

Doctoral thesis proposal

# Orexin and uncertainty effects on food-seeking behavior

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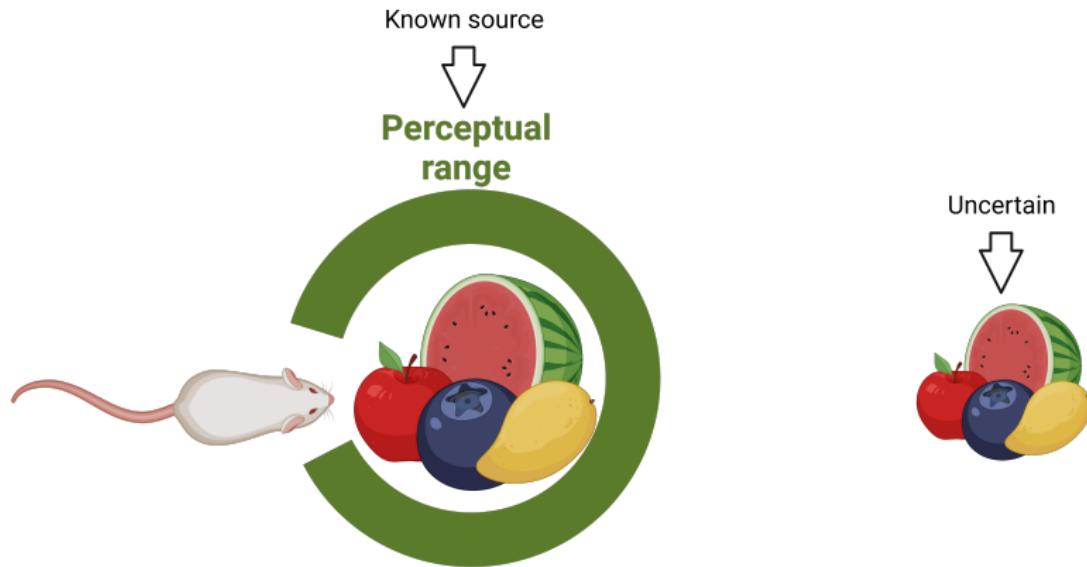
Neurobiology and Obesity (NBO) lab <https://www.nbolab.cl/>

Food-seeking and uncertainty

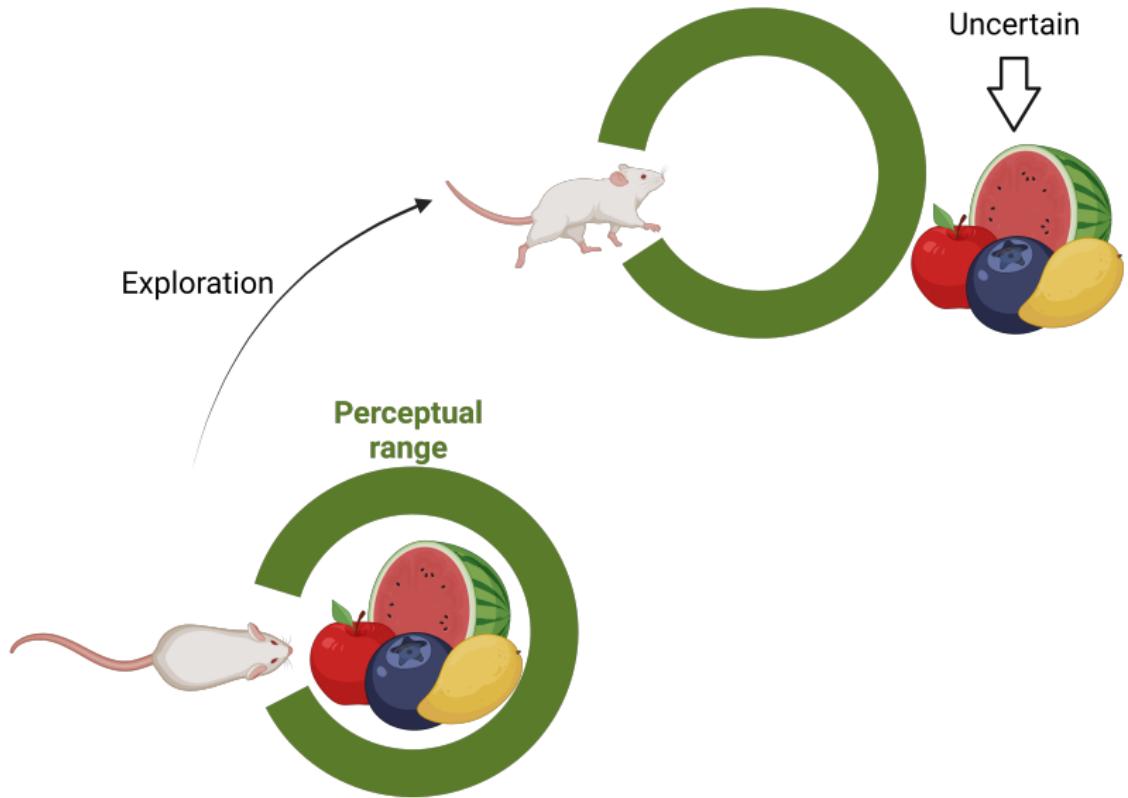
Food-seeking behavior is the coordination of locomotor activity with internal and external cues to procure food



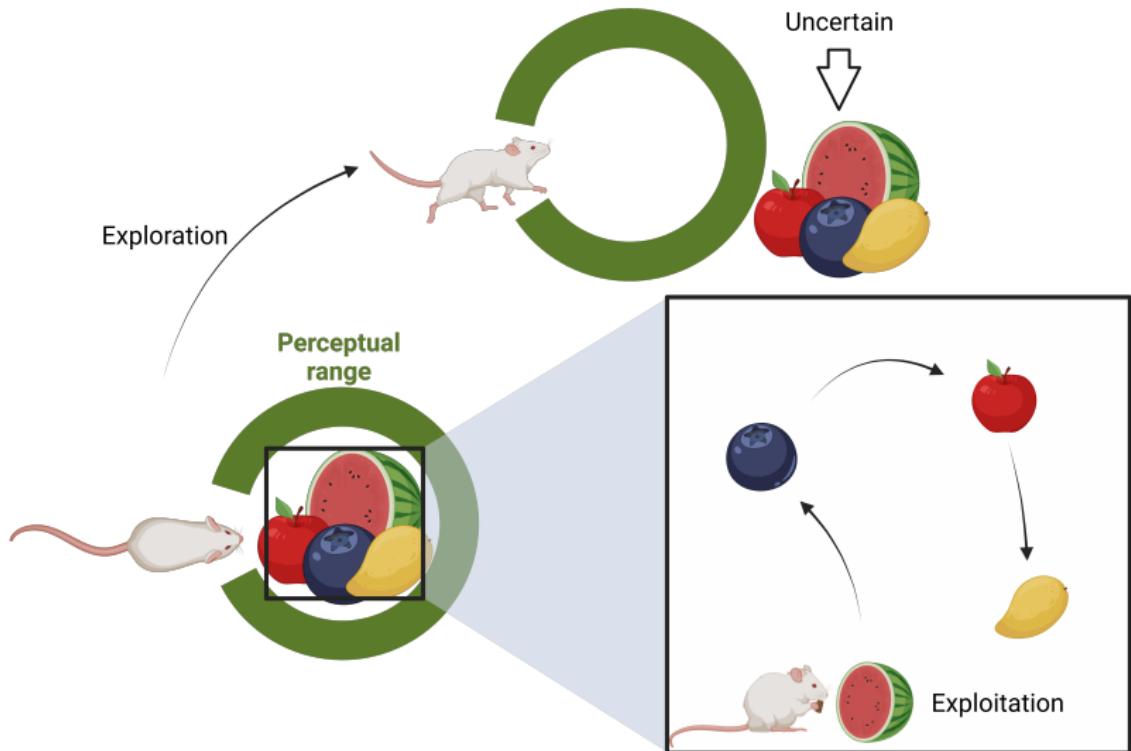
# Food-seeking behavior implies a state of partial knowledge



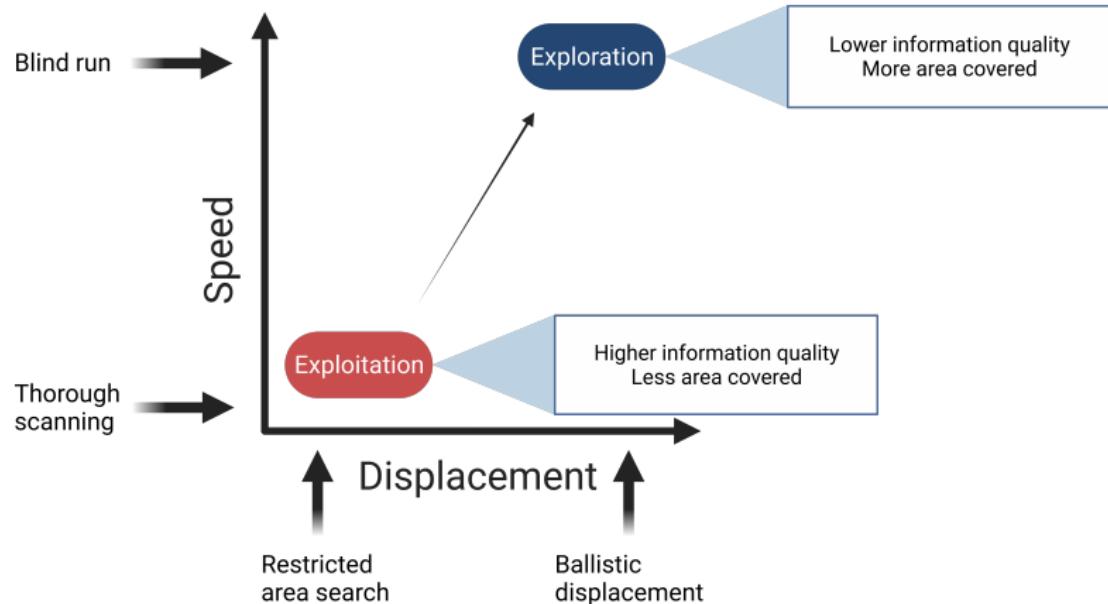
# Partial knowledge forces animals to explore for new food sources



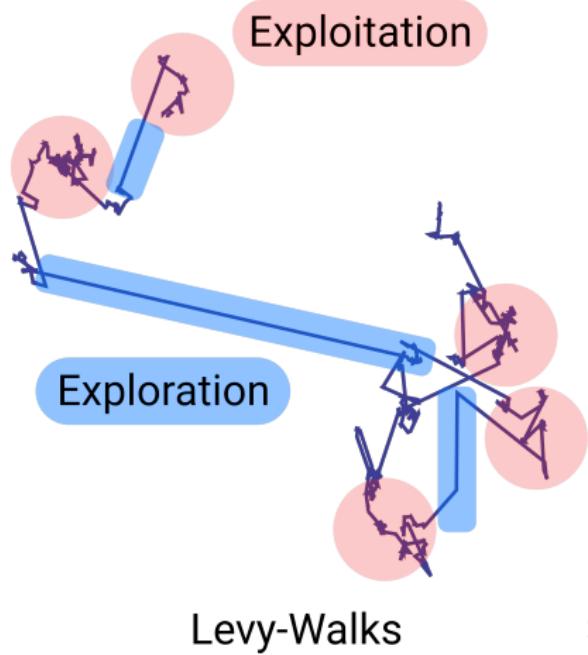
At some point animals need to stop exploring and start exploiting



# Uncertainty is inherent to food-seeking behavior



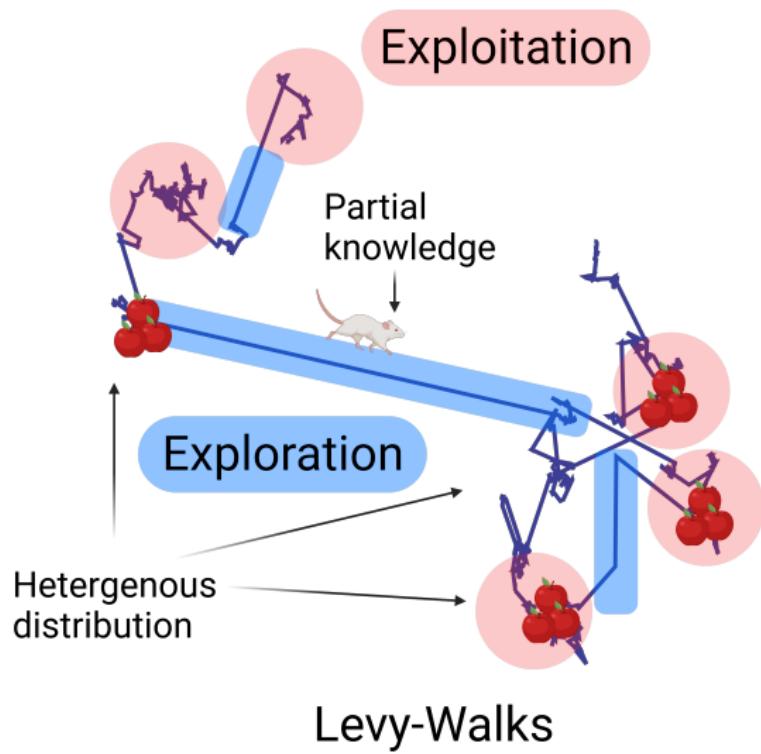
Food-seeking behavior evolved to deal with uncertainty,  
balancing between exploration and exploitation



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<sup>2</sup>Sims et al. (2014); Raichlen et al. (2014); Wosniack et al. (2017)

Food-seeking behavior evolved to deal with uncertainty, balancing between exploration and exploitation

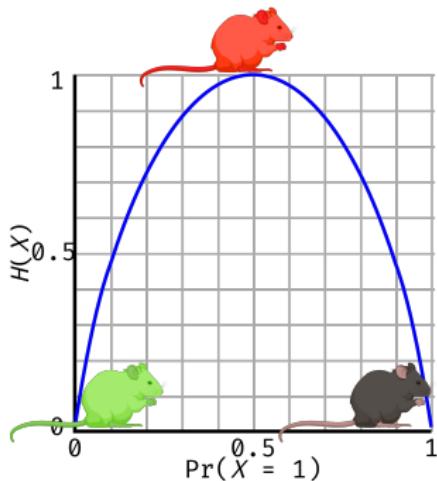


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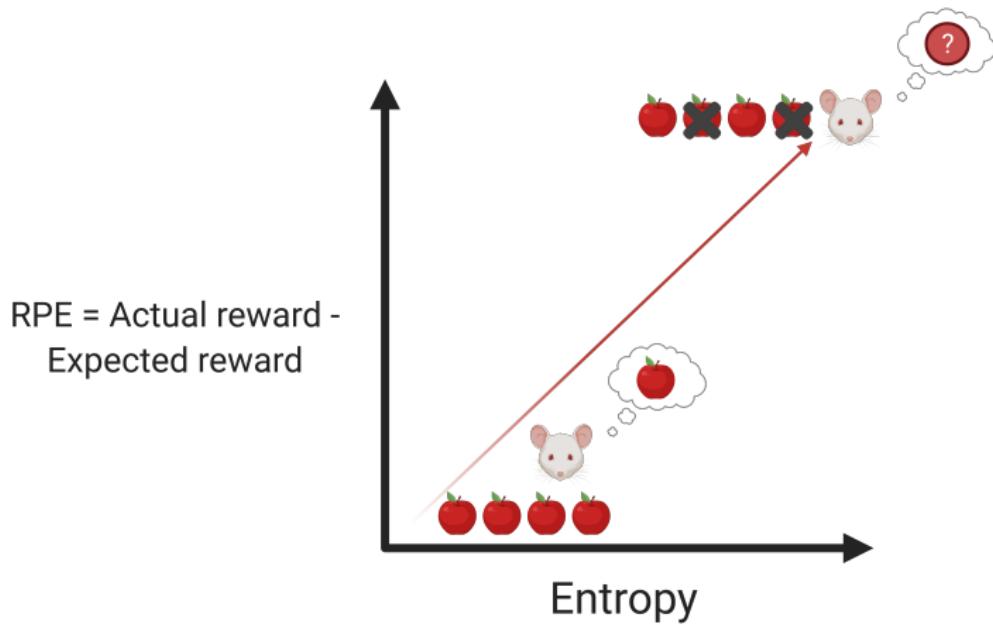
## Key points

- 1 Due to limited perceptual ranges, animals must balance between exploration and exploitation
- 2 Exploratory behavior is triggered to reduce uncertainty of unknown food-sources
- 3 Food-seeking behavior adapted to deal with uncertainty by balancing between exploration and exploitation

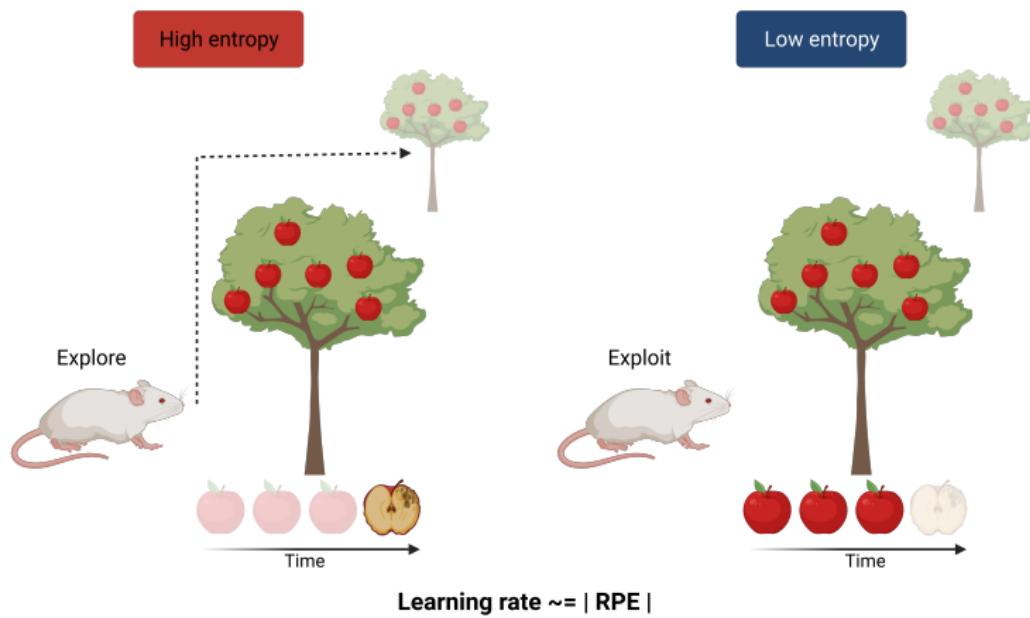
# Uncertainty and behavior: entropy relates the probability of obtaining food with uncertainty



Increasing entropy makes prediction harder, leading to larger reward prediction errors



# Reward prediction error changes the learning rate, adapting behavior to environment uncertainty



## Key points

- ① Entropy allows us to link food-access probability with uncertainty
- ② The reward prediction error offers an indirect measure of environment uncertainty
- ③ The reward prediction error bias exploration/exploitation through the learning rate

Modeling food-seeking behavior in uncertain environments

# Food-seeking behavior modeling starts by expected value computation



Expected value  $\sim=$  Past value + (RPE \* Learning rate)

Expected value  $\sim=$  Action | State

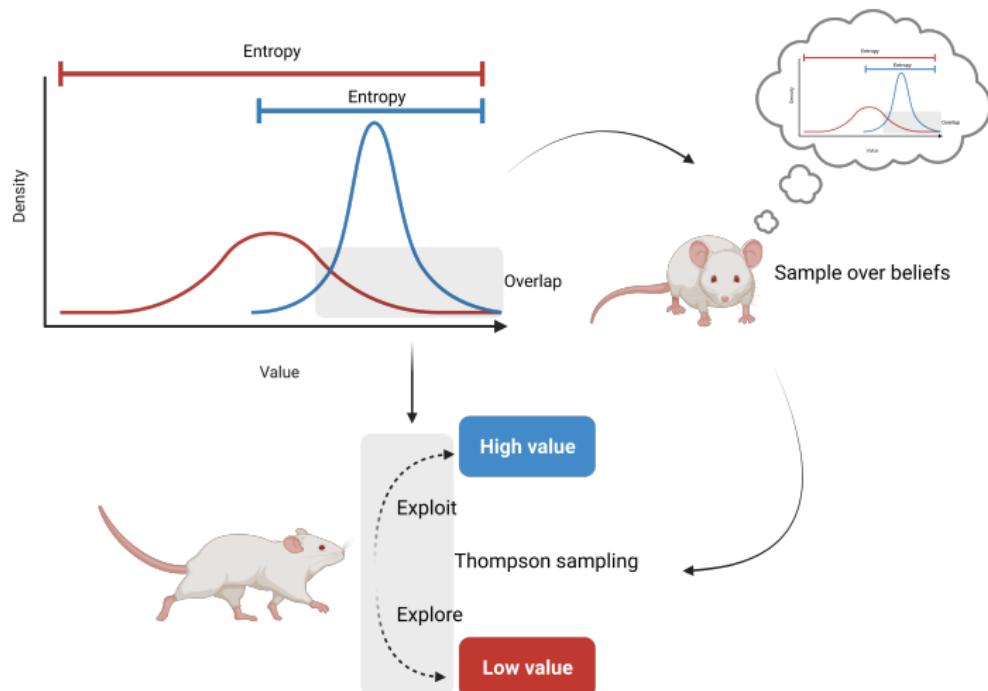
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# Food-seeking behavior modeling starts by expected value computation

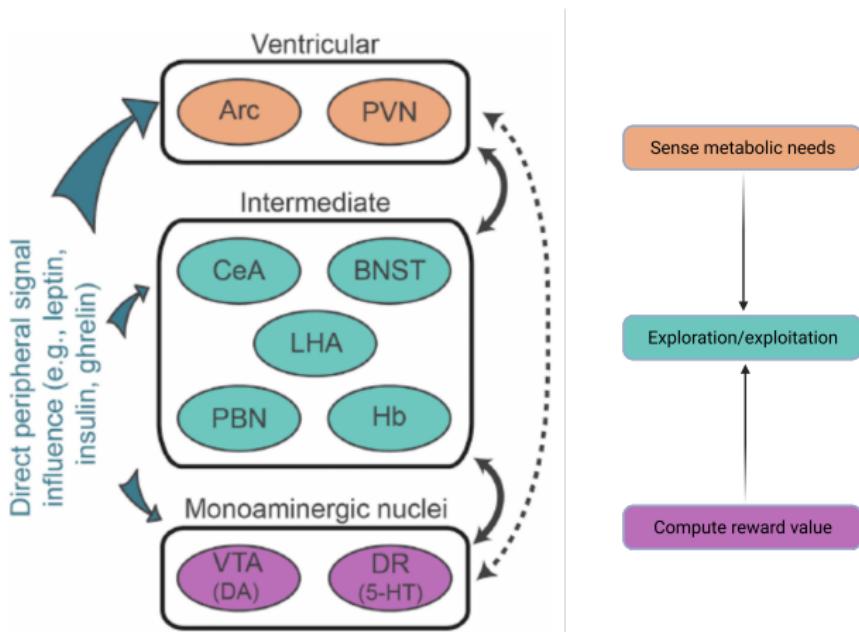


## Key points

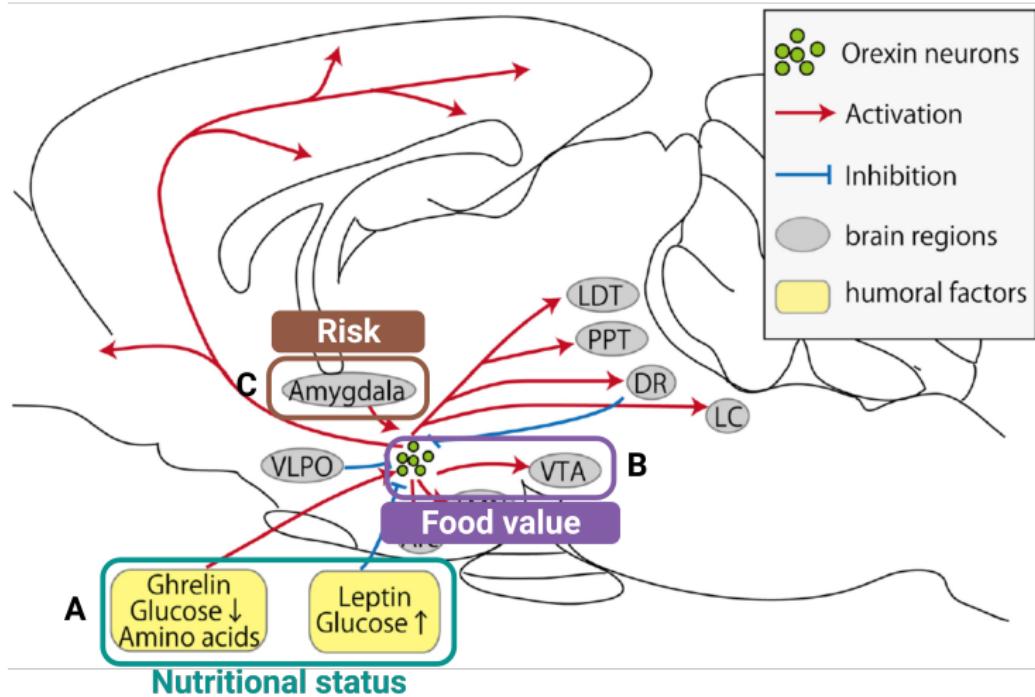
- 1 Uncertainty is inherent to food-seeking behavior and forces the animal to balance between exploration and exploitation
- 2 Uncertainty can be sensed indirectly through direct experience
- 3 The main aspects of food-seeking behavior can be modeled with RPE, learning rate and thompson sampling

Neural basis of uncertainty-driven food-seeking behavior

# Reward and feeding centers connectivity permits procuring rewarding food to meet metabolic demands

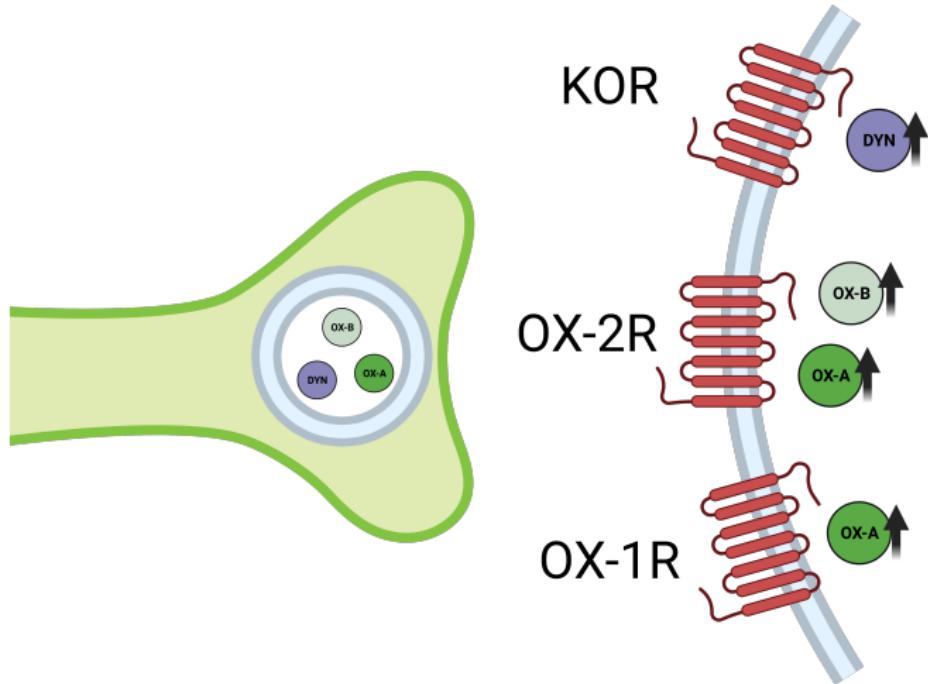


# Reward and feeding centers connectivity permits procuring rewarding food to meet metabolic demands

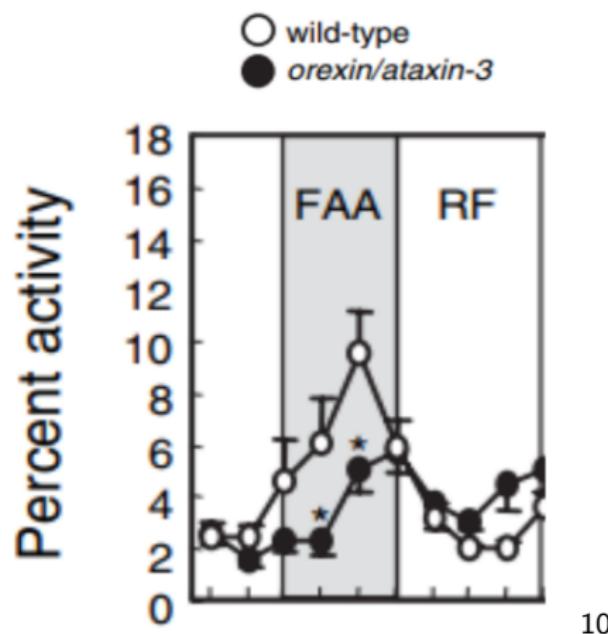


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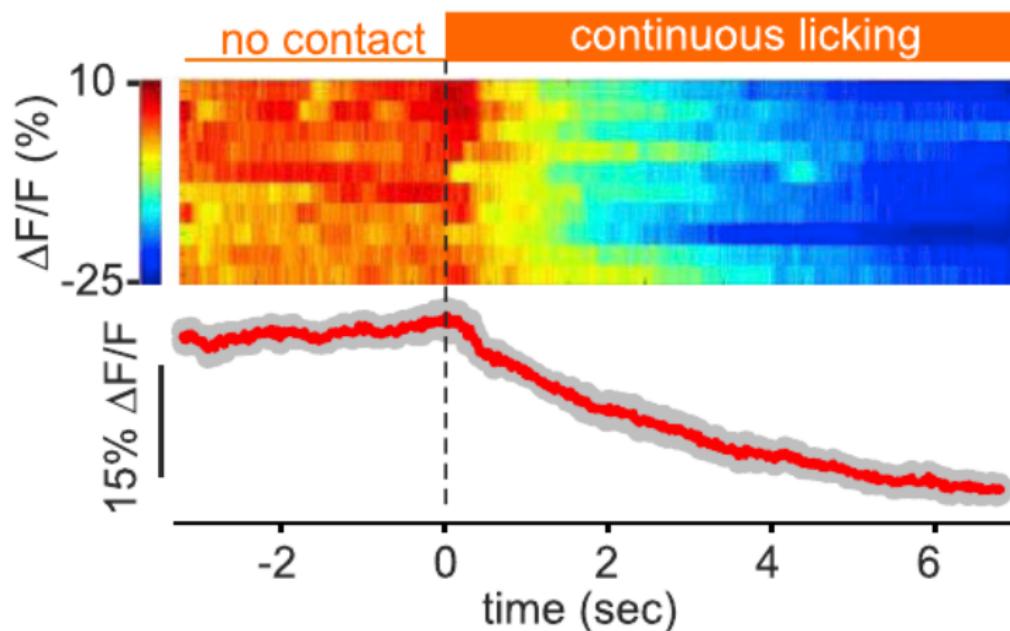
# Orexin could modulate exploration/exploitation through VTA DA activity



# LHA orexin activity role in food-seeking behavior

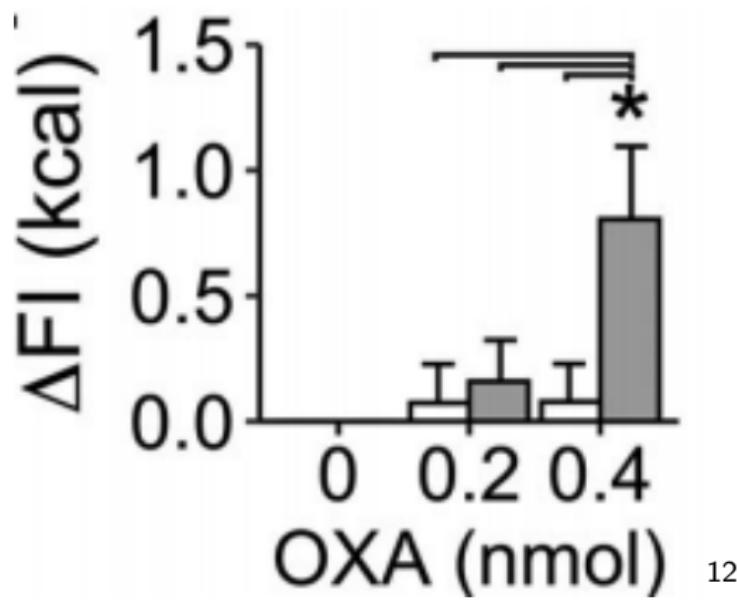


# LHA orexin activity role in food-seeking behavior

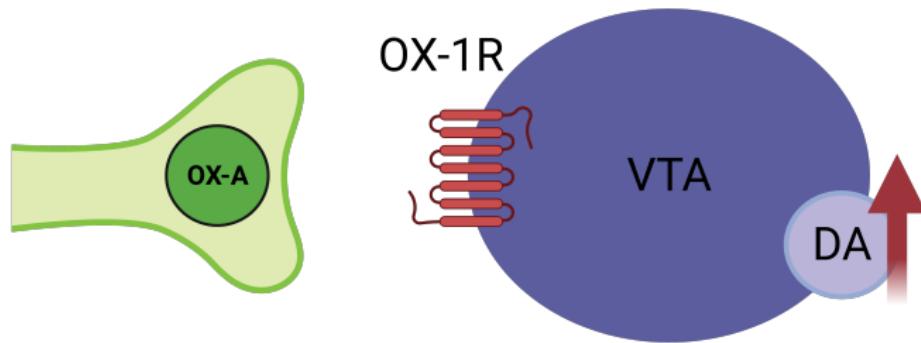


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# LHA orexin activity role in food-seeking behavior

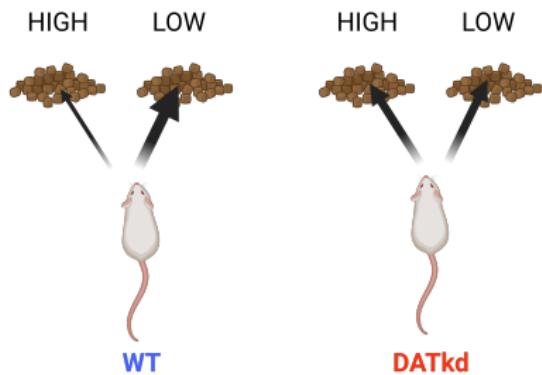
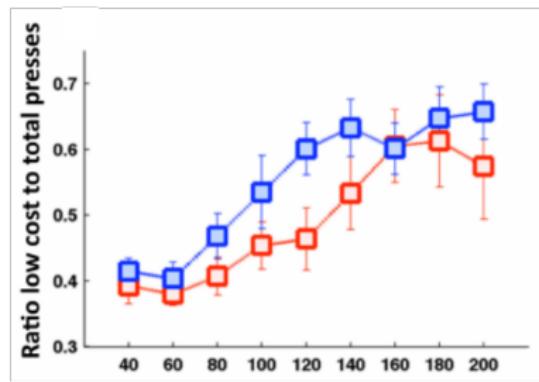


# Orexin could modulate exploration/exploitation through VTA DA activity

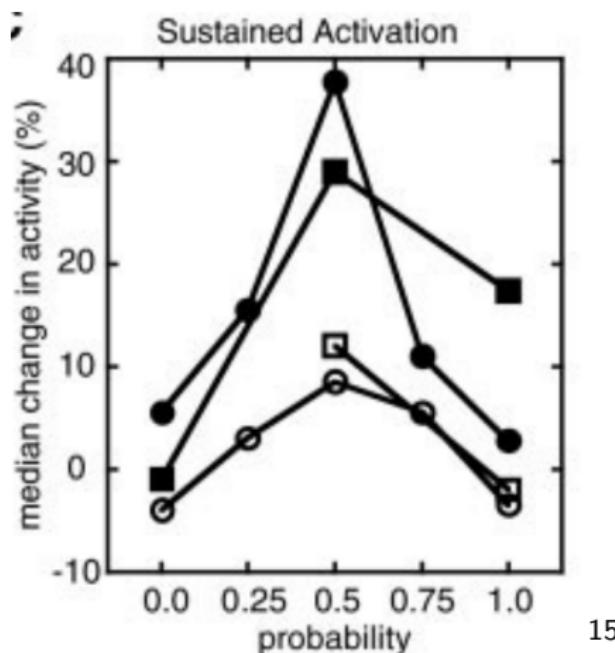


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# Orexin could modulate exploration/exploitation through VTA DA activity

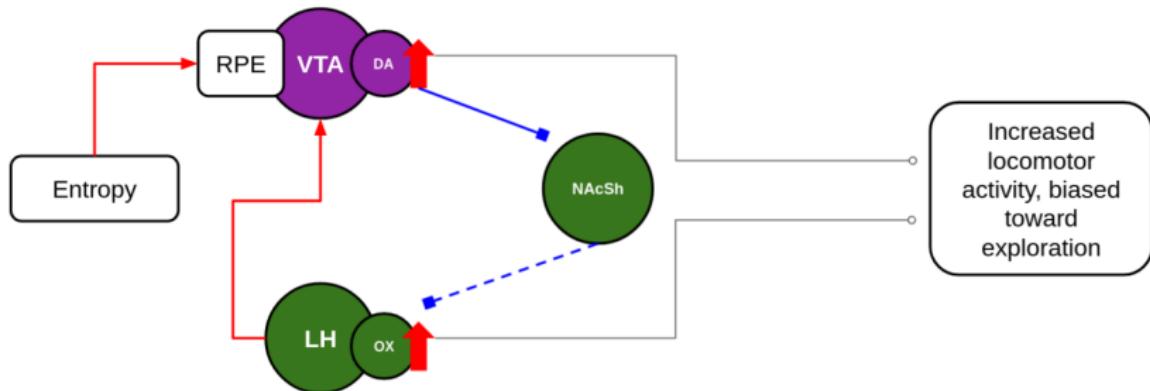


# VTA DA tonic activity encodes entropy



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# Proposed connectivity

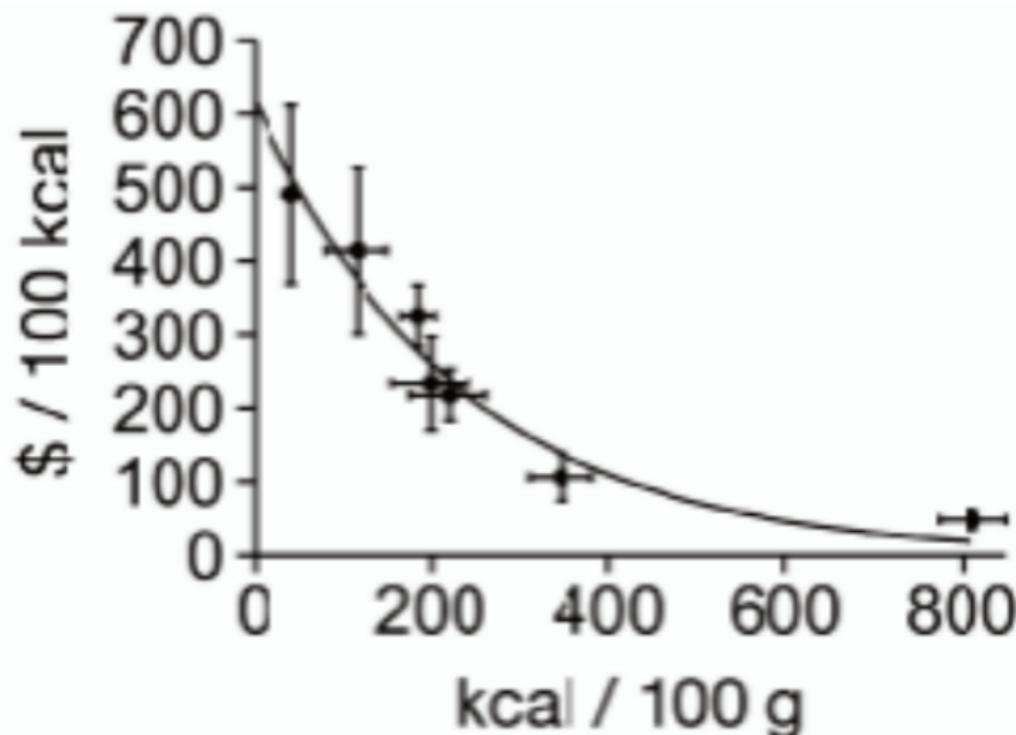


## Key points

- 1 Orexin coordinates locomotor activity towards procuring food
- 2 VTA DA tonic activity encodes entropy
- 3 Orexin functional connectivity with VTA, allows modulation of exploration/exploitation in food-seeking behavior

# Food-seeking in modern obesogenic environments

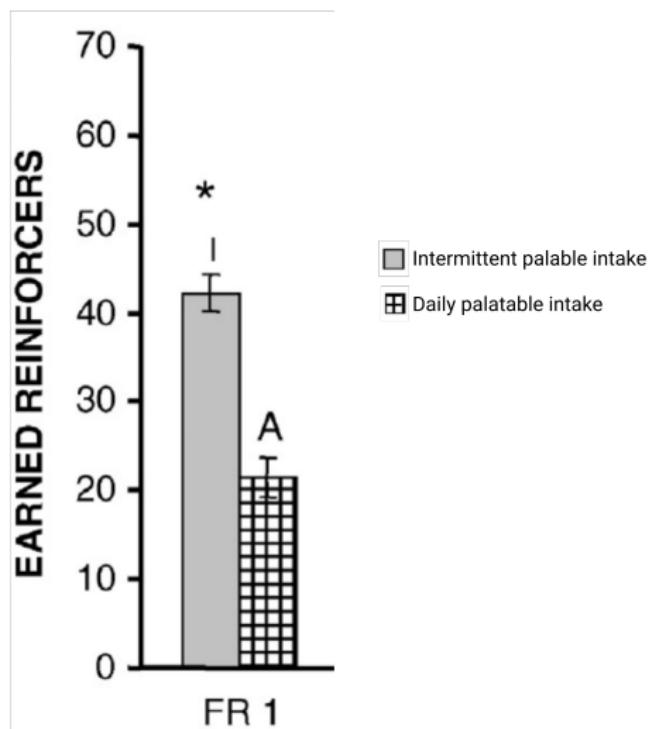
High calorie food items are of easy access



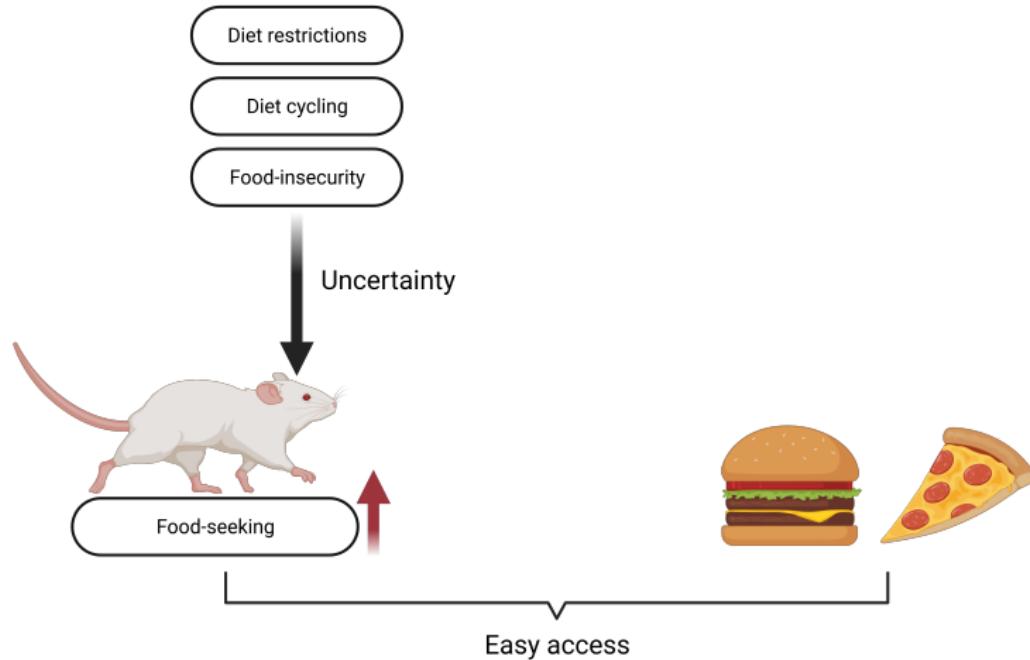
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<sup>16</sup>Verdugo, Giannina, Arias, Vanessa, & Perez Leighton Claudio. (2016)

# Uncertainty increases motivation to obtain food



# Modern environments turn food-seeking behavior maladaptive



## General overview

- 1 Uncertainty is inherent to food-seeking behavior
- 2 Animals sense uncertainty through RPE, and modulate its behavior through the learning rate
- 3 Orexin modulates uncertainty-drive VTA-DA activity
- 4 Easy-access to calorically dense foods turns food-seeking behavior maladaptive

## Hypothesis and objectives

## Main hypothesis and general objective

- Objective: Determine how uncertainty in food-access increases food-seeking behavior, and how orexin mediates uncertainty-driven increased food-seeking behavior
- Hypothesis: Food-access uncertainty increases food-seeking behavior, and this increase is modulated by orexin neurons activity

## Specific objectives

- 1 Determine whether uncertainty in food access required for subsistence increase motivation for palatable foods, and if this correlates with orexin gene expression
- 2 Determine whether uncertainty in obesogenic environments increases food-seeking behavior and assess if increased food-seeking behavior correlated with orexin gene expression
- 3 Determine if orexin/dynorphin neurons projecting to the VTA are active during sucrose intake
- 4 Determine whether orexin in VTA elicits increased food-seeking behavior towards uncertain options, and orexin agonists inhibits food-seeking behavior towards uncertain options

## Methods

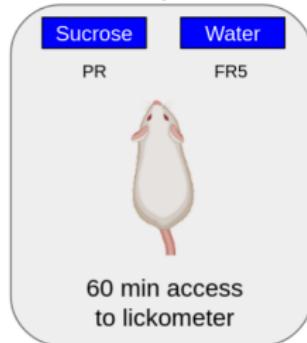
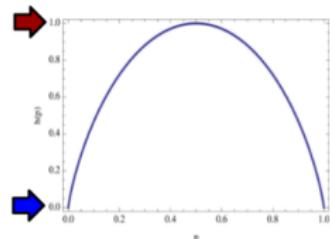
# Specific objective 1: setting



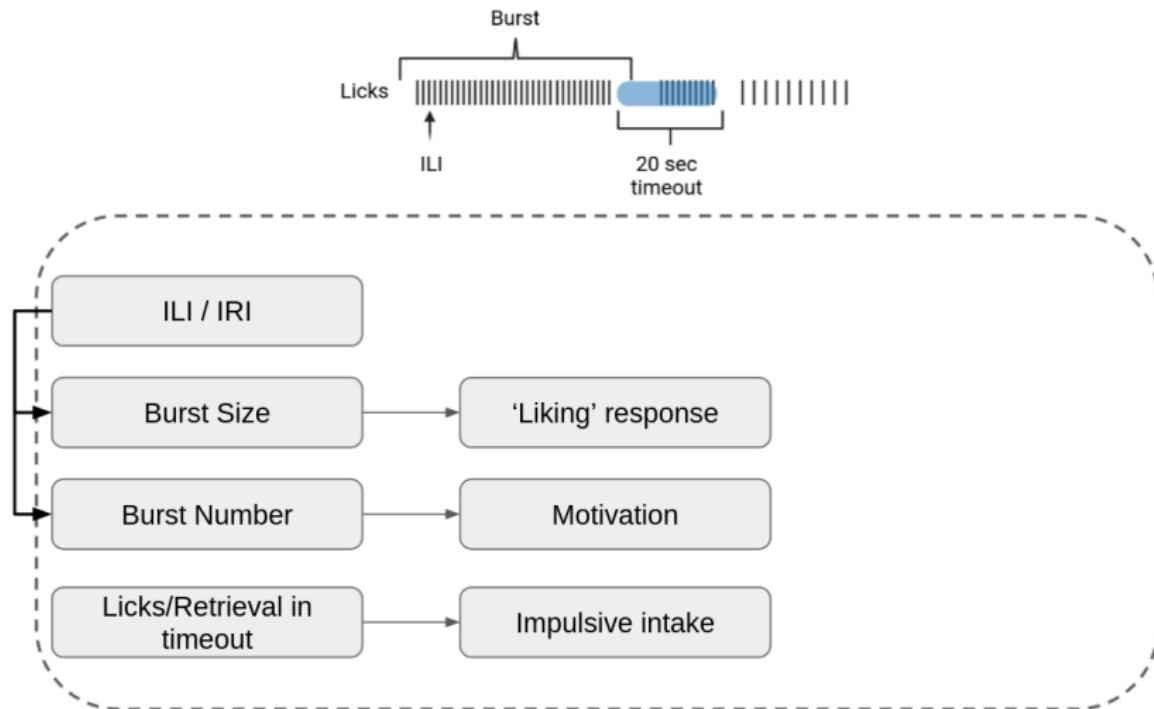
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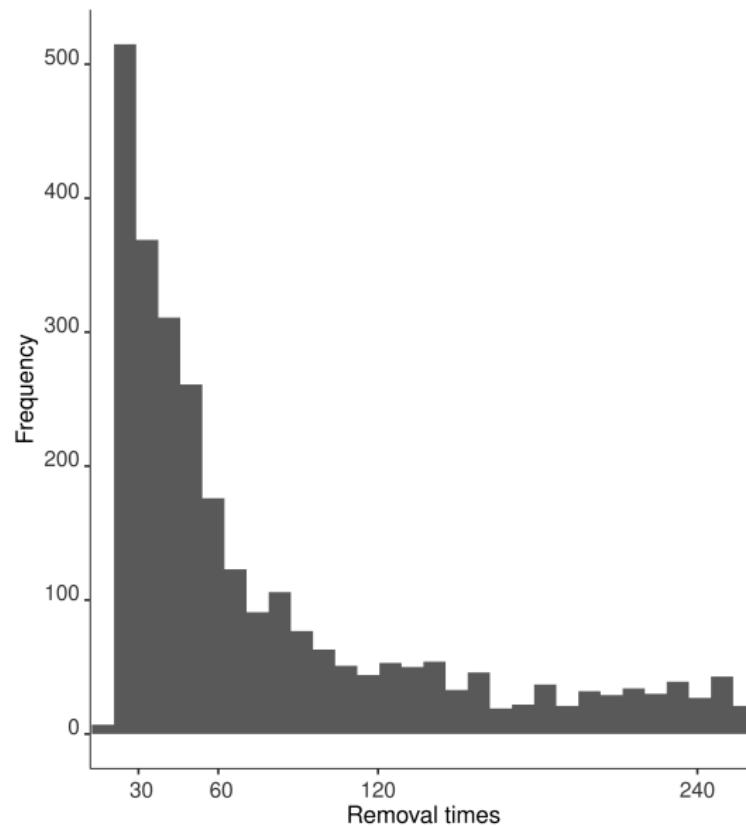
15 - 30 - 120 - 240 sec



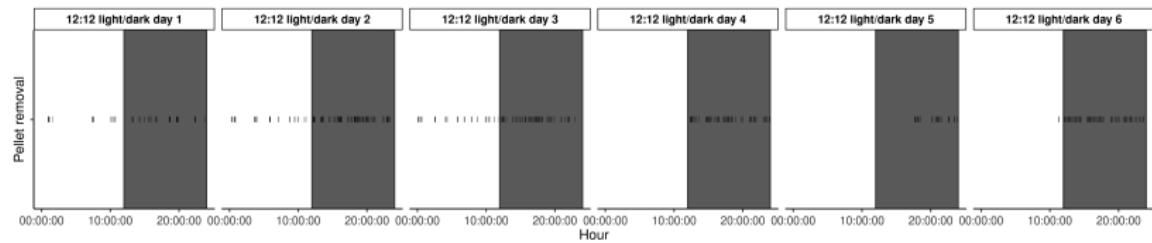
# Specific objective 1: behavioral analysis



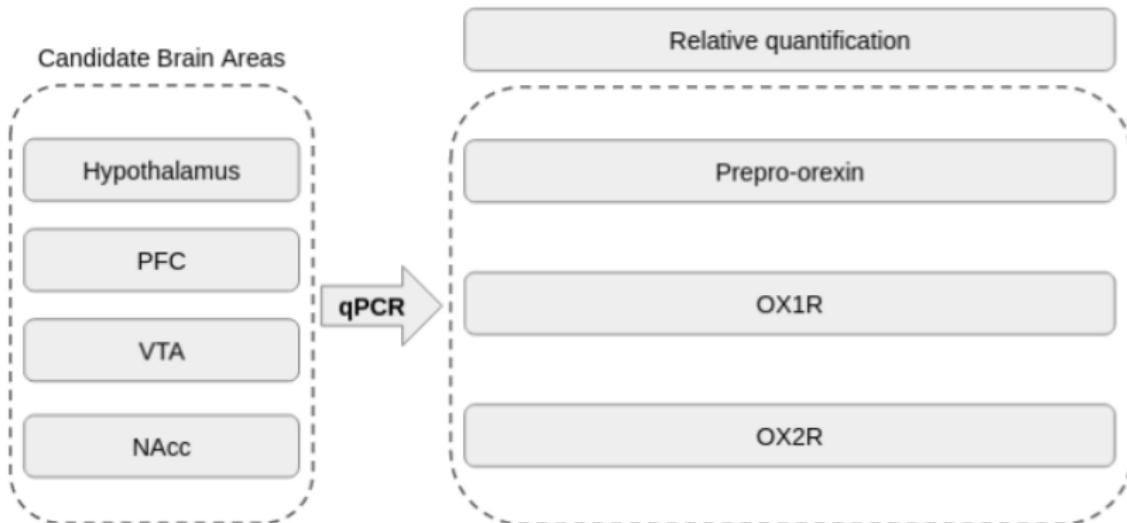
# Inter removal intervals



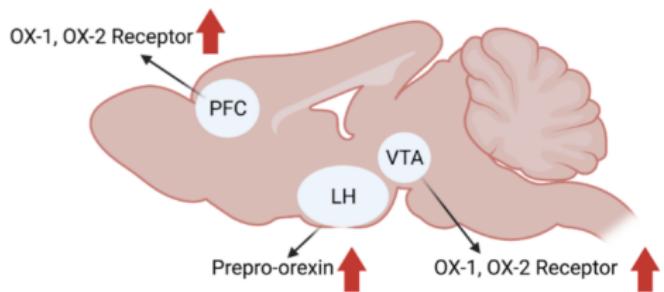
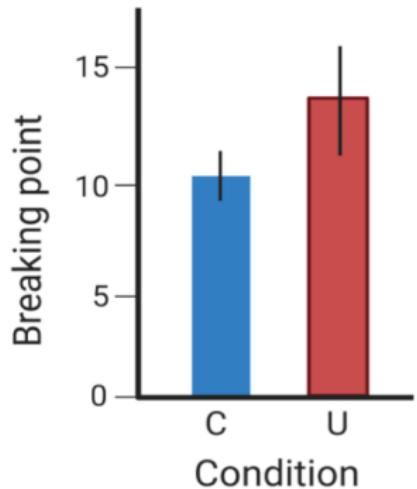
# Circadian pellet intake



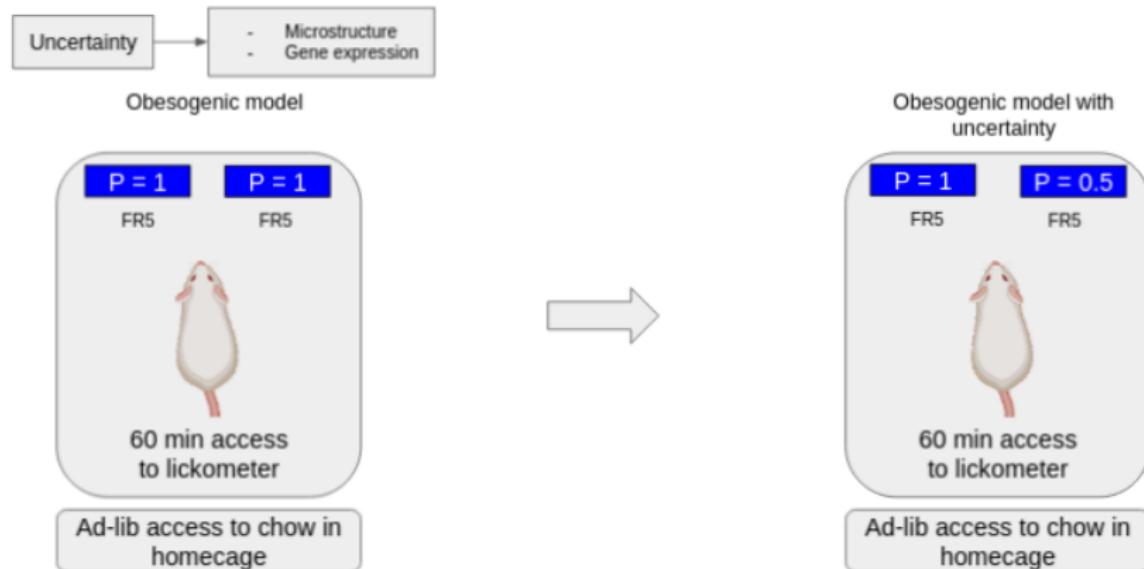
# Specific objective 1: gene expression



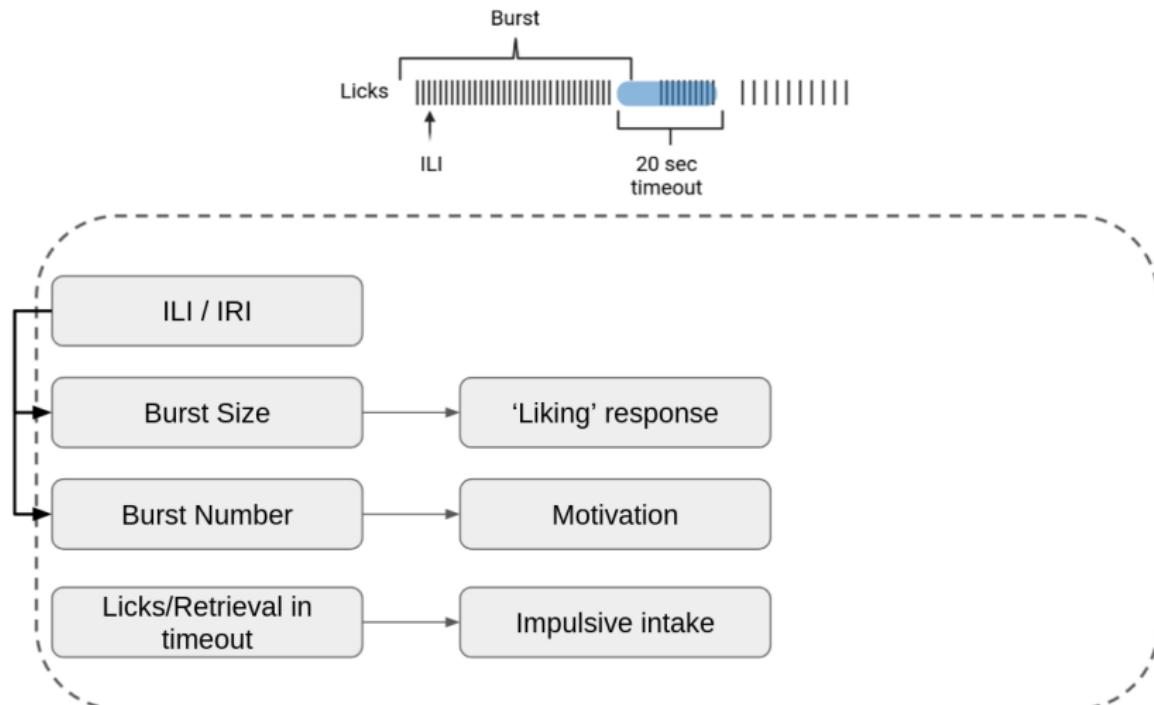
## Specific objective 1: expected results



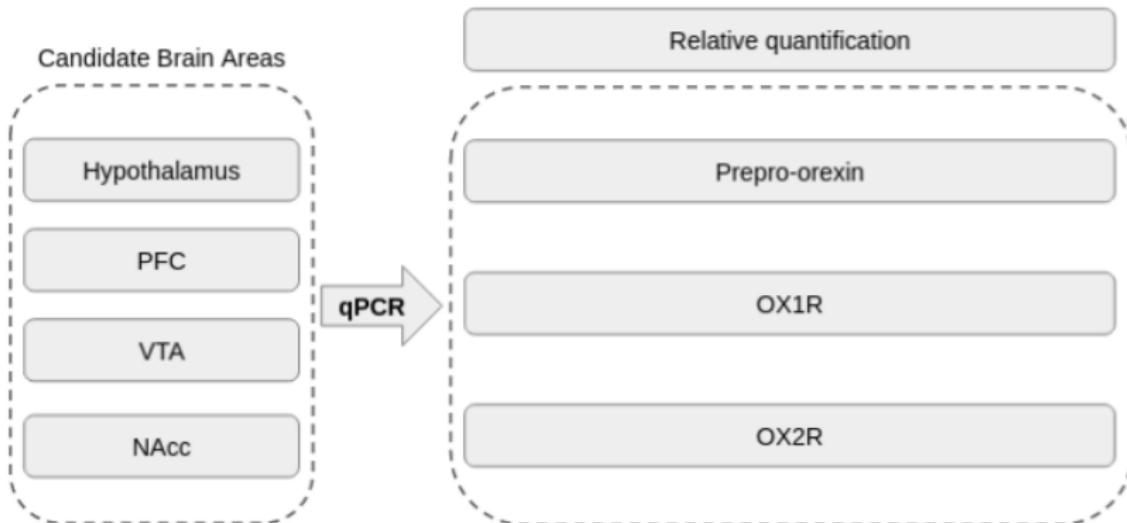
## Specific objective 2: setting



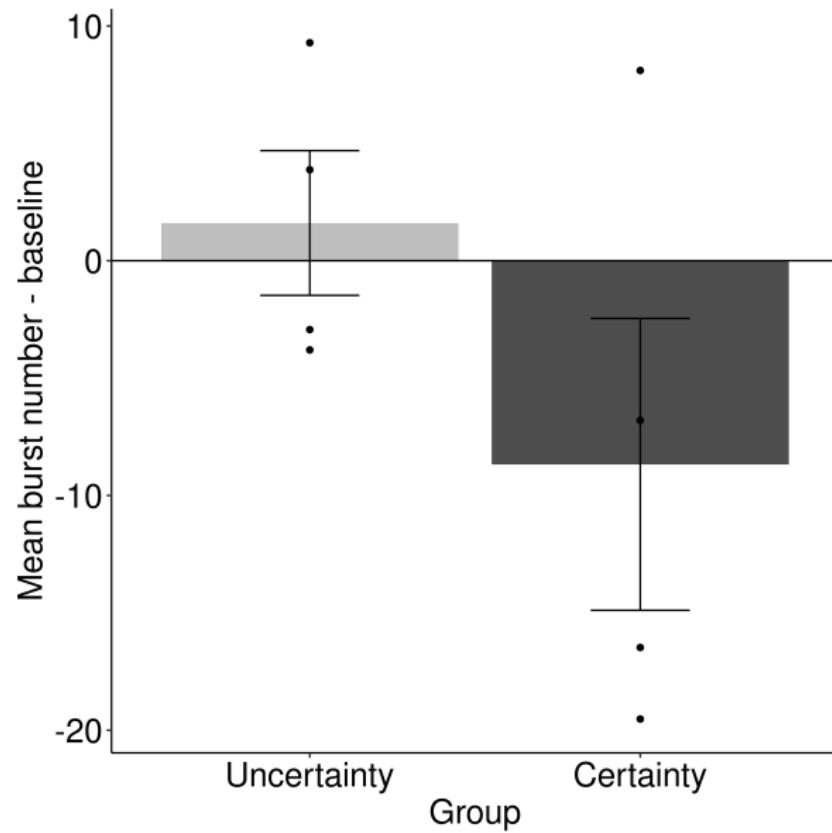
## Specific objective 2: behavioral analysis



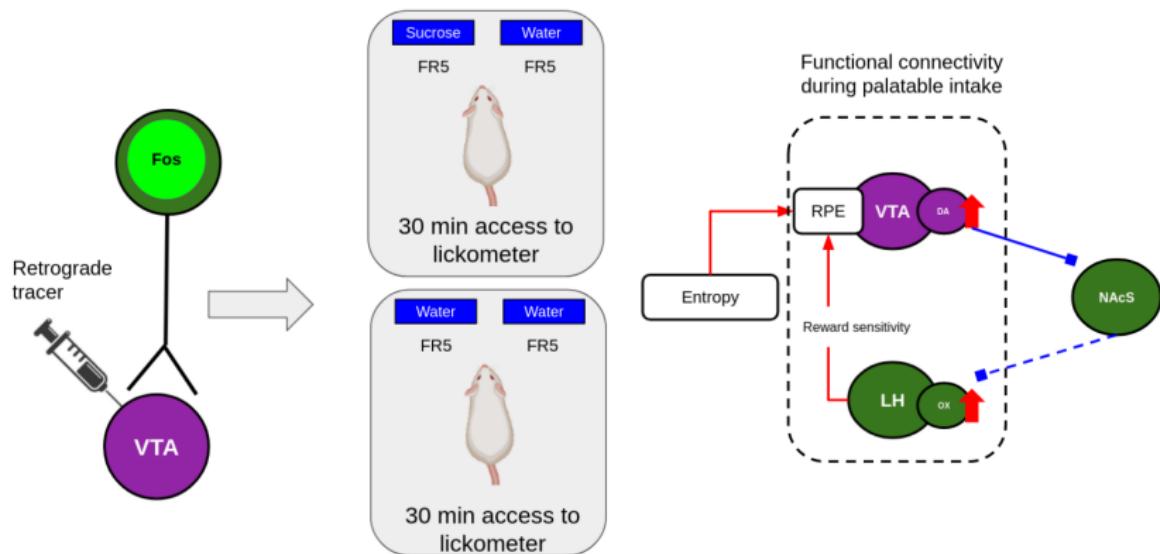
## Specific objective 2: gene expression



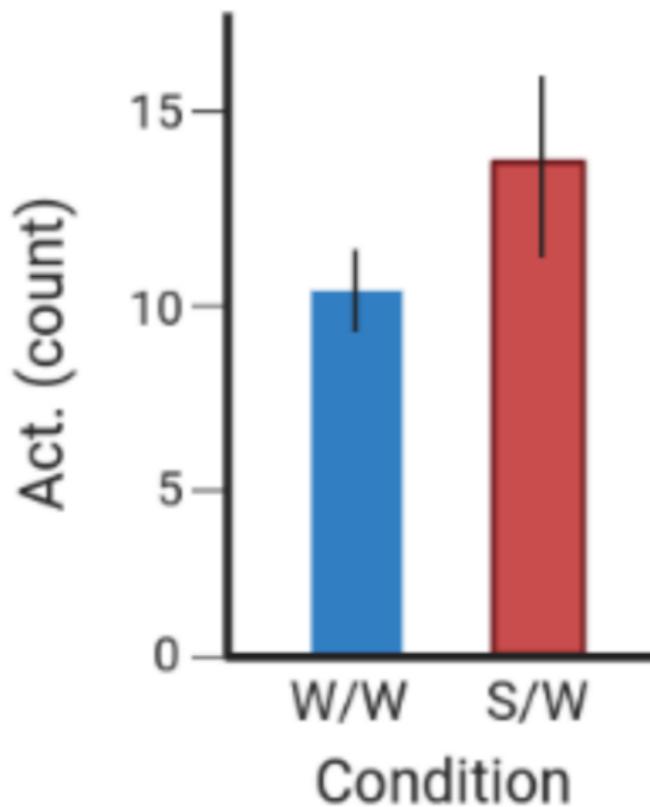
## Specific objective 2: pilot study



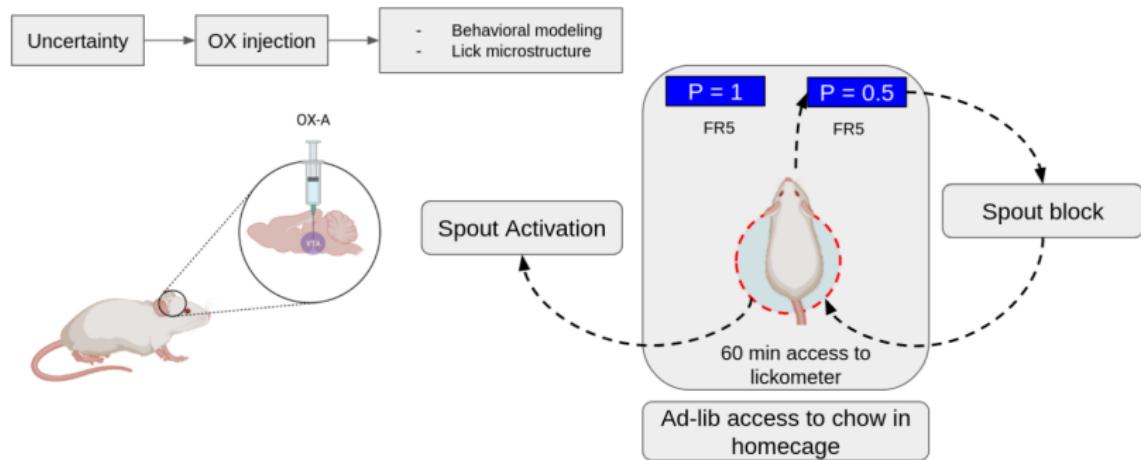
## Specific objective 3: setting



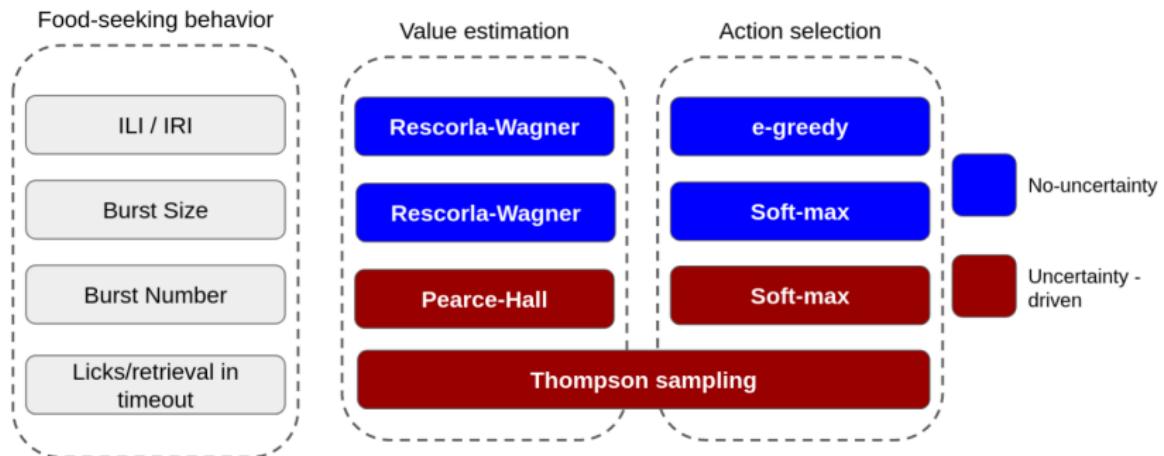
## Specific objective 3: expected results



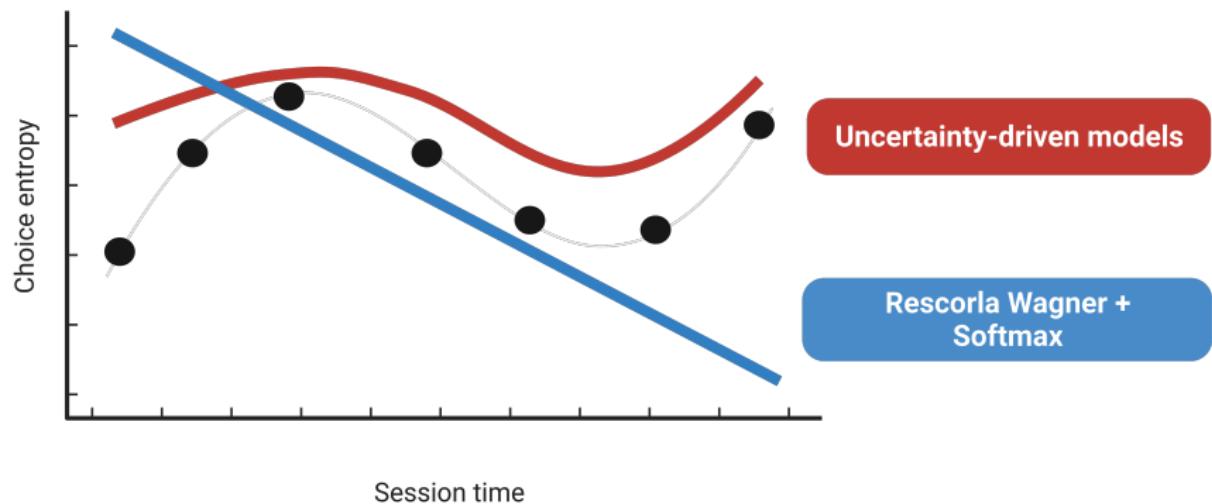
## Specific objective 4: setting



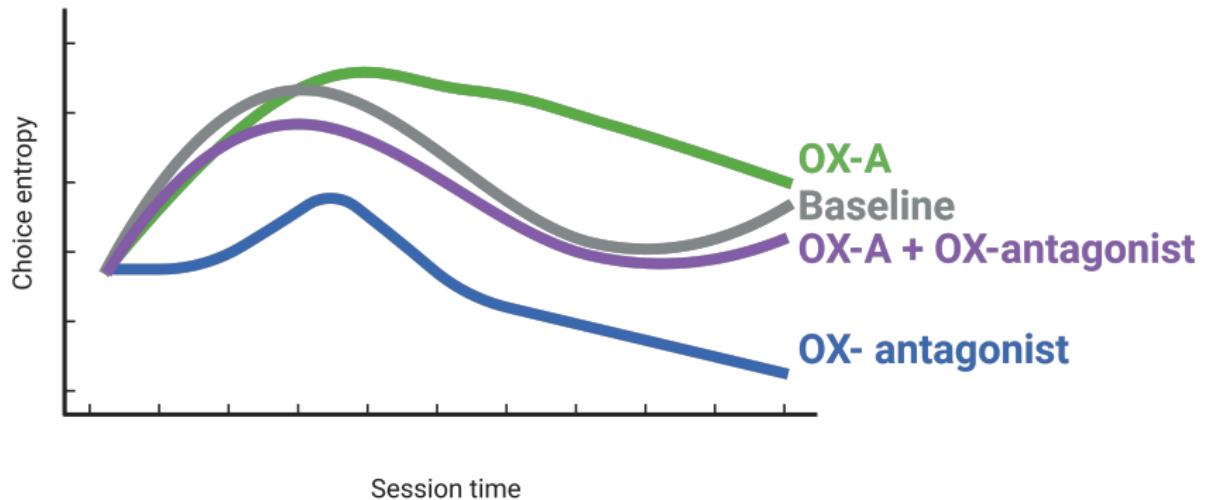
# Specific objective 4: behavioral analysis



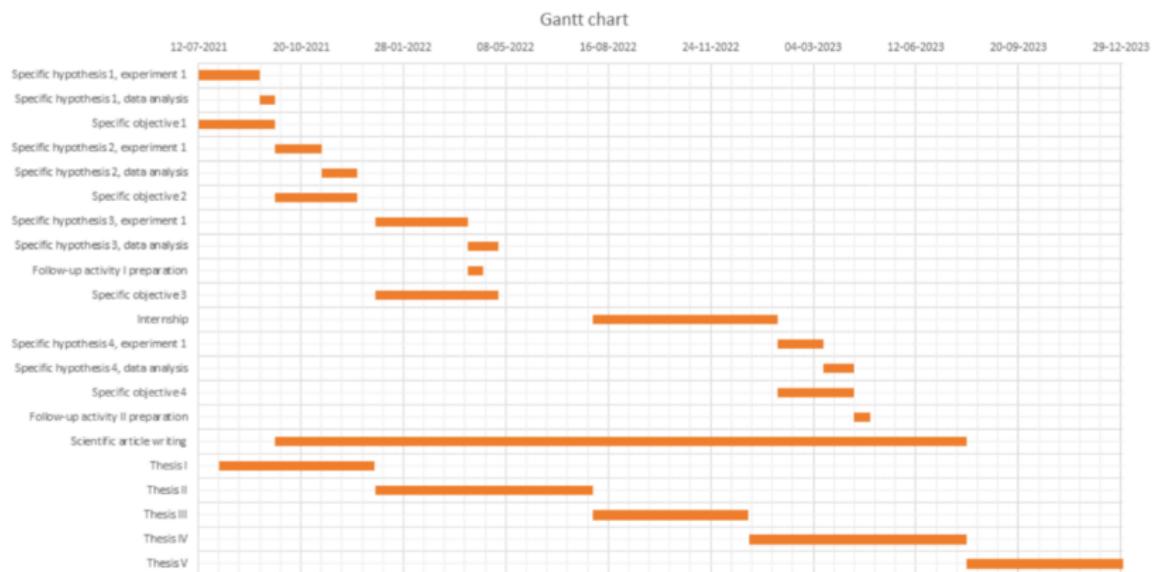
## Specific objective 4: expected results



## Specific objective 4: expected results



# Workplan



Thanks!

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