

Meta-analysis: Dose-dependent Effects of Methylphenidate on Neurocognitive Functioning in Children with Attention-Deficit/Hyperactivity Disorder

Karen Vertessen 1, Marjolein Luman 2, Anouck Staff 2, Pierre Bet 3, Ralph de Vries 2, Jos Twisk 3, Jaap Oosterlaan 4

J Am Acad Child Adolesc Psychiatry. 2021 Sep 11;S0890-8567(21)01709-3.
doi: 10.1016/j.jaac.2021.08.023. Online ahead of print.

Classification: drug-treatment

Abstract

Objective: Neurocognitive deficits are at the heart of explanatory models of ADHD and lead to significant impairments in daily life. Determine dosing effects of methylphenidate (MPH) on a broad range of neurocognitive functions and investigate possible impairing effects of high doses is therefore important.

Method: Placebo-controlled trials were included that investigated MPH dosing effects on neurocognitive functions in children (5-18 years) diagnosed with ADHD. Effect sizes (SMD) were calculated for different neurocognitive functions (baseline speed, variability in responding, non-executive memory and executive memory, inhibitory control and cognitive flexibility) and, if available, for ADHD symptoms. Meta-regression analysis were used to investigate linear effects of dose (mg/kg/dose) and separate meta-analyses compared SMDs for three MPH dose ranges: low (0.10-0.30 mg/kg/dose), medium (0.31-0.60 mg/kg/dose) and high dose (0.61-1.00 mg/kg/dose).

Results: Thirty-one studies fulfilled inclusion criteria comprising 804 children with ADHD. MPH had beneficial effects on all neurocognitive functions ($d=0.20-0.73$). Significant linear dosing effects were found for ADHD symptoms and lower-order neurocognitive functions (baseline speed, variability in responding, non-executive memory), with greater enhancement of functioning with increasing dose. No dosing effects were found for higher-order neurocognitive functions (executive memory, inhibitory control and cognitive flexibility). No detrimental effects for MPH were found on any of the investigated functions.

Conclusion: MPH is superior to placebo in improving ADHD symptoms and a broad range of neurocognitive functions, however effects sizes regarding the effects of dose vary substantially between functions. Our data highlights the importance of

considering both neurocognitive and symptomatic aspects of ADHD in clinical practice.