

ORAL CONTRACEPTIVES IMPROVE SPATIAL LEARNING AND ANXIETY IN A RODENT MODEL DESPITE OPPOSING ANDROGENICITY

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Introduction

- 14% of women aged 15-49 use oral contraceptives (OC), or “the pill.”¹ Despite this, the impact of oral contraceptives on cognition and affect are not well understood.

- OC can be classified as androgenic or antiandrogenic. Androgenic pills contain androgenic progestins, which act like androgens (i.e. testosterone) in the body and have masculinizing effects on the brain. Antiandrogenic pills do the opposite, producing feminizing effects on the brain.

- “Masculinizing” refers to the increase in structural or functional traits in the brain typically found in men.²

- “Feminizing” refers to increases in traits found in women.²

- Men typically exhibit better spatial learning and memory than women, so masculinizing (androgenic) pills may improve spatial abilities and feminizing (antiandrogenic) pills may hinder spatial ability.^{3,4}

- Few studies on OCs have found effects on cognition and anxiety. However, these studies do not differentiate between pill type. The current study looks at both types of pills in isolation to ensure that possible opposing effects of androgenic and antiandrogenic OCs can be seen.

Hypothesis

Spatial Learning:
Best Performance ----- Worst Performance
Androgenic treatment > Control > Antiandrogenic treatment

Anxiety:
High ----- Low
Androgenic treatment > Control > Antiandrogenic treatment

Methods

Control
N = 7

Androgenic
Falmina (LNG)
N = 7

Antiandrogenic
Yasmin
(DRSP)
N = 7

Timeline

Pill at 7 weeks old

5 weeks treatment

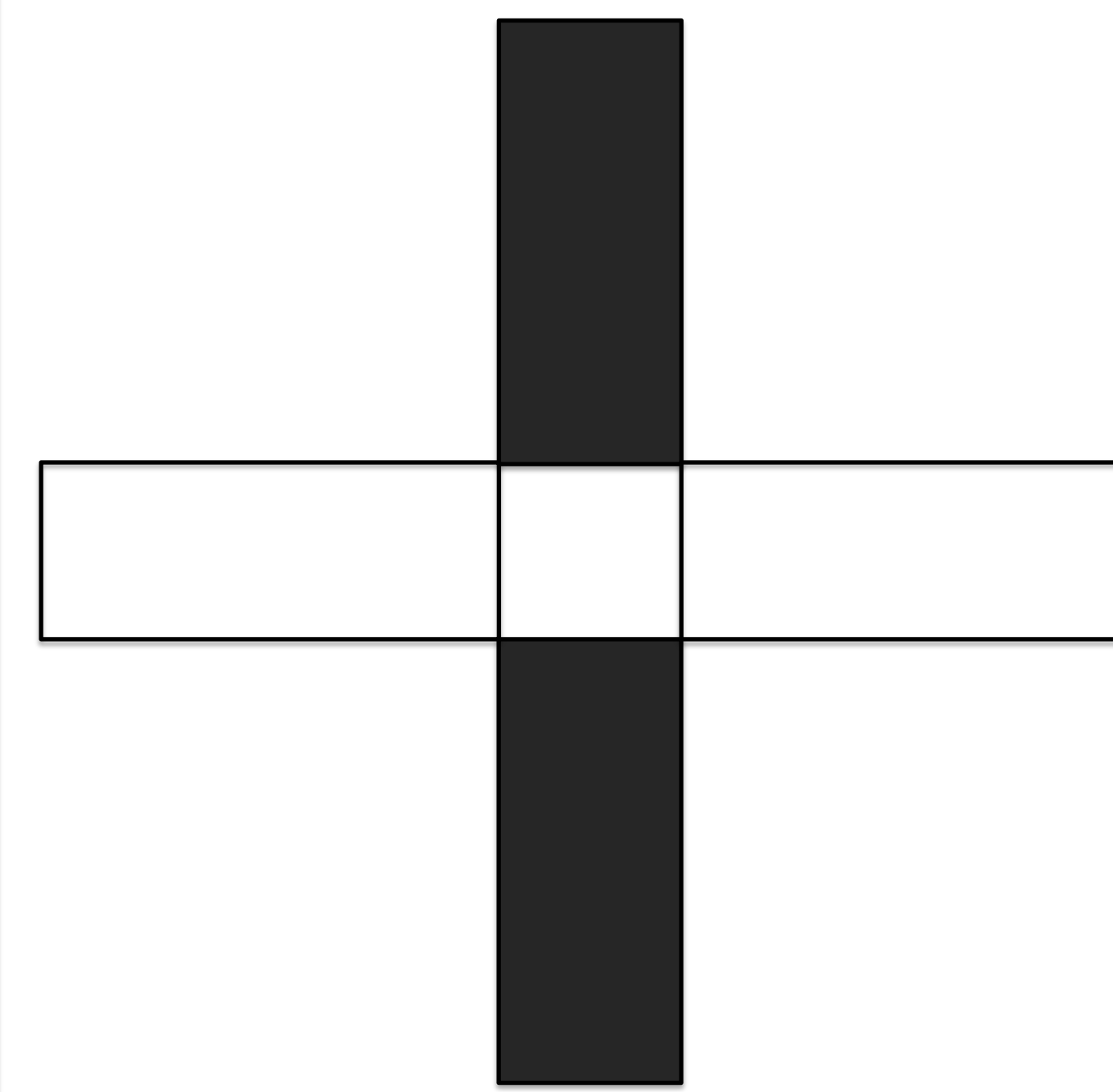
Elevated Plus Maze
1 day

24 hours

Morris Water Maze
6 days

Materials

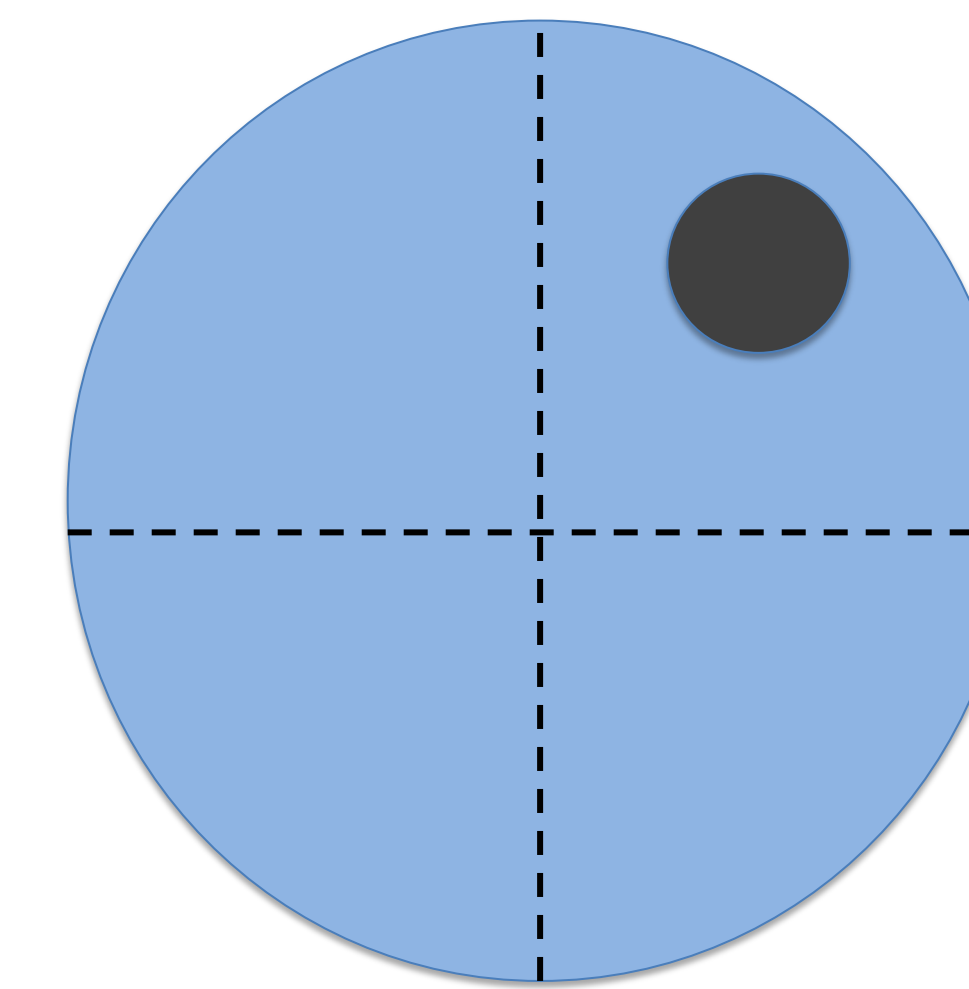
Elevated Plus Maze



Assesses anxiety

- One 5 minute trial per animal
- Animal placed in center
- More time in closed arms and less time in open arms indicates more anxiety

Morris Water Maze

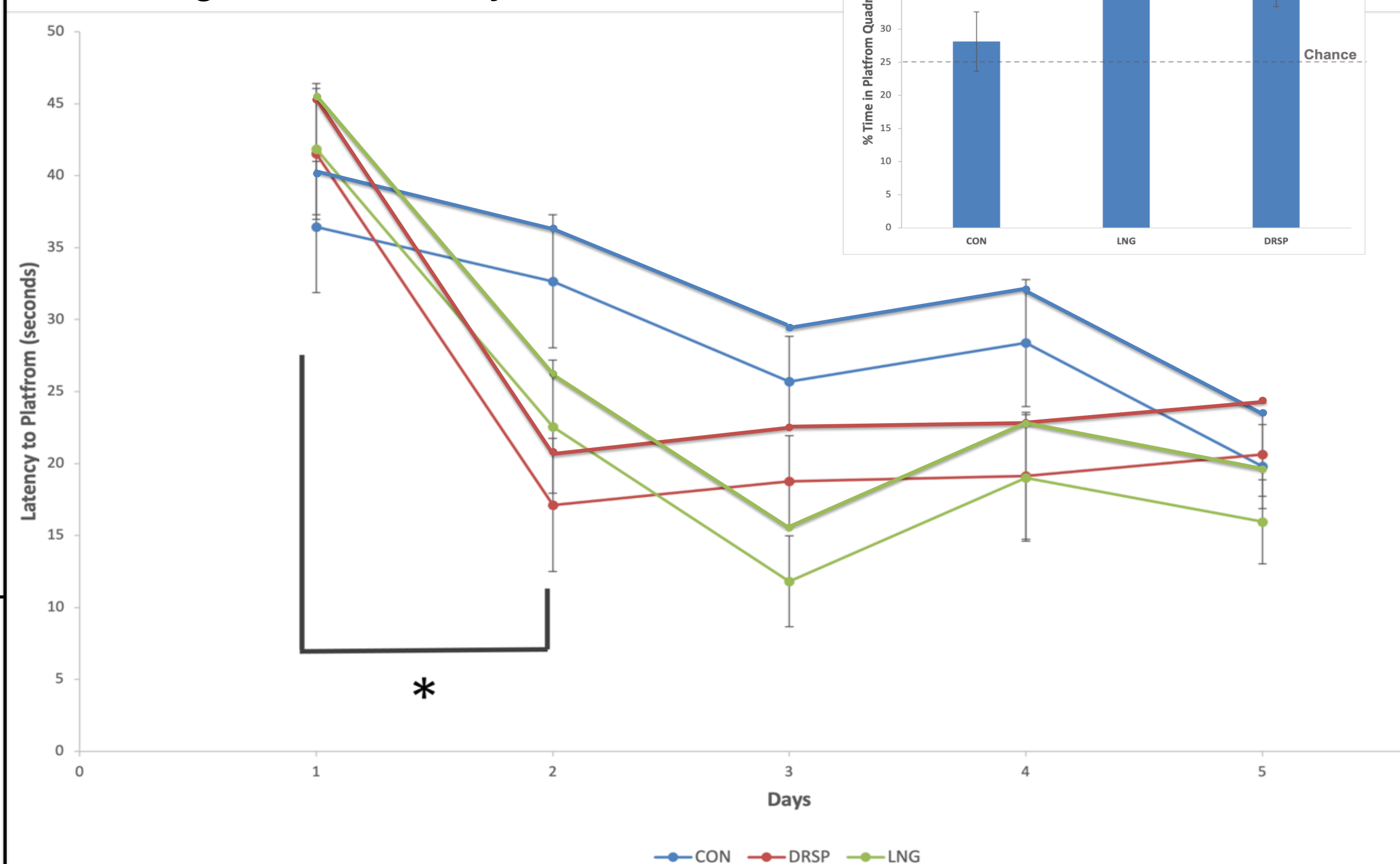


Assesses spatial learning/memory

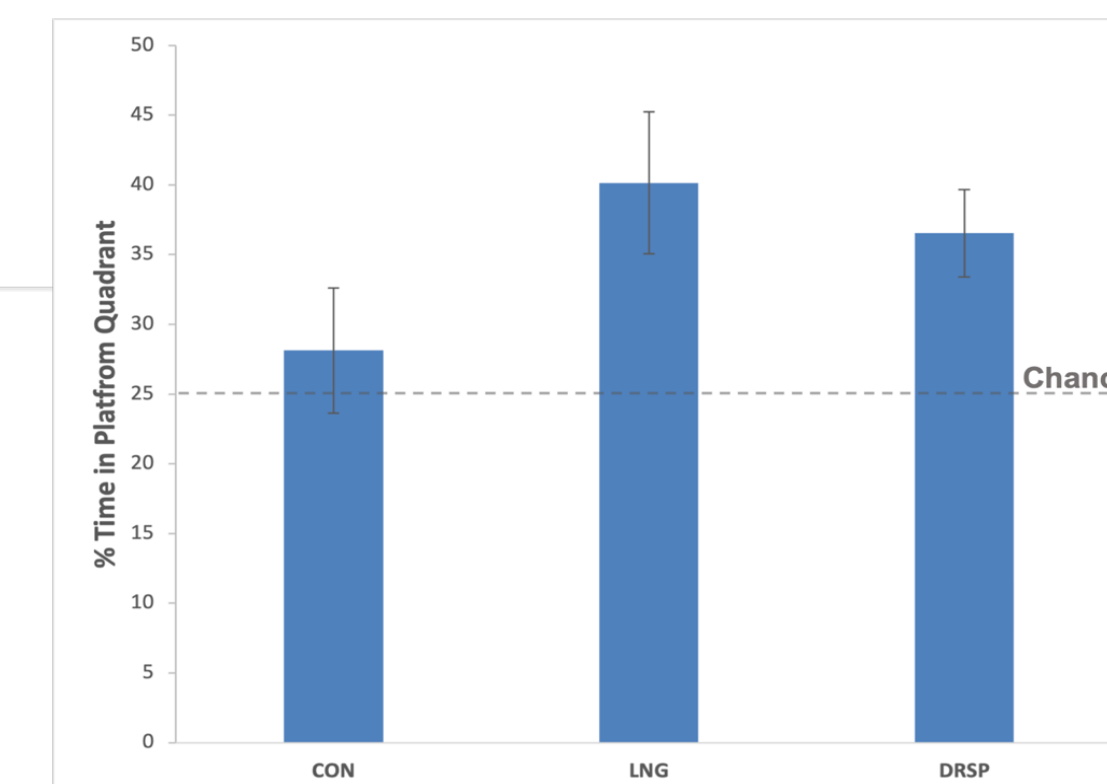
- 5 days, 4 trials/day, 1 minute/trial, to find the hidden platform
- Probe trial: hidden platform removed, one minute
- More time in quadrant with platform indicates better spatial learning

Spatial Learning Results

Learning Data: Latency to Platform



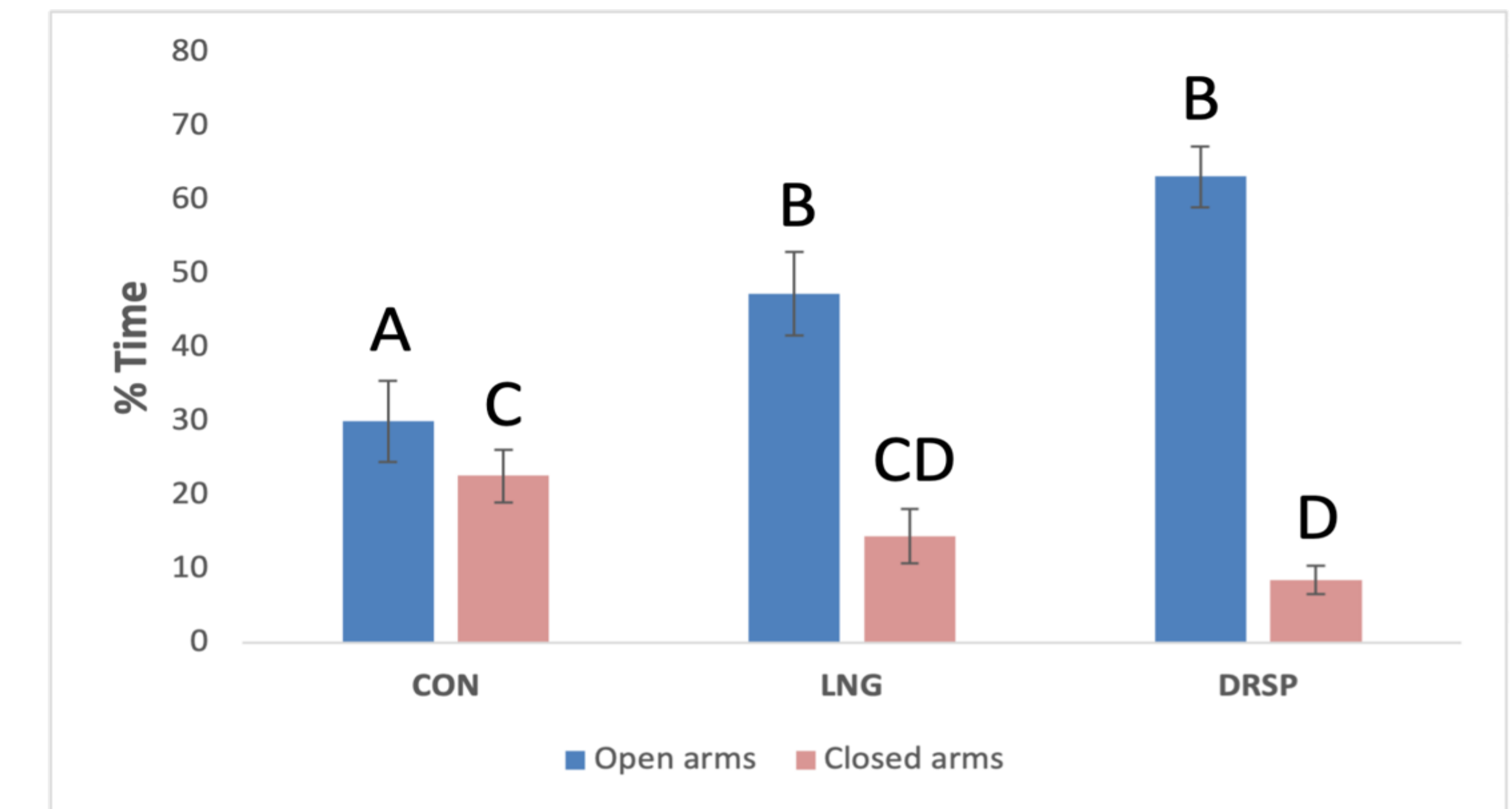
Probe Trial Data



- All groups showed learning through the 5 days of testing
- LNG and DRSP groups learned more quickly than control group from day 1 to day 2 (indicated by asterisk)
- The LNG and DRSP groups spent significantly more time than chance in the platform quadrant during the probe trial (see inset)

Anxiety Results

Elevated Plus Maze Data



- LNG and DRSP spent more time in open arms than control, indicating less anxiety
- Control spent the most time in closed arms, indicating more anxiety
- DRSP spent least time in closed arms, indicating less anxiety

Discussion

Spatial Learning

- Unexpectedly, both groups given an OC performed better in this spatial learning task compared to control animals as evidenced by:
 - Both LNG and DRSP groups had shorter latencies and distances on day 2 of training compared to controls
 - LNG and DRSP groups spent more time in the platform quadrant

Anxiety

- Unexpectedly, both groups given an OC showed less anxiety as evidenced by:
 - DRSP group exhibited the least anxiety with most time in open arms and the least time in closed arms
 - The LNG group showed some anxiety with spent less time in open arms than the DRSP group but more than the control group

Future Directions

- Use larger sample size to replicate results
- Use different dosage route to ensure that pill is working
- Study progestins in isolation without estrogen in the formulation—estrogen may have impacted results

Implications

- Oral contraceptives do impact spatial learning and anxiety in rodents, so it must be investigated in a human model as well.
- Effects on anxiety especially may have implications on which pill a person chooses to take
- All individuals choosing to take OCs should be made aware of these possible effects brain functions

1. Daniels, K. (2020). Current Contraceptive Status Among Women Aged 15–49: United States, 2017–2019. 388, 8.

2. Pletzer, B. A., & Kerschbaum, H. H. (2014). 50 years of hormonal contraception—Time to find out, what it does to our brain. *Frontiers in Neuroscience*, 8, 256. <https://doi.org/10.3389/fnins.2014.00256>

3. Weiss, E. M., Kemmler, G., Deisenhammer, E. A., Fleischhacker, W. W., & Delazer, M. (2003). Sex differences in cognitive functions. *Personality and Individual Differences*, 13.

4. Peragine, D., Simeon-Spezzaferro, C., Brown, A., Gervais, N. J., Hampson, E., & Einstein, G. (2020). Sex difference or hormonal difference in mental rotation? The influence of ovarian milieu. *Psychoneuroendocrinology*, 115, 104488. <https://doi.org/10.1016/j.psyneuen.2019.104488>