Understanding Cilia Function on POMC Neurons in Appetite and Satiety

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Over one-third of adults in the United States are obese. Obese individuals are at an increased risk for cardiovascular diseases, type 2 diabetes, cancer, and other health conditions, resulting in premature death. Interestingly, cilia have been linked to controlling satiety in both mice and humans, and individuals with dysfunctional cilia are often obese. Cilia are cellular appendages composed of microtubules and can be motile or immotile. Primary (immotile) cilia function as sensors for important signaling pathways. The loss of cilia, specifically from hypothalamic proopiomelanocortin (POMC) expressing cells, disrupts satiety, leading to overeating and obesity. While it is known that cilia loss in POMC cells in the hypothalamus causes obesity, the age or developmental stage at which cilia loss is important for this phenotype remains unclear. The aim of this research is to determine the time point critical for proper cilia function on POMC neurons to maintain normal feeding behaviors. To do this, we utilize an inducible POMC-CreER mouse model. This model allows us to disrupt cilia formation and maintenance at specific stages of life. We take a multifaceted approach to analyze the impact of cilia loss by measuring long-term body weight and feeding behavior in adult mice, studying changes in embryonic development, as well as analyzing physiological changes in cultured primary neurons. These studies will contribute to a better understanding of the role of cilia in satiety signaling which will help lead to the development of effective treatments for weight related diseases.