

Commentary

Randomised controlled trial of the short-term effects of osmotic-release oral system methylphenidate on symptoms and behavioural outcomes in young male prisoners with attention deficit hyperactivity disorder (ADHD): CIAO-II study: commentary, Asherson et al

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Keywords

ADHD; prevalence; forensic; prisoners; comorbidity.

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Response

We thank Professor Seena Fazel for his thoughtful comment. We agree there is a possibility of over-diagnosis of attention deficit hyperactivity disorder (ADHD) in this and other studies of prisoners with ADHD. He notes that in the CIAO-II study the prevalence is around 24%, which is greater than the 95% CI (14–21%) reported in a recent meta-analysis.¹ He raises the possibility that the lack of efficacy in our study might have been due to the inclusion of mostly subthreshold cases. In our view this is unlikely for several reasons. First, we applied DSM-5 criteria including an assessment of both childhood and adult symptoms, applying all criteria such as onset before age 12, significant impairment from the symptoms and symptoms not being better explained by another disorder. The final diagnosis was made in each case by trained senior psychiatrists, under supervision for this project, following an interview assessment for both ADHD and other common mental health disorders that frequently co-occur with ADHD. Nevertheless, we did not include informant report as this was not feasible to obtain in many cases, and the accuracy of patient report among prisoners is unknown, raising the possibility of false positive cases. False positive cases could arise either due to the inclusion of subthreshold cases, as suggested, or the inclusion of other disorders that might mimic ADHD, such as post-traumatic stress disorders, or the effects of drug use.

To address these possibilities, we conducted several post-hoc subgroup analyses (see additional materials to this publication). Firstly, we included a subgroup who reported seven or more symptoms of both hyperactivity/impulsivity and inattention in both childhood and adulthood. This is much higher than the usual threshold in DSM-5 of five or more symptoms in either domain, and therefore very unlikely to be subthreshold cases. A total of 102 participants met this higher diagnostic threshold criterion. In this subgroup, the estimated score difference between the OROS-MPH and placebo arms was estimated to be 1.83 (95% CI [–2.34, 6.01]), ($t = 0.87$, $P = 0.386$), reflecting a small but non-significant improvement in the OROS-MPH arm.

Regarding the possibility for other mental health disorders to mimic ADHD, we conducted further subgroup analyses without any comorbidity ($n = 36$), without an anxiety disorder ($n = 162$), without a mood disorder ($n = 137$) and without antisocial personality disorder ($n = 51$). Cases of borderline personality disorder ($n = 15$) and post-traumatic stress disorder ($n = 13$) were too small to warrant further subgroup analyses. Finally, we conducted a subgroup analysis of 73 participants with low-risk scores for drug and alcohol use. None of these subgroup analyses indicated any significant differences in the primary outcome between OROS-MPH and placebo groups, with the highest difference being for the group with no alcohol use problems (1.88, 95% CI [–3.65, 7.41]), ($t = 0.68$, $P = 0.499$).

Overall, while we cannot rule out the possibility that the high rates of comorbidity and drug use could potentially mask some of the effects of OROS-MPH in this study, we also found no evidence to support this. In our view, the analysis of 102 cases with very high levels of symptoms likely excludes the possibility of sub-threshold cases as an explanation for the study's findings.

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Data availability

A pseudo-anonymised data-set is available following a data sharing request to the corresponding author for consideration.

Author contribution

All authors contributed to the writing and revision of this report.

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Declaration of interest

P.A. has speaker and/or consultancy fees from Jansen-Cilag, Medice and Takeda. All others have no conflict of interest.

Reference

- 1 Beaudry G, Yu R, Långström N, Fazel S. An updated systematic review and meta-regression analysis: mental disorders among adolescents in juvenile detention and correctional facilities. *J Am Acad Child Adolesc Psychiatry* 2021; **60**(1): 46–60.

Psychiatry in history

Equanimity in psychiatric medicine: the mind in the middle

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Equanimity made a dramatic appearance in the field of medicine in the late nineteenth century. In his 1889 address to medical graduates at the University of Pennsylvania which also served as his farewell lecture before he departed to become chief of staff at Johns Hopkins Hospital, the Canadian physician Sir William Osler (1849–1919), FRS, FRCP, advised his students to understand the relationship of imperturbability with equanimity. Drawing upon the philosophical ideal of *aequanimitas*, he stressed that their future careers as physicians depended in no small part upon ‘coolness and presence of mind under all circumstances, calmness amid storm, clearness of judgment in moments of grave peril’.¹ As the ‘mental equivalent’¹ to imperturbability, a concept, he pointed out, involving ‘immobility, impassiveness, or, to use an old and expressive word, phlegm’,¹ equanimity involves ‘educat[ing] your nerve centers’¹ in order to find a balance between constriction and expansion. What Osler, one of modern medicine’s most influential and admired physicians, means by this is not the concealment of empathy but rather an open attitude of equilibrium that patients find calming, reassuring.

Equanimity has deep roots in Western sources (e.g. the Stoic philosophy upon which Osler explicitly drew) and Eastern ones, especially in Buddhist and Taoist traditions. For example, in Buddhism, there is a wonderful synonym for *upeksā* (Sanskrit) – or *upekkha* (Pali) – the term most commonly translated as equanimity. The word is *tatramajjhataṭṭā*, a compound of three Pali elements meaning *standing there in the middle of everything*. (Pali is the language of the *Tiṭiṭaka*, the sacred canon of Theravāda Buddhism.) This middle position is a privileged one. Here, because experience is not split into the categories of pleasant or unpleasant, immunity to immersion and avoidance may be found.

The awakened mind in the middle possesses a broad state of awareness, and is like an undivided context for the experience of things. In the ‘The Parable of the Plants’ of the *Lotus Sūtra*, it is compared to falling rain:

The rain falls everywhere,
Coming from all sides,
Flowing everywhere without limit,
Reaching over the face of the earth.²

Never reducible to a state of stillness, true equanimity has the conditions of vibrancy and range characterising the awakened mind. As an image of how consciousness operates generatively, it is like falling rain – it ‘goes to all’. Equanimity is thus the function of a flexible perceptual system, ranging over whatever may appear and fluidly noticing both the pleasant and the unpleasant with an awareness that one depends on the other for its meaning. Through an orientation toward the fullness of what is, equanimity is most recognisable.

References

- 1 Osler W. *Aequanimitas* 3rd ed. The Blakiston Company, 1932, p. 4.
- 2 *The Lotus Sutra*. Trans. Reeves G. Wisdom Publications, 2008, p. 162.

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