusion without any type of restriction.

Quality assessment / Risk of bias analysis: None.

Strategy of data synthesis: None.

Subgroup analysis: None.

Sensitivity analysis: None.

Country(ies) involved: Italy.

Keywords: brain network; dopamine; glutamate; serotonin; postsynaptic density; connectivity; schizophrenia; immediate early genes; antipsychotics; Homer.

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