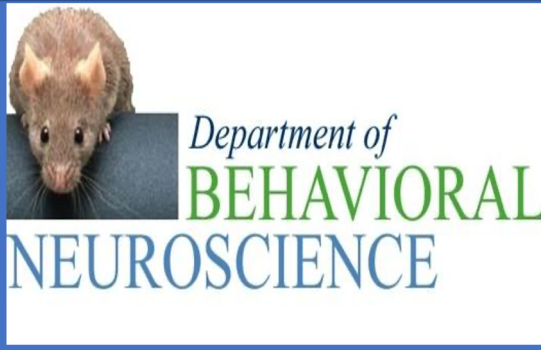


MODULATING RELATIONSHIPS WITH SMALL MOLECULES: WHAT IF THE FUTURE IS ALREADY HERE?

Andrey Ryabinin, PhD

Oregon Health & Science University

NOGIN Workshop 2023

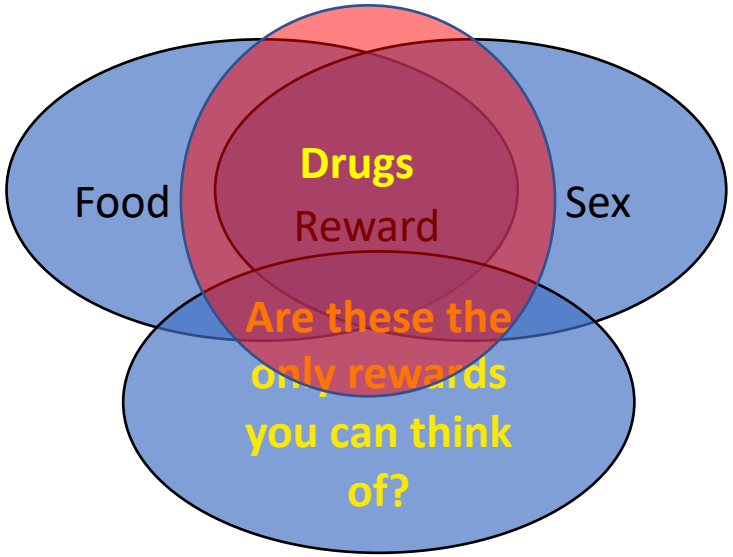
Why study alcohol and drug addiction?

Tremendous health and societal problem:
8 mln annual deaths globally are associated with tobacco use,
4 mln annual deaths globally are associated with alcohol use.
About 1 mln annual deaths globally – due to other drugs

Allows us to think about fundamental questions:
what it means to want, to crave, to love, to be dependent on something or someone?

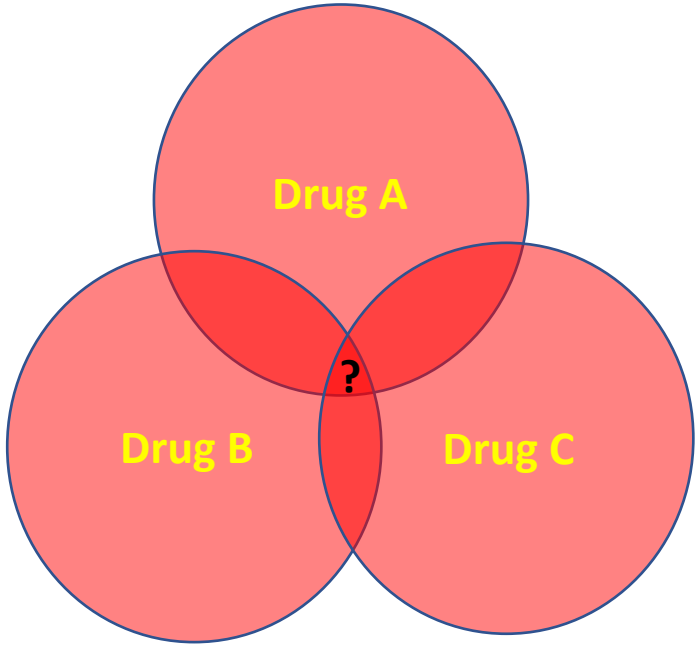
Theorizing about causes of addiction

Addictive drugs “hijack” natural reward systems



Mechanisms of addiction

Different for different drugs



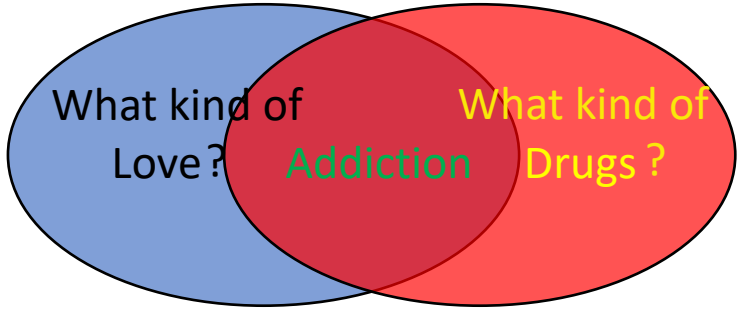
Love/social attachment as addiction

Psychopharmacology (2012) 224:1–26
DOI 10.1007/s00213-012-2794-x

REVIEW

The behavioral, anatomical and pharmacological parallels between social attachment, love and addiction

James P. Burkett · Larry J. Young



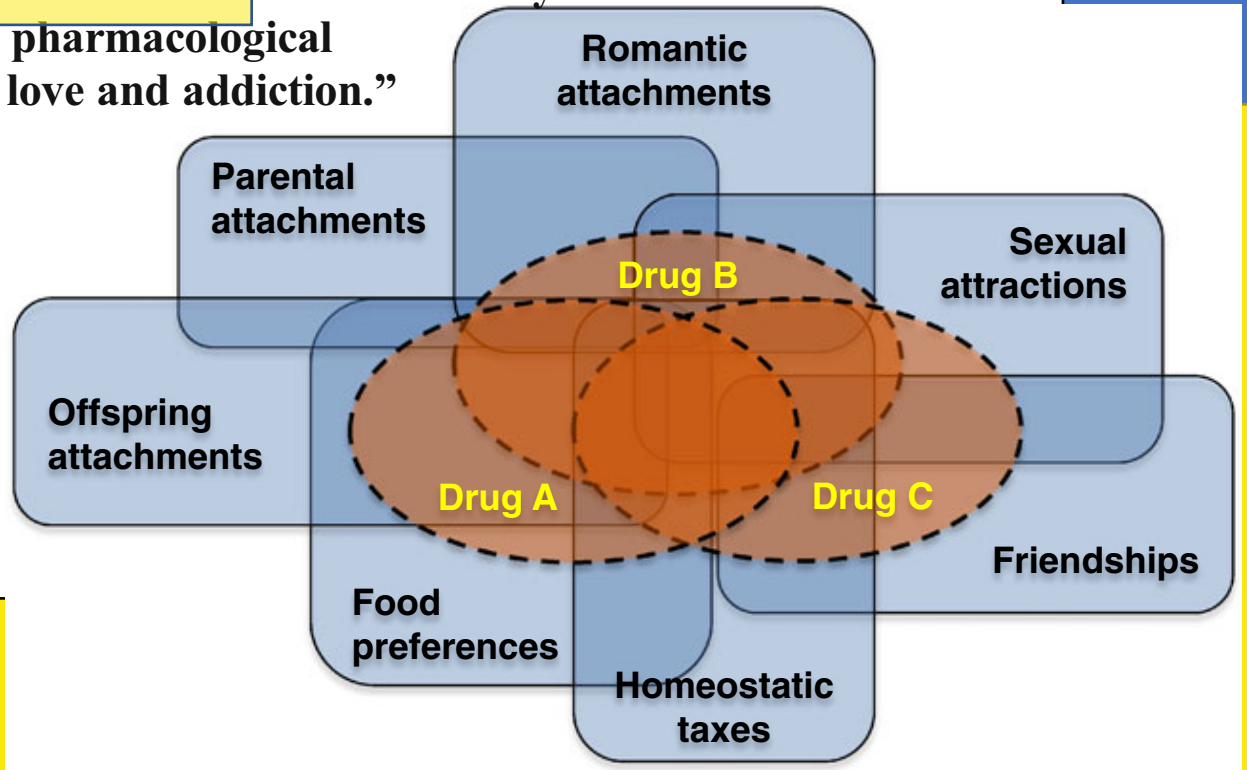
Things are much more complicated

Psychopharmacology (2012) 224:27–29
DOI 10.1007/s00213-012-2858-y

COMMENTARY

Love and addiction: the devil is in the differences: a commentary on "The behavioral, anatomical and pharmacological parallels between social attachment, love and addiction."

Caroline M. Hostetler · Andrey E. Ryabinin



Am I a "splitter"?

“Doctor, help! I need something now!”

Is it possible to pharmacologically manipulate social attachments?

Oxytocin

Parturition

Milk Production

Social attachment

Anxiety

Pain

Memory

Addiction

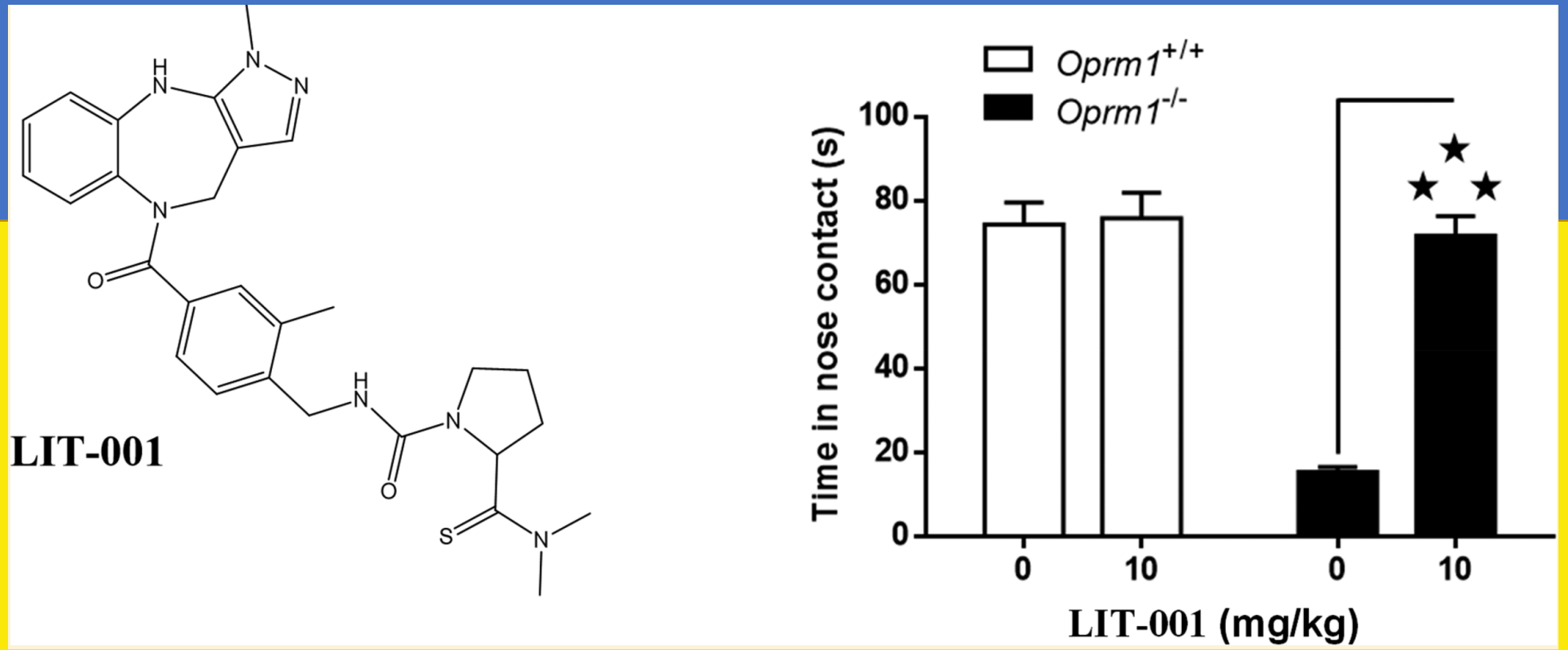
Potential problems with using oxytocin in clinical settings

- Short half life

- Poor brain penetrance

- Nonspecific effects, including actions on AVPR1a receptors

A new development:
LIT-001
- first OXTR-specific small molecule agonist



Frantz et al, *J Med Chemistry,* 2018

Prairie voles – a remarkable rodent model for social neurobiology

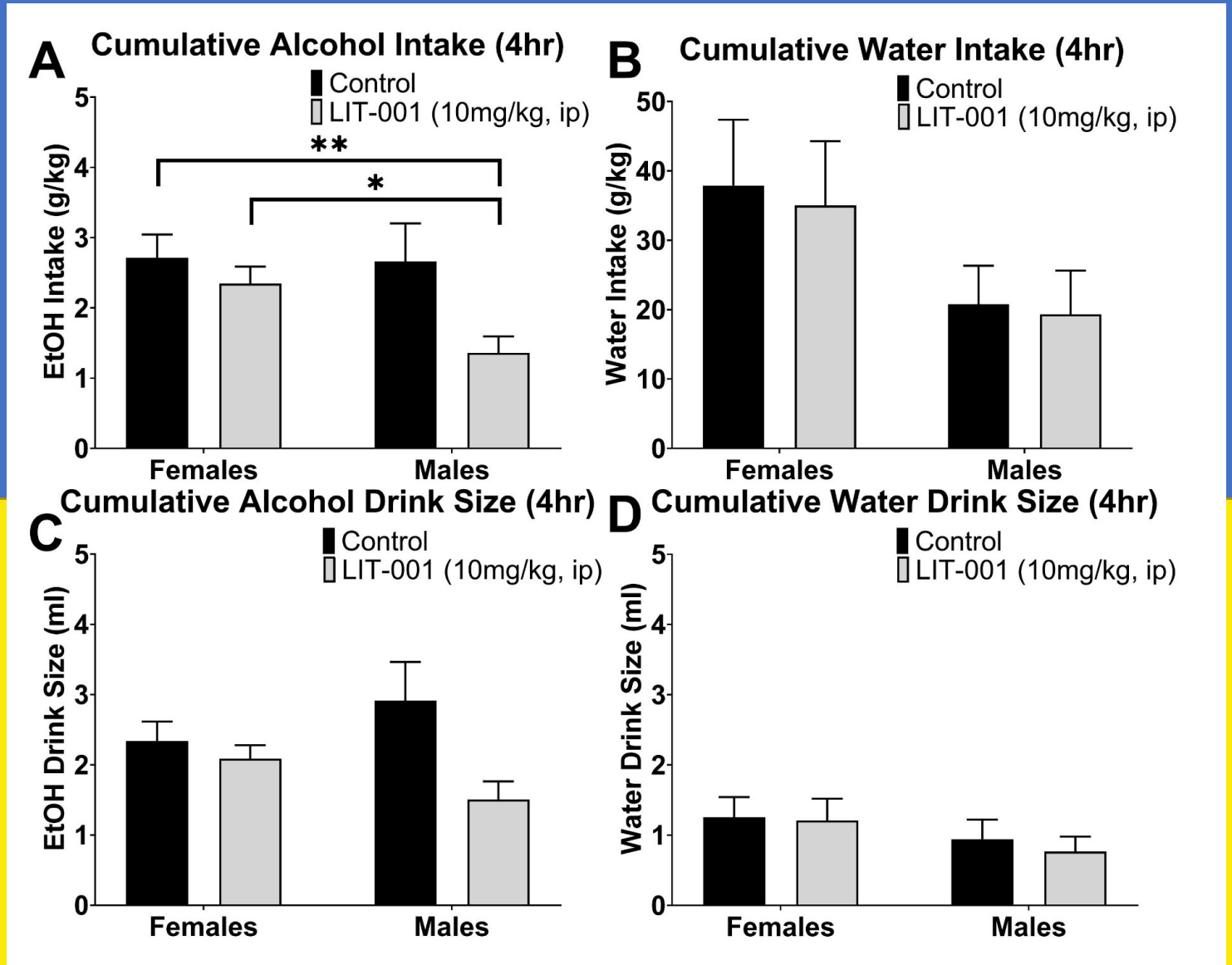
Highly affiliative, facultatively monogamous. Like humans, can form long-term emotional bonds between adult individuals.

Like humans, show biparental and alloparental behaviors.

Translational/predictive validity for mechanisms regulating social behaviors

They like drinking alcohol .

LIT-001 decreases alcohol consumption in socially housed male prairie voles



Potretzke et al,
Neuropsychopharm, 2022

How will LIT-001 affect

pair bonding?

Unpublished data removed

(being submitted for publication)

Summary and Conclusions

Highly selective brain-penetrant oxytocin agonist affects pair-bonding in prairie voles.

The effects of this agonist depend on the phase of pair bonding.

These data are consistent with the idea that binding of oxytocin receptors signals presence of the social partner – promising for PGD or PLSD.

It is likely that in humans, the effects of manipulating the oxytocin system will have differential effects on social bonding depending on the social context of relationships.

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