# Do effects of methylphenidate decline after long-term use? A double-blind, placebo-controlled cross-over study of effects of methylphenidate on cognitive functioning and real world behavior in treatment naïve children compared to effects after 9 months of treatment in clinical practice

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| **Ethical review** | Approved WMO |
| **Status** | Pending |
| **Health condition type** | Cognitive and attention disorders and disturbances |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON49265

**Source**
ToetsingOnline

**Brief title**
MEDUSA

### Condition

- Cognitive and attention disorders and disturbances

**Synonym**
Attention Deficit Hyperactivity Disorder (ADHD)

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Accare
**Source(s) of monetary or material Support:** intern gefinancierd

## Intervention

**Keyword:** ADHD, Classroom behavior, Cognitive functioning, Methylphenidate

## Outcome measures

### Primary outcome

Measures include observations of classroom behavior rated by trained investigators and as perceived by the teacher (e.g. hyperactivity, off-task behavior, disobedient behavior, and (verbal) aggression), as well as the performance on the neuropsychological test battery measuring spatial working memory, sustained attention, response inhibition, and motor and mental response speed. Furthermore, EEG measures during rest (i.e. theta and beta power, theta/beta ratio) and during a response inhibition task (P300 peak) will be analyzed.

### Secondary outcome

Physical activity during classroom observation and everyday cognitief functioning as rated by the parents (BRIEF-P).

# Study description

### Background summary

Many children and adolescents with attention-deficit hyperactivity disorder (ADHD) use methylphenidate for extended periods of time, despite the lack of data on its long-term effectiveness. There is an ongoing debate whether individuals may develop tolerance towards methylphenidate over the longer term. It has been suggested that the acute short-term effects of methylphenidate diminish after prolonged use, but current evidence is lacking.

In addition to the characteristic pattern of symptoms of inattention, hyperactivity, and impulsivity, ADHD is also associated with cognitive functioning impairments, which may improve by using methylphenidate. However, it is currently unclear whether long-term methylphenidate use leads to changes in underlying brain functioning as expressed by effects on behavior (in the classroom) and neurocognitive measures (neuropsychological tasks, electroencephalography), and how this relates to each other.

## Study objective

The main objective of this study is to compare the acute effects of methylphenidate on behavioral and cognitive functioning in 6 to 12 year old treatment naïve children compared to the effects after nine months of treatment with methylphenidate in general clinical practice. We also aim to investigate if there is an association between the performance on the cognitive tasks, EEG measures, and classroom behavior.

## Study design

This study will consist of two series of double-blind, placebo-controlled cross-over trials: an initial trial to assess the effects of methylphenidate on behavioral and neurocognitive functioning prior to the start of treatment with methylphenidate in methylphenidate naïve children. The participants will also perform a test battery of cognitive tasks and an EEG-recording will be made, again once on a placebo and once on methylphenidate, one week apart. Participants will be observed in the classroom, once on a placebo and once on methylphenidate, one week apart. . After nine months of treatment the trial will be repeated.

## Intervention

Four day use of methylphenidate in a regular dose and four days use of placebo

## Study burden and risks

The burden for the participating families will include four visits to the clinical center. Each visit takes around 180 minutes. During each visit the participant will receive one tablet of study medication. During the first visit, an IQ screener will be taken right after taking the study medication

(approximately 20 - 30 min). Then an EEG recording (approximately 1 hour, including 30 min of recordings and 30 min of preparation time) will be made. The EEG recording will consist of two resting state periods (each 5 minutes, one at the start and one at the end of the recording) and a recording during a Stop Signal Task (20 min). Thereafter, participant will complete the test battery of cognitive tasks (approximately 5045 m inutes per test battery). One parent will complete two questionnaires (30 min) while they wait for the participant to finish the assessment. and The following day two investigators will observe the participant in the classroom (approximately 30 minutes).The risks of participating in this study are negligible and the possible physical and psychological discomfort mild. Participation in this study will benefit the individuals as the effectiveness of methylphenidate will be assessed at multiple levels (i.e. classroom behavior, cognitive functioning, brain activity). As ADHD is particularly prevalent during young age and the aim of the study is to compare the acute effect in drug naïve participants when they start treatment with methylphenidate and after they have been using it for nine months, this study requires a population of children and adolescents.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

## Inclusion criteria

• Children between the ages 6 and 12, any ethnicity or cultural background
• Who have been diagnosed with ADHD as confirmed with the Parent Interview for Child Symptoms (PICS) (obtained during routine clinical assessment)
• Who are going to start methylphenidate as per clinical decision
• No use of methylphenidate for the past six months
• Have a bodyweight of at least 20 kilograms
• Deemed reliable and compliant with the protocol
• Parents (or the legal guardian) and children (twelve years) have provided informed consent to participate in the study.

## Exclusion criteria

• Intellectual disability (based on available IQ below 70 or the clinical opinion of the investigator, taking into account relevant psychosocial information, e.g. educational level/academic achievements; or as confirmed by the IDS-2 IQ screener obtained in each participant, see section 7.1.2)

# Study design

## Design

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| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Crossover |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

### Recruitment

NL

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|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-08-2023 |
| Enrollment: | 60 |
| Type: | Anticipated |

### Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Medikinet |
| Generic name: | Methylphenidate |
| Registration: | Yes - NL intended use |

## Ethics review

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| Approved WMO Date: | 21-12-2020 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 06-12-2023 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
| --- | --- |
| EudraCT | EUCTR2020-003660-11-NL |
| CCMO | NL74817.042.20 |