



Inappropriate Conclusions Regarding Neurotoxicity in Methadone and Methamphetamine Users

Comment on “Investigating cognitive functions in methadone users in comparison with methadone and methamphetamine users and control group”

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I read with great interest the study by Eslami-Shahrbabaki et al investigating the cognitive effects of concomitant opioid and stimulant use.¹ Given the important shifting patterns in polysubstance drug use, a better understanding of the interaction effects between opioids and stimulants, such as methamphetamine, is needed. However, I am concerned that the authors of this manuscript extrapolate conclusions far beyond the presented data. For example, the main conclusion of the study is that concomitant methadone and methamphetamine use has a “cumulative toxic effect on the brain”.¹ However, this statement extends beyond the data collected because the dependent measure does not evaluate toxic effects on the brain. Furthermore, I believe additional issues warrant further discussion, such as inappropriate study design and use of language that is less than precise in drug research.

In the primary conclusions, the manuscript states that the “MMT+MAMP group obtained the least [BACS] score compared to MMT and controls, [indicating] a cumulative toxic effect of concomitant use of methadone and MAMP”.¹ However, since the Brief Assessment of Cognition in Schizophrenia (BACS) is not a validated measure for neurotoxicity, the manuscript inappropriately concludes that as the BACS score for the methadone maintenance treatment (MMT) + amphetamine (MAMP) group is lower, opioid and methamphetamine use causes brain toxicity. This paper does not include a measure which could accurately assess neurotoxicity. To assess neurotoxicity, researchers typically analyze brain morphology data. Often, this requires the use of brain imaging techniques (i.e., MRI, PET) to collect evidence of changes in grey or white matter volume, white matter

tract integrity, or tissue oxygenation changes. Since the dependent measure does not provide any meaningful information about toxicity, such data should not be extrapolated to encompass conclusions regarding neurotoxicity and drug use.

Additionally, the study concludes that “Concomitant use of methadone and stimulants such as MAMP affects the cognitive function of consumers more than each other alone”.¹ However, the experimental design of the study does not include a methamphetamine-only group and this precludes statements comparing the effects of using MAMP alone vs. in combination with methadone. The study included three experimental groups: an MMT group, an MMT+MAMP group, and a control non-substance group. There is no data comparing the BACS scores between the MMT+MAMP group and an MAMP-only group. Thus, there is no evidence to support the conclusion that concomitant use of methadone and stimulants affects cognitive function more than methamphetamine use alone.

Another concern in this paper is the use of language that is less than precise. At several points, the piece notes the risks of combining opioids with “stimulants,” but this blanket term extrapolates data based on methamphetamine to an entire class of drugs with different chemical compositions and cognitive effects. Stimulants typically include amphetamines, ecstasy (MDMA), cocaine, nicotine, and caffeine. As this study focuses on the effects of methamphetamine drug use, conclusions indicating causation between broader stimulant use and cognitive impairment are unsupported extrapolations.

In addition, a broader concern is that the manuscript offers a less than careful interpretation which can



perpetuate a harmful narrative regarding drug use. The reality is, when used safely, opioids play a beneficial role in the treatment and management of debilitating chronic pain.² Many pain patients who use opioids concurrently use amphetamines to help manage other conditions, such as attention-deficit/hyperactivity disorder.^{3,4} These combinations help individuals maintain a daily routine and sustain a life worth living. Less than careful interpretations, which exaggerate the extent of neurological drug effects without enough supporting data, have the potential to contribute to the stigmatization and vilification of such individuals. It is increasingly important to understand the scientific reality of drug use without vilifying individuals, such as pain patients, who struggle with chronic conditions.

Finally, the manuscript selectively narrows focus on important drug issues in South and East Asia, calling these regions “a global hub for MAMP production and trafficking”.¹ However, the paper reports this finding without mentioning the equally disturbing extrajudicial killings that occur in the Philippines, and have occurred in Thailand.^{5,6} In these countries, government bodies believe that drug users are unredeemable because of irreversible brain damage and choose to perform extrajudicial killings of convicted drug users.⁶ There is overwhelming evidence that overstating the negative consequences of drugs, such as methamphetamines, contributes to these killings.⁷ Thus, I am concerned that the conclusions made in this manuscript linking methamphetamine use with toxicity and brain damage will further exacerbate such global responses..

Conclusion

Given the important shifting patterns in polysubstance drug use, a better understanding of the interaction effects between opioids and stimulants, such as methamphetamine, is needed. Future research must prioritize accurate study design and precise language to

ensure appropriate conclusions in drug research.

Authors' Contribution

Conceptualization: Jacqueline A. Erler, Carl Hart, Christopher Medina-Kirchner.

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Competing Interests

None.

Ethical Approval

Not applicable.

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