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Comparative Analysis of the Effects of Actual Versus Assumed Opioid Experience on the Regulation of Ventral Striatal Opioid Receptor Gene Expression

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Introduction

- The opioid crisis has surged across the United States, with a staggering 75% of drug overdose fatalities in 2020 involving an opioid¹. A 38% increase in opioid-related deaths was observed from 2019 to 2020, emphasizing the urgent need for understanding the neurobiological mechanisms underlying opioid addiction¹.
- The mu (MOR) and kappa-opioid receptors (KOR) in the ventral striatum are thought to play a critical role in the addictive potential of opioids, as well as possible therapeutic interventions²⁻⁶.

Aim

This study aims to compare current methods and a new quantitative approach to more accurately assess the role of drug experience in the regulation of opioid receptor expression levels in an oxycodone self-administration and abstinence model.

Methods

- 36 male Sprague Dawley rats were used.
- Jugular catheters were inserted.
- Animals were trained for 20 days under two different conditions: short access condition and extended access condition.
- Short access:** n = 15 oxycodone n = 3 saline; 0.1 mg/kg/infusion; 3 h/day
- Extended access:** n = 15 Oxycodone n = 3 saline; 0.1 mg/kg/infusion; 9 h/day

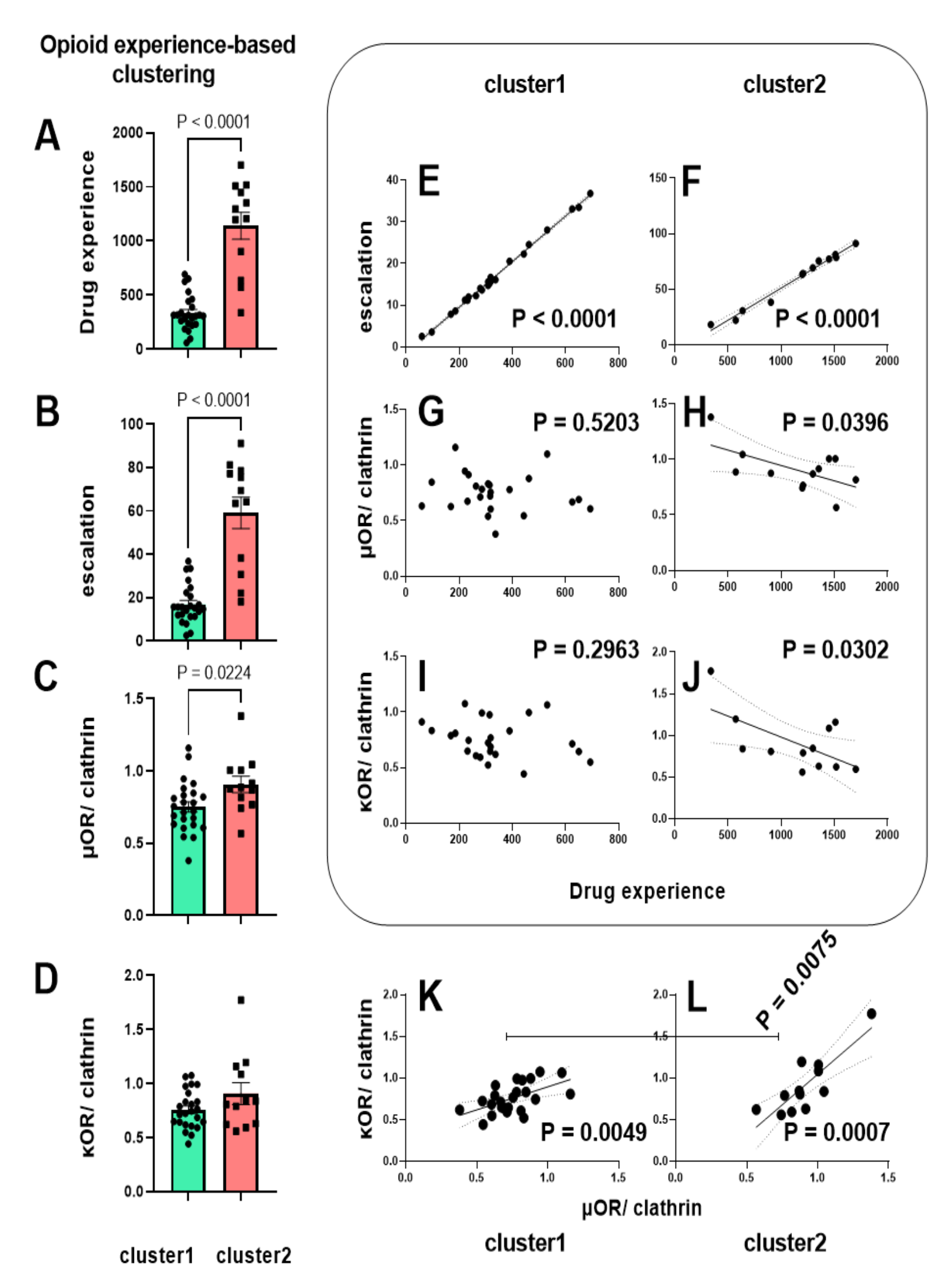
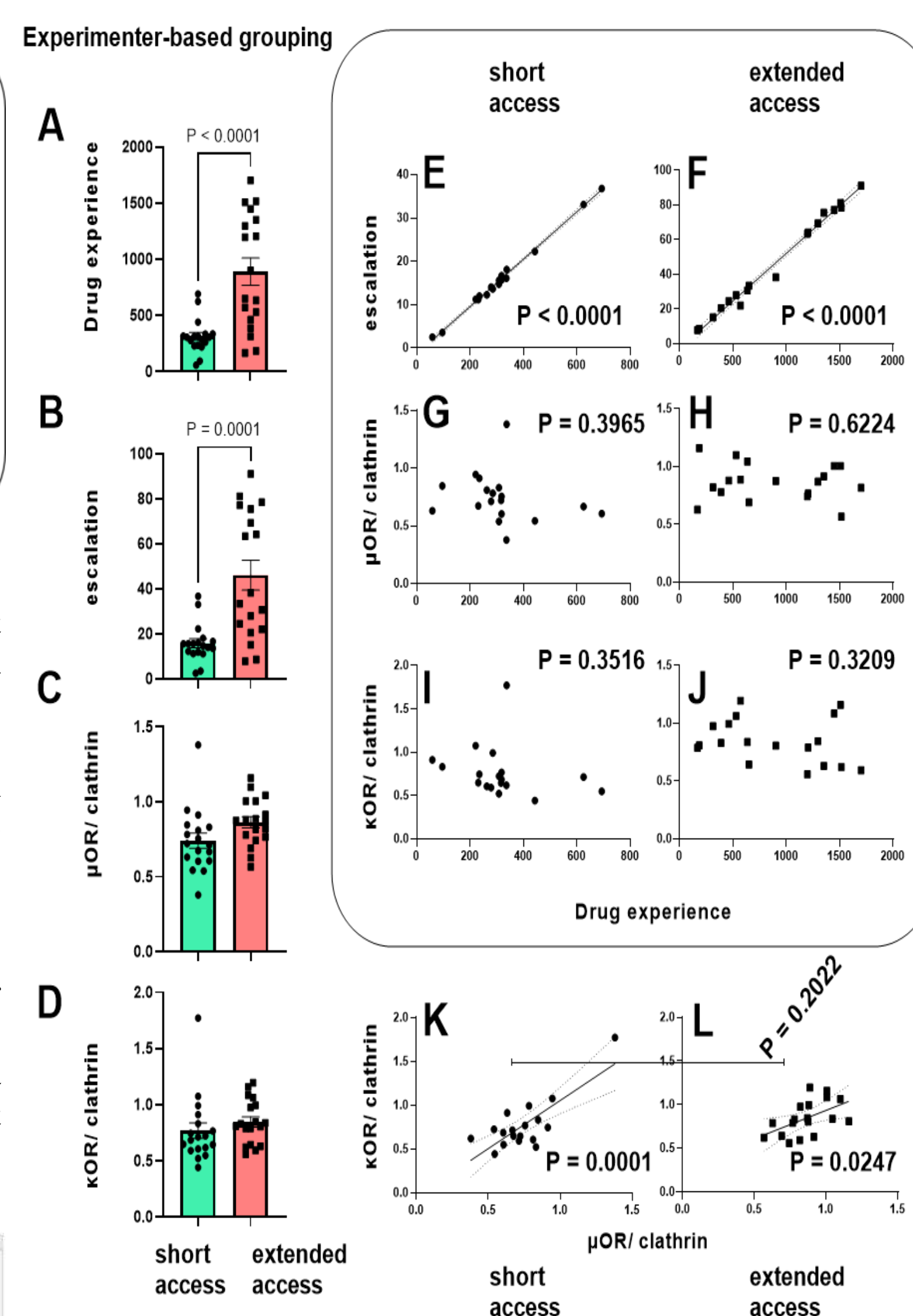
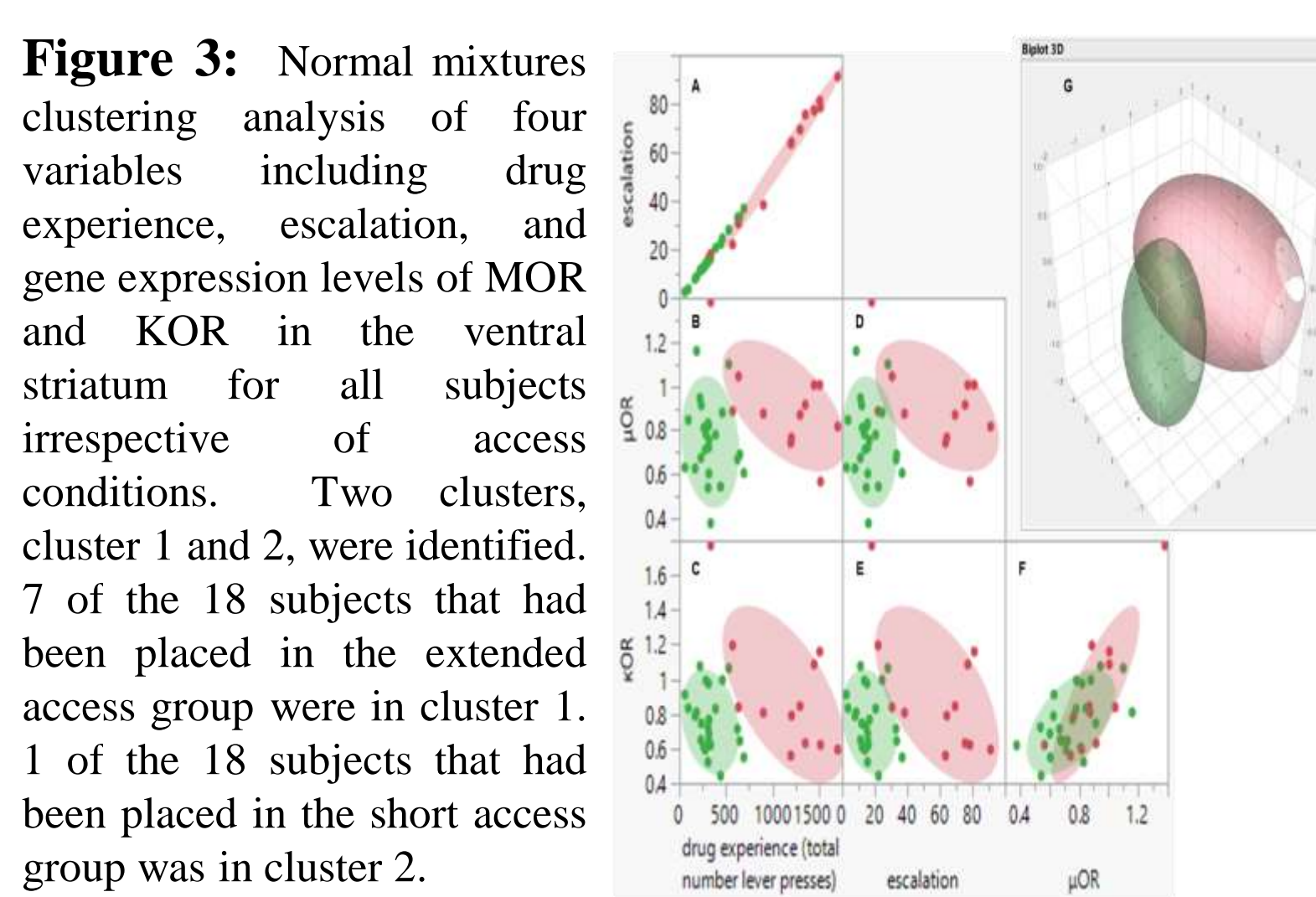
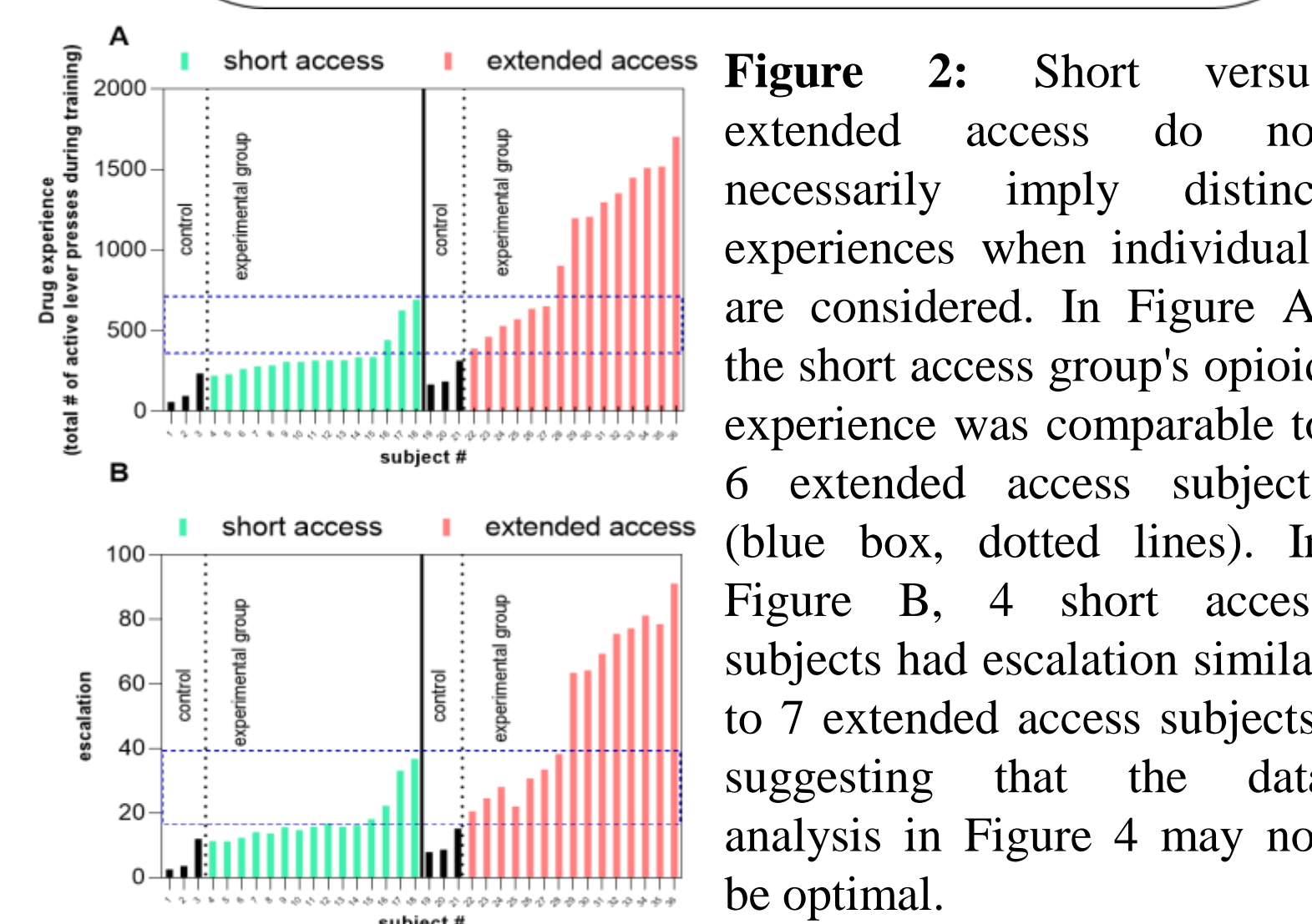
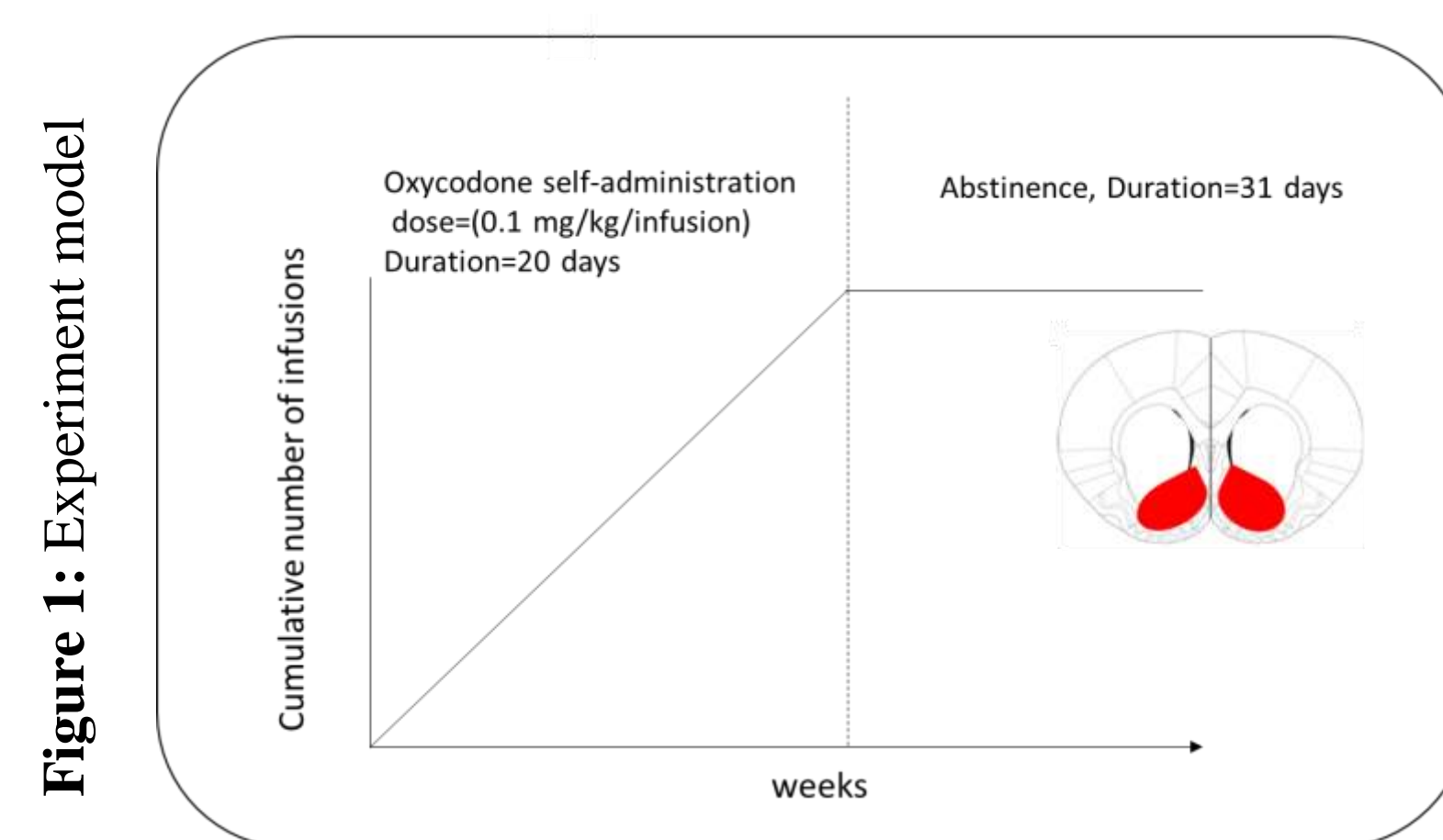
Post- Experimentation and Euthanasia

- I.V catheters were closed, and rats were returned to individual cages. They had no more access to oxycodone.
- 31 days after the last exposure, rats were euthanized, and brains were extracted. Ventral striatum was isolated and RT-PCR analysis was carried out to assess mu and kappa gene expression levels.
- Gene expression level was measured by comparing it to a control gene within the same sample (Clathrin mRNA) and expressed as a fold change.

Variables

Drug Use Experience: Total number of drug infusions animal obtained; **Escalation:** Rate of change of drug use over the 20 day-training period

Figures



Conclusion

- The quantitative method with clustering is more sensitive in identifying the influence of opioid experience on opioid receptor (mu and kappa) expression levels in the ventral striatum.
- Opioid experience, irrespective of access conditions, plays a role in the regulation of opioid receptor expression levels in the ventral striatum following prolonged abstinence from oxycodone self-administration.

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