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Enduring effects of methylphenidate on sleep in children with attention-deficit/hyperactivity disorder: a double-blind randomized controlled trial

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Background: Methylphenidate (MPH), the most commonly prescribed stimulant for Attention Deficit Hyperactivity Disorder (ADHD), effectively improves behavioral symptoms of ADHD [1]. However, possible (side) effects of MPH on sleep have not been well studied [2]. The question whether or not ADHD medications affect sleep poses a serious concern for parents and psychiatrists [3], also because preclinical studies suggest that exposure to ADHD medications

during brain development can induce long-lasting changes [4]. The aim of the current study was therefore twofold. Our first aim was to investigate the effects of MPH on sleep in medication-naive children for a relatively long treatment period of 16 weeks. Our second aim was to investigate whether the effects of MPH on sleep would outlast the pharmacological clearance of MPH. Based on the available literature, we hypothesized a negative effect of MPH on sleep, that would persist after treatment cessation.

Methods: In a double-blind, placebo controlled randomized clinical trial (Effects of Psychotropic Drugs on Developing Brain-Methylphenidate; ePOD-MPH) 50 medication-naive boys with ADHD between 10 and 12 years of age were included. Subjects were treated for 16 weeks with either MPH or placebo. Sleep was assessed using actigraphy and a sleep diary. Sleep was assessed at three time-points: prior to randomization, during treatment (week 8) and one week after treatment discontinuation (in week 17). Our main outcome measure was sleep efficiency, which is defined as the objective total sleep time divided by the objective time in bed, multiplied by 100 (%), and is thought to best summarize the quality, composition, continuity and consolidation of sleep. Our secondary outcome measures focused on timing and duration of sleep. Linear mixed models were used to analyze the data. Covariates included melatonin use (N = 9 at all time-points) and restless legs syndrome severity scores (N = 13 above cut-off prior to randomization).

Results: A significant time x treatment interaction effect was found for actigraphically estimated sleep efficiency ($p = 0.007$). MPH significantly improved sleep efficiency at trial end compared to baseline (+4.94%; $p = 0.005$), whereas no such effect occurred in the placebo condition (+0.97%; $p = 0.868$). Furthermore, after trial end the MPH condition showed higher sleep efficiency than the placebo condition (+5.84%; $p < 0.001$). In addition, positive effects of MPH treatment were found on timing and duration of sleep, indicating that the subjects treated with MPH fell asleep earlier, had a shorter sleep onset latency, and slept longer compared to the placebo condition and/or baseline. Inclusion of the covariates did not affect the findings.

Conclusions: In this RCT involving medication-naive boys with ADHD, we found a strong, positive effect of 16 weeks MPH treatment on the timing, duration and quality of sleep in boys with ADHD. As prior studies with shorter study durations found no-, or negative effects, our results indicate that a longer treatment period is needed to properly evaluate MPH related sleep problems. Interestingly, these effects persisted at least one week after drug clearance, in line with our findings on dopamine function in these children [5].

References

[1] Volkow, N.D., Wang, G.J., Fowler, J.S., Gatley, S.J., Logan, J., Ding, Y.S., Hitzemann, R., Pappas, N., 1998. Dopamine transporter occupancies in the human brain induced by therapeutic doses of oral methylphenidate. Am J Psychiatry 155, 1325–1331.

[2] De Crescenzo, F., Armando, M., Mazzone, L., Ciliberto, M., Sciannamea, M., Figueroa, C., Janiri, L., Quested, D., Vicari, S., 2014. The use of actigraphy in the monitoring of methylphenidate versus placebo in ADHD: a meta-analysis. ADHD Atten Deficit Hyperact Disord 6, 49–58.

[3] Hvolby, A., Jørgensen, J., Bilenberg, N., 2008. Actigraphic and parental reports of sleep difficulties in children with attention-deficit/hyperactivity disorder. Arch Pediatr Adolesc Med 162, 323–329.

[4] Andersen, S.L., 2005. Stimulants and the developing brain. Trends Pharmacol Sci 26, 237–243.

[5] Schrantee, A., Tamminga, H.G.H., Bouziane, C., Bottelier, M.A., Bron, E.E., Mutsaerts, H.M.M., Zwinderman, A.H., Groote, I.R., Rombouts, S.A.R.B., Lindauer, R.J.L., Klein, S., Niessen, W.J., Opmeer, B.C., Boer, F., Lucassen, P.J., Andersen, S.L., Geurts, H.M., Reneman, L., 2016. Age-dependent effects of methylphenidate on the human dopaminergic system in young vs adult patients with attention-deficit/hyperactivity disorder. JAMA Psychiatry 56, 1073–1086.

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