

Proyecto de tesis doctoral para optar al grado de  
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## Introduction

Mammals evolved in an environment where food sources are limited and often scarce; thus, maintaining fat reserves and overall caloric intake is extremely important. Most animals accomplish this by increasing food-seeking behavior when food access is limited, resulting in extended foraging bouts. However, foraging and larger fat reserves can increase predation risk by increasing exposure and reducing mobility, respectively. Therefore, increasing foraging bouts should only occur when the risk of starvation outweighs the risk of predation. One environmental clue that animals use to make this decision is uncertainty in food access: higher levels of food access uncertainty predicts future food scarcity, triggering food-seeking behavior to prevent starvation. This prediction effectively allows animals to act upon proximal cues without the need to know the complete state of the environment. Currently, it is unclear how animals use uncertainty to drive food-seeking behavior. We propose that the prediction error between expected and actual intake from foraging bouts translates into a measure of food-access uncertainty. Increasing uncertainty generates unreliable expectations, therefore, more prediction errors. Then, exploratory behavior should increase proportionally to the prediction error. Relating uncertainty to food scarcity is a successful adaptive strategy when food is limited, but food sources are ubiquitous in modern environments. These environments increase food-seeking behavior leading to excessive intake, raising the risk of overweight and obesity. Even though the effects of uncertainty (through intermittent diet schemes) are known to increase food intake in a binge-like fashion, the specific behavioral events and the neurobiological substrate mediating these effects remain unclear. The neurobiological mechanisms that regulate food-seeking behavior and foraging must use information about a nutrient deficit to increase alertness and physical activity to forage successfully. The neuropeptide orexin has the potential to be a mediator of foraging behavior. Fasting and intake respectively increase and decrease the activity of orexin neurons, and its activation increases physical activity and food intake, but this effect seems to be brain site-specific. Together, these data support that orexin might promote foraging behavior by increasing

locomotor activity in response to a nutrient deficit before food intake. Orexin could provide the mechanism to drive increased food-seeking behavior when uncertainty increases. Together, these data led us to hypothesize that orexin promotes food-seeking-related behaviors when facing uncertainty related to food access. Our overall aim is to determine how uncertainty in food-access increases food-seeking behavior, and how orexin mediates uncertainty-drive increased food-seeking behavior.