

# Cognitive Function in Patients with Opioid Use Disorder Treated with Opium Tincture or Methadone: Results from Opium Trial

James Wong<sup>1</sup>, Mohammadali Nikoo<sup>1</sup>, Shahin Akhondzadeh<sup>2</sup>, & Michael Krausz<sup>1</sup>

## Introduction

- Cognitive function in patients with opioid use disorder (OUD) and receiving opioid agonist treatment (OAT) is crucial as it impacts everyday functioning and rehabilitation [1].
- Chronic opioid use induces progressive changes in central brain regions related to learning, memory, reward, motivation, and cognitive control [2-4].
- Cognitive effects of OAT have been examined in studies, but findings are limited and inconsistent [5].
- We aimed to compare the cognitive function in patients with OUD treated with opium tincture (OT) or methadone over the course of a randomized controlled trial (RCT).

## Methods

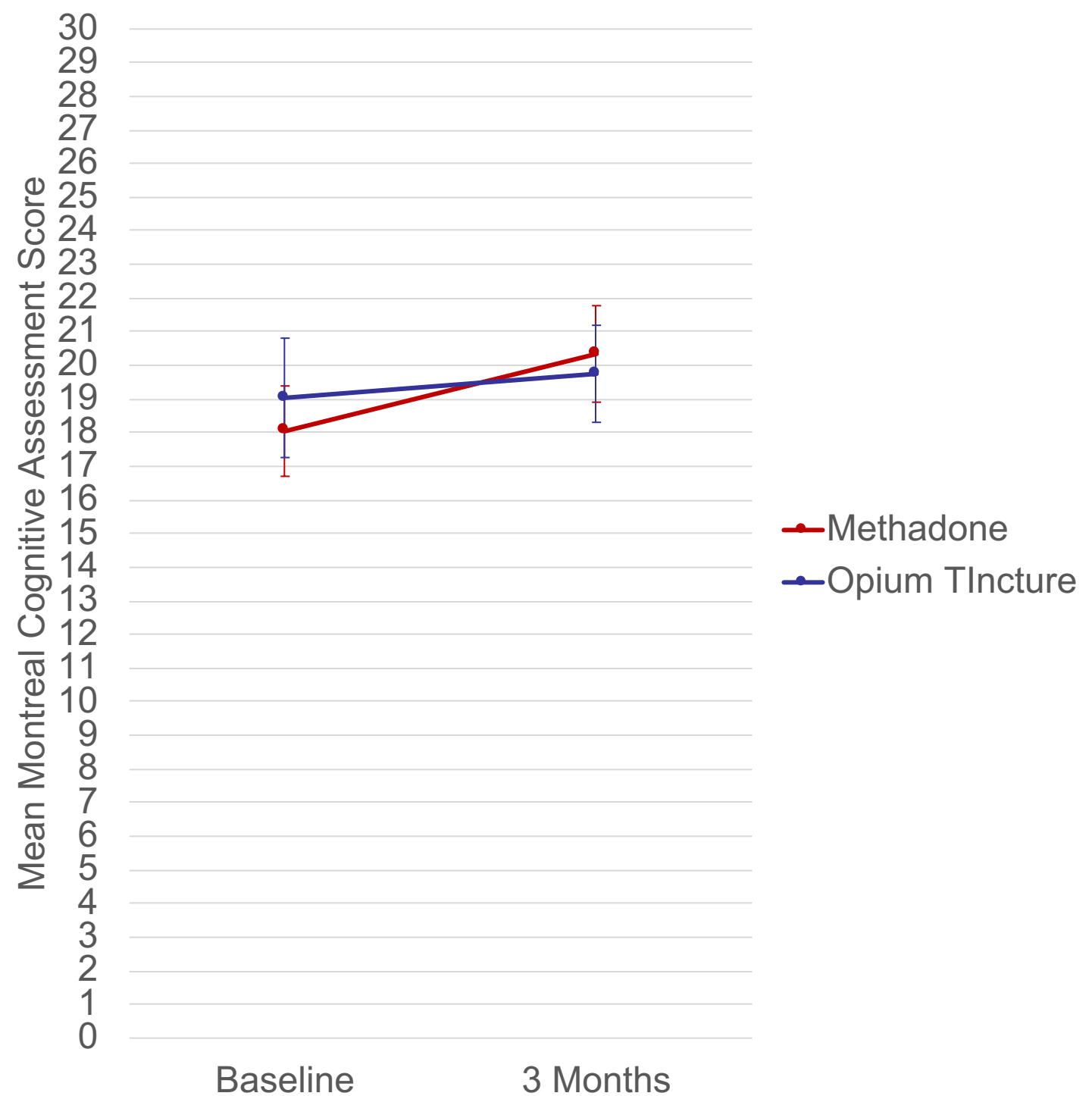
- A multi-center, double-blind, non-inferiority RCT comparing OT and methadone was completed [6].
- A stratified sample of 204 participants with OUD was randomized to OT or methadone with an allocation ratio of 1:1 using a patient-centered flexible dosing strategy.
- Participants were followed for 3 months.
- A key secondary outcome was cognition, measured by the Montreal Cognitive Assessment (MoCA), a brief screening measure designed to identify cognitive impairment using a 30-point test format [7].
- Participants completed the MoCA four times – at baseline, month 1, month 2, and month 3.

## Results

- A total of 72 of 204 participants fully completed the MoCA from baseline to 3 months.
- The mean MoCA scores of the 72 participants at baseline and 3 months were 18.431 (SEM = 0.535) and 20.111 (SEM = 0.518) respectively.
- A significant improvement in the mean MoCA scores of these participants was seen from baseline to 3 months,  $p = 0.001$ .
- Out of the 72 participants, there were 28 participants in the OT arm and 44 participants in the methadone arm.
- At baseline, there was no significant difference in the mean MoCA scores between the two arms,  $p = 0.371$ .
- In the OT arm, there was no significant difference in the mean MoCA scores between baseline and 3 months,  $p = 0.417$  (Figure 1).
- In the methadone arm, there was a significant improvement in the mean MoCA scores between baseline and 3 months,  $p < 0.001$  (Figure 1).

## Discussion & Conclusion

- Cognitive function in the 44 participants on methadone maintenance treatment (MMT) improved over the course of the clinical trial.
- Previous research on the effects of MMT on cognitive function have yielded conflicting evidence.
- Some studies have demonstrated decline in cognitive function with MMT in cognitive domains, such as memory and verbal function [5, 8, 9], and associated this to factors such as polysubstance use and psychiatric comorbidities.
- Other studies have demonstrated improvement in cognitive function consistent with our findings. The improvement was seen in domains such as concentration and cognitive control [5, 10], and may partly be due to associated reductions in illicit drug use and a less harmful lifestyle.
- Furthermore, some studies have not shown any changes in cognitive function [1, 5].
- There seems to be a lack of convincing hypothesis explaining the above-mentioned findings in either direction.
- This study supports evidence in favor of cognitive improvement with MMT and suggests some possible relation to the effects of methadone as opposed to other opioids. However, the lack of significant difference in the OT arm could be due to the arm's smaller sample size.
- Further studies are warranted to unravel the underlying mechanism for effects of MAT on cognitive function.



**Figure 1.** Changes in mean MoCA Score from Baseline to 3 Months in OT and Methadone arms