

INPLASY PROTOCOL

To cite: de Bartolomeis et al.
Dysregulated signaling at postsynaptic density: a systematic review and translational appraisal for the pathophysiology, clinics, and antipsychotics' treatment of schizophrenia. Inplasy protocol 2022110129. doi: 10.37766/inplasy2022.11.0129

Received: 25 November 2022

Published: 25 November 2022

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Support: No external funding was provided for the present systematic review.

Review Stage at time of this submission: Process of systematization and review of results.

Conflicts of interest:
None declared.

Dysregulated signaling at postsynaptic density: a systematic review and translational appraisal for the pathophysiology, clinics, and antipsychotics' treatment of schizophrenia

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Review question / Objective: The present systematic review aims to provide an updated overview of the available evidence on the implication of postsynaptic density proteins in dysregulated signaling transduction and their potential implications in antipsychotic treatment in schizophrenia.

Condition being studied: Schizophrenia is a severe psychiatric disorder whose prevalence worldwide is 1%, associated with aberrant synaptic plasticity potentially linked with dysregulated signaling at the postsynaptic density. Increasing evidence has accumulated in the last two decades on the pivotal role of synaptic plasticity alterations and aberrant cortical-subcortical connectivity in schizophrenia pathophysiology, as well as on the molecular underpinnings of antipsychotics' effects on the structure of the synaptic architecture, relevant to psychotic disorders. Despite the emerging role of postsynaptic density proteins in behavioral disorders, there is currently no systematic review that integrates preclinical and clinical findings addressing dysregulated postsynaptic density signaling and translational implications for antipsychotic treatment in the aberrant postsynaptic function context.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 November 2022 and was last updated on 25 November 2022 (registration number INPLASY2022110129).

INTRODUCTION

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METHODS

Search strategy: (psd) AND (schizophrenia) + 'psd schizophrenia' OR (psd AND ('schizophrenia'/exp OR schizophrenia)); ((schizophrenia) AND (psd)) AND (antipsychotic*) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'antipsychotic*'; ((schizophrenia) AND (psd)) AND (clozapine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'clozapine'; ((schizophrenia) AND (psd)) AND (aripiprazole) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'aripiprazole'; ((schizophrenia) AND (psd)) AND (brexpiprazole) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'brexpiprazole'; ((schizophrenia) AND (psd)) AND (cariprazine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'cariprazine'; ((schizophrenia) AND (psd)) AND (risperidone) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'risperidone'; ((schizophrenia) AND (psd)) AND (haloperidol) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'haloperidol'; ((schizophrenia) AND (psd)) AND (olanzapine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'olanzapine'; ((schizophrenia) AND (psd)) AND

(chlorpromazine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'chlorpromazine'; ((schizophrenia) AND (psd)) AND (fluphenazine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'fluphenazine'; ((schizophrenia) AND (psd)) AND (lurasidone) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'lurasidone'; ((schizophrenia) AND (psd)) AND (xanomeline) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'xanomeline'; ((schizophrenia) AND (psd)) AND (quetiapine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'quetiapine'; ((schizophrenia) AND (psd)) AND (iloperidone) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'iloperidone'; ((schizophrenia) AND (psd)) AND (sulpiride) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'sulpiride'; ((schizophrenia) AND (psd)) AND (amisulpride) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'amisulpride'; ((schizophrenia) AND (psd)) AND (asenapine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'asenapine'; ((schizophrenia) AND (psd)) AND (bromperidol) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'bromperidol'; ((schizophrenia) AND (psd)) AND (clotiapine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'clotiapine'; ((schizophrenia) AND (psd)) AND (loxapine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'loxapine'; ((schizophrenia) AND (psd)) AND (paliperidone) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'paliperidone'; ((schizophrenia) AND (psd)) AND (perphenazine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'perphenazine'; ((schizophrenia) AND (psd)) AND (pimozide) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'pimozide'; ((schizophrenia) AND (psd)) AND (promazine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'promazine'; ((schizophrenia) AND (psd)) AND (thioridazine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'thioridazine'; ((schizophrenia) AND (psd)) AND (tiapride) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'tiapride'; ((schizophrenia)

AND (psd)) AND (trifluoperazine) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'trifluoperazine'; ((schizophrenia) AND (psd)) AND (ziprasidone) + ('schizophrenia'/exp OR schizophrenia) AND psd AND 'ziprasidone'.

Participant or population: We included all clinical and preclinical studies investigating the signaling dysregulations at postsynaptic density in patients with schizophrenia and animals modeling psychotic disorders.

Intervention: We included all clinical and preclinical studies investigating signaling dysregulations at the postsynaptic density level in patients with schizophrenia and in animals modeling psychotic disorders, to assess the pathophysiology of the disease, the clinical implications, and the impact of treatment with antipsychotics.

Comparator: Healthy controls, wild type, and vehicle-treated rodents.

Study designs to be included: Original clinical, preclinical research studies and reviews

Eligibility criteria: English-written articles, published in peer-reviewed journals, exploring the involvement of dysregulated signaling of PSD proteins in schizophrenia and their implication in antipsychotic treatment.

Information sources: The search was carried out on EMBASE, Scopus, and PubMed on 1st August 2022. Four independent co-authors systematically searched for studies to include. Any disagreements were resolved by consulting the other two authors.

Main outcome(s): Any protein or transcript levels of postsynaptic density molecules in schizophrenia or models of psychosis.

Quality assessment / Risk of bias analysis: Not related.

Strategy of data synthesis: Not related.

Subgroup analysis: Not related.

Sensitivity analysis: Not related.

Country(ies) involved: Italy.

Keywords: synaptic signaling, antipsychotics, postsynaptic density, schizophrenia, signalome, connectome, synaptosome, synaptopathy.

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