Plan Overview

A Data Management Plan created using DMPTool

DMP ID: https://doi.org/10.48321/D1561Z

Title: Estrogenic Regulation of Hypothalamic Circuits Involved in Energy Balance

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Project abstract:

Obesity is an epidemic with few signs of abatement. Nearly half of the adult US population is considered overweight or obese and many of the leading causes of death are considered co-morbidities. Furthermore, obesity is marked by a significant health disparity in which females are more susceptible than males. Of particular concern, hypoestrogenic states like menopause are marked by a non-aging related increase in body weight driven by decreased physical activity and enhanced food motivation. However, females are under-represented in basic and clinical research. Consequently, the biological underpinnings are poorly understood and there are few therapeutic options currently available. Orexin neurons of the perifornical region, dorsomedial hypothalamus, and lateral hypothalamus are involved in both circadian activity and food motivation, particularly for palatable food (*i.e.,* those high in fat and sugar). Women tend to have greater orexin signaling than men. Furthermore, orexin peptide levels are increased in post-menopausal compared to women in their reproductive years or those on hormone replacement therapy. Clearly, the orexin system exhibits both sex differences and estrogenic regulation, yet the mechanisms are largely unknown. In this application, we propose to use a combination of molecular, cellular, and behavioral techniques in conjunction with CRISPR/SaCas9 gene editing to address the following aims: (1) Cellularly and behaviorally delineate the putative subpopulations of orexin neurons. (2) Elucidate the estrogenic regulation of orexin signaling onto hunger neurons. (3) Establish the role of Neuropeptide Y in orexin excitability and associated behaviors. The long-range goal of our research is to elucidate the mechanisms by which E2 regulates hypothalamic neural circuits and how dysregulation contributes to disease risk. The current proposal aims to exploit differential estrogenic regulation to assemble our knowledge of the orexin system into a useful framework for future study. Not only will these findings help address health disparities in obesity, but potentially identify novel therapeutic targets to treat insomnia, addiction, anxiety, and attention deficit disorder.

Start date: 01-01-2024

End date: 01-01-2029

Last modified: 01-18-2024

Copyright information:

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This project will produce primarily three types of data.

1) Mouse behavioral data to be collected from ~50 subjects evenly divided among males and females.

2) Electrophysiological data recorded in vitro from brain slices using pClamp 11 software. Raw data will be in pClamp abf format. Processed data will be in Excel spreadsheets (*.xls) and GraphPad Prism files for statistical analysis.

3) Micrographs of immunocytochemical labeling of proteins in cryostat sections take from mouse brains. Raw images will be in .czi format with processed images exported to RGB Tiff format.

Data will be generated from several mouse behavioral assays, including body weight and food intake measurements. Groups will be divided between those undergoing CRISPR mediated gene knockdown or just control virus. Electrophysiological recordings will be done in vitro using whole-cell recordings. GFP and CRE transgenic mice will be used to identify or optogenetically stimulate neurons. Immunocytochemical labeling will be used to visualize protein localization.

In this proposed project, the cleaned, item-level spreadsheet data for all variables will be shared openly, along with example quantifications and transformations from initial raw data. Final files used to generate specific electrophysiological analyses to answer the Specific Aims and related results will also be shared. The rationale for sharing only cleaned data is to foster ease of data reuse. However, raw behavioral data and image files will be shared. This will not only enable others to confirm our findings, but potential perform additional analyses.

Effort will be made to preserve all meta data associated with data files. Such data is particularly useful when others may wish to do types of data analysis not originally envisioned by research group.

pClamp 11 is free to download and use for basic viewing and analysis.

ImageJ is freely distributed and can be used to view and analyze image files.

Excel and GraphPad are not free, but are commercially available.

Data will be stored in common or open formats. Information needed to make use of this data such as the meaning of variable names or subject information will be provided in excel or text documents along with data files. Metadata will be preserved whenever possible and care will be taken in file naming and folder organization.

Imaging data will be deposited into NCI’s Imaging Data Commons or the Brain Image Library. All other data described above in the “data to be shared” section will be deposited into the DANDI Archive.

For electrophysiolgical data, recordings will be organized by Aim and subaim into dated folders. A spreadsheet will be provided with all key information (Subject #, Sex, Treatment, etc).

For imaging data, pictures will be preserved in raw format with metadata indicating subject, sex, antibodies used, and brain region. Metadata will provide information as to settings used to image. Images will be organized into folders based on Aim and subaim.

Behavioral data will be organized by Experiment->Behavioral Assay->Group. Raw video or excel data (exported from tracking software) will be provided.

All scientific data generated from this project will be made available as soon as possible, and no later than the time of publication or the end of the funding period, whichever comes first. The duration of preservation and sharing of the data will be a minimum of 10 years after the funding period.

There are no anticipated factors or limitations that will affect the access, distribution or reuse of the scientific data generated by the proposal.

Controlled access will not be used. The data that is shared will be shared by unrestricted download.

N/A

Lead PI Todd STincic, ORCID: 0000-0001-7504-2422, will be responsible for the day-to-day oversight of lab/team data management activities and data sharing. Broader issues of DMS Plan compliance oversight and reporting will be handled by the PI and Co-I team as part of general [campus(es)] stewardship, reporting, and compliance processes.
