Doctoral thesis proposal

Orexin and uncertainty effects on food-seeking behavior

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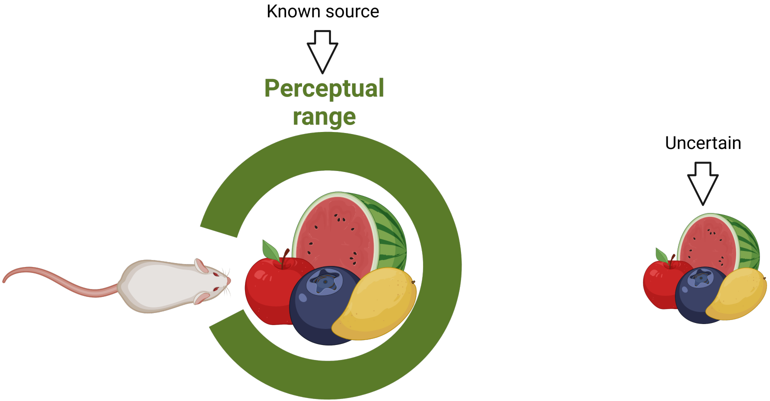
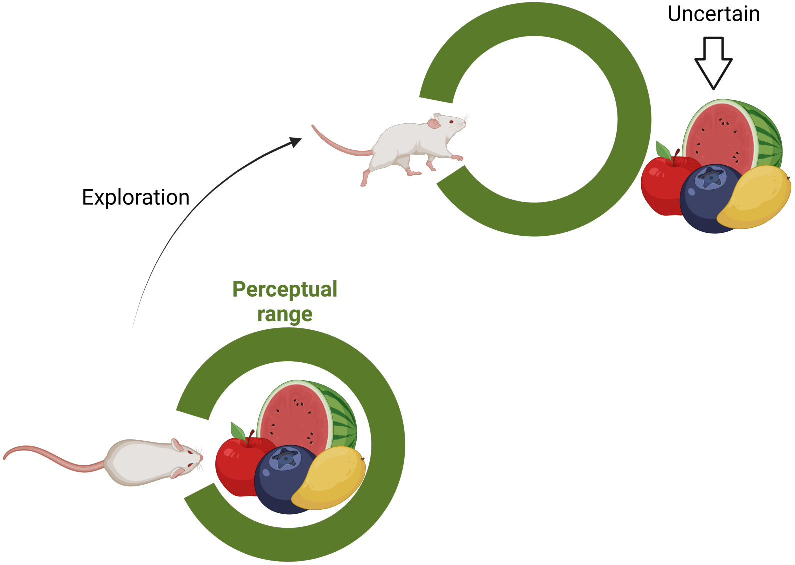
Food-seeking and uncertainty

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

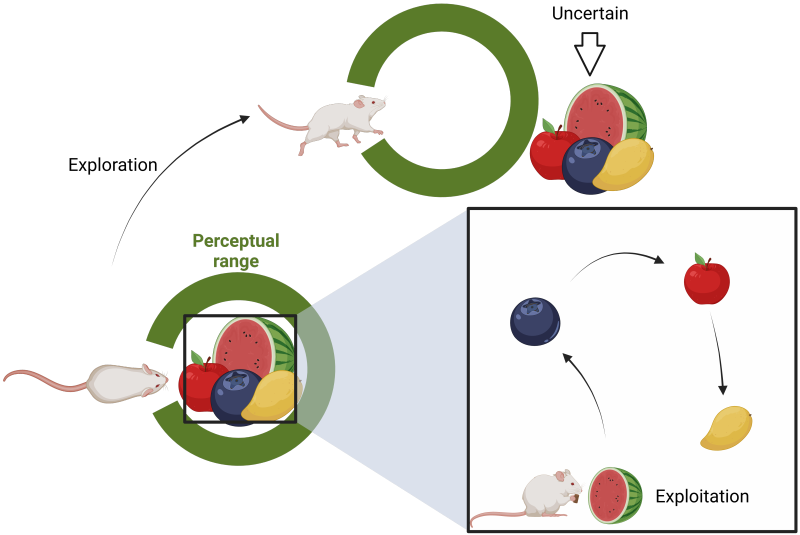
Food-seeking behavior implies a state of partial knowledge



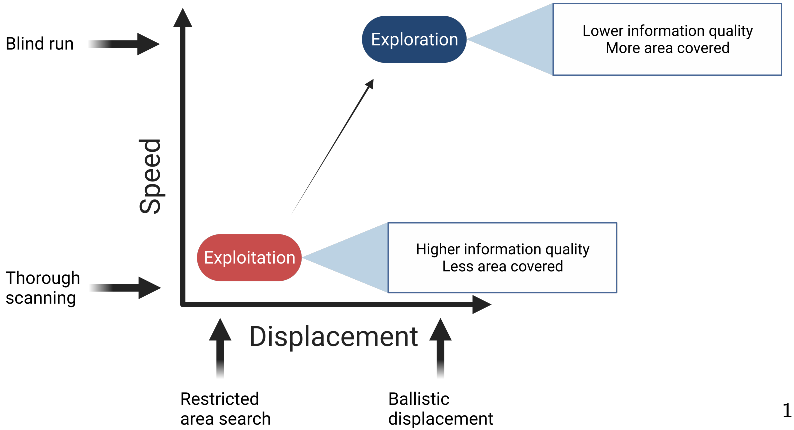
Partial knowledge forces animals to explore for new food sources



At some point animals need to stop exploring and start exploiting



Uncertainty is inherent to food-seeking behavior



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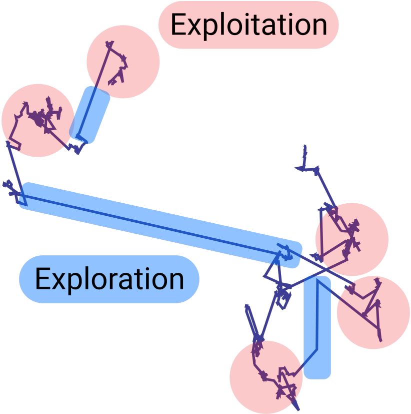
[1] Bartumeus et al. (2014)

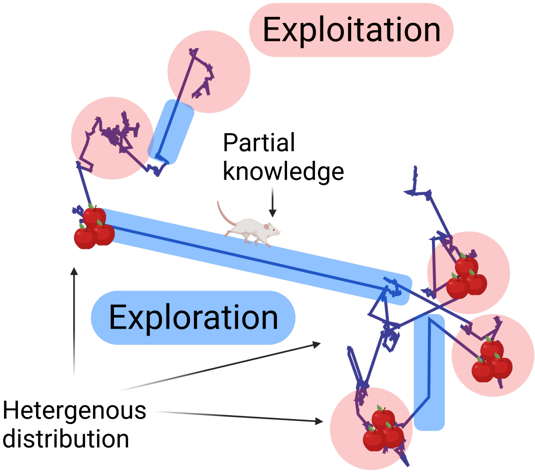
Food-seeking behavior evolved to deal with uncertainty, balancing between exploration and exploitation



Levy-Walks [2]

[2] 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



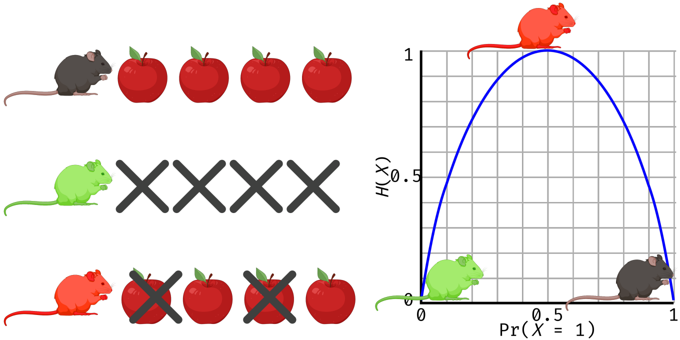
Levy-Walks [3]

[3] Sims et al. (2014); Raichlen et al. (2014); Wosniack et al. (2017)

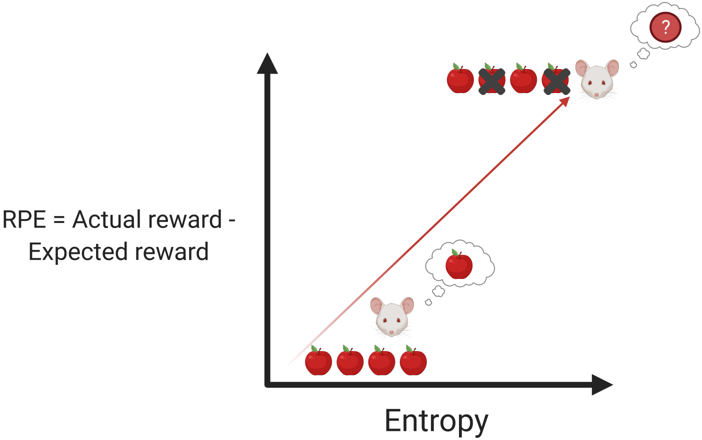
Key points

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

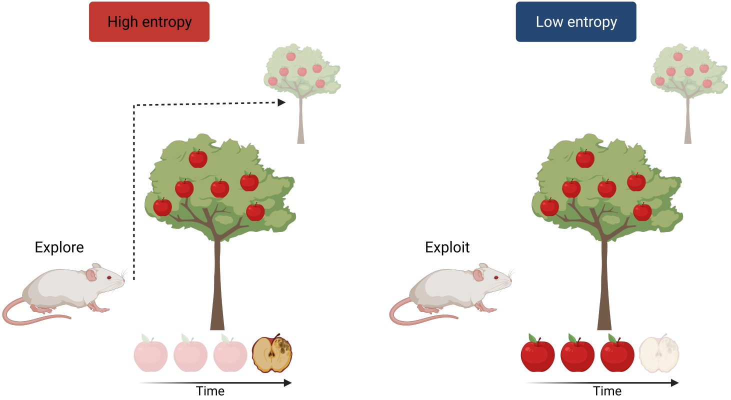
Uncertainty and behavior: entropy relates the probability of obtaining food with uncertainty



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



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



Learning rate ~= | RPE |

[4] Pearce and Hall (1980)

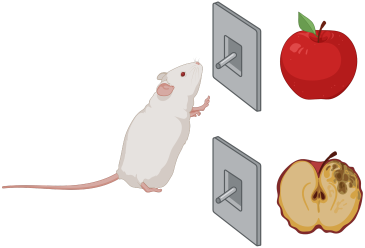
Key points

1. Entropy allows us to link food-access probability with uncertainty
2. The reward prediction error offers an inderect 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 ~= Past value + (RPE * Learning rate)



Expected value ~= Action | State

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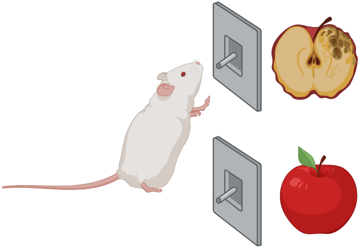
[5]Sutton and Barto (2018)

Food-seeking behavior modeling starts by expected value computation

Expected value ~= Past value + (RPE * Learning rate)

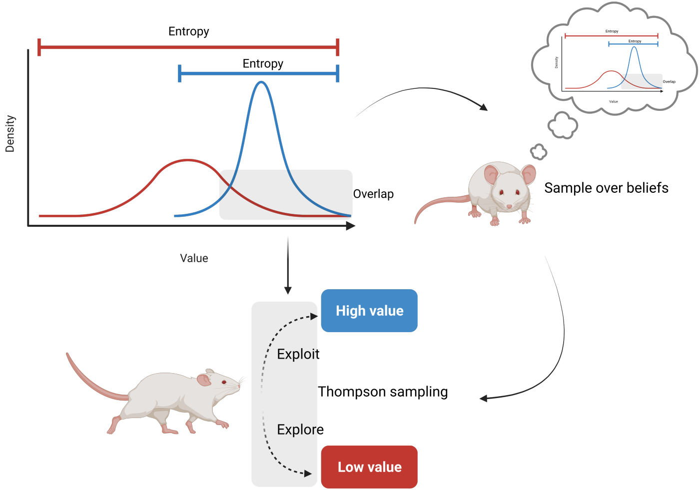


Expected value ~= Action | State

[6]

[6] Sutton and Barto (2018)

Food-seeking behavior modeling starts by expected value computation



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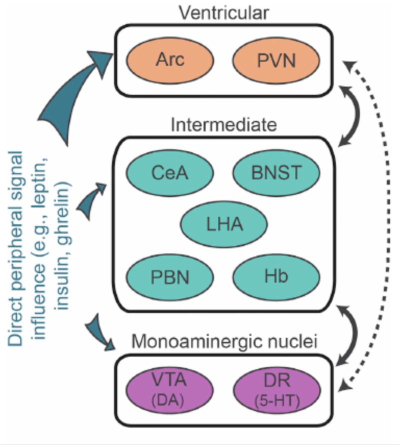
[7] Thompson (1933); Wang et al. (2017)

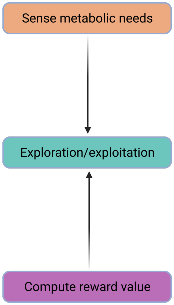
Key points

1. Uncertainty is inherent to food-seeking behavior and forces the animal to balance between exploration and exploitation
2. Uncertainty can be sensed inderectly 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





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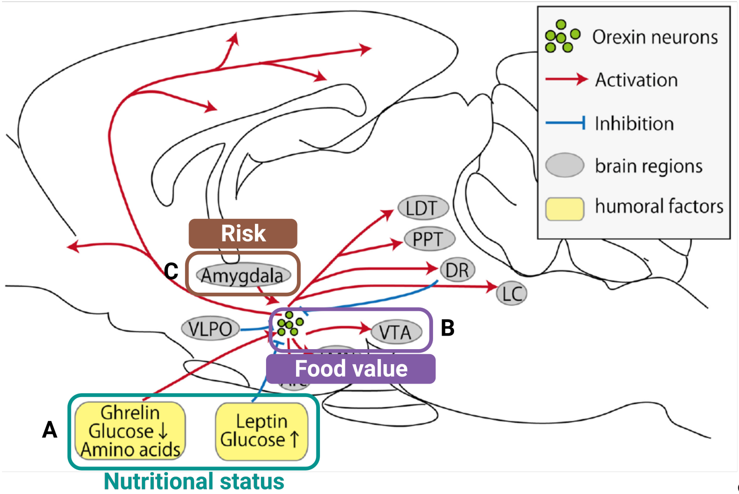
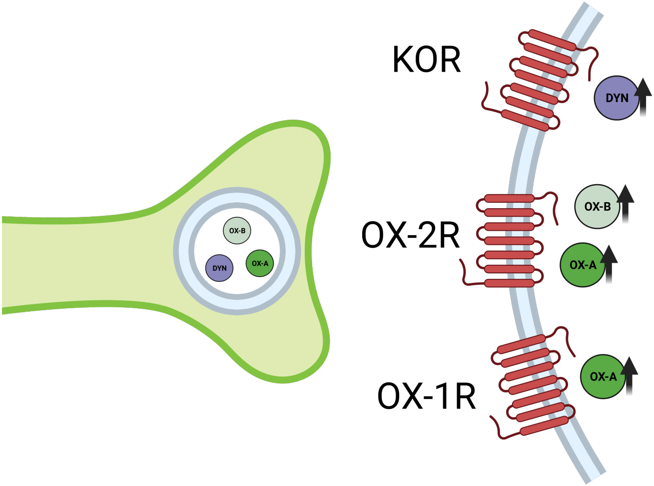
[8] Rossi and Stuber (2018)

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

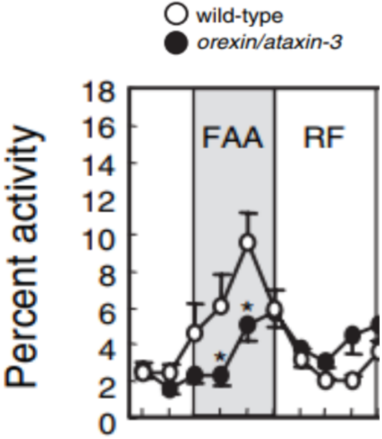


[9] Inutsuka and Yamanaka (2013)

Orexin could modulate exploration/exploitation through VTA DA activity



LHA orexin activity role in food-seeking behavior



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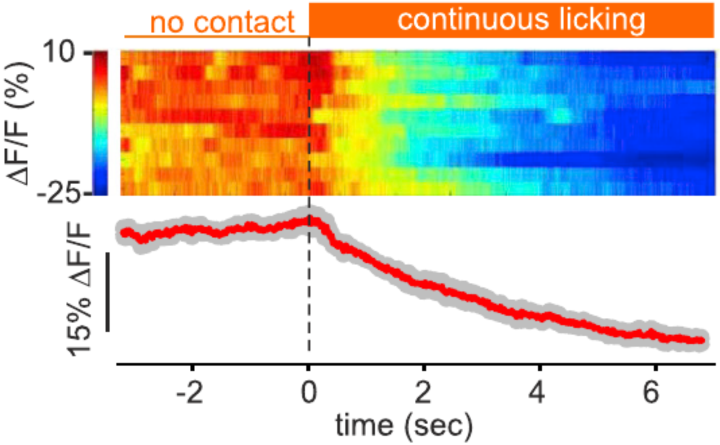
[10] Akiyama et al. (2004)

LHA orexin activity role in food-seeking behavior



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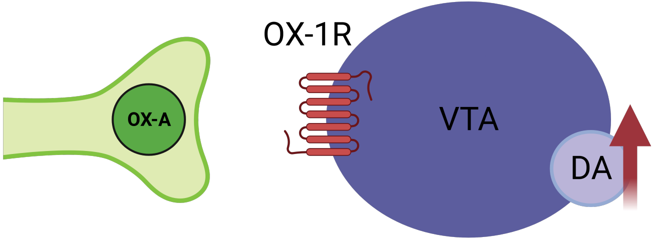
[11] González et al. (2016)

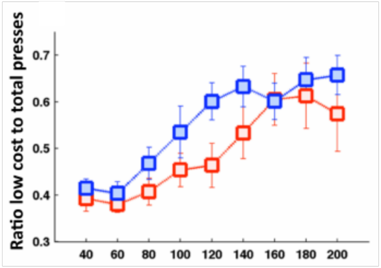
Orexin could modulate exploration/exploitation through VTA DA activity

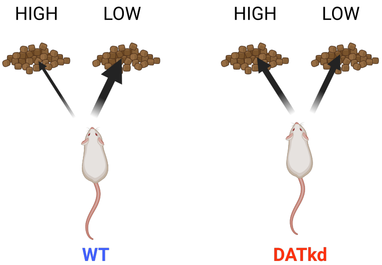


[12]

[12] Baimel et al. (2017)

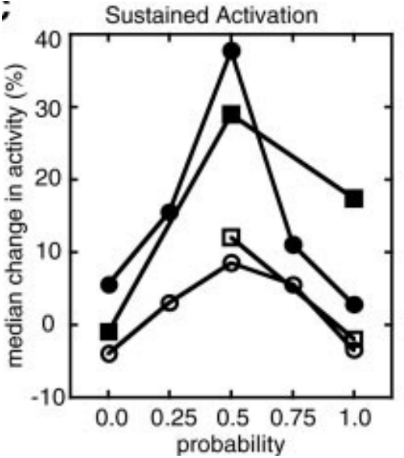
Orexin could modulate exploration/exploitation through VTA DA activity





[13] Beeler et al. (2010)

VTA DA tonic activity encodes entropy



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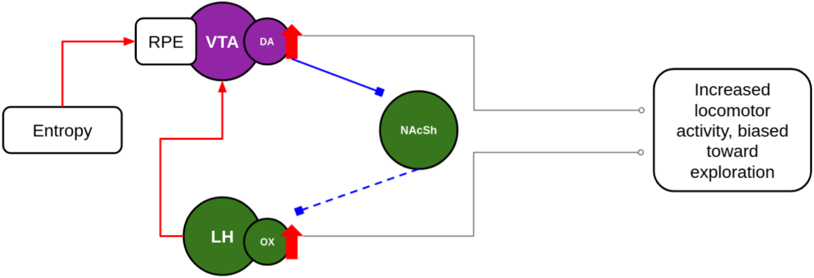
[14] Fiorillo (2003)

Proposed connectivity

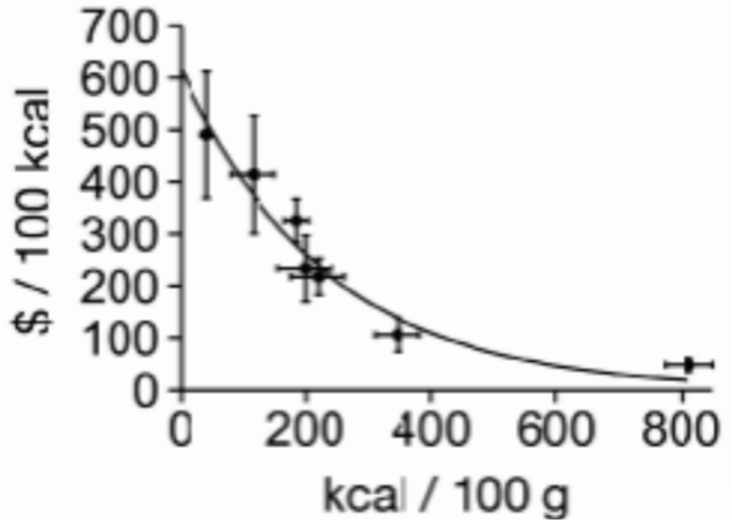


Key points

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

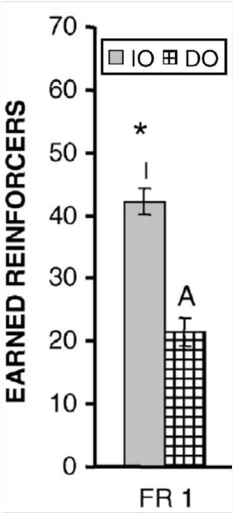
Food-seeking in modern obesogenic environments

High calorie food items are of easy access



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

Uncertainty increases motivation to obtain food



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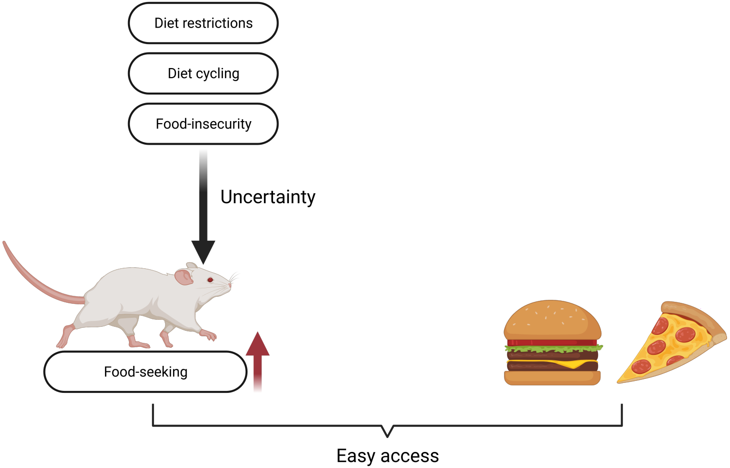
[16] Wojnicki et al. (2015)

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

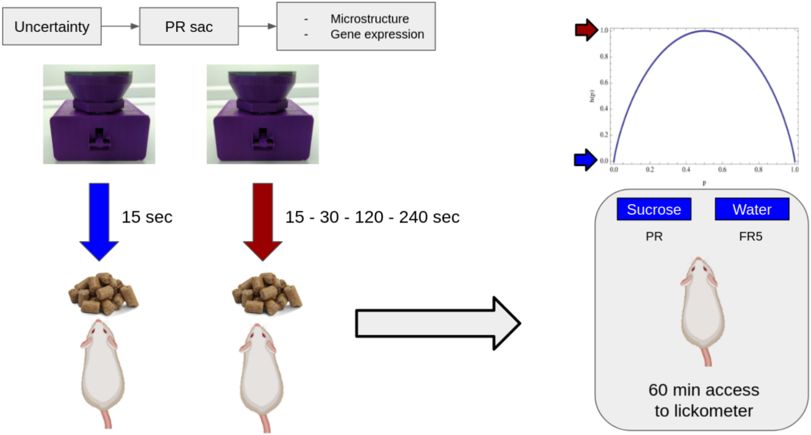
- Objective: Determine how uncertainty in food-access increases food-seeking behavior, and how orexin mediates uncertainty-driven increased food-seeking behavior
- Hypothesis: Food-access uncertainty increases food-seeking behavior, and this increase is modulated by orexin neurons activity

Specific objectives

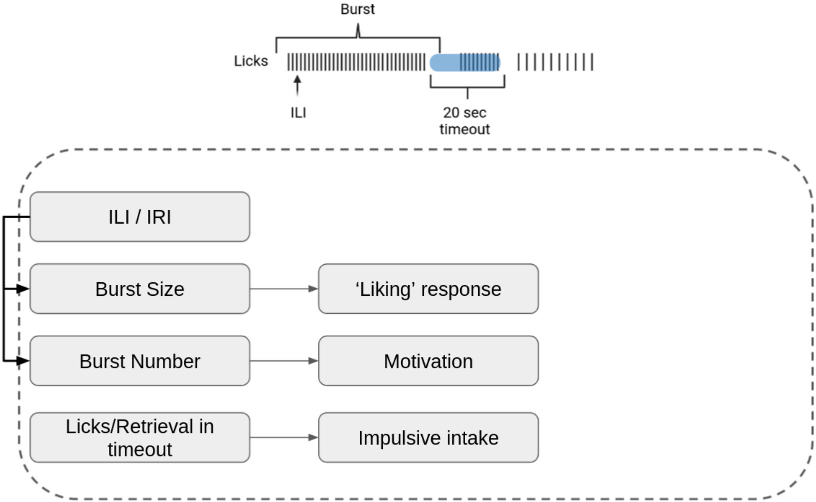
1. Determine whether uncertainty in food access required for subsistence increase motivation for palatable foods, and if this correlates with orexin gene expression
2. Determine whether uncertainty in obesogenic environments increases food-seeking behavior and assess if increased food-seeking behavior 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

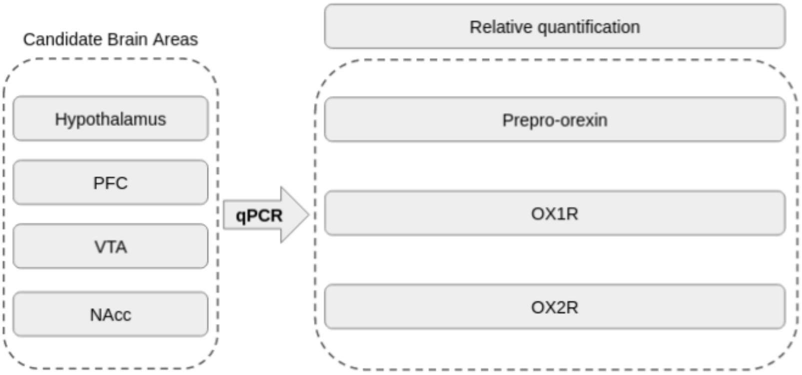
Specific objective 1: setting



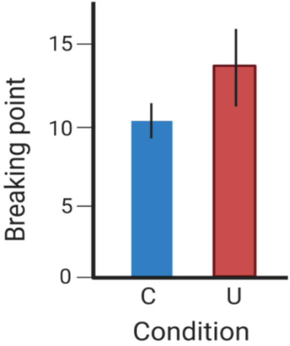
Specific objective 1: behavioral analysis

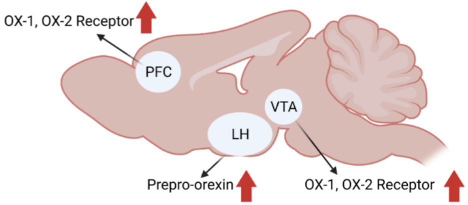


Specific objective 1: gene expression

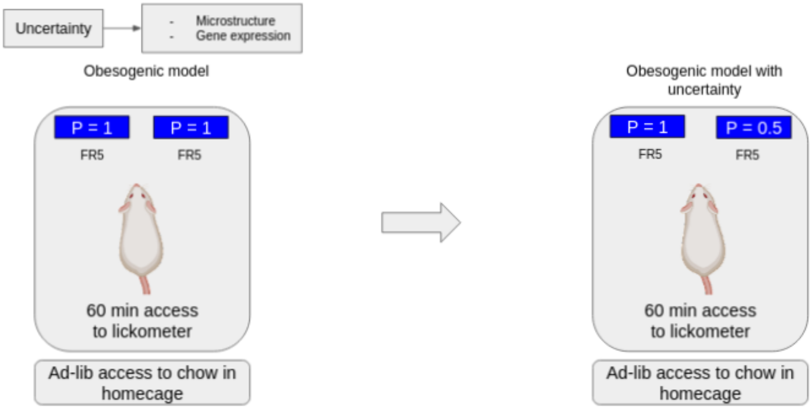


Specific objective 1: expected results

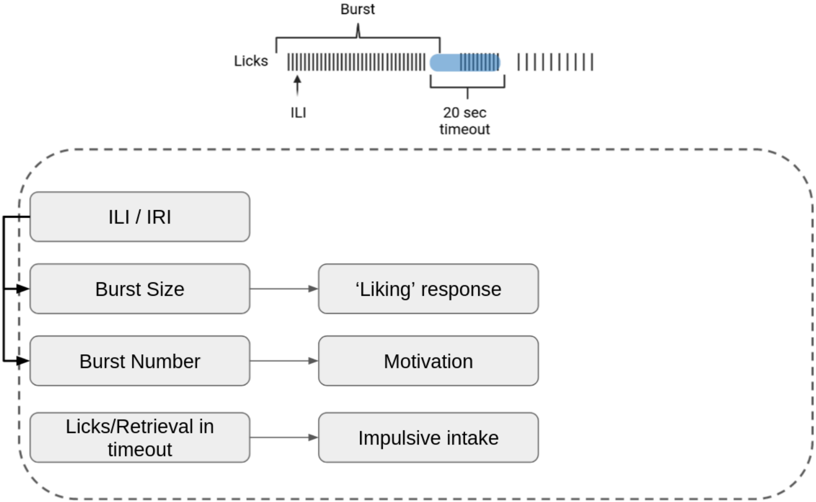




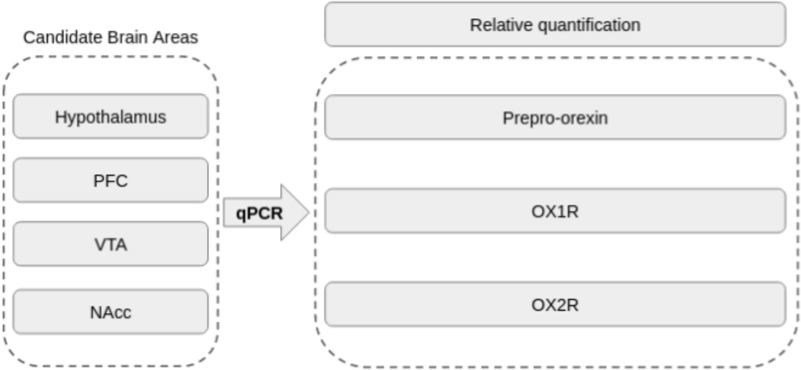
Specific objective 2: setting



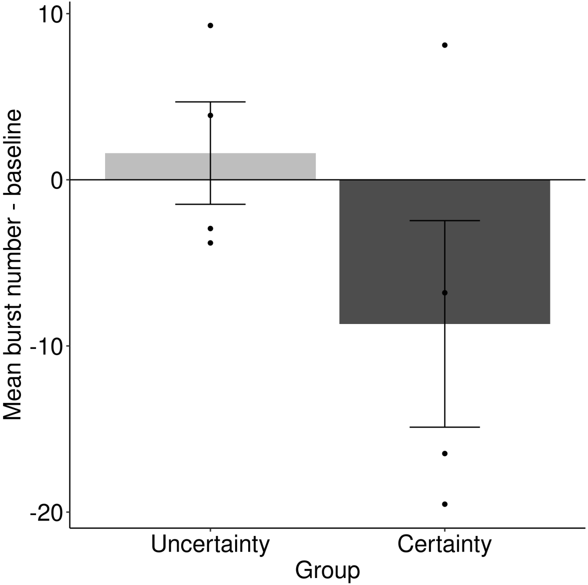
Specific objective 2: behavioral analysis



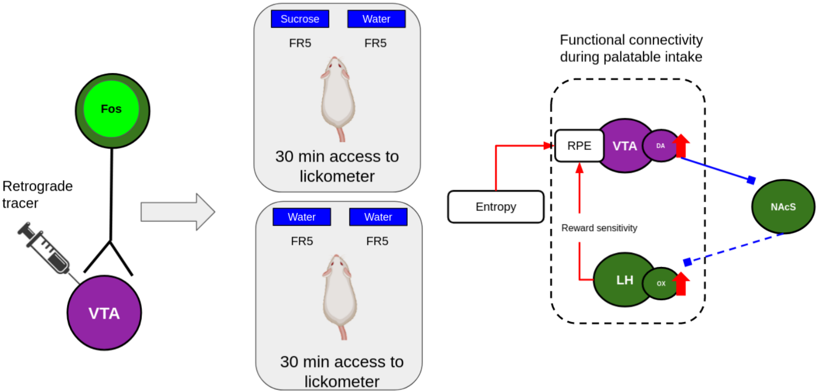
Specific objective 2: gene expression



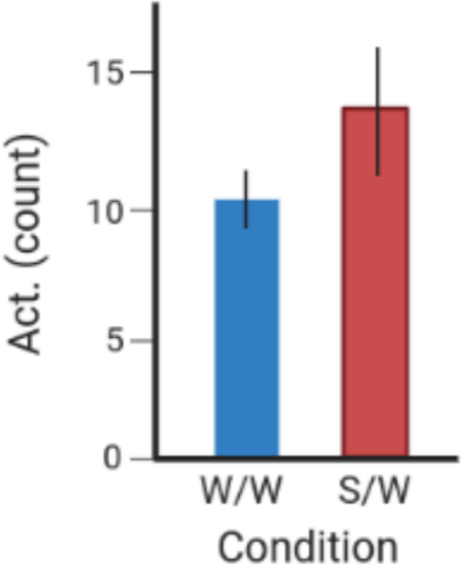
Specific objective 2: pilot study



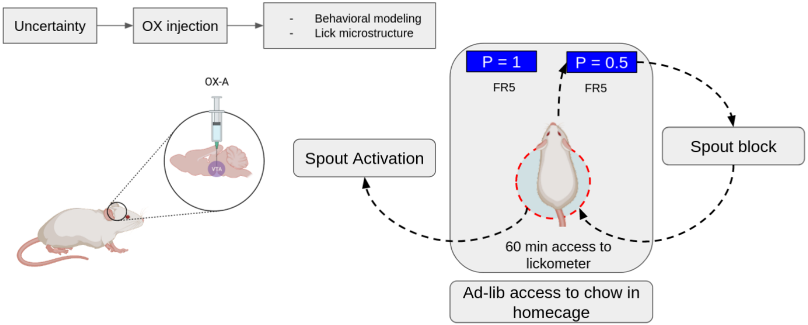
Specific objective 3: setting



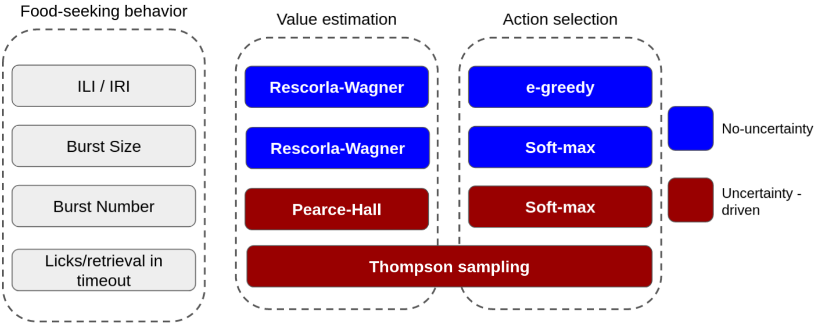
Specific objective 3: expected results



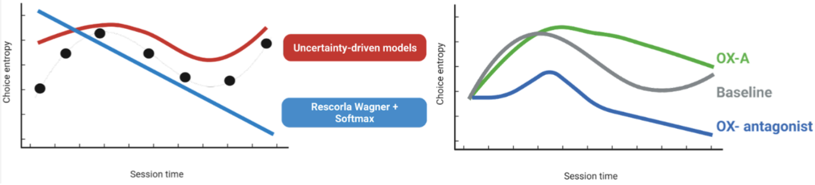
Specific objective 4: setting



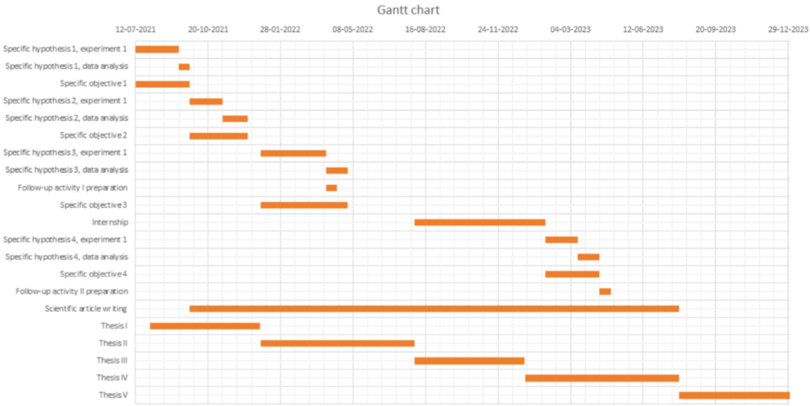
Specific objective 4: behavioral analysis



Specific objective 4: expected results



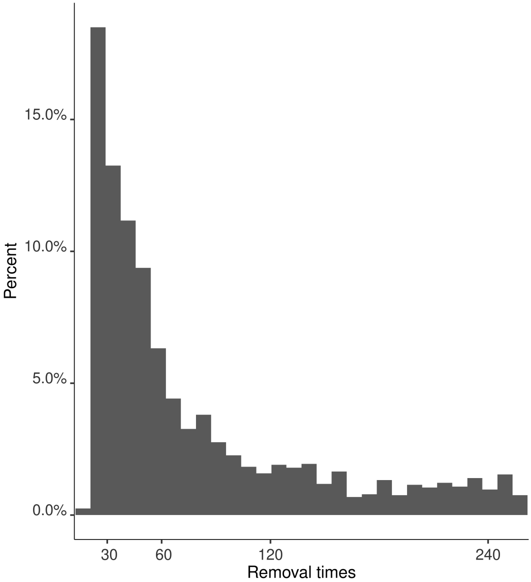
Workplan


Gantt chart
12-07-2021
20-10-2021
28-01-2022
08-05-2022
16-08-2022
24-11-2022
04-03-2023
12-06-2023
20-09-2023
29-12-2023
Specific hypothesis 1, experiment 1
Specific hypothesis 1, data analysis
Specific objective 1
Specific hypothesis 2, experiment 1
Specific hypothesis 2, data analysis
Specific objective 2
Specific hypothesis 3, experiment 1
Specific hypothesis 3, data analysis
Follow-up activity I preparation
Specific objective 3
Internship
Specific hypothesis 4, experiment 1
Specific hypothesis 4, data analysis
Specific objective 4
Follow-up activity II preparation
Scientific article writing
Thesis I
Thesis II
Thesis III
Thesis IV
Thesis V

Thanks!

Inter removal intervals FED

Inter removal intervals FED



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