Received: 6 June 2023 | Revised: 25 September 2023 | Accepted: 16 October 2023

DOI: 10.1111/acps.13630

Acta Psychiatrica Scandinavica WILEY

RESEARCH LETTER

No association between methylphenidate use and psychotic experiences in a population-based sample of adolescents at risk of emotional and behavioral problems

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Funding information
Erasmus Universitair Medisch Centrum Rotterdam; GGz Breburg; GGz Delfland; GGz Westelijk Noord-Brabant; Parnassia Psychiatric Institute Antes; Yulius

1 | INTRODUCTION

Methylphenidate is a psychostimulant commonly prescribed for the symptoms of attention-deficit/hyperactivity disorder (ADHD). Subclinical symptoms of psychosis, referred to as psychotic experiences, have been reported in individuals with ADHD when prescribed methylphenidate.[1] Amphetamines are hypothesized to trigger or exacerbate latent psychosis vulnerabilities among those predisposed for such conditions.[2] Consequently, clinical guidelines advise cessation of methylphenidate if psychotic symptoms are reported.[3] To investigate the empirical evidence behind these concerns, a recent Cochrane review synthesized randomized and observational data on the topic.[4] The authors report a small effect size of an increased risk of psychotic symptoms after methylphenidate use. They also reported, however, critical risk of bias in the studies they identified. Thus, the low quality of empirical evidence did not permit a substantive conclusion.

The current short report investigates the association between methylphenidate use in the past 3 months and currently reported psychotic experiences.

2 | METHODS

The iBerry (Investigating Behavioral and Emotional Risk in Rotterdam Youth) cohort[5] consists of 1022 adolescents. The Strengths and Difficulties-Questionnaire-youth (SDQ-Y), a screener for emotional and behavioral problems, was used at age 13 as part of preventive healthcare at schools to select participants for the cohort: 71% of adolescents were selected with high scores on the SDQ-Y (≥85th percentile) and were therefore at high risk of developing emotional and behavioral problems. The rest of the sample was a random selection of adolescents with lower SDQ-Y scores. The current cross-sectional analysis uses data from 855 adolescents who took part in the baseline measurement and had data for psychotic experiences and medication use available. The mean age was 14.8 years and 52% were female. The majority of adolescents fell within the medium-to-high household income range (€2400–4399; 50%), while 22% were in the high-income bracket (>€4400). Their average IQ matched the population average with a mean score of 100, and 45% of these adolescents had completed prevocational secondary education.

Outcome	IRR[1]	95% CI[2]	*p*-Value	*p*-Value (equivalence test)[3]
PQ-16 total score	1.07	[0.95, 1.20]	0.265	<0.001
PQ-16 hallucinations	1.11	[0.93, 1.32]	0.241	0.024
PQ-16 delusions	1.00	[0.82, 1.22]	0.976	0.005

[1]Incidence rate ratio.
[2]95% confidence interval.
[3]Practical equivalence was set to a half point PQ-16 score difference.

TABLE 1 Results from Poisson regression with methylphenidate use (past 3 months) as predictor and three PQ-16 scores as outcome. Estimates adjusted for age, sex, monthly household income and IQ.

To assess psychotic experiences, the self-report Prodromal Questionnaire-16 (PQ-16) was used.[6] A total sum score was calculated using all 16 items. Additionally, two subscales were calculated—hallucinatory and delusional experiences—using nine and four items, respectively. All items of the PQ-16 inquire about psychotic experiences at the time the questionnaire is completed. Methylphenidate use in the past 3 months was reported by the primary caregiver and coded as a binary "yes" or "no" variable. The PQ-16 and the medication use questions were filled out on the same day. As a proxy for socio-economic status, monthly household income was also reported by the primary caregiver.

We used Poisson regressions to investigate the association between methylphenidate use as predictor and PQ-16 scores as outcomes. We first tested associations adjusted for age and sex, then included monthly household income and IQ as covariates following past literature.[4] We report additionally on *p*-values from equivalence tests to provide evidence against the methylphenidate use hypothesis. We used multiple imputation to impute missing data on household income ($n = 56$). All analyses were conducted in R version 4.1.[7]

3 | RESULTS

A total of 98 (11.3%) adolescents in the cohort had used methylphenidate in the past 3 months. There were no age differences between users and non-users. There were more boys using methylphenidate (7.1%) than girls (4.2%). There were no considerable differences among educational level categories or in IQ scores.

The age and sex adjusted association between methylphenidate use in the past 3 months and psychotic experiences was nonsignificant for the PQ-16 psychotic experiences total score, nor was it significant for the hallucination and delusion subscales (all $p > 0.39$). Results did not change meaningfully after additional adjustment for household income and IQ. Fully adjusted associations are presented in Table 1. All remained nonsignificant. Additionally, the equivalences test rejected a difference between methylphenidate users and non-users for all psychotic experience outcomes (all $p < 0.05$).

4 | DISCUSSION

In this current study, we provide evidence against an association between methylphenidate use and psychotic experiences. Neither hallucinatory nor delusional experiences were associated with methylphenidate use in the past 3 months. A major strength of the cohort used for the current analysis was the high prevalence of psychotic experiences due to its design. This makes the current analysis a particularly well-powered one to investigate the association with methylphenidate. Spurious associations possibly reported in smaller studies were less likely to have occurred in the current report.[4] Indeed, national registry data from Sweden found no evidence for an association between methylphenidate and hospital visits related to psychosis.[8] Two important limitations from previous studies were addressed. First, the adolescents in the current study were old enough to clearly distinguish psychotic experiences from common transient experiences in early ages.[9] Second, we used a general population-based cohort as opposed to selected patients in a healthcare setting.[10] Selection bias was thus avoided. The current study was not randomized and thus confounding remains a possibility. However, confounding usually produces non-causal associations rather than masking them.[11] We therefore conclude the evidence does not support a link between methylphenidate and psychotic experiences.

FUNDING INFORMATION

The iBerry Study is funded by the Erasmus University Medical Center and the following institutes of mental health care (GGz): Parnassia Psychiatric Institute Antes, GGz Breburg, GGz Delfland, GGz Westelijk Noord-Brabant and Yulius. All funding organizations participate in the Epidemiological and Social Psychiatric Research Institute (ESPRi), a consortium of academic and non-academic research groups. The funding bodies had no role in the

conduct of the study, design, management, analysis, or interpretation of the data.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/acps.13630.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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How to cite this article: Zarchev M, Bouter D, Grootendorst van-Mil NH. No association between methylphenidate use and psychotic experiences in a population-based sample of adolescents at risk of emotional and behavioral problems. *Acta Psychiatr Scand*. 2023;1-3. doi:10.1111/acps.13630