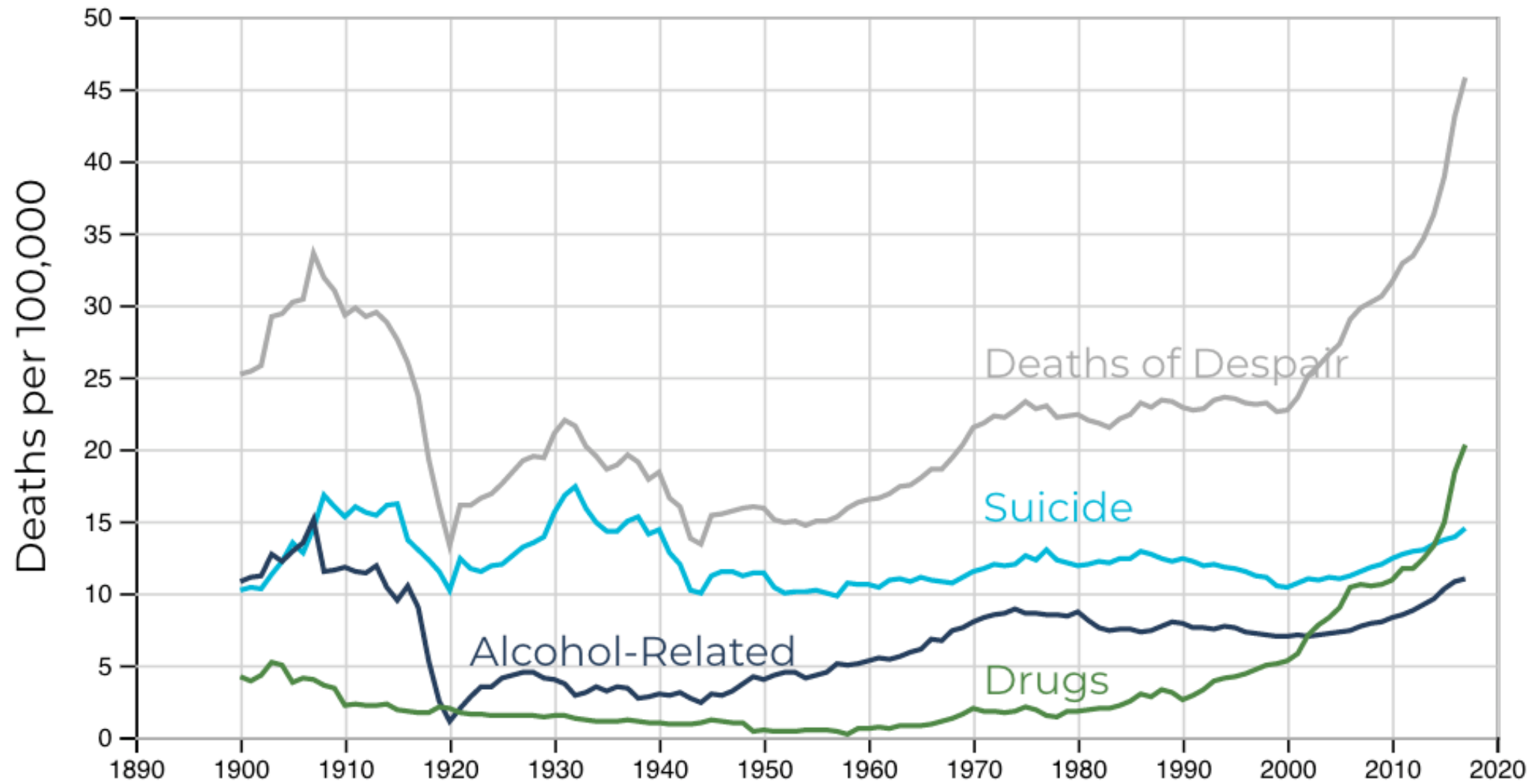


Deaths of Despair and Its Components, 1900-2017, Crude Rates



Source: Social Capital Project analyses of CDC data

Addiction is a Chronic, Treatable Brain Disorder

FRONTIERS IN NEUROSCIENCE: THE SCIENCE OF SUBSTANCE ABUSE

1997

Addiction Is a Brain Disease, and It Matters

Alan I. Leshner

Science

The NEW ENGLAND JOURNAL of MEDICINE

2016

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Neurobiologic Advances from the Brain Disease Model of Addiction

Nora D. Volkow, M.D., George F. Koob, Ph.D., and A. Thomas McLellan, Ph.D.

Neuropsychopharmacology

2021

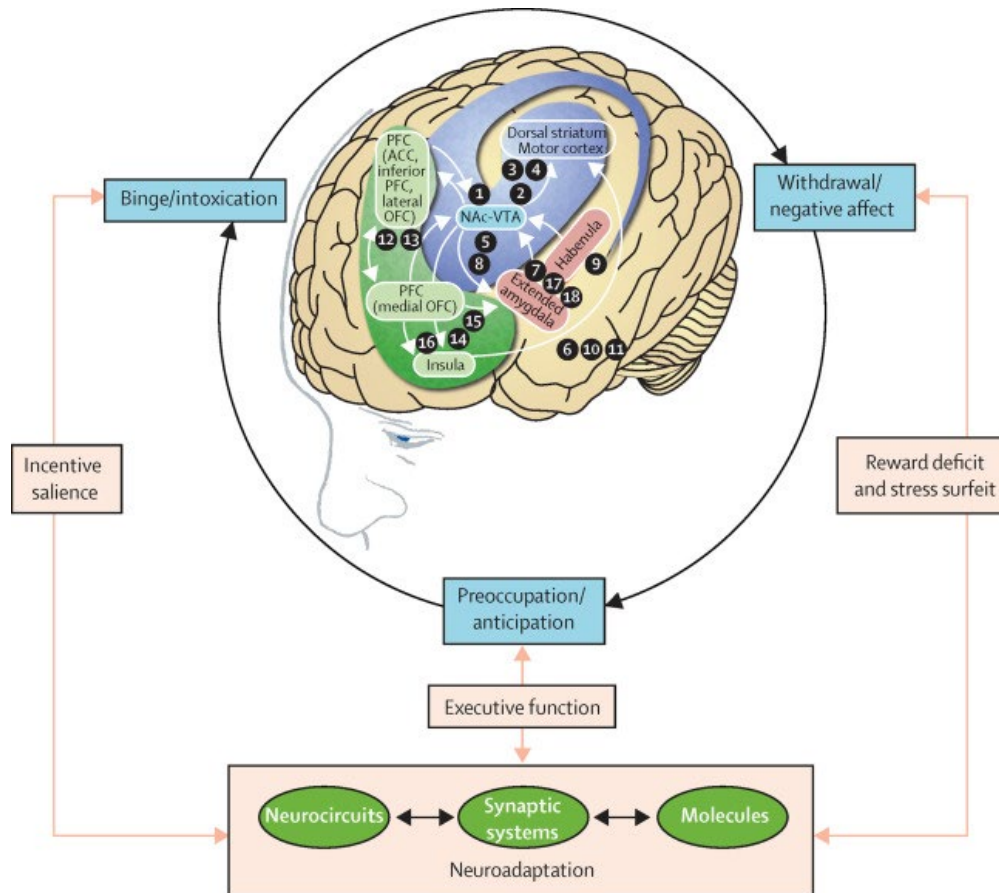
REVIEW ARTICLE

OPEN

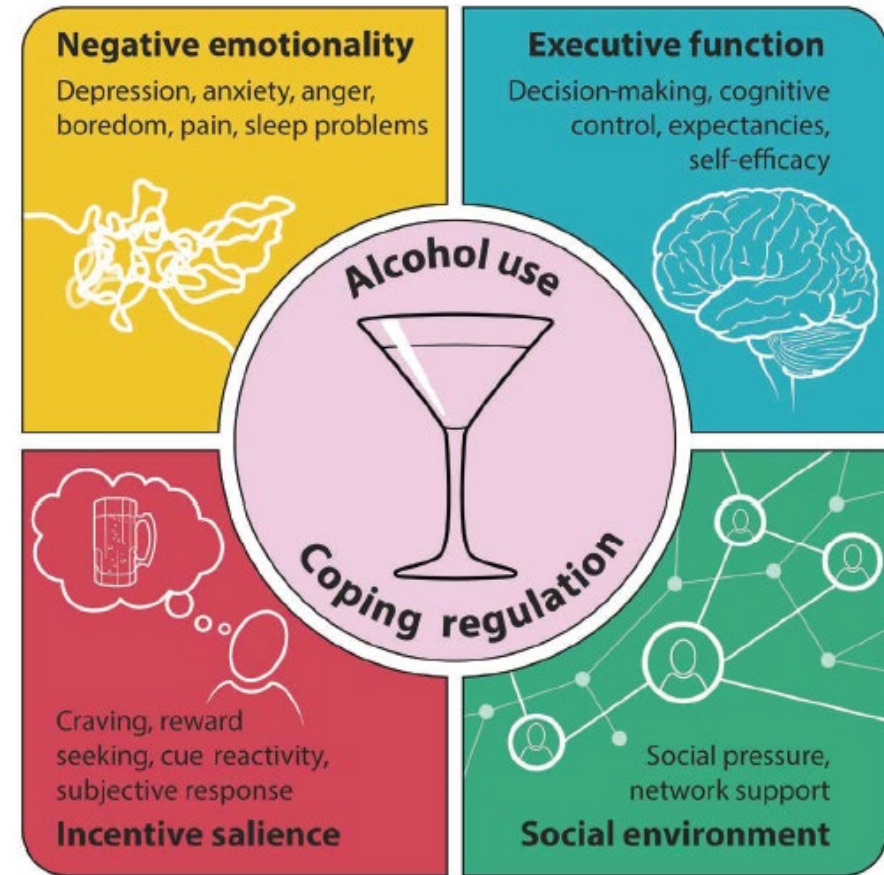
Addiction as a brain disease revised: why it still matters, and the need for consilience

Markus Heilig¹, James MacKillop^{2,3}, Diana Martinez⁴, Jürgen Rehm^{5,6,7,8}, Lorenzo Leggio⁹ and Louk J. M. J. Vanderschuren¹⁰

Addiction is a Complex Multifactorial Medical Disorder



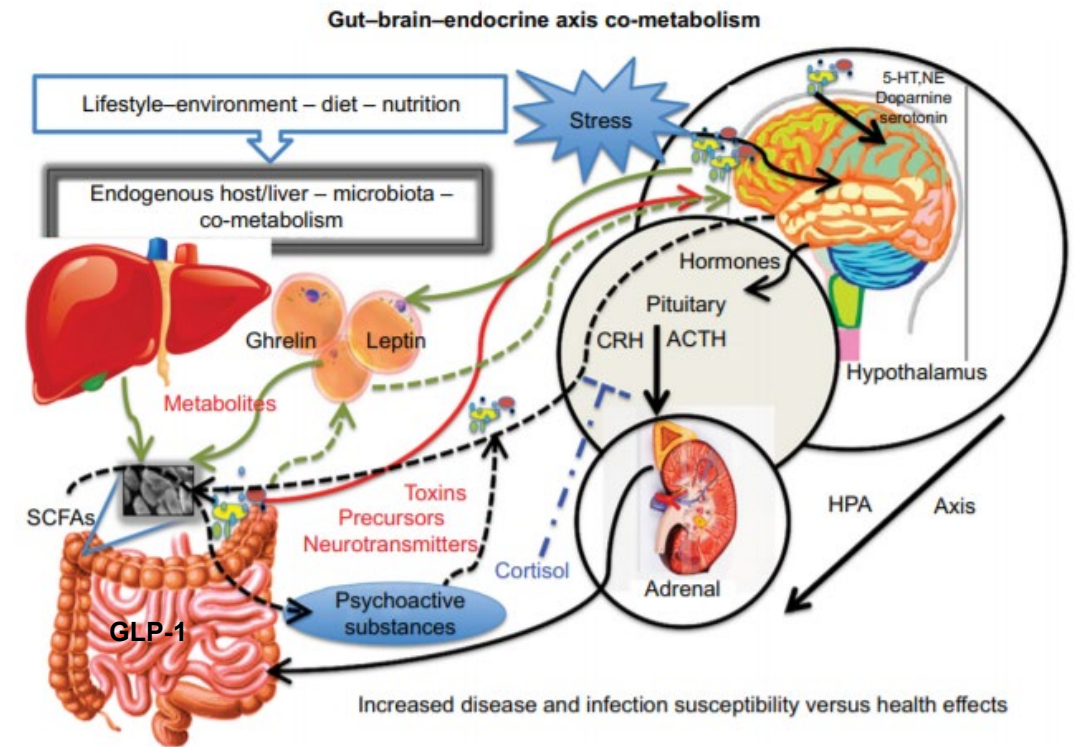
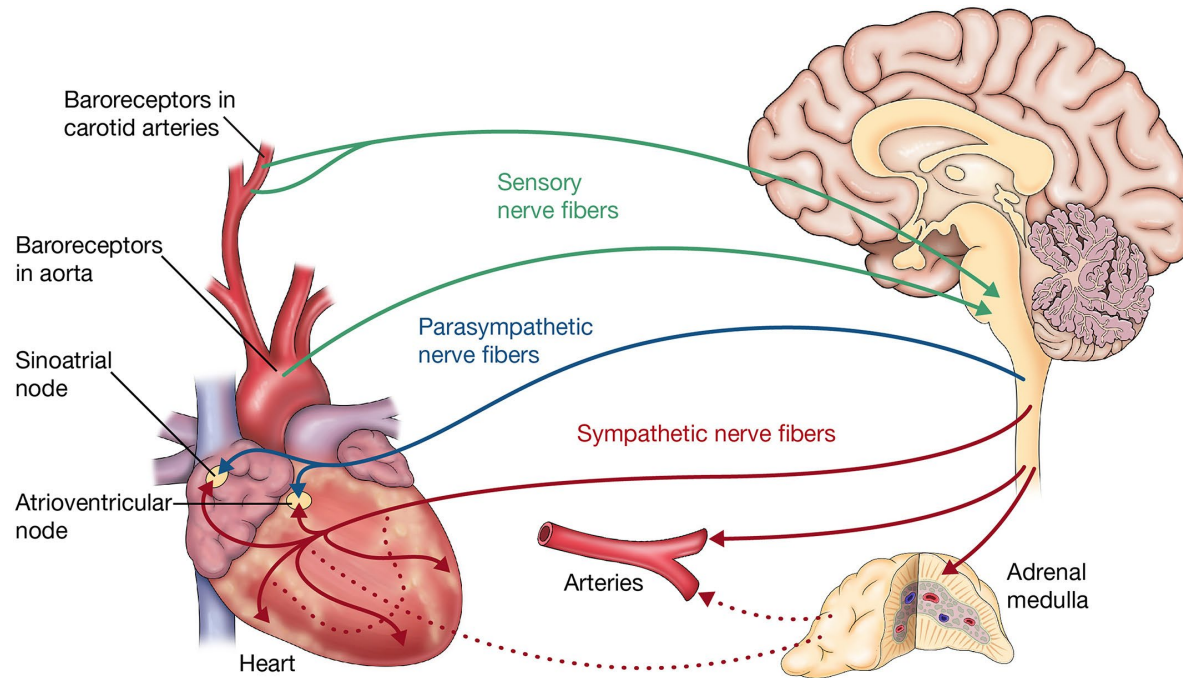
Koob & Volkow. Lancet Psychiatry 2016



Witkiewitz, Litten & Leggio. Science Advances 2019

Thinking Outside the Box? Targeting Outside the Brain

Addiction is a brain disorder ... and the brain connections with the periphery matter



GLP-1 System: A New Target to Treat Addictions?

GLP-1 System: A New Target to Treat Addictions?

health Life, But Better Fitness Food Sleep Mindfulness Relationships

Weight-loss meds like Ozempic may help curb addictive behaviors, but drugmakers aren't running trials to find out

By Meg Tirrell, CNN

Updated 1:11 PM EDT, Thu June 1, 2023



LIVING BETTER

Ozempic seems to curb cravings for alcohol. Here's what scientists think is going on

August 28, 2023 · 5:00 AM ET



Michaela Doucette



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Weight-loss drugs may also curb addictions

By CNN Newsroom staff



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AMERICAN UNIVERSITY RADIO

Is Semaglutide a New Treatment for AUD?

GLP-1 System: A New Target to Treat Addictions?

Pharmacological Research 207 (2024) 107312



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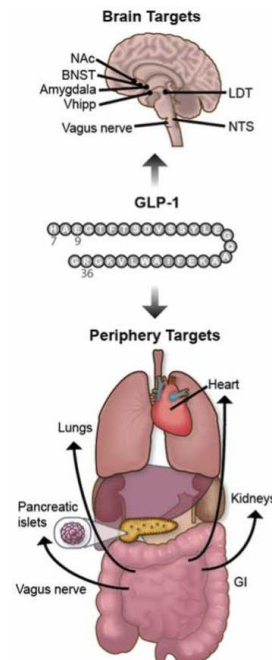
Pharmacological Research

journal homepage: www.elsevier.com/locate/yphrs

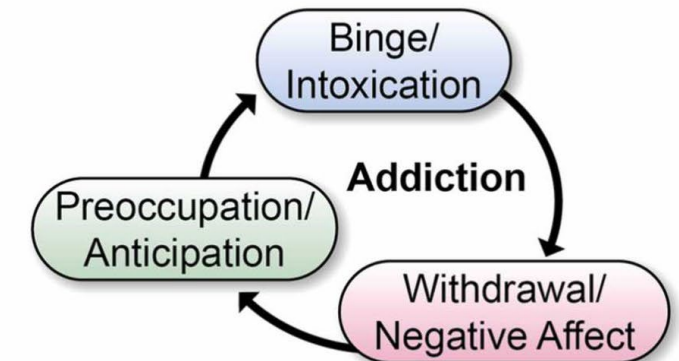


IUPHAR review – Glucagon-like peptide-1 (GLP-1) and substance use disorders: An emerging pharmacotherapeutic target

Nicolaus Bruns VI^{a,b,c,1}, Elizabeth H. Tressler^{a,b,c,1}, Leandro F. Vendruscolo^c, Lorenzo Leggio^{a,*}, Mehdi Farokhnia^{a,*}



- GLP-1R agonists have shown to reduce alcohol, psychostimulants, opioids, and nicotine use and other addiction-related outcomes in preclinical models.
- Initial clinical studies support the safety and potential efficacy of GLP-1R agonists in addiction treatment. Several randomized controlled trials are underway.



TODAY SPEAKERS

Session Overview

Lorenzo Leggio, National Institute on Drug Abuse &
National Institute on Alcohol Abuse and Alcoholism

Speaker Presentations

Elisabet Jerlhag Holm, University of Gothenburg (*Zoom*)

Heath Schmidt, University of Pennsylvania

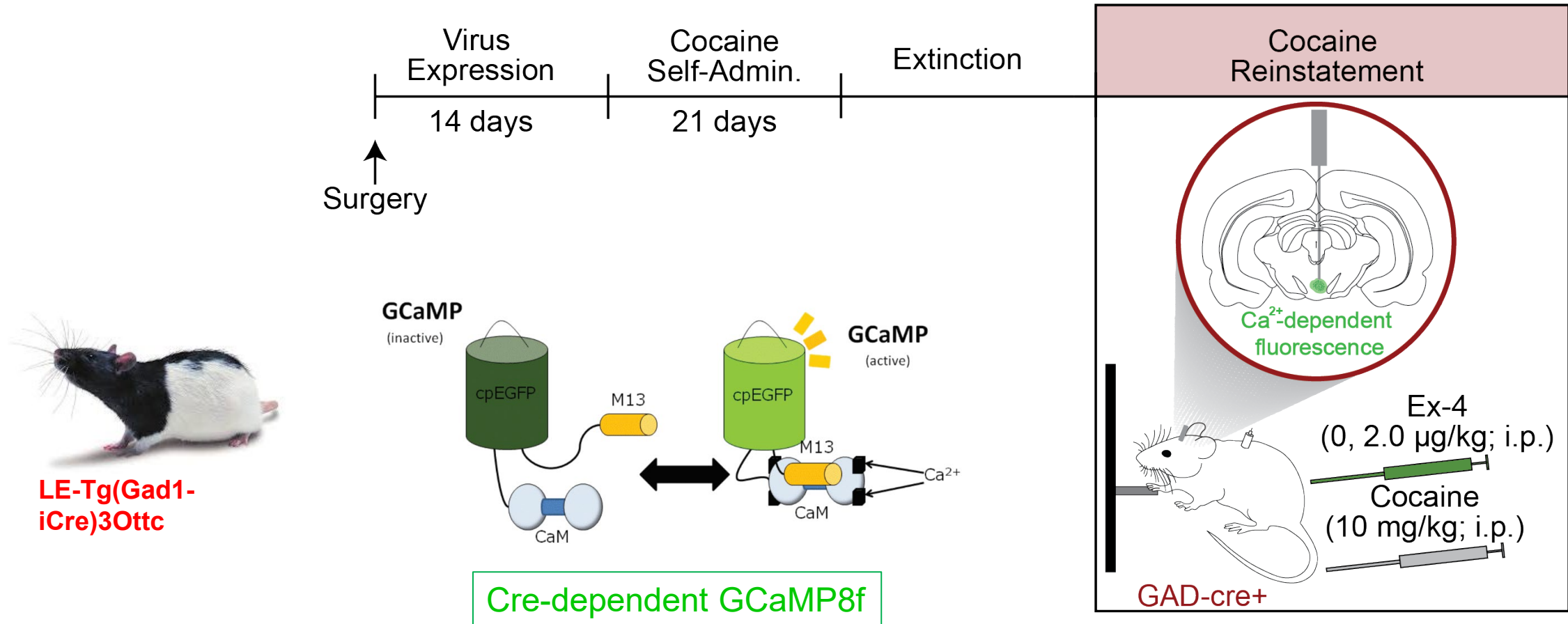
Mehdi Farokhnia, National Institute on Drug Abuse &
National Institute on Alcohol Abuse and Alcoholism

Rong Xu, Case Western Reserve

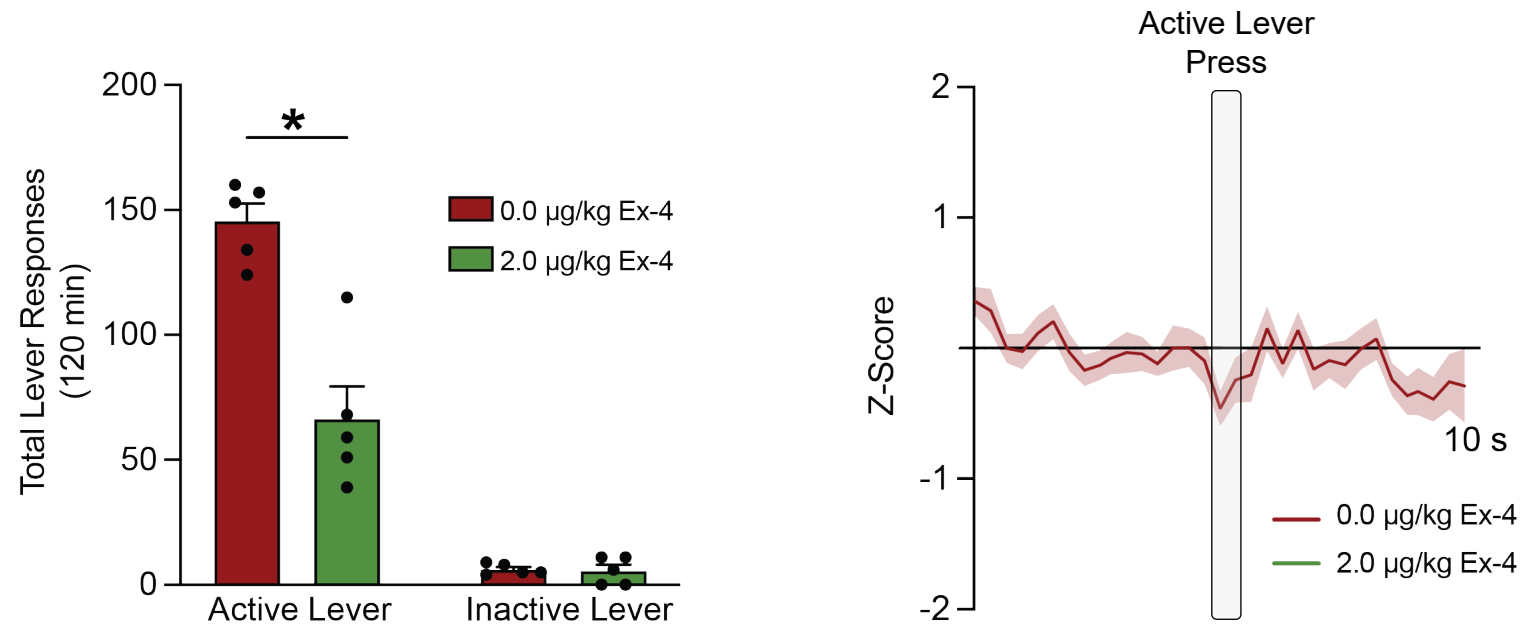
Patricia (“Sue”) Grigson, Penn State University

Moderated Discussion and Audience Q&A

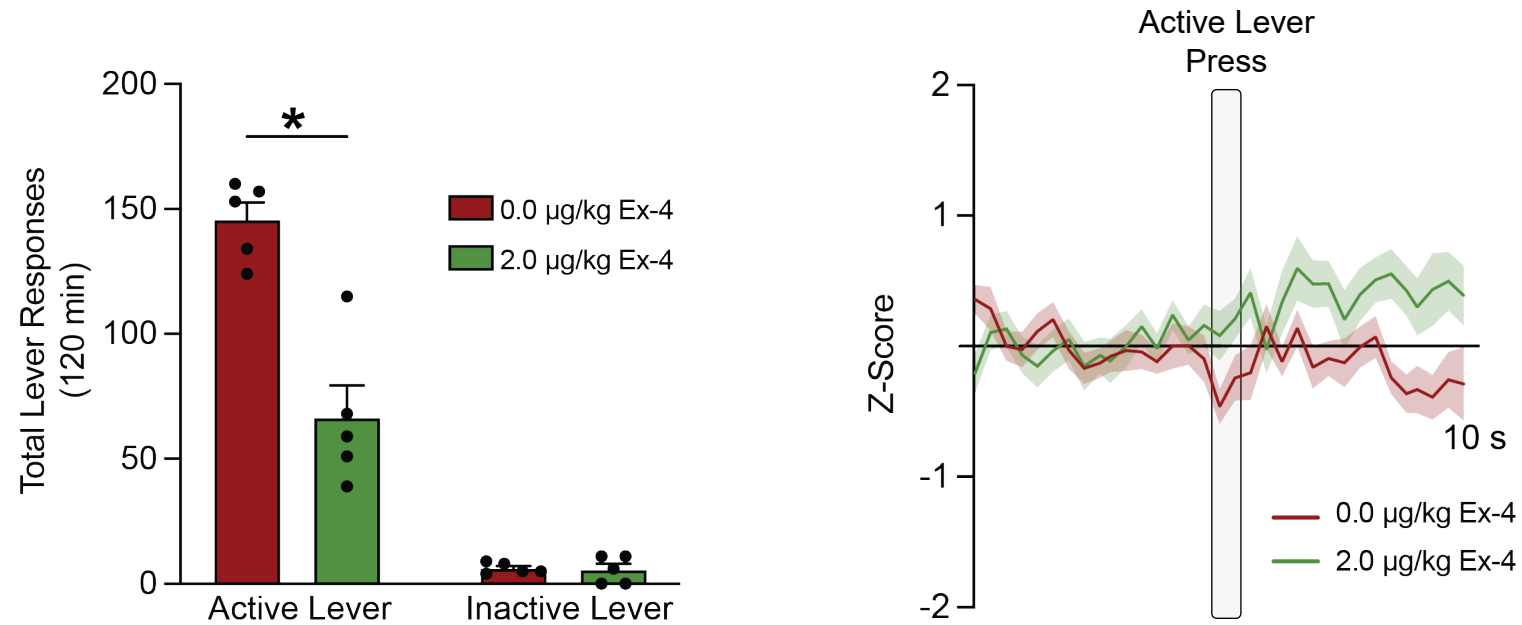
GLP-1R pharmacotherapy increases activity of VTA GABA neurons and attenuates cocaine seeking



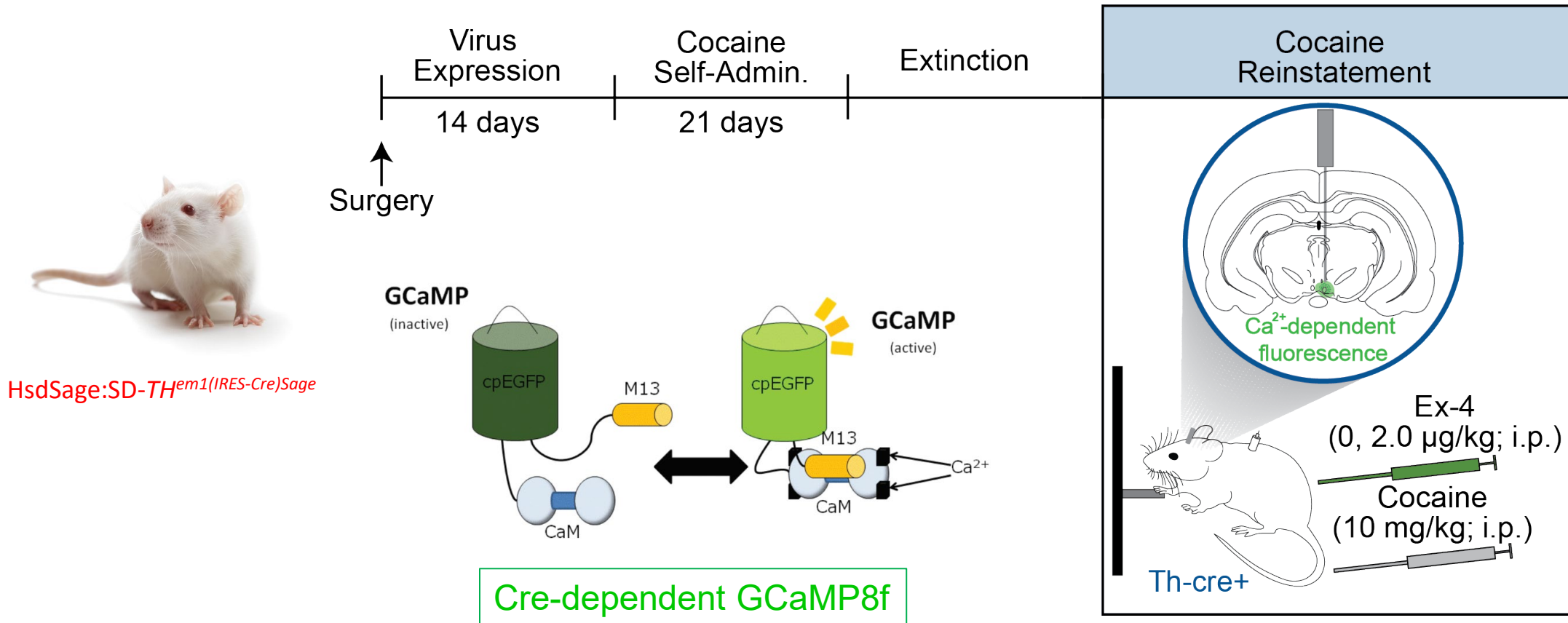
GLP-1R pharmacotherapy increases activity of VTA GABA neurons and attenuates cocaine seeking



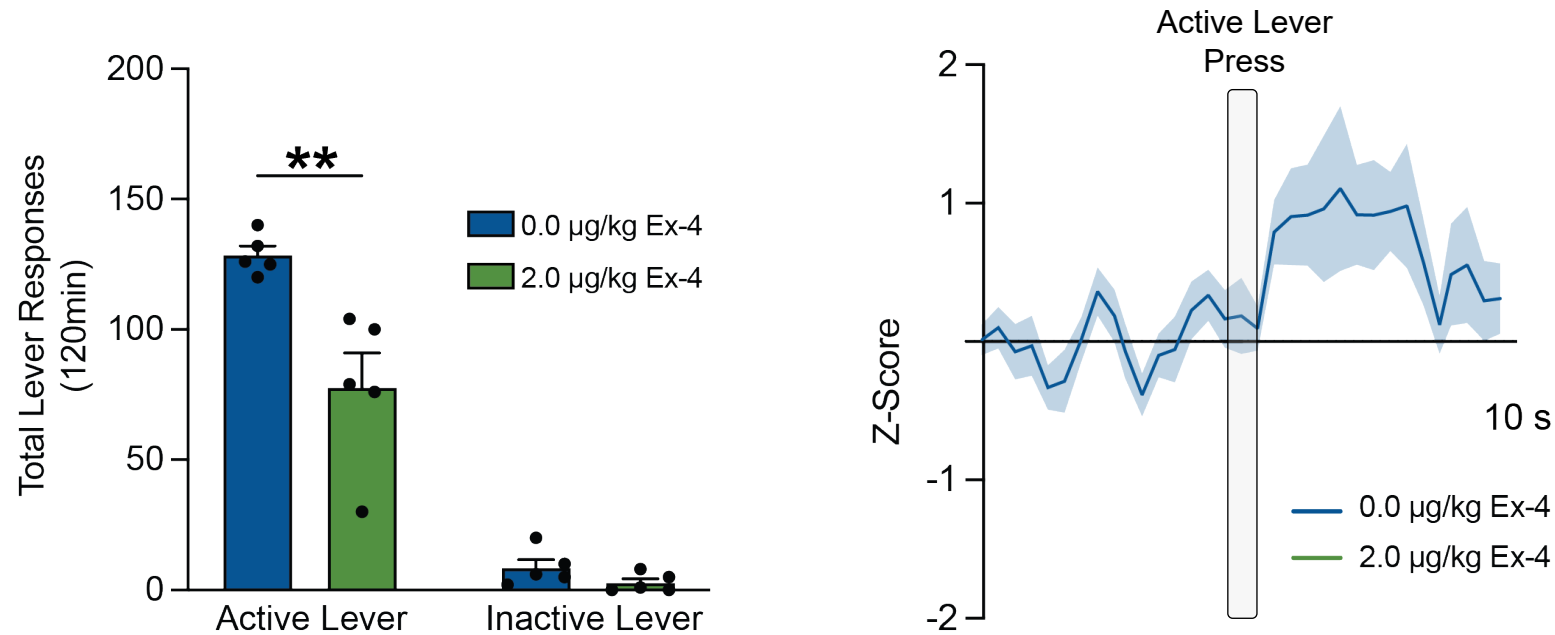
GLP-1R pharmacotherapy increases activity of VTA GABA neurons and attenuates cocaine seeking



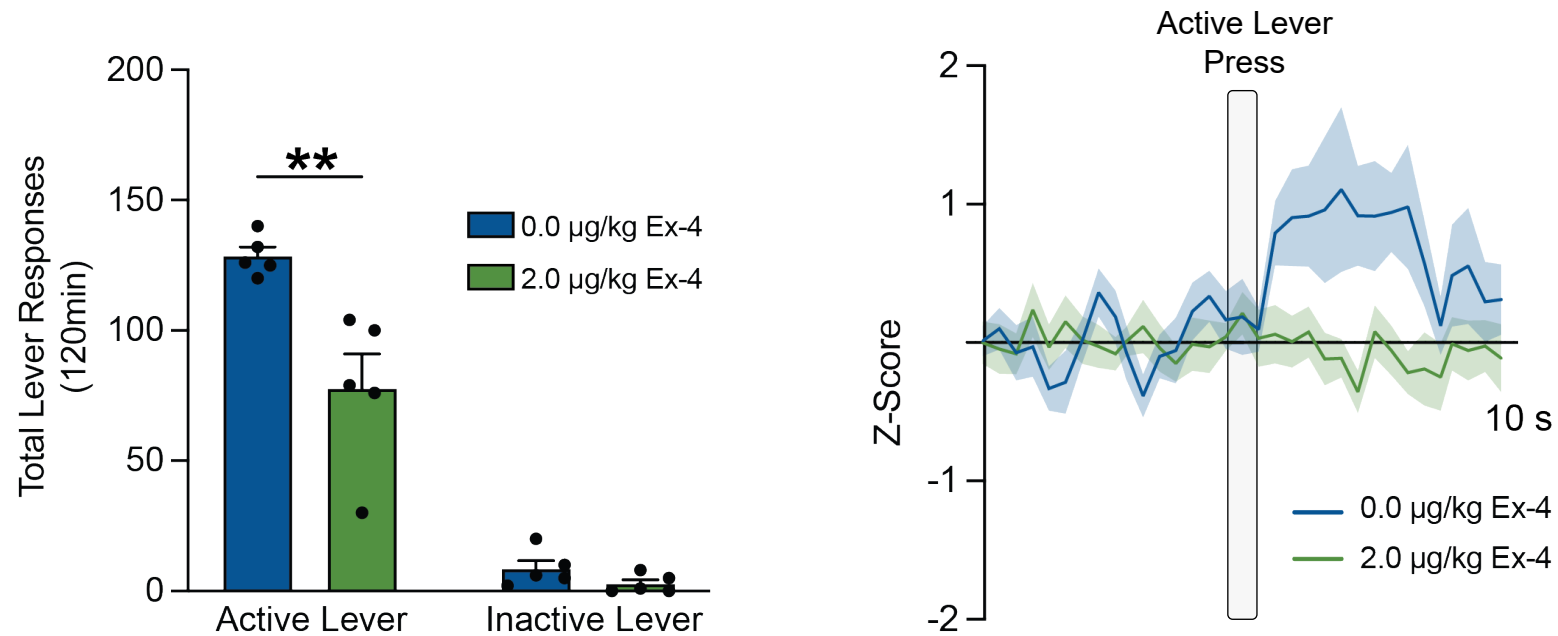
GLP-1R pharmacotherapy decreases activity of VTA dopamine neurons and attenuates cocaine seeking



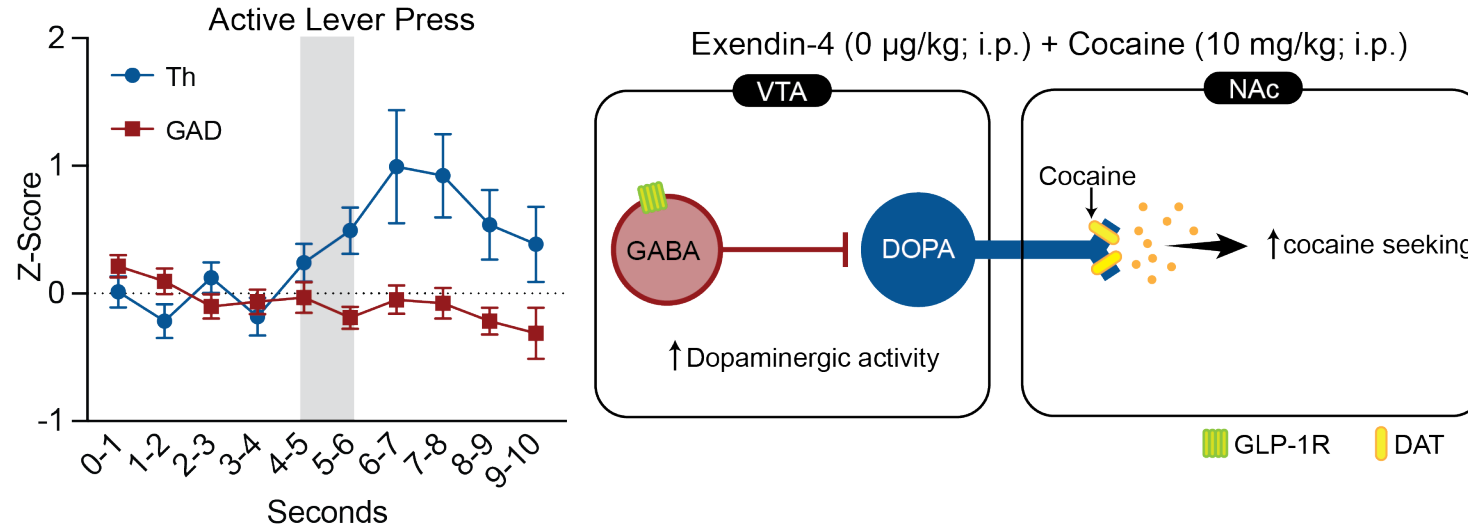
GLP-1R pharmacotherapy decreases activity of VTA dopamine neurons and attenuates cocaine seeking



GLP-1R pharmacotherapy decreases activity of VTA dopamine neurons and attenuates cocaine seeking



GLP-1R pharmacotherapy engages VTA GABA neurons to regulate mesolimbic dopamine neurons and attenuate cocaine seeking



Summary & Conclusions

- Systemic administration of a GLP-1 receptor agonist attenuates drug-seeking behavior at doses that are well-tolerated in cocaine-experienced rats. These findings suggest that GLP-1R agonists could be re-purposed for treating cocaine use disorder.
- The efficacy of systemic exendin-4 to reduce cocaine seeking is associated with increased activity of VTA GABA neurons and decreased activity of VTA dopamine neurons.

Outstanding Questions & Future Directions

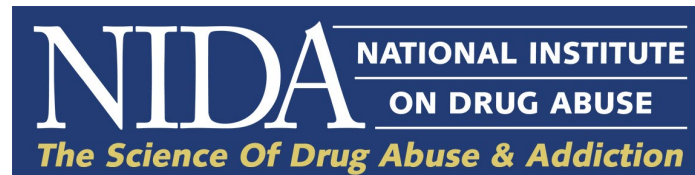
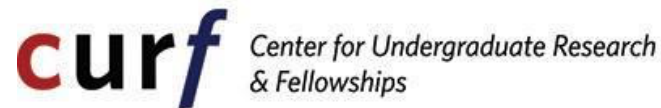
- What are the downstream molecular and cellular mechanisms underlying the efficacy of GLP-1R agonists on voluntary drug-taking and -seeking behaviors?
- Define post-synaptic versus pre-synaptic mechanisms of action.
- Can we target central GLP-1-producing circuits to selectively reduce drug-mediated behaviors?
- Are next-generation GLP-1R agonists more efficacious?
- What are the adverse effects of GLP-1R agonists in humans with SUDs?
- Will approaches that target GLP-1Rs and additional neuropeptide systems with overlapping functional activity be more efficacious and/or better tolerated than GLP-1R agonist monotherapy alone?

Acknowledgments



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- Austin Pothikamjorn
- **Kael Ragnini**
- **Vanessa Weir**
- Yafang Zhang, Ph.D.

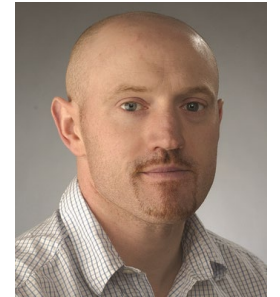
Check us out:



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Rick Crist,
UPenn