

Doctoral thesis proposal

Orexin and uncertainty effects on food-seeking behavior

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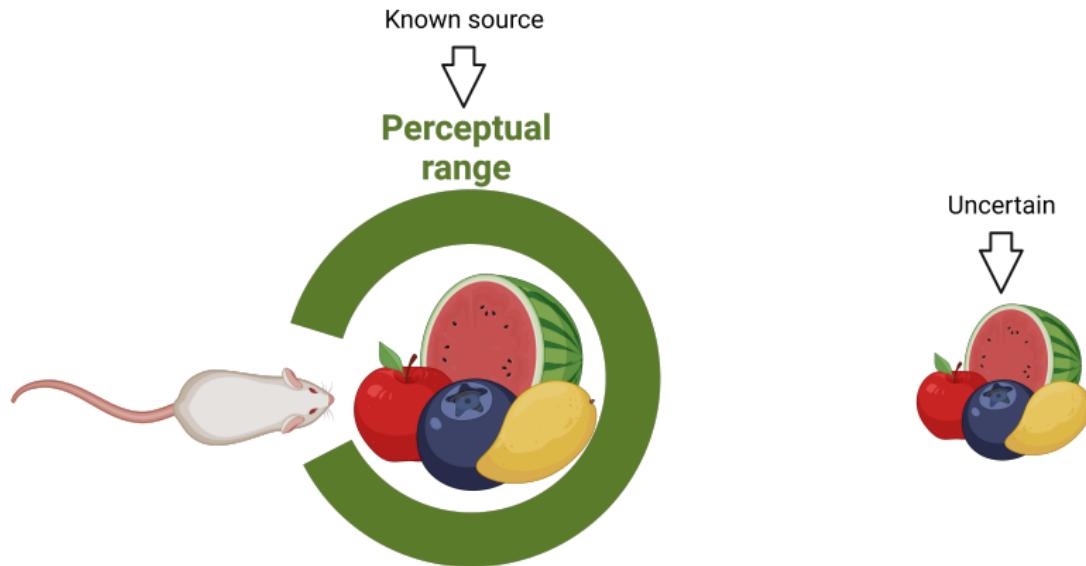
Neurobiology and Obesity (NBO) lab <https://www.nbolab.cl/>

Food-seeking and uncertainty

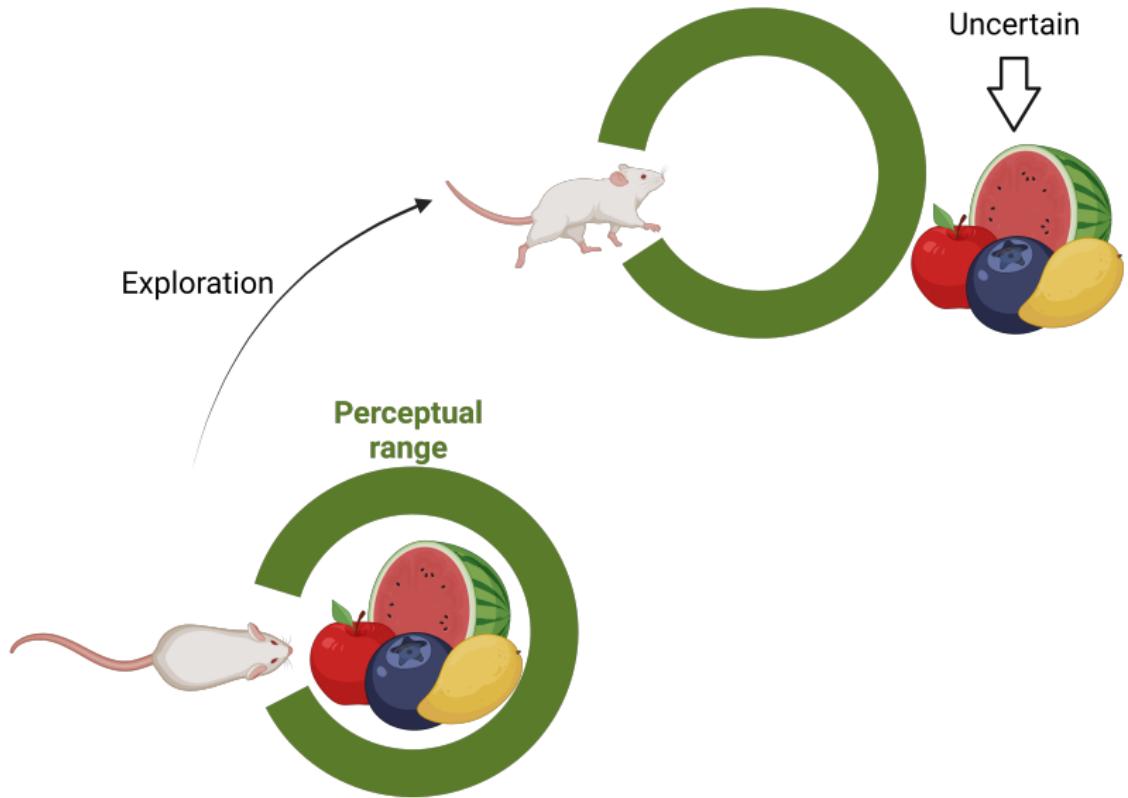
Food-seeking behavior is the coordination of locomotor activity with internal and external cues to procure food



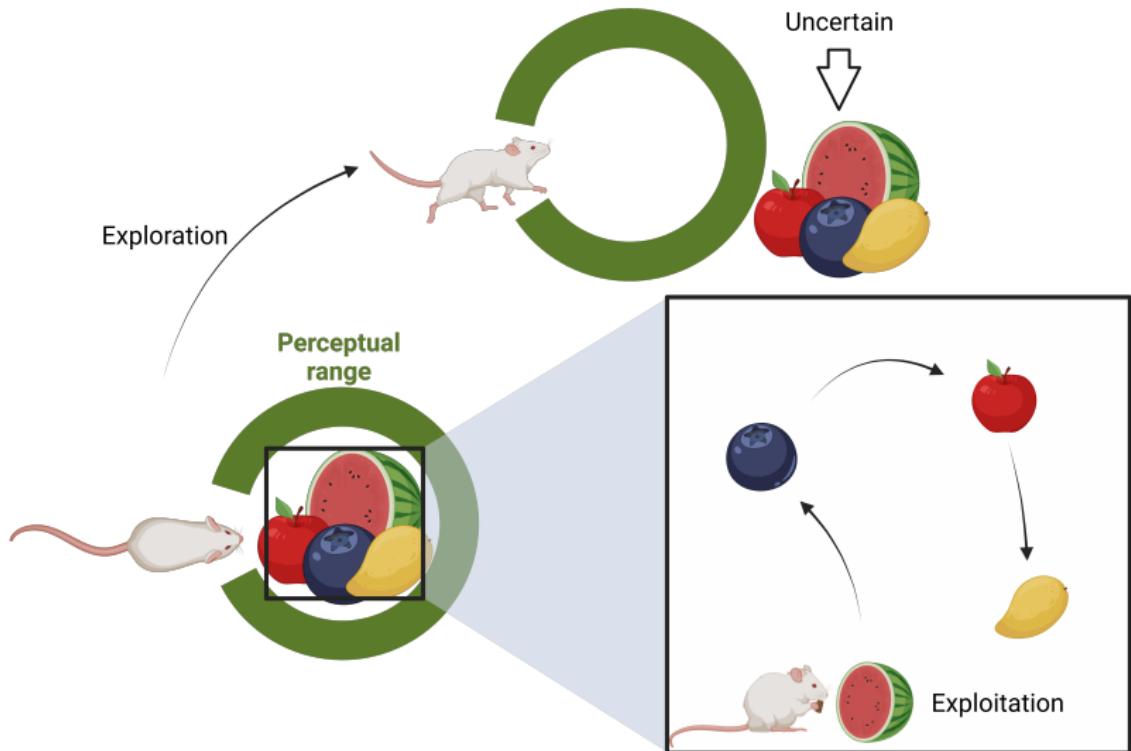
Food-seeking behavior implies a state of partial knowledge



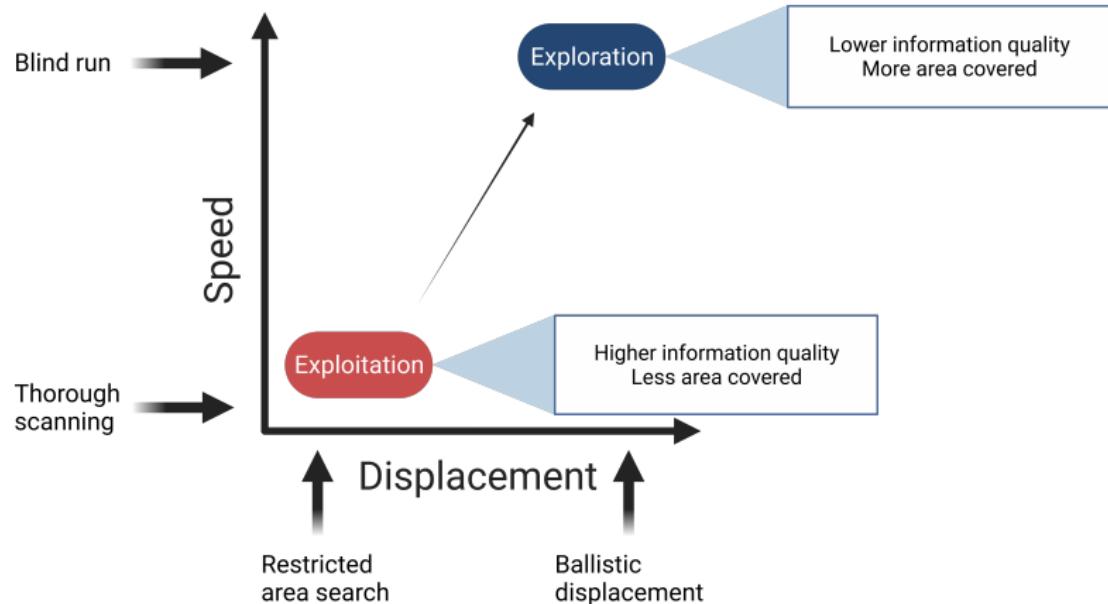
Partial knowledge forces animals to explore for new food sources



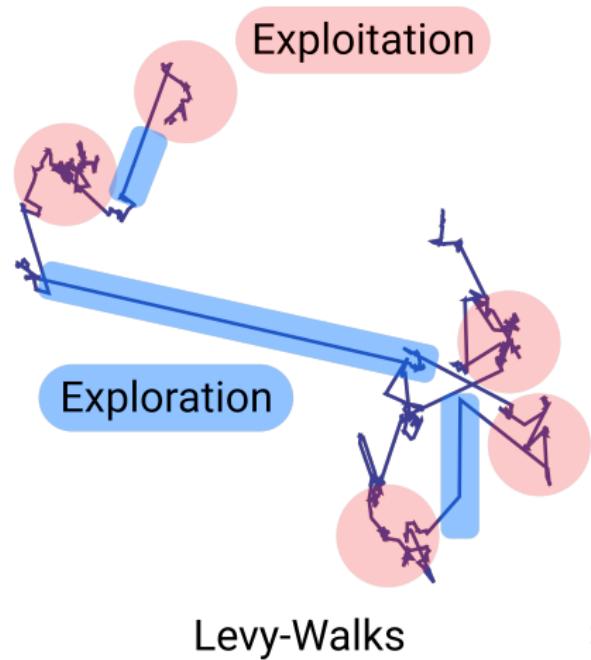
At some point animals need to stop exploring and start exploiting



Uncertainty is inherent to food-seeking behavior



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

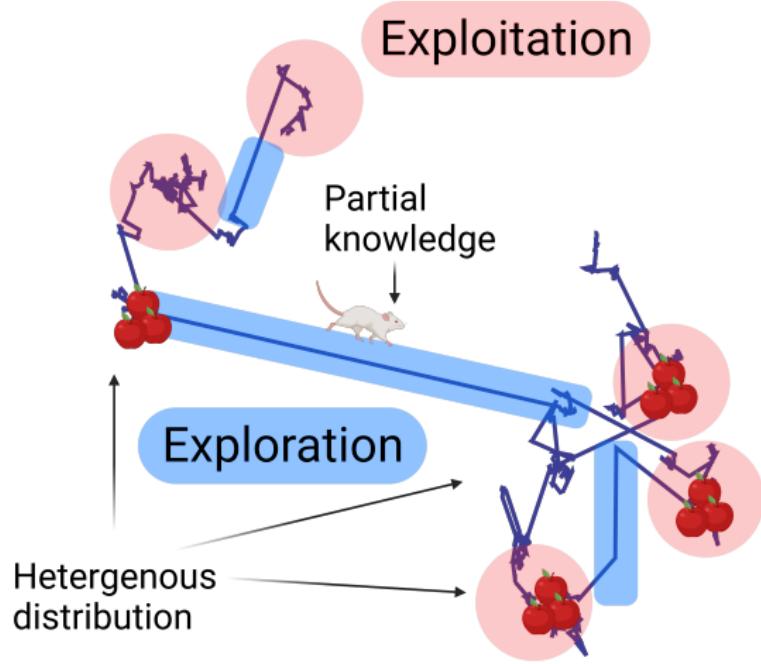


Levy-Walks

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²(V2K7D7TC#Sims_Etal_2014?);
(GA2XPWXX#Raichlen_Etal_2014?);
(SMMK9V45#Wosniack_Etal_2017?)

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



Levy-Walks

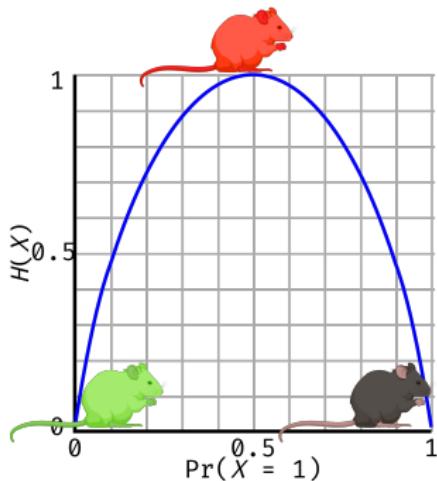
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³(V2K7D7TC#Sims_Etal_2014?);
(GA2XPWXX#Raichlen_Etal_2014?);
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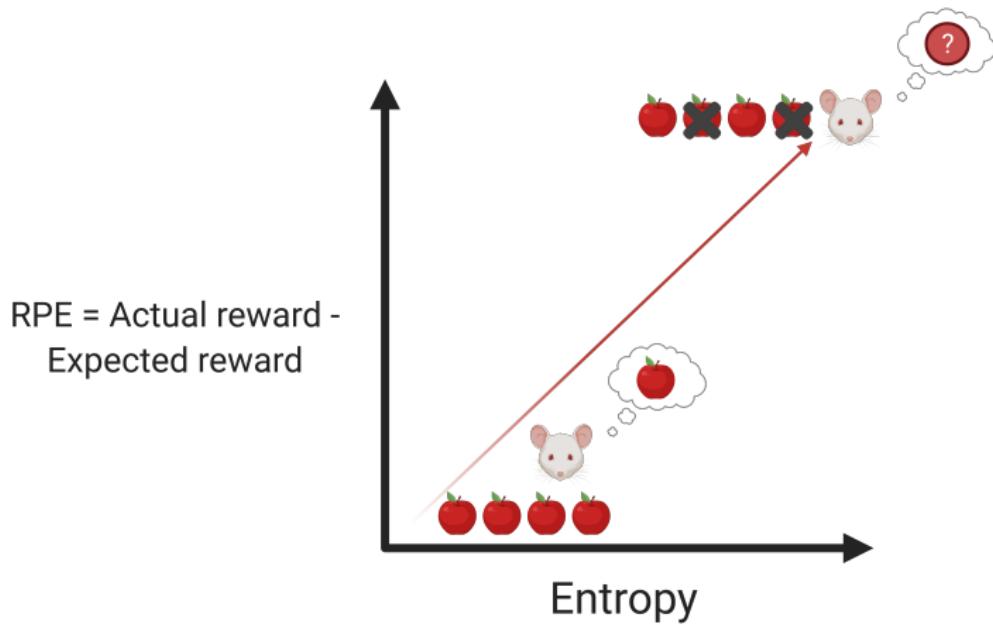
Key points

- 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

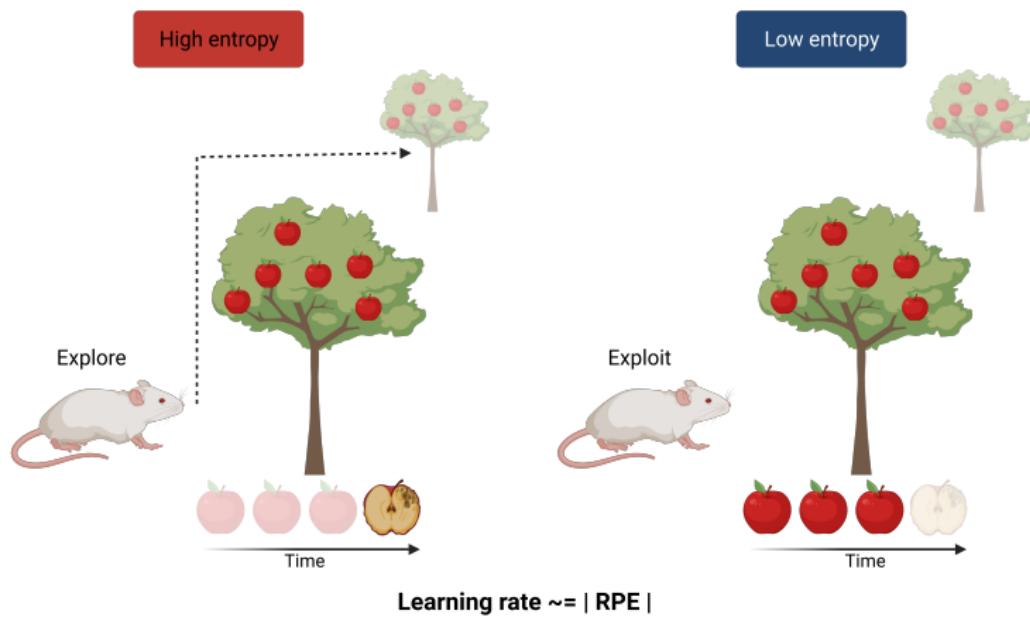
Uncertainty and behavior: entropy relates the probability of obtaining food with uncertainty



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

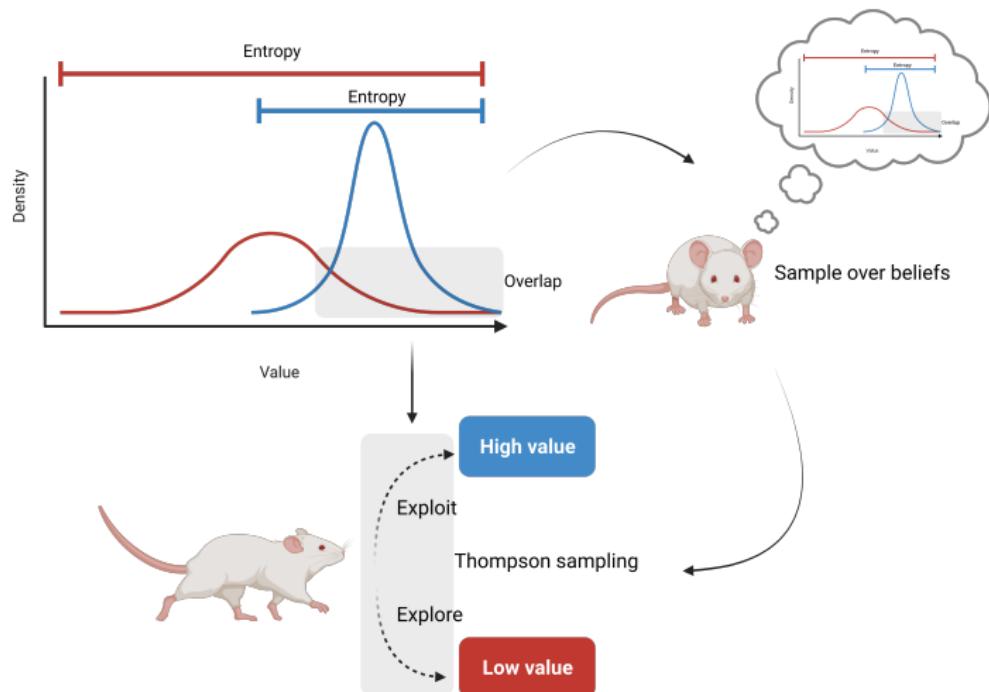
Food-seeking behavior modeling starts by expected value computation



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

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Food-seeking behavior modeling starts by expected value computation

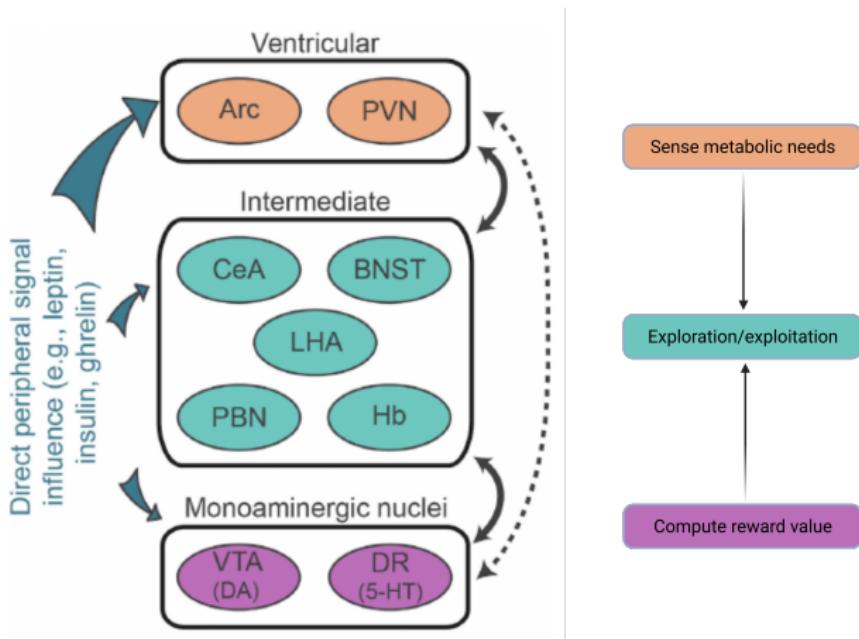


Key points

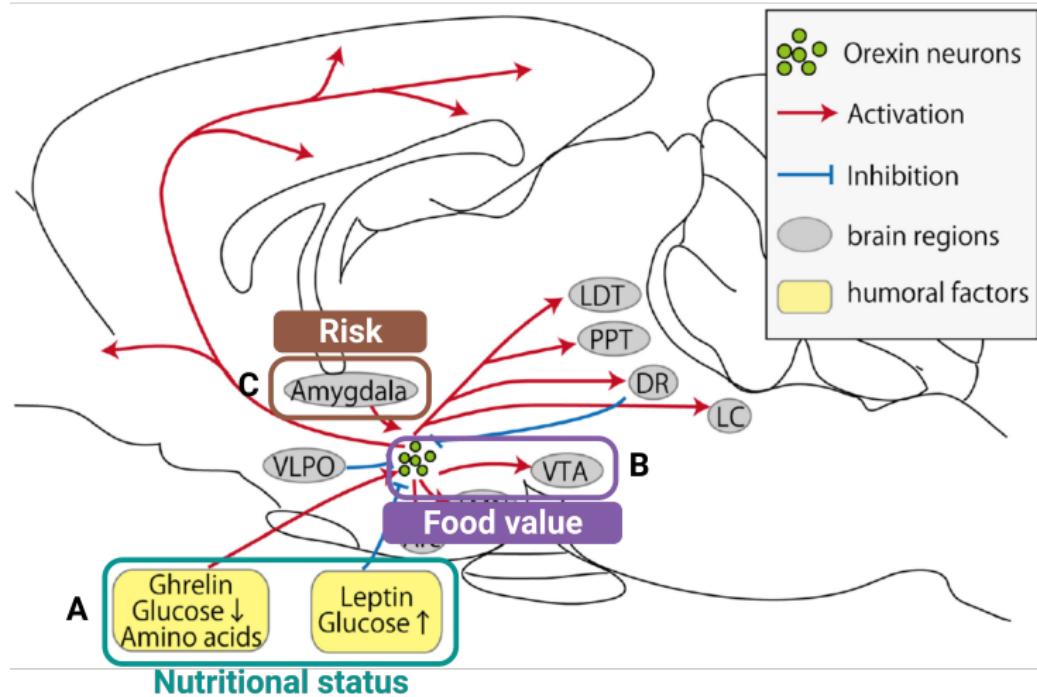
- 1 Uncertainty is inherent to food-seeking behavior and forces the animal to balance between exploration and exploitation
- 2 Uncertainty can be sensed indirectly through direct experience
- 3 The main aspects of food-seeking behavior can be modeled with RPE, learning rate and thompson sampling

Neural basis of uncertainty-driven food-seeking behavior

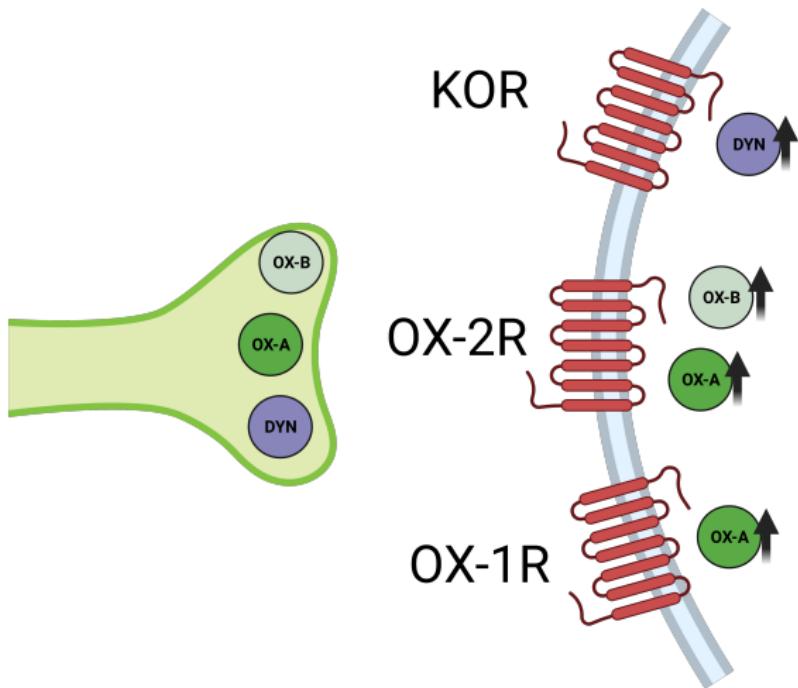
Reward and feeding centers connectivity permits procuring rewarding food to meet metabolic demands



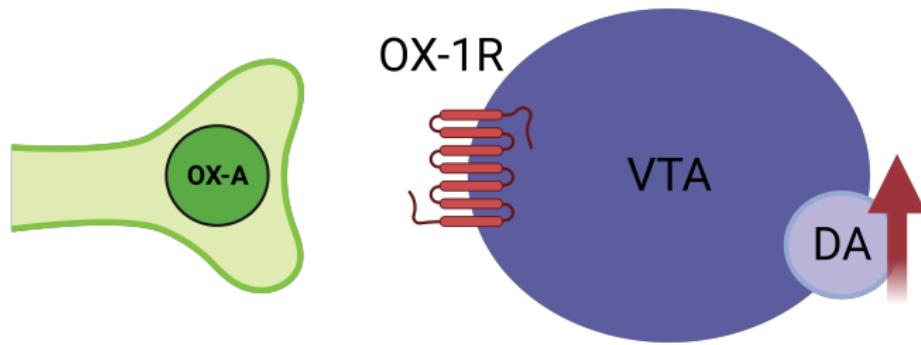
Reward and feeding centers connectivity permits procuring rewarding food to meet metabolic demands



Orexin could modulate exploration/exploitation through VTA DA activity

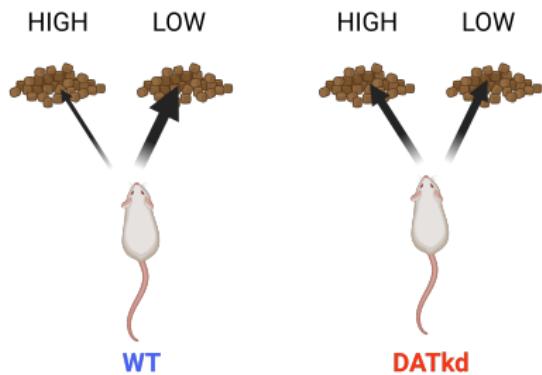
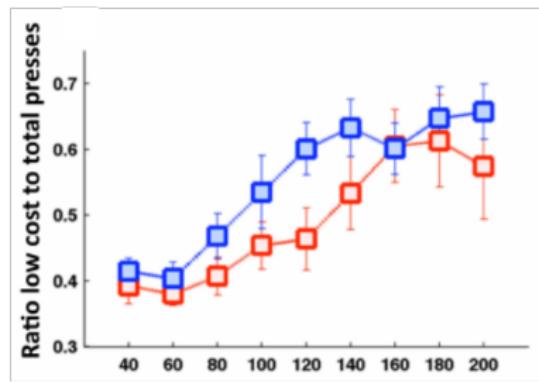


Orexin could modulate exploration/exploitation through VTA DA activity

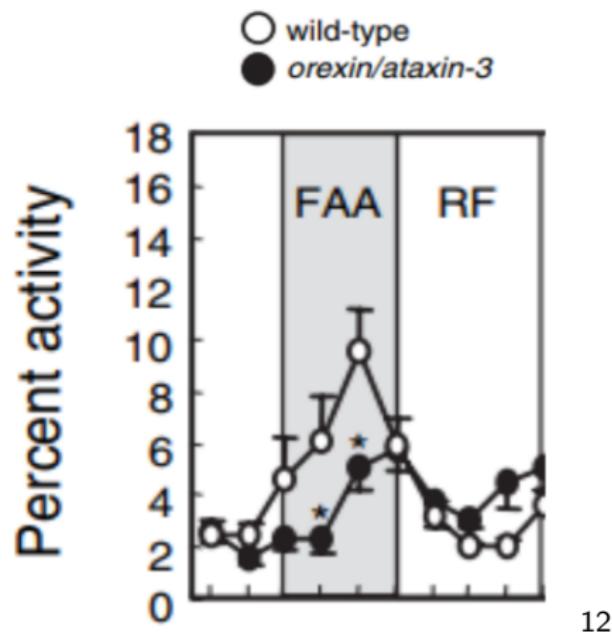


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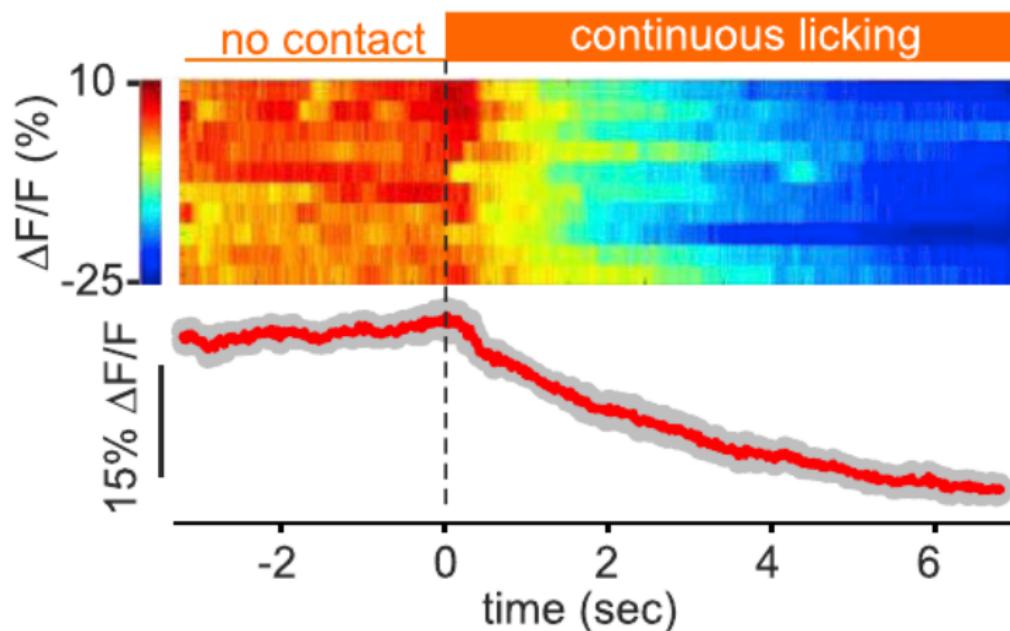
Orexin could modulate exploration/exploitation through VTA DA activity



LHA orexin activity is specific to food-seeking behavior



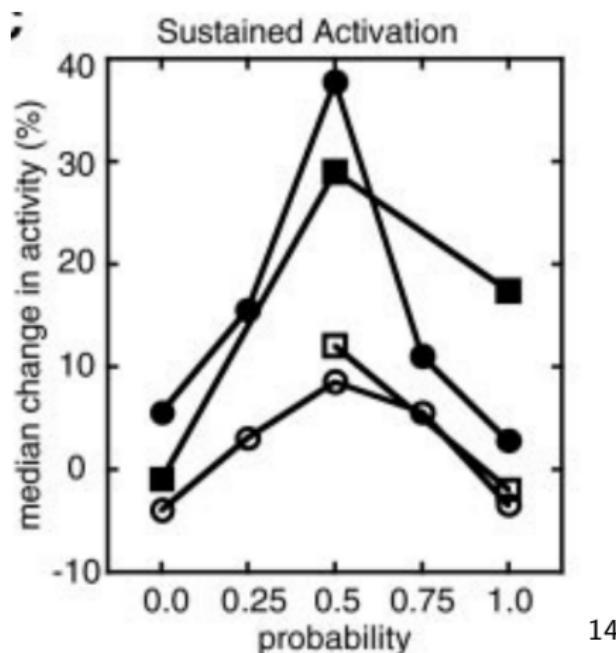
LHA orexin activity is specific to food-seeking behavior



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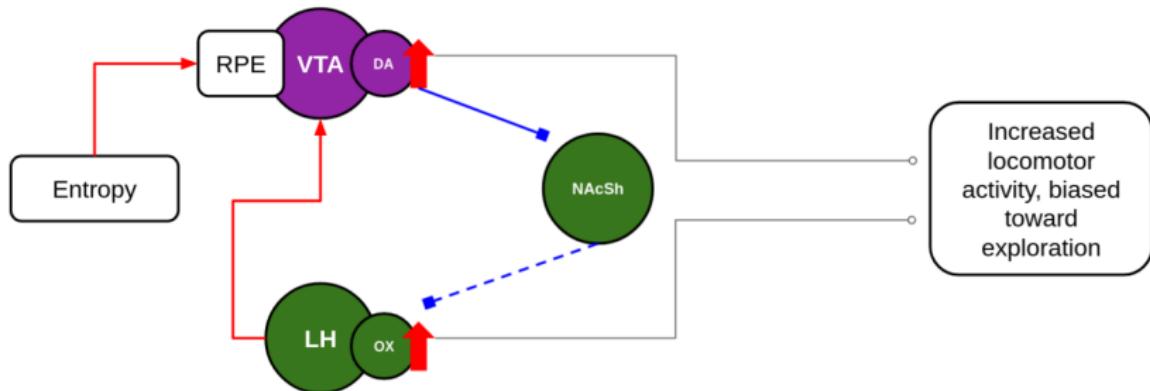
¹³(7GXEINLY#González_Etal_2016?)

VTA DA tonic activity encodes entropy



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Proposed connectivity

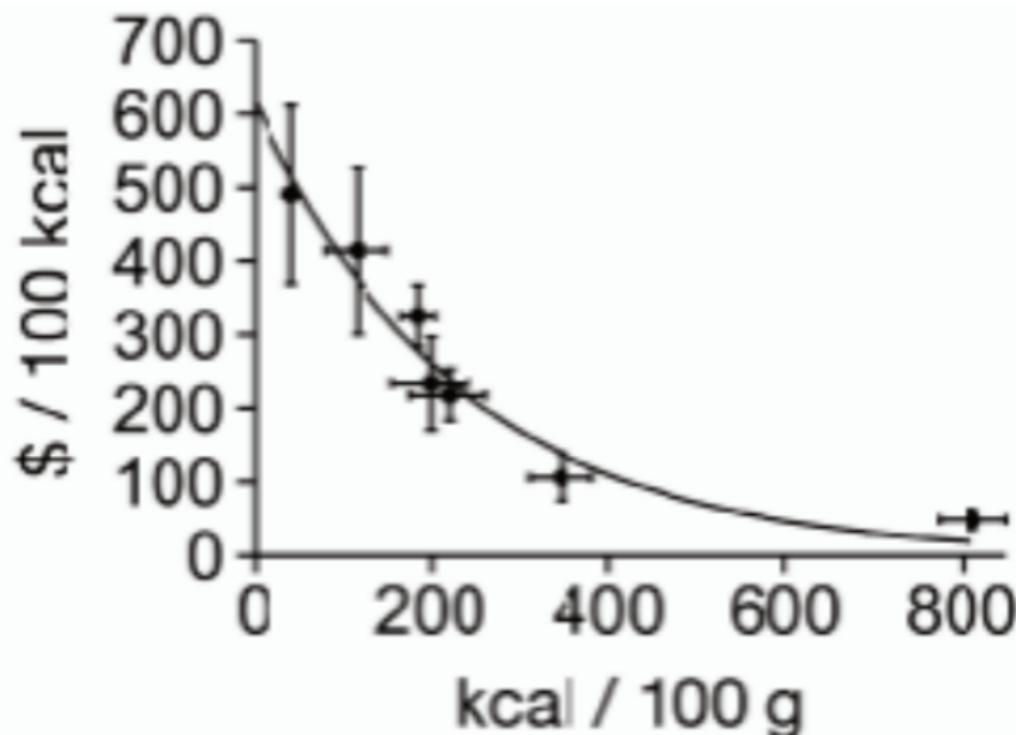


Key points

- 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

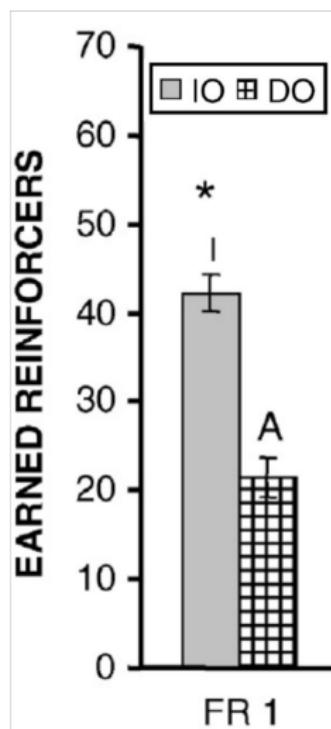
High calorie food items are of easy access



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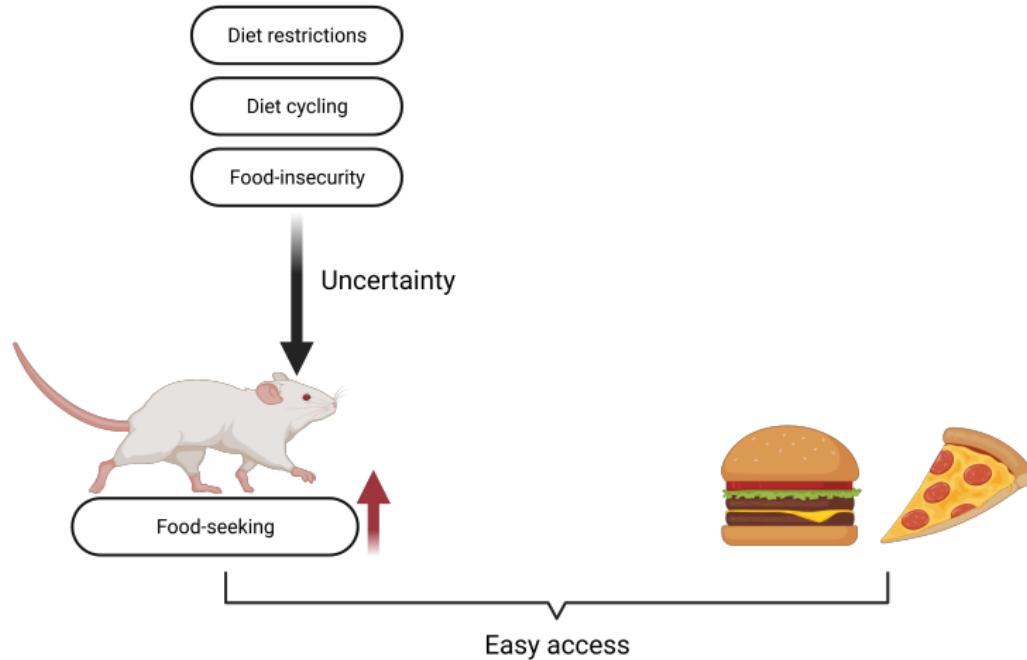
¹⁵Verdugo, Giannina, Arias, Vanessa, & Perez Leighton Claudio. (2016)

Uncertainty increases motivation to obtain food



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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

Methods

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

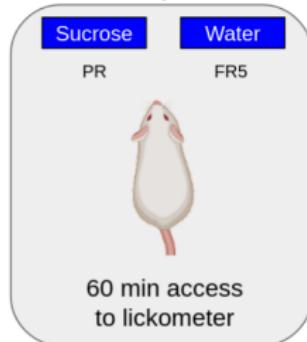
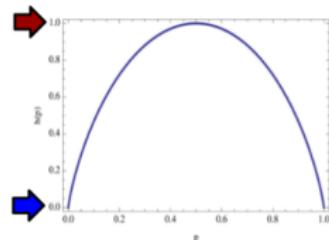
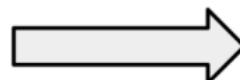
Specific objective 1: setting



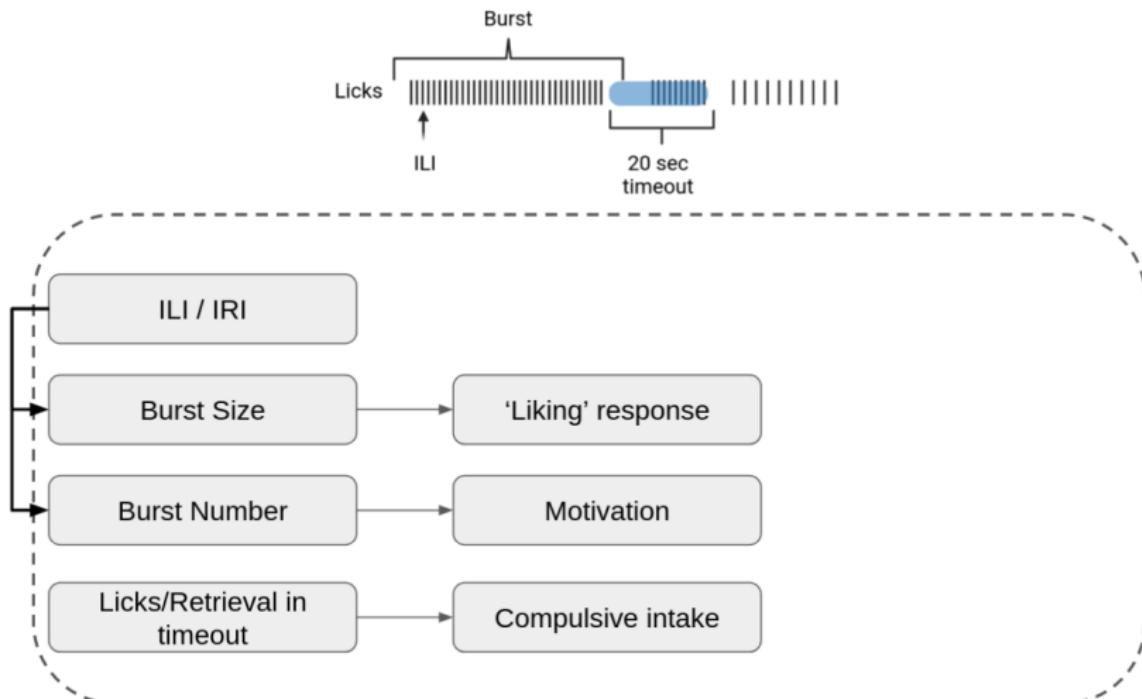
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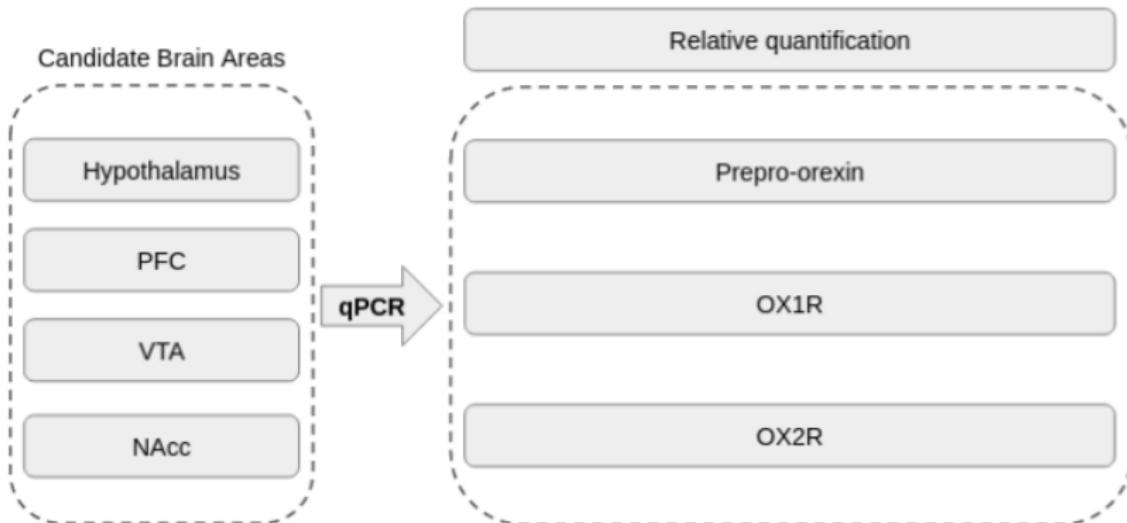
15 - 30 - 120 - 240 sec



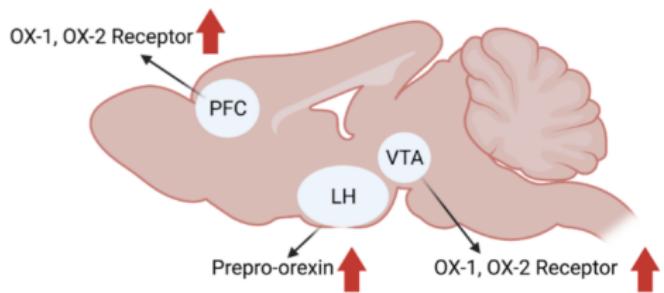
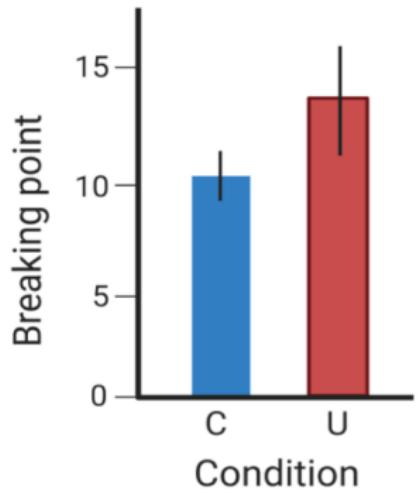
Specific objective 1: behavioral analysis



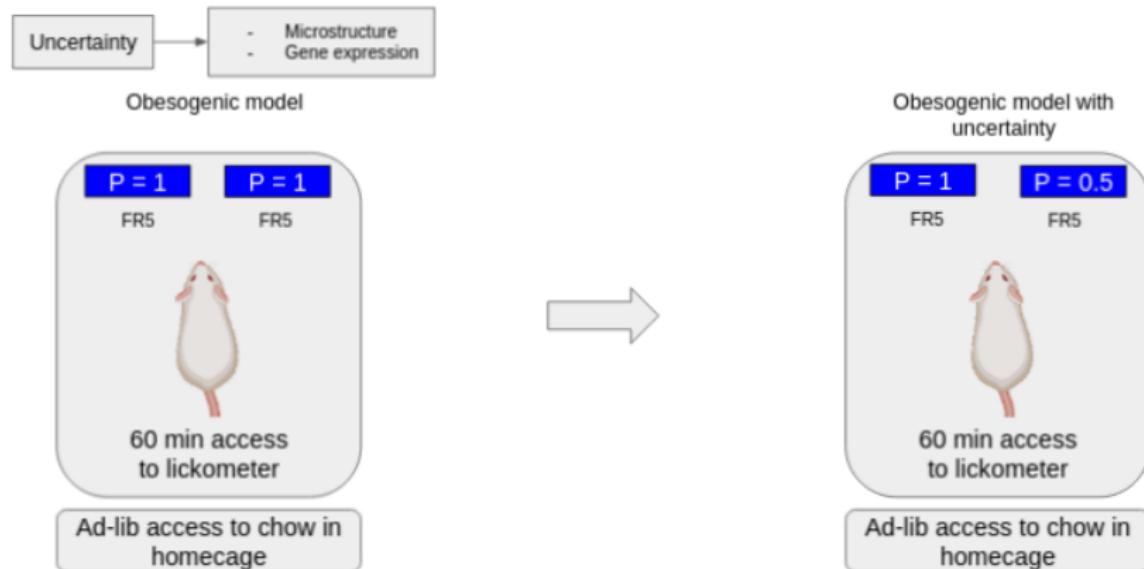
Specific objective 1: gene expression



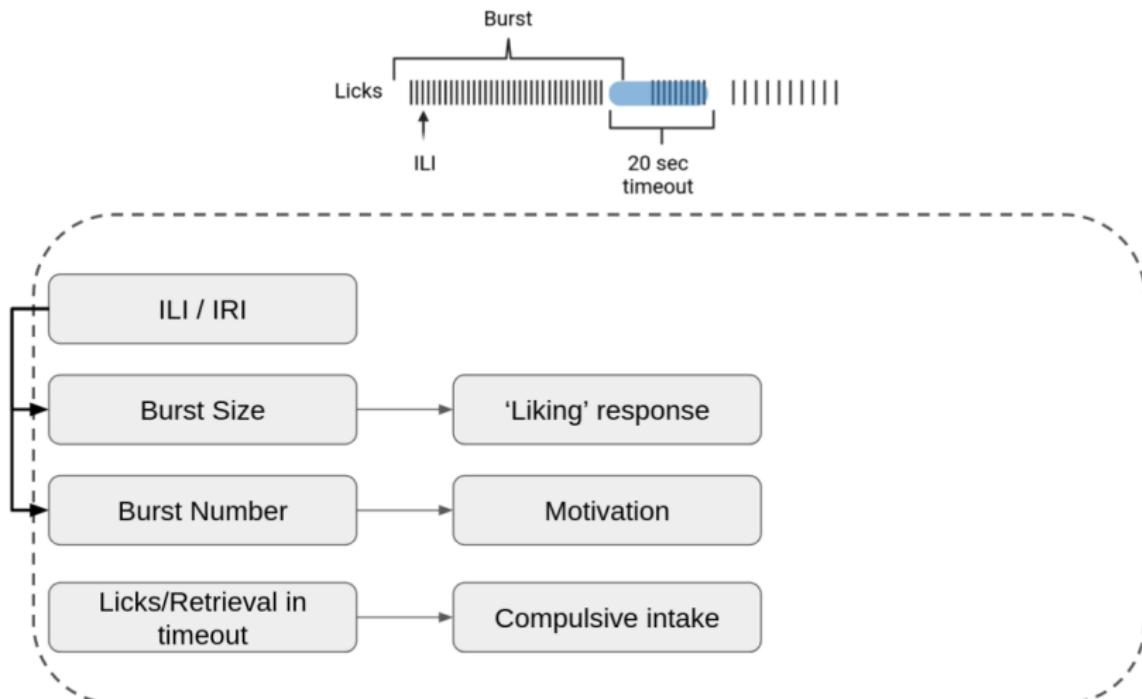
Specific objective 1: expected results



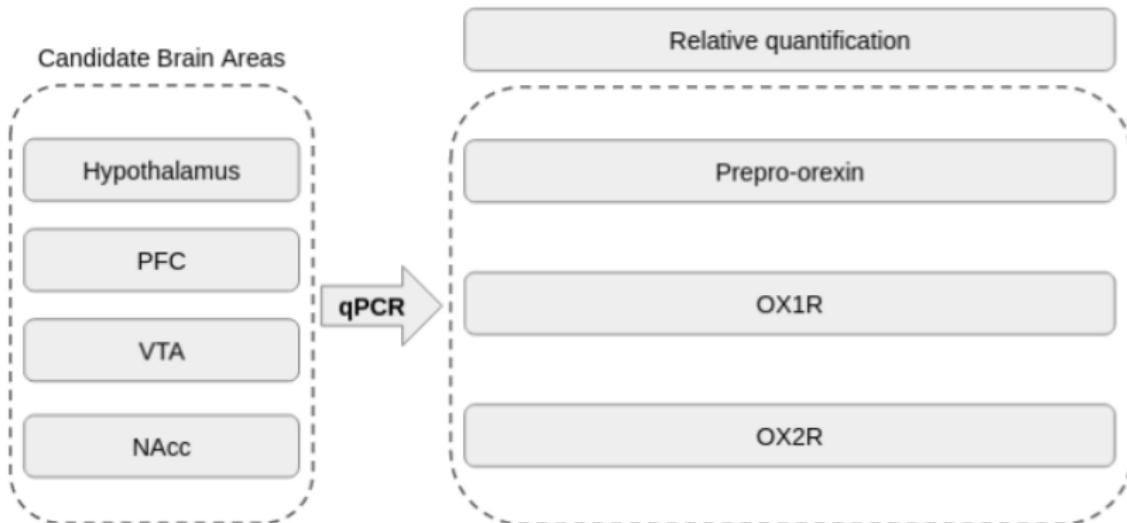
Specific objective 2: setting



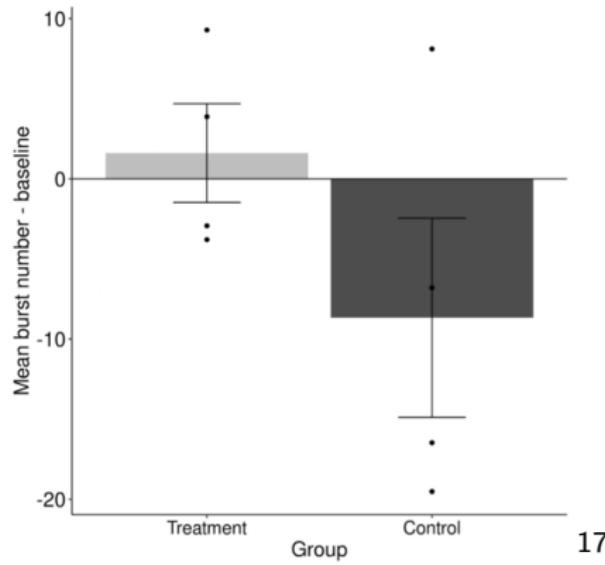
Specific objective 2: behavioral analysis



Specific objective 2: gene expression

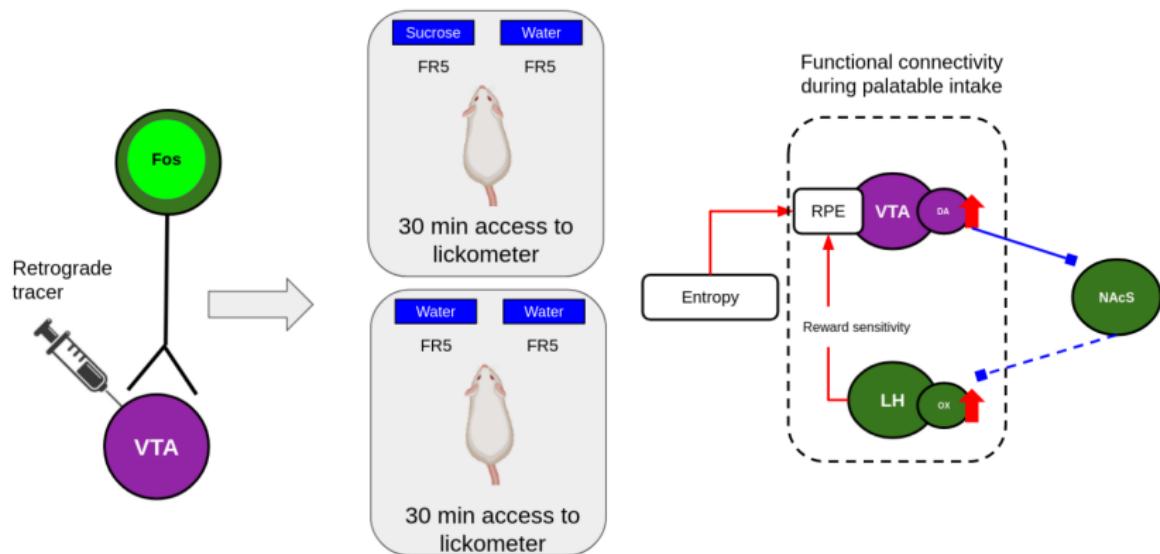


Specific objective 2: pilot study

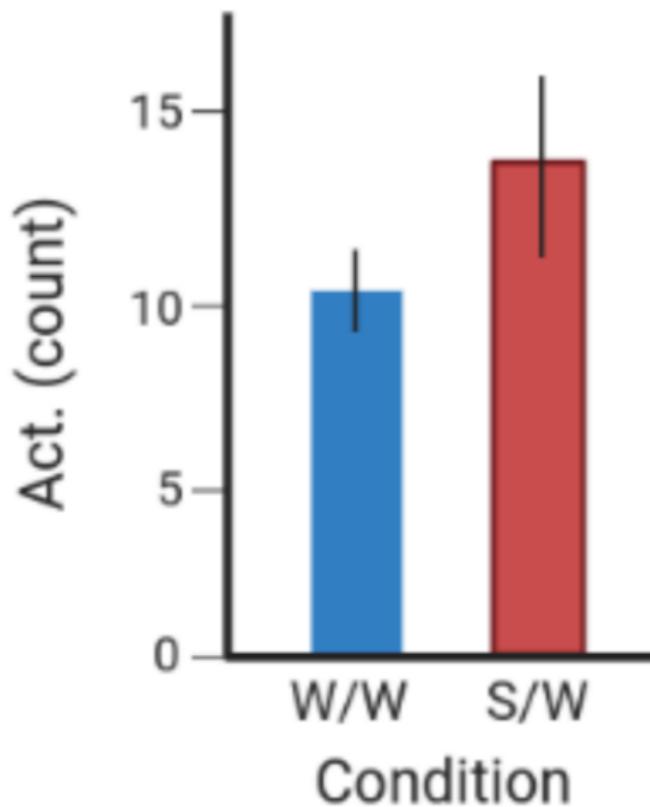


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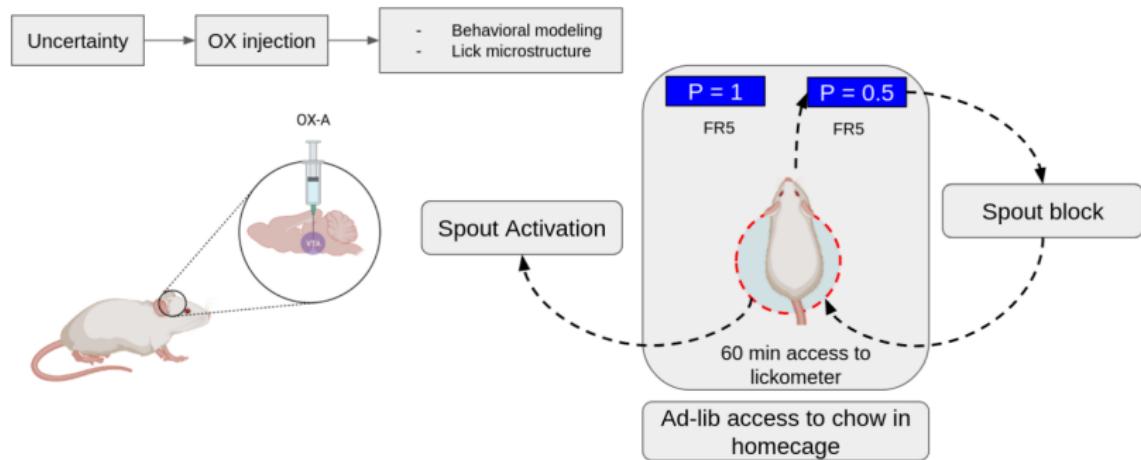
Specific objective 3: setting



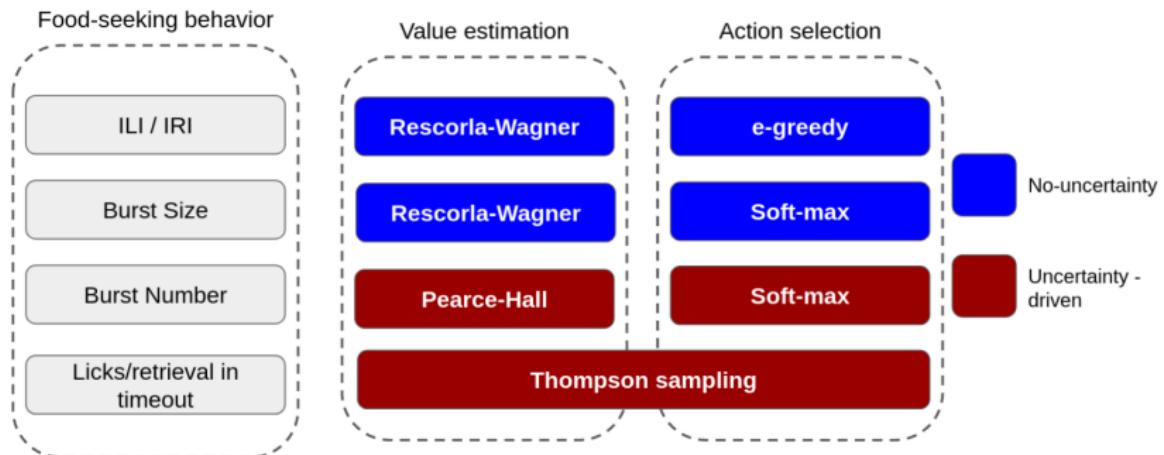
Specific objective 3: expected results



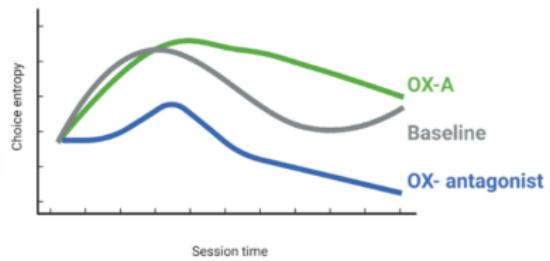
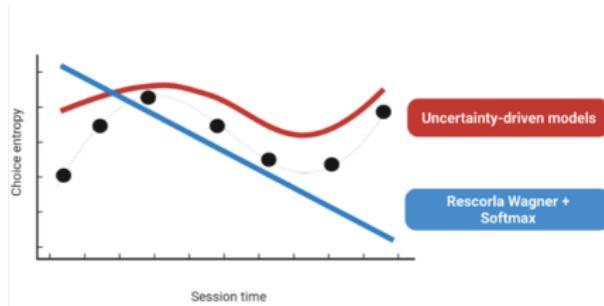
Specific objective 4: setting



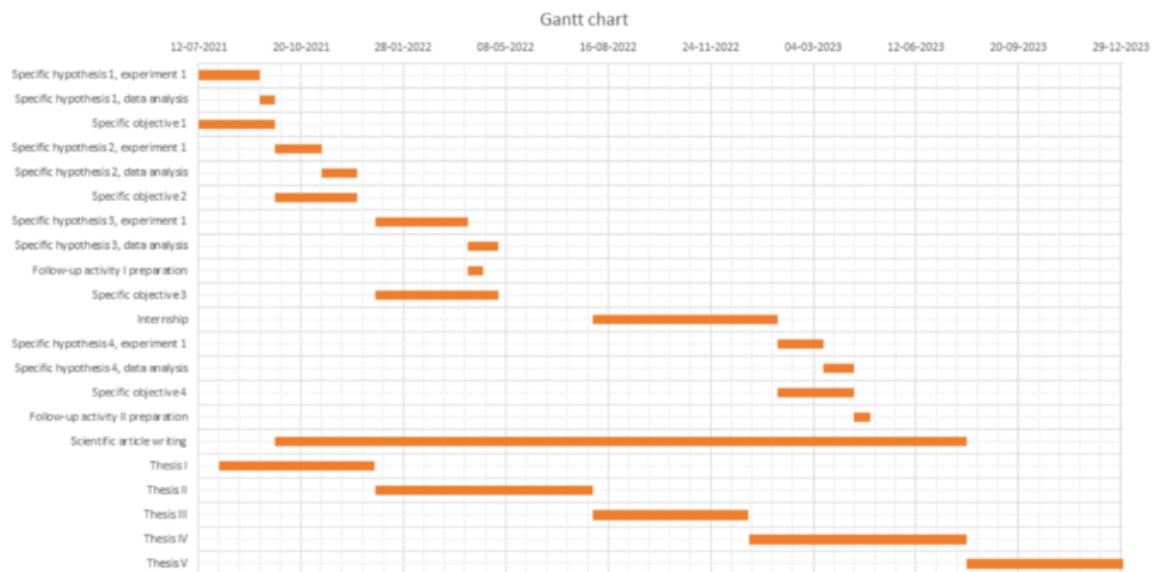
Specific objective 4: behavioral analysis



Specific objective 4: expected results



Workplan



Thanks!

References { .allowframebreaks }.