OPEN ACCESS

Scientific Letters

III 1H-TOXRUN
International Congress 2024
02-03 May, 2024 | Porto, Portugal

Poster 80

Oral methylphenidate effects on GAP43 and PSD95 expression in the developing brains of Wistar Kyoto rats

Patrícia Soares-Couto [1,2,*], Vera Marisa Costa [1,2], Ana Dias-Carvalho [1,2], Susana Isabel Sá [3], Mariana Ferreira [1,2], Félix Carvalho [1,2] and João Paulo Capela [1,2,4]

[1] Associate Laboratory i4HB - Institute for Health and Bioeconomy, Faculty of Pharmacy, University of Porto, 4050-313 Porto, Portugal
[2] UCIBIO -Applied Molecular Biosciences Unit, Laboratory of Toxicology, Department of Biological Sciences, Faculty of Pharmacy, University of Porto, 4050-313 Porto, Portugal
[3] CINTESIS@RISE, Department of Biomedicine, Unit of Anatomy, Faculdade de Medicina, Universidade do Porto, Porto, Portugal
[4] FP-I3ID, Faculty of Health Sciences, University of Fernando Pessoa, Porto, Portugal

* Correspondence: up202204235@up.pt

Abstract

Background: Attention Deficit Hyperactivity Disorder (ADHD) is a prevalent neuropsychiatric disorder in childhood and adolescence [1]. Differences in brain structure, function, and connectivity were seen between ADHD and healthy individuals [2,3] but the underlying cellular and neurobiological mechanisms of ADHD are not fully understood [3,4]. **Objective:** To evaluate how clinically relevant oral doses of methylphenidate (MPH), a first-line ADHD treatment, affect body growth and the expression of brain proteins involved in synaptic plasticity, integrity, and neuronal growth. **Methods:** Wistar-Kyoto rats (18 males and 19 females) were randomly assigned to two groups. The treated group received a daily dose of MPH (5mg/kg in a 5% sucrose solution) by gavage, while the control group received an equivalent volume of 5% sucrose solution [5]. Administration began on postnatal day 15 (equivalent to childhood in humans) and lasted for 15 days, with the doses adjusted individually based on the animal's weight (25g per 100μL of drug or vehicle). The animal's weight was monitored throughout the experiment. On postnatal day 30, the animals were sacrificed, the brain was dissected in separate relevant areas. Liver, heart, and kidneys were also collected. Subsequently, the brain areas were processed by Western Blotting. **Results:** No statistically significant changes in body and peripheral organ weight were noticed among the control and treated groups in either males or female rats. Furthermore, MPH did not affect the expression of GAP43 and PSD95 proteins in the diencephalon and prefrontal cortex. Moreover, no notable sex differences were observed for these same parameters. **Conclusions:** Although MPH induced no significant changes in the analyzed parameters in males, females and even no sex related changes, further investigation into new brain areas, markers, and mainly ADHD models is crucial to understand the role of MPH on development.

Keywords: attention deficit dyperactivity disorder (ADHD); methylphenidate (MPH); neuroplasticity; Wistar-Kyoto

Acknowledgments

This research was funded by national funds from Fundação para a Ciência e a Tecnologia (FCT), I.P., project UIDP/04378/2020 and UIDB/04378/2020 of the Research Unit on Applied Molecular Biosciences (UCIBIO) and the project LA/P/0140/2020 of the Associate Laboratory Institute for Health and Bioeconomy—i4HB. Also, supported by national funds through Fundação para a Ciência e a Tecnologia (FCT), I.P., in the scope of the project "EXPL/MED-FAR/0203/2021".

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