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Ashley N. Fricks-Gleason

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Running away from addiction: Can exercise attenuate methamphetamine-induced neurotoxicity?

Ashley N. Fricks-Gleason, Ph.D.

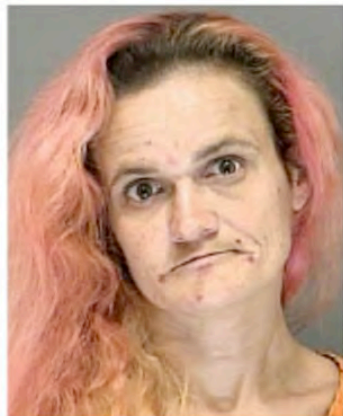
Dept. of Psychology & Neuroscience



What do you think of when I say “METH”?



1 AGE: 22



2 AGE: 33

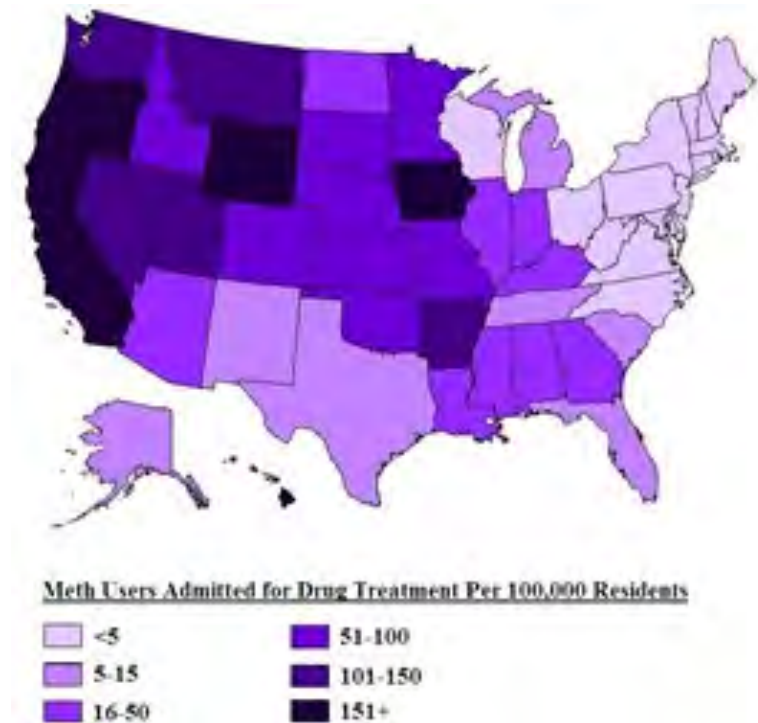


How big is our drug problem?

- How many people worldwide reported using an illicit drug in 2010?
- The extent of global illicit drug use remained stable between 2005 and 2010
- In 2010, how many Americans aged 12+ reported using an illicit drug in the past month?

How big is our METH problem?

- The abuse of methamphetamine (METH) continues to be a major public health concern
- Use has increased markedly in the last 15 years
 - Ease of manufacture
 - Long-lasting euphoria
- Use is endemic in the Western States
 - Where does Colorado rank?

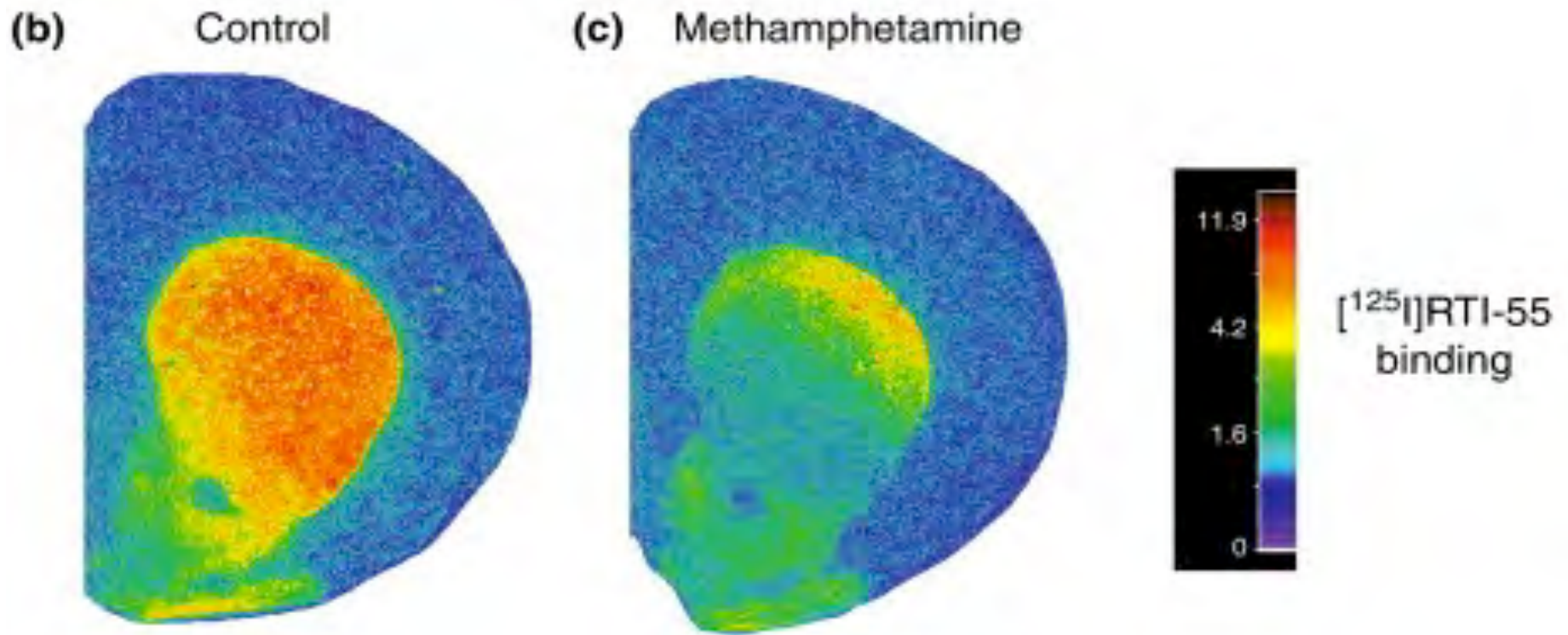


METH effects

- METH is a powerful psychostimulant
- Acute effects
 - Psychosis
 - Aggressive behavior
- Long-term consequences
 - Structure and function of the central nervous system
 - Concomitant cognitive deficits
 - Addiction



Exposure to METH decreases dopamine levels in the brain



METH neurotoxicity in humans



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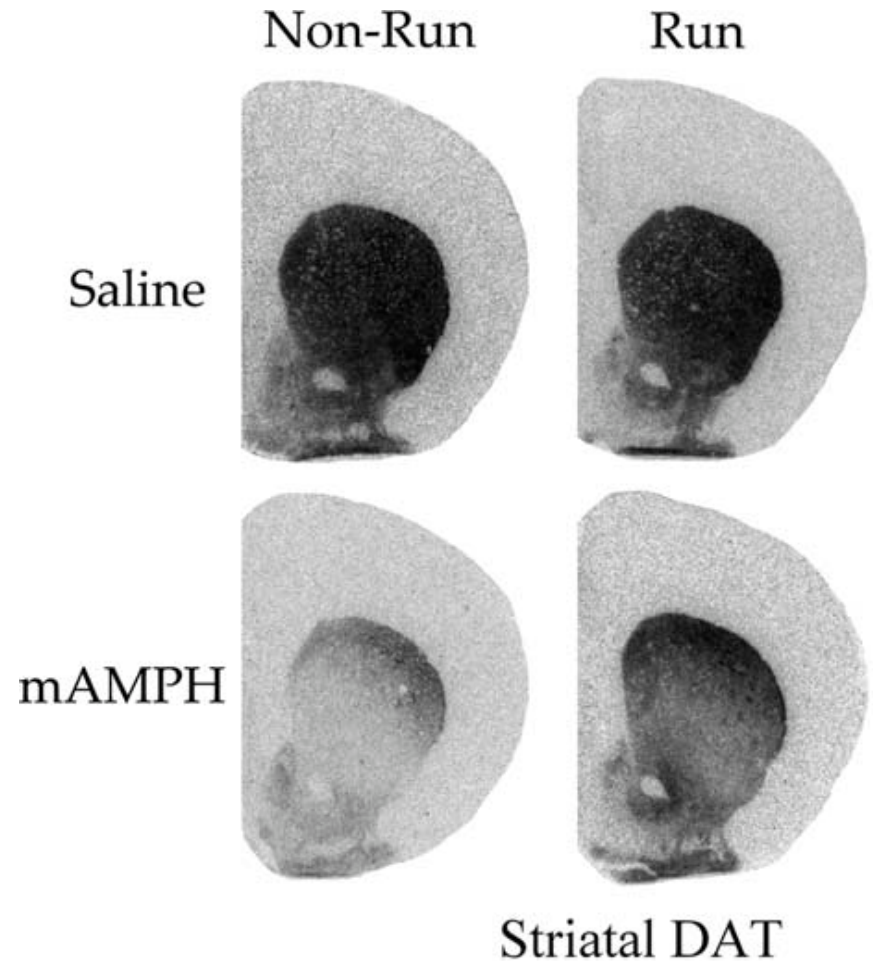
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METH-induced neurotoxicity leads to cognitive impairments

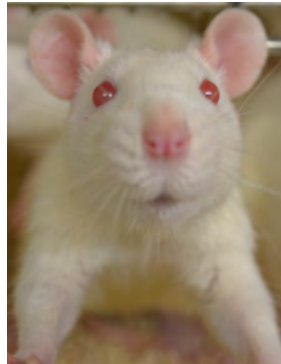
- Impaired cognition persists over time
- Deficits include impairments in:
 - Memory
 - Decision making
 - Executive Function
- Significantly impacts the ability of METH abusers to engage in, and ultimately benefit from, drug treatment programs

Exercise is good for you

- Rodent models of PD have demonstrated a beneficial role for exercise on both neurochemical and behavioral outcomes
- Exercise has also recently been shown to ameliorate METH-induced neurotoxicity



Experimental Plan

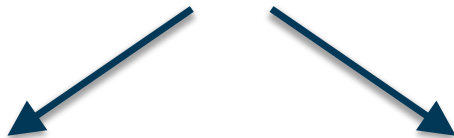


(+)-METH

4 x 4 mg/kg, s.c., at 2-hr intervals

Saline

4 x 1 ml/kg, s.c., at 2-hr intervals



Exercise

Free
access to
running
wheels for
3 weeks

Sedentary

Housed with
a locked
running
wheel for
3 weeks



Exercise

Free
access to
running
wheels for
3 weeks

Sedentary

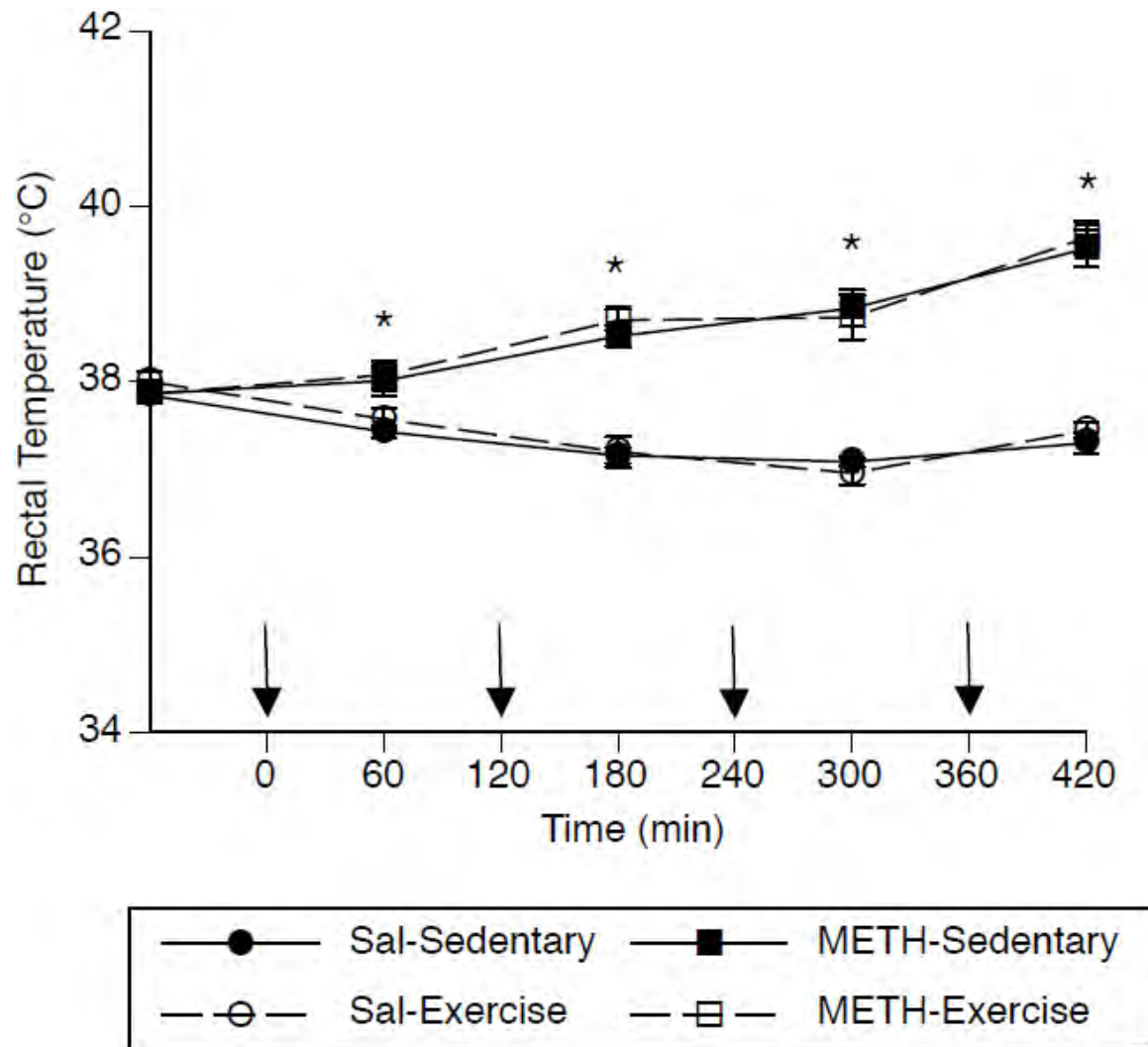
Housed with
a locked
running
wheel for
3 weeks

Why won't this thing spin?

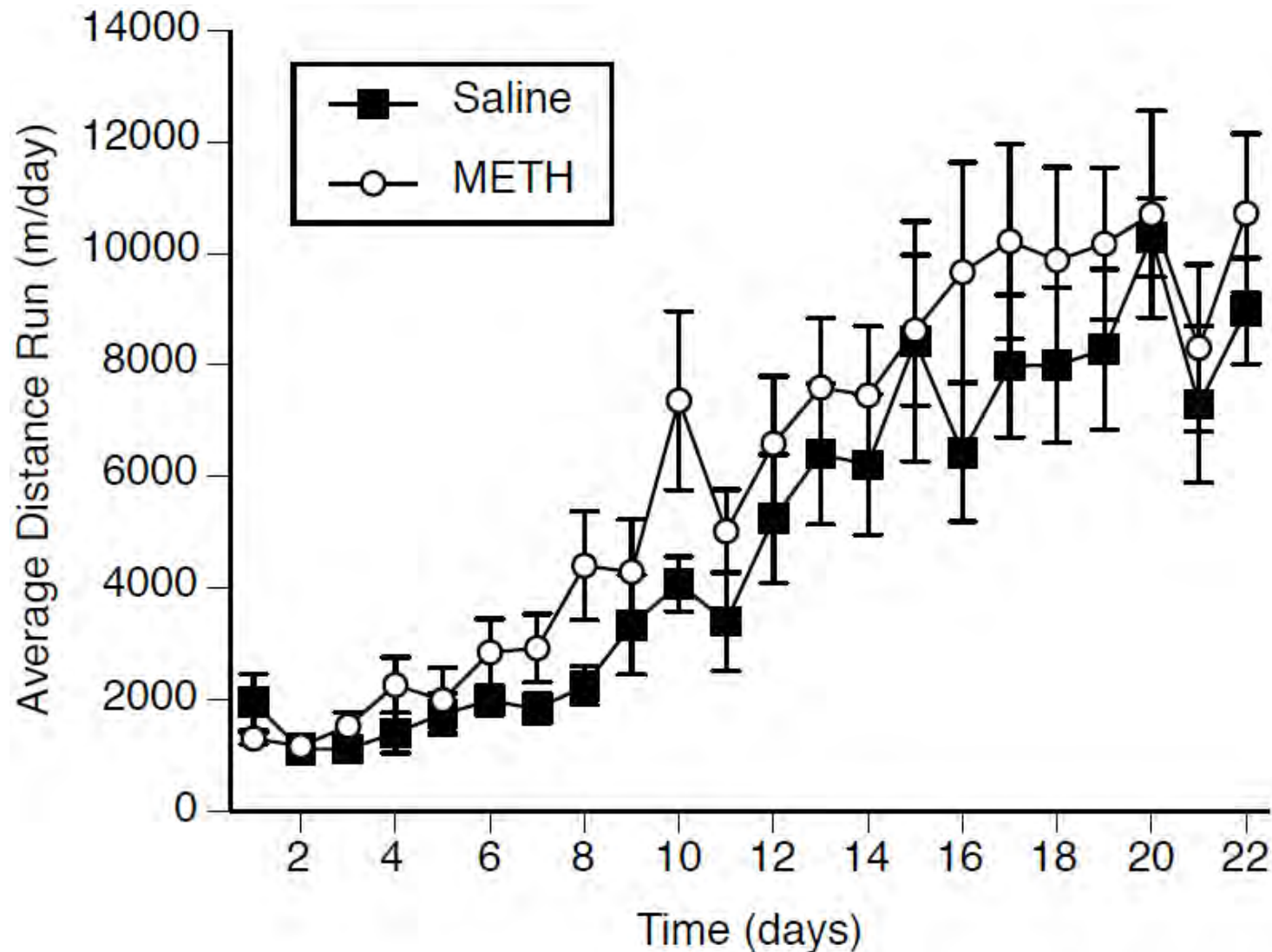


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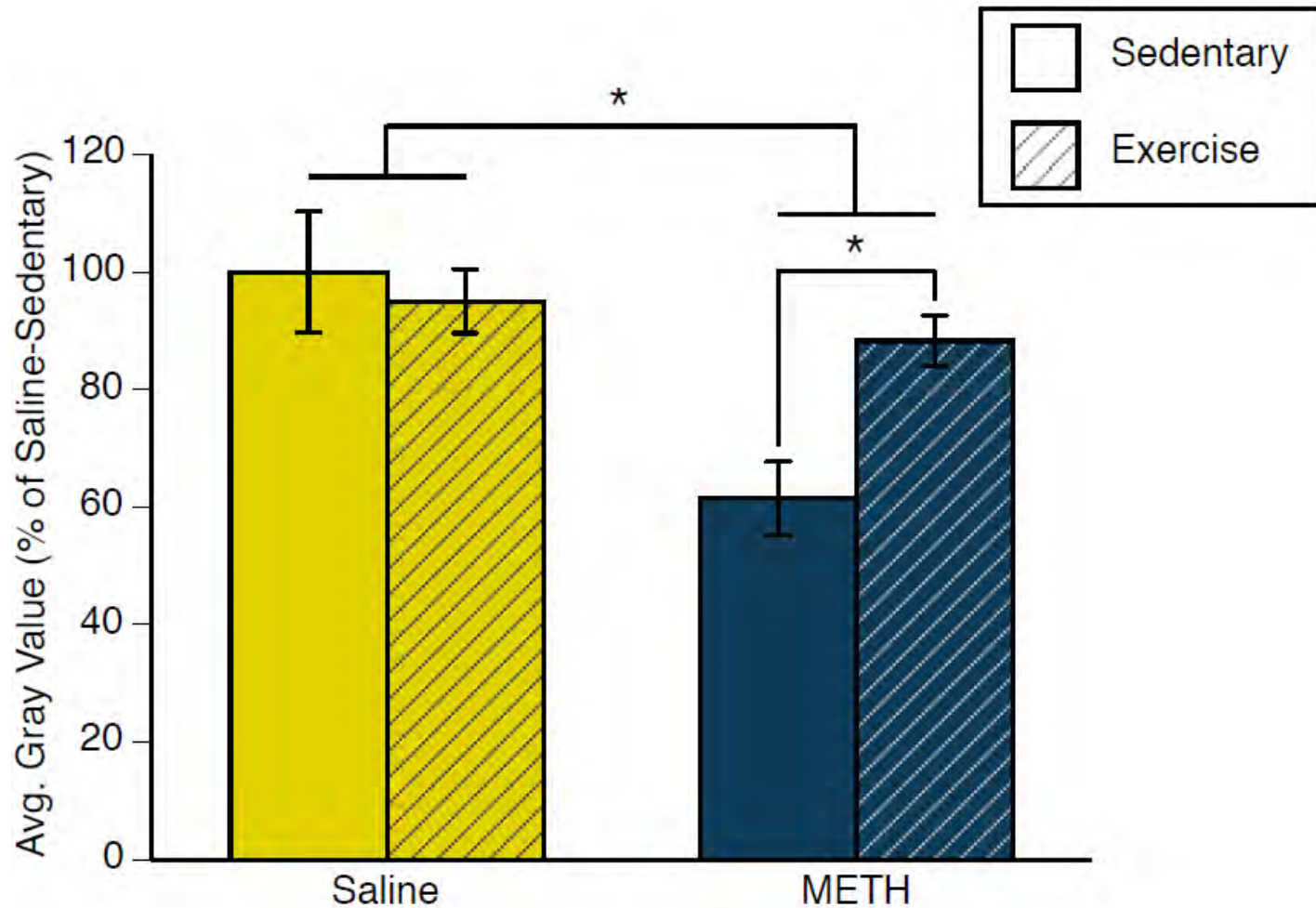
METH pretreatment induced significant hyperthermia



METH-pretreated animals ran as well as saline-pretreated controls



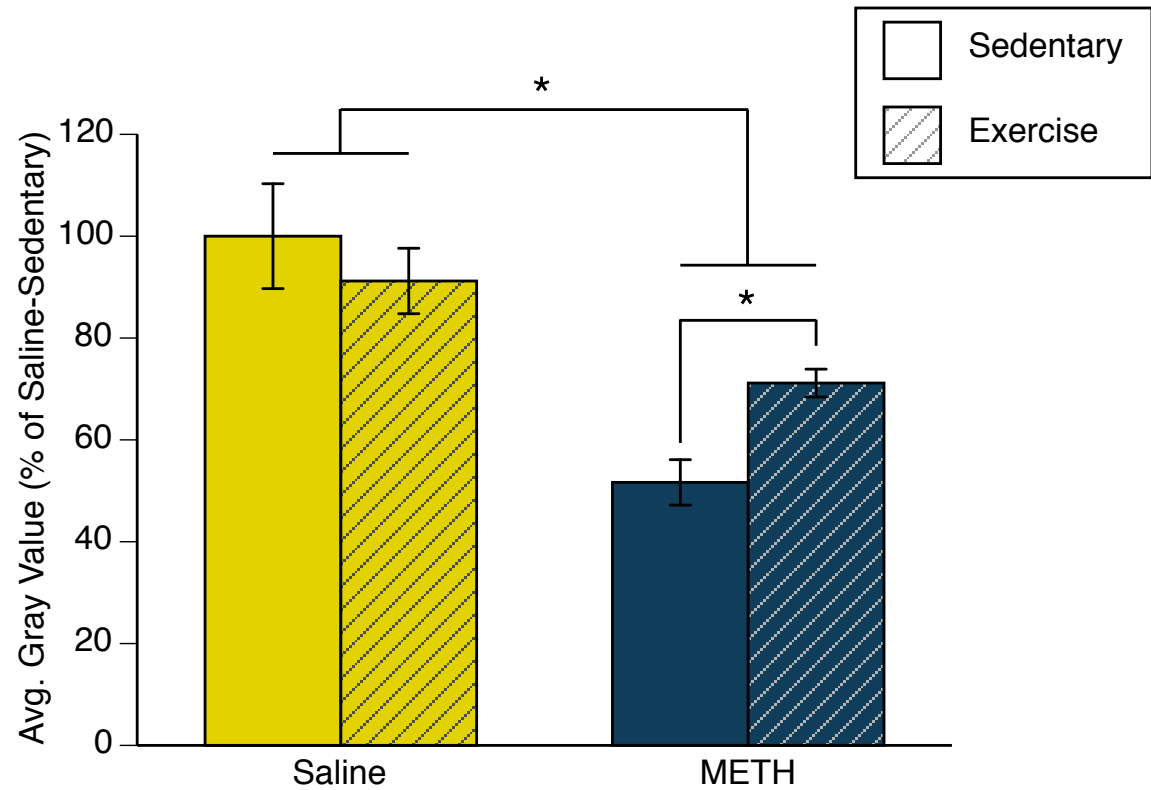
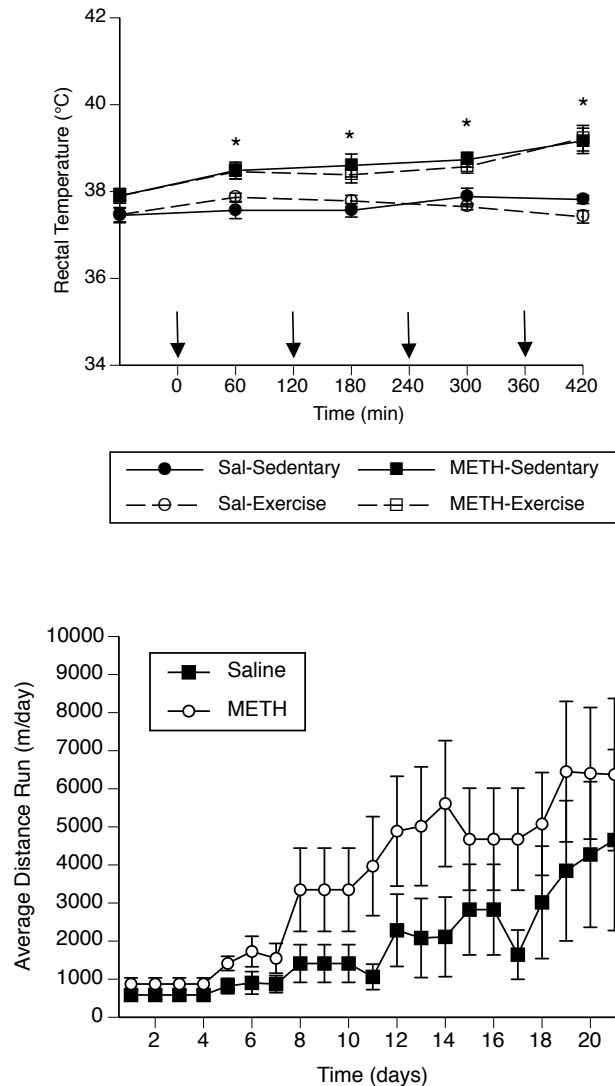
Voluntary exercise attenuated METH-induced dopaminergic neurotoxicity



That's great and all, but how therapeutically relevant is it?

- Arguably, starting the exercise regimen 24 hours after the METH binge isn't likely to translate directly to the clinic
- So, can we delay the start of the exercise regimen and still see an effect?

Delayed exercise attenuates METH-induced dopaminergic neurotoxicity



Implications

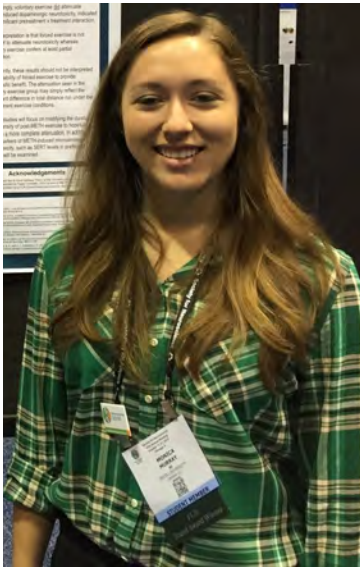
- Limiting exposure to running wheels solely to the post-METH period resulted in attenuation of neurotoxicity
 - Suggests that exercise is a non-pharmacological treatment with therapeutic relevance
- Importantly, this attenuation was still seen in the 7 day delay experiment
 - Suggests that exercise isn't simply disrupting the mechanisms that lead to neurotoxicity, but rather is reversing the neurotoxic effects post-hoc

So, what's next?

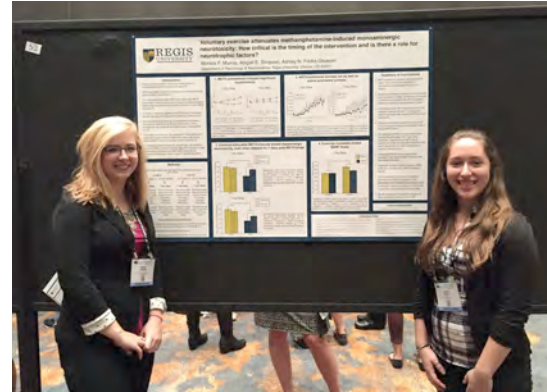
- Can we modify the duration and intensity of post-METH exercise to hopefully achieve a more complete attenuation?
- Can we begin to elucidate potential mechanisms?
 - Neurotrophic factors (BDNF and GDNF)
- Perhaps most interestingly, can exercise also improve performance on cognitive tasks known to exhibit METH-induced deficits?

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Haley Jenkins