Psychotic events during stimulant treatment in children and adolescents with Attention-Deficit Hyperactivity Disorder (ADHD): A Systematic Review

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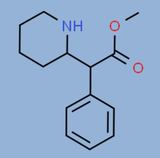
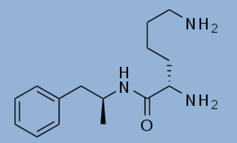
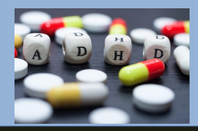






INTRODUCTION

The treatment of **Attention Deficit Hyperactivity Disorder (ADHD)** includes pharmacological and non-pharmacological interventions.[1]

Stimulants, encompassing **methylphenidate** and **amphetamines**, are the recommended first line pharmacological treatment.[2]

Even though they are highly efficacious, at least in the short terms, stimulants may be associated with clinically relevant adverse events. Among these, psychotic events may be particularly traumatic for patients and their families.[1]

An updated systematic evidence synthesis of the literature on psychotic events during stimulant treatments is currently lacking.

Aim: To fill this gap, we conducted an updated systematic review of studies assessing psychotic events during treatment with stimulant medications for children and adolescents with ADHD

METHOD

We followed the 2020 PRISMA recommendations. The registration of the protocol is ongoing.

Search: We searched PubMed, PsycInfo, EMBASE + EMBASE classic, OVID Medline, and Web of Science (up to 8 April 2021) with no language or type of document restrictions.

Inclusion criteria: We included randomised controlled trials (RCTs) or observational studies reporting data on the prevalence and/or type of psychotic events following stimulant treatment in children or adolescents (< 18 years) with a formal diagnosis of ADHD.

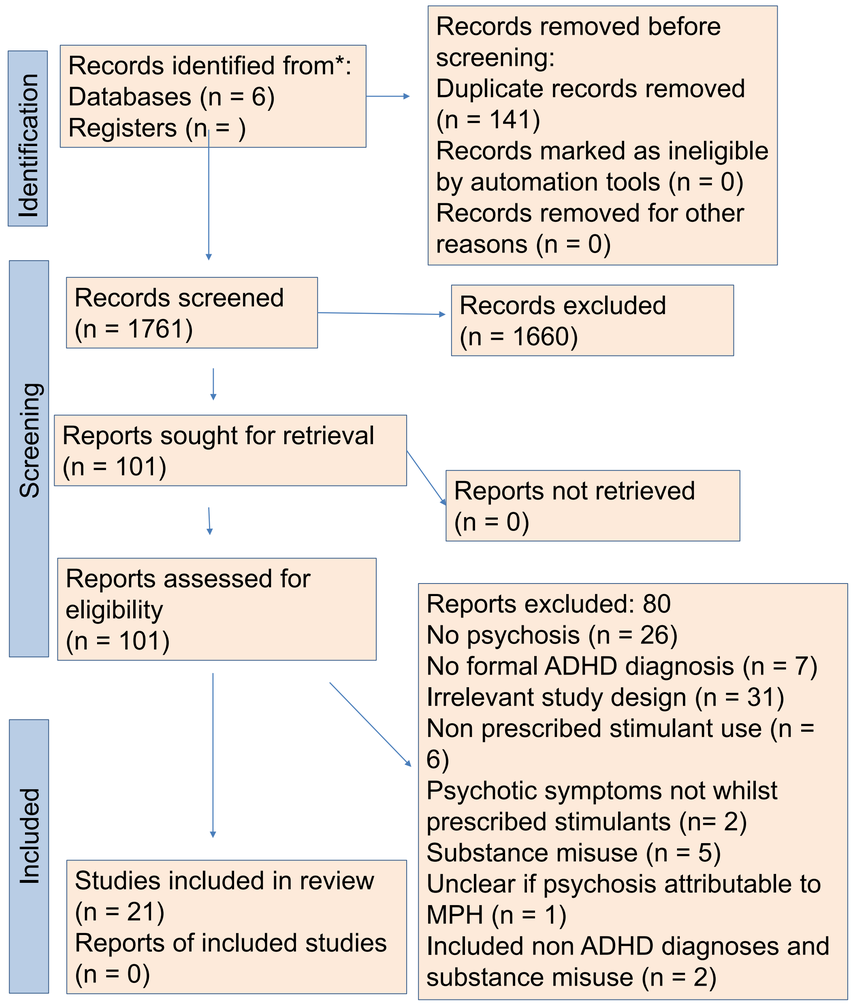
Case reports and case series were also allowed. Narrative reviews or editorial/commentaries were excluded.

Procedure: Two investigators performed independently the screening and date extraction. Any disagreement was arbitrated by the senior author.

RESULTS

We found a total of 1902 potentially eligible references. After screening, 21 references were included (Fig 1).

Fig 1. PRISMA flowchart



Study design	Number of studies included
DB-RCT	3
OL RCT	1
Prospective Cohort	1
Retrospective Cohort	3
Case series	3
Case report	11

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Types of psychotic symptoms reported on Stimulant treatment

Type	MPH	LDX	Mixed salts
VH	11	5	1
AH	7	2	-
SH	2	-	-
Other; e.g. Paranoia,	11	2	1
UH	3	-	-
Unspecified psychotic sx	2	1	-

VH: Visual hallucinations; AH: Auditory hallucinations; SH: Somatic hallucinations; UH: Unspecified hallucinations

Table 2

We report mainly on the findings from case reports/series, as there was a paucity of detail on the associated psychotic events in the other types of studies (Table 1).

Patients were all prescribed methylphenidate, with the exception of one patient prescribed mixed amphetamine salts.

- Time of onset of psychotic symptoms whilst on stimulant treatment ranged from 24 hours to months to 3 years.
- Psychotic symptoms ranged from paranoia and bizarre behaviour reported, to visual, auditory and somatic hallucinations. (Table 2)

The majority of articles reported spontaneous resolution on discontinuation of the medication. Most cases resolved within a week, one case took 3 weeks to resolve with an antipsychotic.

15 cases rechallenged with pharmacological treatment after remission:

- 8 were successfully rechallenged on same medication but sometimes with a different dose or preparation.
- 7 patients were switched to alternative medications, including Lisdexamfetamine, Dexamphetamine, Atomoxetine, and Clonidine.

DISCUSSION and CONCLUSIONS

The bulk of the literature is descriptive, reporting on the type of psychotic event, its temporal onset and resolution.

Prescribers should be aware that, in the majority of cases, psychotic events during stimulant treatment remit after stopping the stimulant, without need to add an antipsychotic.

Further research is needed to understand cause-effect relationships and underlying pathophysiological mechanisms.

References

1. Cortese S. Cortese S. Pharmacologic Treatment of Attention Deficit-Hyperactivity Disorder. N Engl J Med. 2020;10;383(11):1050-1056.
1. National Institute for Health and Care Excellence (NICE). Attention deficit hyperactivity disorder: diagnosis and management. 2018. https://www.nice.org.uk/guidance/ng87