

# Investigating cognitive function in people with chronic non-cancer pain prescribed opioids: A longitudinal study

---

JANE AKHURST<sup>1</sup>, AMY PEACOCK<sup>1,2</sup>, & RAIMONDO BRUNO<sup>1,2</sup>

<sup>1</sup>UNIVERSITY OF TASMANIA

<sup>2</sup>NATIONAL DRUG AND ALCOHOL RESEARCH CENTRE



# Conflicts of interest

---

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

JA is supported by an Australian government Research Training Program stipend. AP is supported by a National Health and Medical Research Council research fellowship (#1109366) and has received an untied educational grant from Seqirus for a post-marketing study of tapentadol. The National Drug and Alcohol Research Centre at UNSW Australia is supported by funding from the Australian Government under the Drug and Alcohol Program.

RB has received investigator-initiated untied educational grants from Reckitt Benckiser/Indivior for the development of an opioid-related behavior scale and a study of opioid substitution therapy uptake among chronic non-cancer pain patients. RB and AP have received an untied educational grant from Mundipharma for a post-marketing study of oxycodone.

**BACKGROUND:**

# Acute cognitive effects of opioids

---

- Psychoactive effects (e.g., sedation) are common
- Cognitive effects in healthy volunteers (Strand, 2019; Zacny, 1995):
  - Impaired task performance vs. baseline, mostly for attention tasks
  - Effects vary by dose, type of opioid
- Real-world consumption: chronic use → tolerance

## BACKGROUND:

# Chronic cognitive effects in CNCP

---

- Cross-sectional studies
  - Opioid group vs. healthy controls: some impairment in attention (Sjogren 2005)
  - Opioid vs. opioid-free CNCP groups: mixed (Sjogren 2005; Schiltewolf 2014)
- Longitudinal studies
  - Pre-opioid vs. 3-12 months follow-up: no change or improvement for attention, executive functions, and memory (Freo 2018; Jamison 2003; Tassain 2003)
  - Only Tassain used control group

**BACKGROUND:**

# Knowledge gaps & aims

---

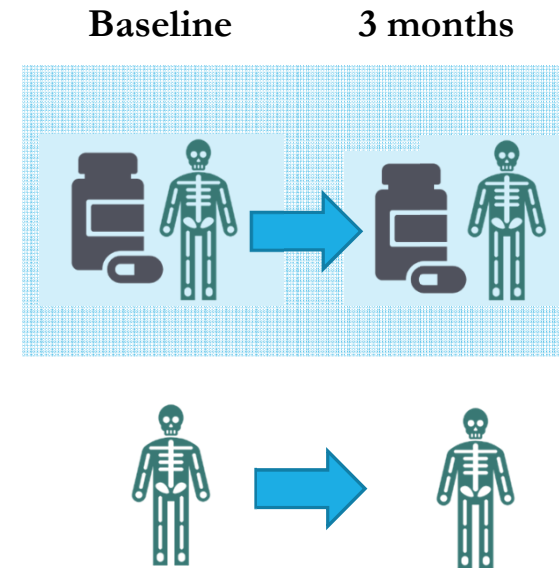
- What is driving cognitive effects: opioids, pain, or practice?
- Within CNCP groups, do chronic opioid consumers improve to the same degree as non-consumers?
  - Differential practice effects: subtle impairment?
- **Research aim:** compare cognitive performance for Opioid group (CNCP, chronic opioid use) vs. Controls (frequent pain, no opioids) across time

## DESIGN & METHODS:

# Study design & measures

---

- Outcomes: cognitive task performance
- Design: mixed 2(Group: Opioid, Control) x2(Time: baseline, 3 months) study
  - Multi-level mixed models for repeated measures; covariates: pain severity & interference, premorbid IQ
  - *t*-tests against normative data

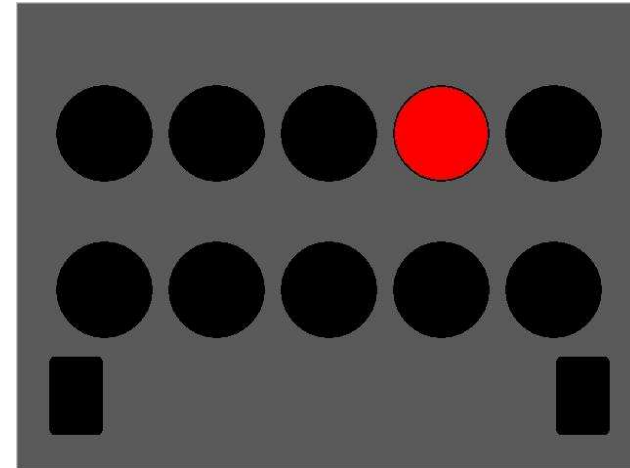


## DESIGN & METHODS:

# Attention tasks

---

- Reaction Test (choice RT)
  - Respond to critical combination of stimuli
  - Score: RT (ms)
- Determination Test (stress tolerance)
  - Respond to all stimuli
  - Score: no. correct responses
- Scores: percentile ranks based on general population ( $M=50$ )
  - Higher score = better performance



## DESIGN & METHODS:

# Memory tasks

---

- Rey's Auditory Verbal Learning Test (verbal memory)
  - 15-item word list, read aloud 5x
  - Score: no. words recalled for immediate (Trial 1), enhanced (Trial 5), & delayed recall
- Royal Prince Alfred Prospective Memory Test
  - 4 scenarios; responses cued by trigger (e.g., alarm)
  - Score: 0-12, based on accuracy & timeliness
- Both tasks: higher score = better memory



## DESIGN & METHODS:

# Other assessments

---

- Demographics:
  - **Age, sex, education**
  - Wechsler Test of Adult Reading [WTAR]: **premorbid IQ**
- Co-morbidities that can affect cognition:
  - Brief Pain Inventory [BPI]: **Pain severity & interference**, past 24 hrs
  - Kessler Scale of Psychological Distress [K10]: **Psych. distress**, past 30 days
  - Alcohol Use Disorders Identification Test [AUDIT]: **Alcohol use**, past year

## RESULTS:

# Sample characteristics

---

- $N=26$  (14 Opioid, 12 Controls)
- Opioid dose same at baseline  
( $M=57.2$ ) & 3 months ( $M=60.0$ ),  
 $p=.738$
- Covariates: BPI severity & interference, WTAR
  - BPI interference:  
Opioid > Control,  $p=.012$
  - WTAR: Opioid < Control,  $p=.028$



### Mean age & gender

Opioid: 42.6 yrs & 71.4% female;  
Control 34.4 yrs & 91.7% female



### Opioid treatment duration

Median 17 months (3–30)



### Average daily opioid dose

Median 40mg/day (OME)

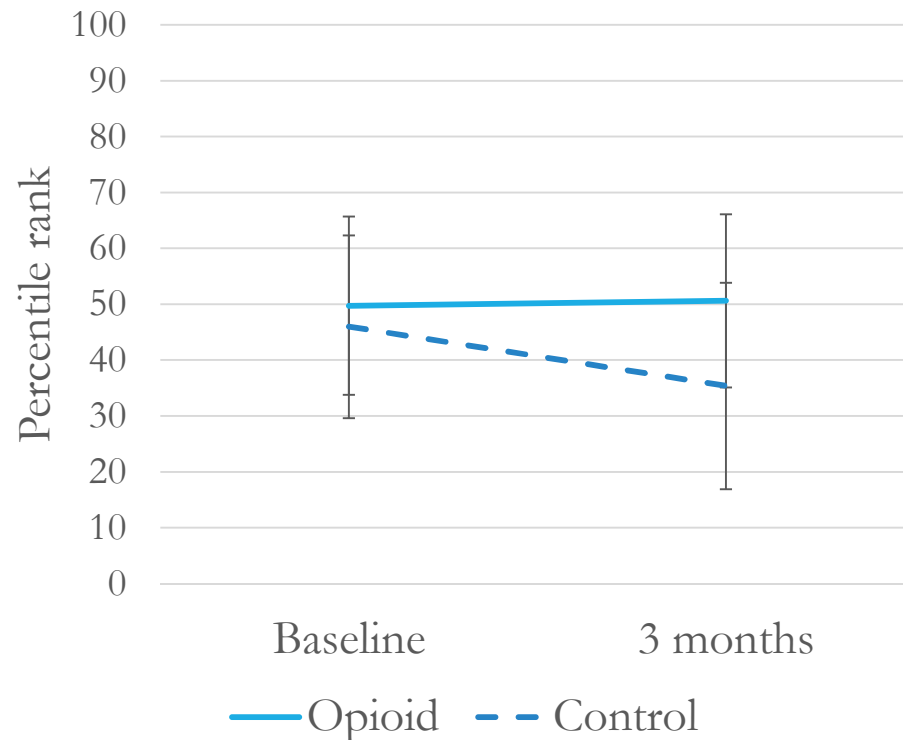


UNIVERSITY of  
TASMANIA

AUSTRALIA

## RESULTS:

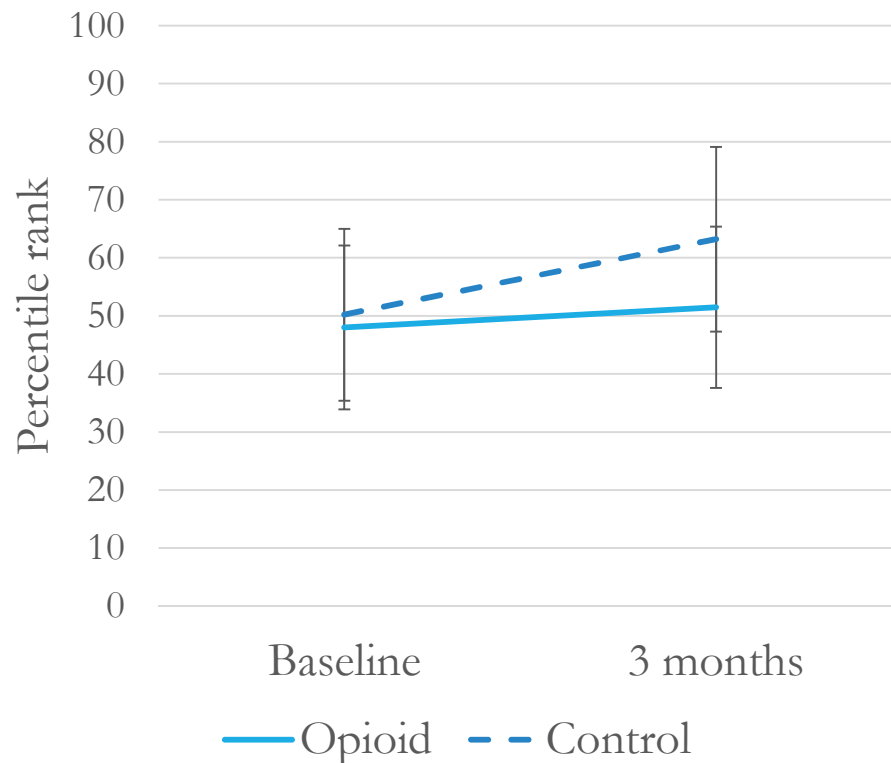
# Attention tasks: Reaction Test



- Non-significant difference to general population ( $M=50$ ),  $p \geq .463$  (raw means)
- Mixed models: N.S. main & interaction effects,  $p_s \geq .258$
- N.S., moderate magnitude decline for Controls from baseline to 3 months,  $p = .136$ ,  $g = 0.43$

## RESULTS:

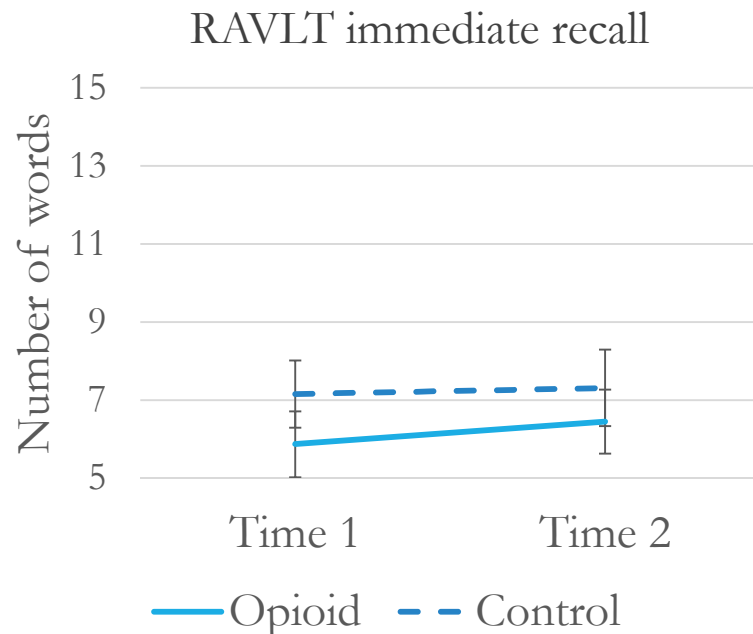
# Attention tasks: Determination Test



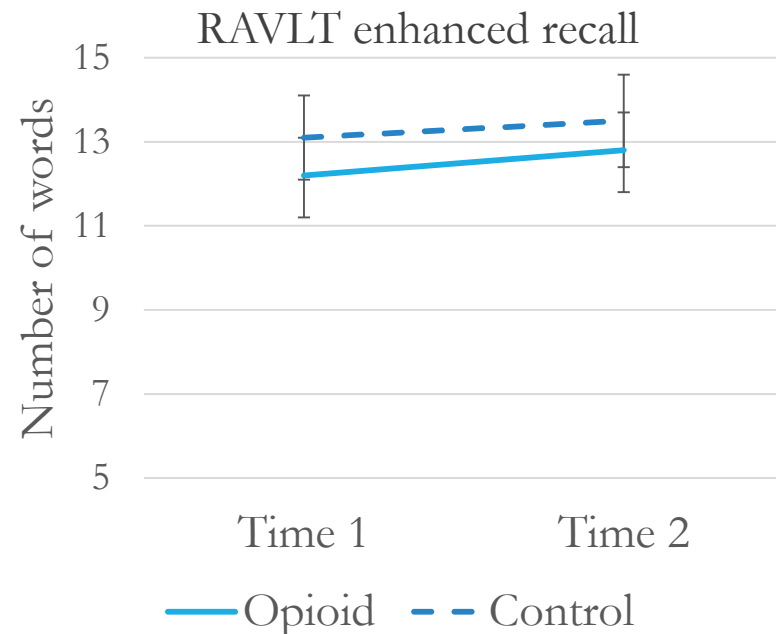
- N.S. difference to general population ( $M=50$ ),  $p \geq .175$  (raw means)
- Mixed models: Group\*Time interaction,  $p = .040$
- Controls significantly improved from baseline to 3 months,  $p = .002$ ,  $g = 1.08$

## RESULTS:

# Memory tasks



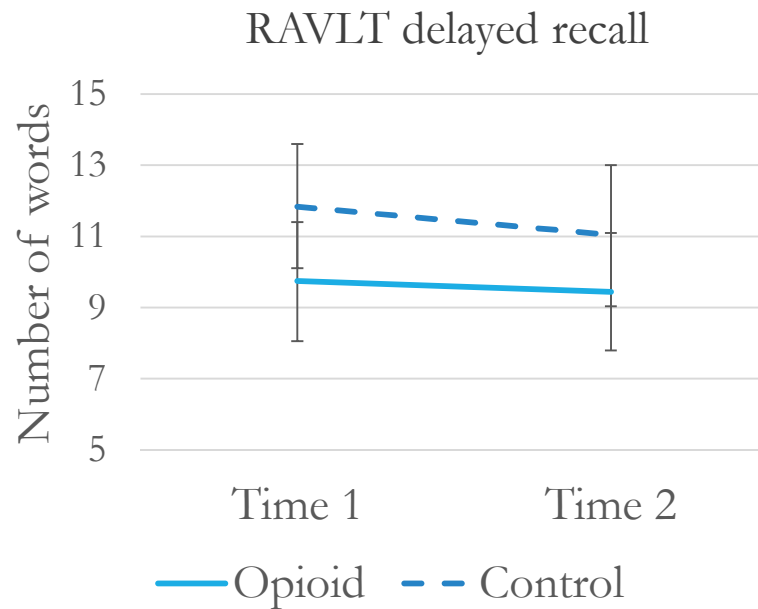
- N.S. main & interaction effects,  $ps \geq .084$
- N.S., moderate magnitude improvement for Opioid group from baseline to 3 months,  $p=1.03$ ,  $g=0.44$



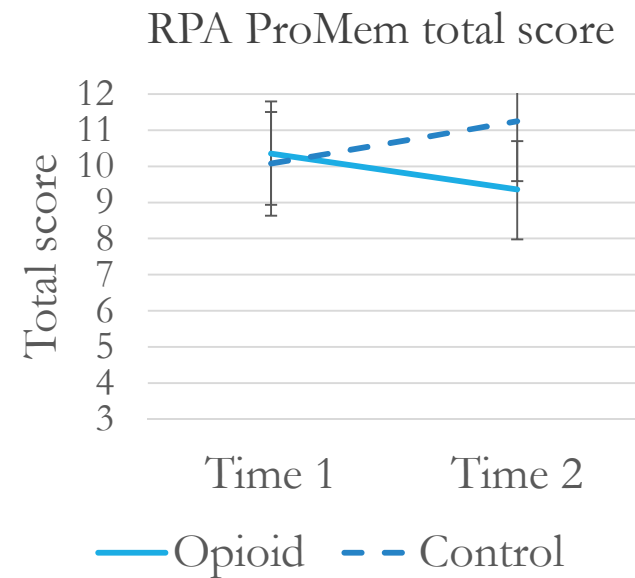
- N.S. main & interaction effects,  $ps \geq .173$

## RESULTS:

# Memory tasks



- N.S. main & interaction effects,  $ps \geq .134$



- N.S. main & interaction effects,  $ps \geq .059$

## DISCUSSION:

# Findings & implications

---

- Summary of findings:
  - No worsening over time, similar to previous research (e.g., Tassain 2003)
  - Choice RT & memory similar between groups, with no change or mild improvement over time for opioid consumers
  - Differential practice effects for stress tolerance
- What does this add?
  - Adds to growing body of work suggesting chronic opioid use does not impair memory function once stable dosing has been achieved
  - Indicates some subtle impairment effects for attention

# Thank you!

---

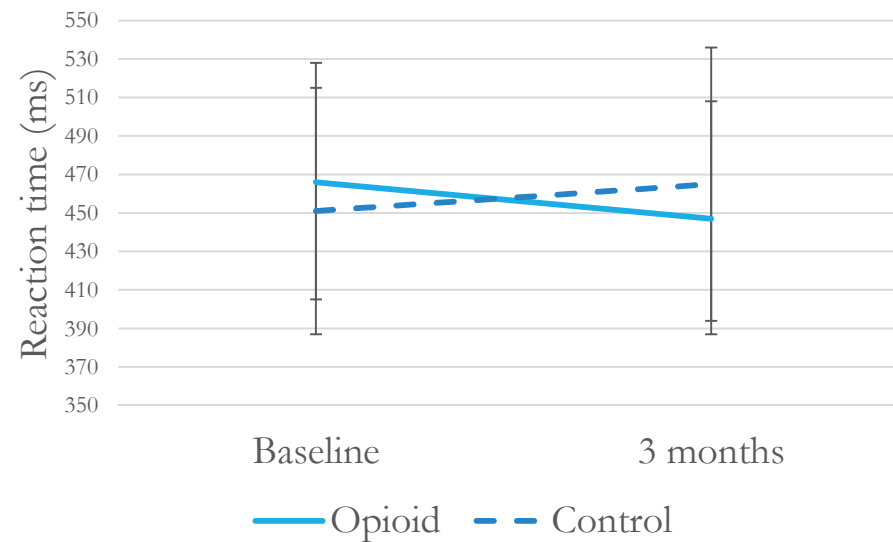
Any questions?



## BONUS RESULTS:

# Reaction Test, raw data

---

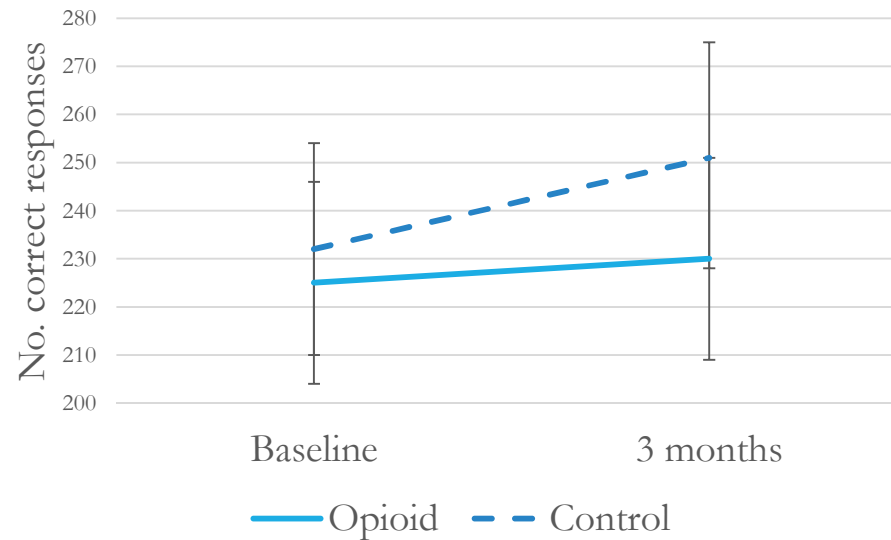


- N.S. main & interaction effects

## BONUS RESULTS:

# Determination Test, raw data

---



- Group\*Time interaction,  $p=.040$
- Significantly > number correct for Controls from baseline  
( $M=232$ ) to 3 months ( $M=251$ ),  $p=.001$ ,  $g=1.19$