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HOW CAN WE INVESTIGATE THE ROLE OF TOPIRAMATE IN THE TREATMENT OF COCAINE USE DISORDER MORE THOROUGHLY?

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We read with interest Darke & Farrell's [1] commentary on our meta-analysis of topiramate published in the eighth issue of 2016 [2]. To elaborate on some of the ideas raised by the commentary, we focus our response on the question of why some studies implied a benefit and others did not. Overall, although the current evidence is not strong enough to support the routine clinical use of topiramate for the treatment of cocaine use disorder, in certain circumstances it may be useful for researching in terms of helping people with cocaine use disorders to stay abstinent from cocaine use.

A possible explanation for the negative findings among the studies may lay in different study designs and populations in the American [3–6] versus the Dutch [7] trials. The diverse study designs ranged from three double-blinded, placebo-controlled trials through the Dutch open label, non-placebo-controlled trial to a four- arm trial combined with contingency management (monetary vouchers), lasting for 18 weeks [7]. Other issues with allocation concealment and attrition bias clearly weakened the study designs. Moreover, the outcome measures were not identical across trials that made them less amenable to meta-analysis. For instance, all trials used different craving scales: craving was assessed using the Brief Craving Scale [3], the Minnesota Cocaine Craving Scale [4], the Brief Substance Craving and Cocaine Selective Severity Assessment Scale [5], the Cocaine Selective Severity Assessment Scale [6] and via the adapted Obsessive Compulsive Drinking Scale [7].

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Declaration of interests

None.

In terms of population diversity, most trials excluded people who had a concurrent use disorder on drugs other than cocaine; however, the excluded substance use disorders varied among the trials. For example, while Umbricht et al. [6] included people receiving methadone who also had a concurrent cocaine use disorder, Kampman et al. [4] included people with concurrent alcohol and cocaine use disorder. Apart from being an open-label design, the only Dutch trial also differed in several other ways: (i) the baseline cocaine use was higher, (ii) the maximal dose of topiramate was lower (200 mg/day) and (iii) the titration period was shorter (3 versus 8 weeks in the American trials). Furthermore, the included Dutch study implied that some type of adherence support intervention is necessary for pharmacotherapeutic approaches to managing cocaine use disorders [7].

In this regard, as contingency management shows promise in the treatment of cocaine use disorder [8–10], it would be interesting to see how topiramate might perform in the context of an adherence-supporting contingency management intervention involving topiramate in comparison to placebo. Robust evaluations of this kind require uniform outcome measures and comparable populations that are amenable to pooling in meta-analyses and that may come later, as the literature on this molecule matures. Until such designs arrive, we will still keep ‘searching for the answer’ to the open question about the role of topiramate in the cocaine use disorder treatment, as posed in Darke & Farrell’s commentary [1].

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References

1. Darke S, Farrell M. Commentary on Singh, et al. Still searching for the answer. *Addiction*. 2016; 111:1347. [PubMed: 27396462]
2. Singh M, Keer D, Klimas J, Wood E, Werb D. Topiramate for cocaine dependence: a systematic review and meta-analysis of randomized controlled trials. *Addiction*. 2016; 111:1337–46. [PubMed: 26826006]
3. Kampman KM, Pettinati H, Lynch KG, Dackis C, Sparkman T, Weigley C, et al. A pilot trial of topiramate for the treatment of cocaine dependence. *Drug Alcohol Depend*. 2004; 75:233–40. [PubMed: 15283944]
4. Kampman KM, Pettinati HM, Lynch KG, Spratt K, Wierzbicki MR, O’Brien CP. A double-blind, placebo-controlled trial of topiramate for the treatment of comorbid cocaine and alcohol dependence. *Drug Alcohol Depend*. 2013; 133:94–9. [PubMed: 23810644]
5. Johnson BA, Ait-Daoud N, Wang XQ, Penberthy JK, Javors MA, Seneviratne C, et al. Topiramate for the treatment of cocaine addiction: a randomized clinical trial. *JAMA Psychiatry*. 2013; 70:1338–46. [PubMed: 24132249]
6. Umbricht A, DeFulio A, Winstanley EL, Tompkins DA, Peirce J, Mintzer MZ, et al. Topiramate for cocaine dependence during methadone maintenance treatment: a randomized controlled trial. *Drug Alcohol Depend*. 2014; 140:92–100. [PubMed: 24814607]
7. Nuijten M, Blanken P, van den Brink W, Hendriks V. Treatment of crack-cocaine dependence with topiramate: a randomized controlled feasibility trial in The Netherlands. *Drug Alcohol Depend*. 2014; 138:177–84. [PubMed: 24629631]

8. Farronato NS, Dürsteler-MacFarland KM, Wiesbeck GA, Petitjean SA. A systematic review comparing cognitive- behavioral therapy and contingency management for cocaine dependence. *J Addict Dis.* 2013; 32:274–87. [PubMed: 24074193]
9. Alwin S, Jan van A, Wim van den B, Anna EG. Efficacy of contingency management for cocaine dependence treatment: a review of the evidence. *Curr Drug Abuse Rev.* 2012; 5:320–31. [PubMed: 23244344]
10. Rawson RA, Huber A, McCann M, Shoptaw S, Farabee D, Reiber C, et al. A comparison of contingency management and cognitive-behavioral approaches during methadone maintenance treatment for cocaine dependence. *Arch Gen Psychiatry.* 2002; 59:817–24. [PubMed: 12215081]