The Connection between the BNST and the LH

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INTRODUCTION

Create a neural network that models how CRF neurons affect hypocretin, how CCK affects GABA, and how GABA affects Hypocretin.

BACKGROUND AND SIGNIFICANCE

The hypocretin or orexin system in the brain is responsible for the sleep-arousal system and reward processing. Hypocretin, a neuromodulator found in the hypothalamus is central to this system. It works by binding onto specific cell receptors and therefore increasing the cell's activity. This allows the body to regulate its states of arousal and sleep. But inputs from other regions of the brain, and their effects on hypocretin neurons aren't completely understood.

One such region is the BNST. The BNST is an area in the brain located upper-left of the brainstem that regulates stress response. It is directly connected to the hypothalamus. This experiment studies the effect of stimulation in the BNST region on hypocretin cells in the hypothalamus. It will use a method of stimulation called optogenetics.

The LH is a region in the brain that houses Hypocretin neurons. It has been linked to sleep as mentioned before.

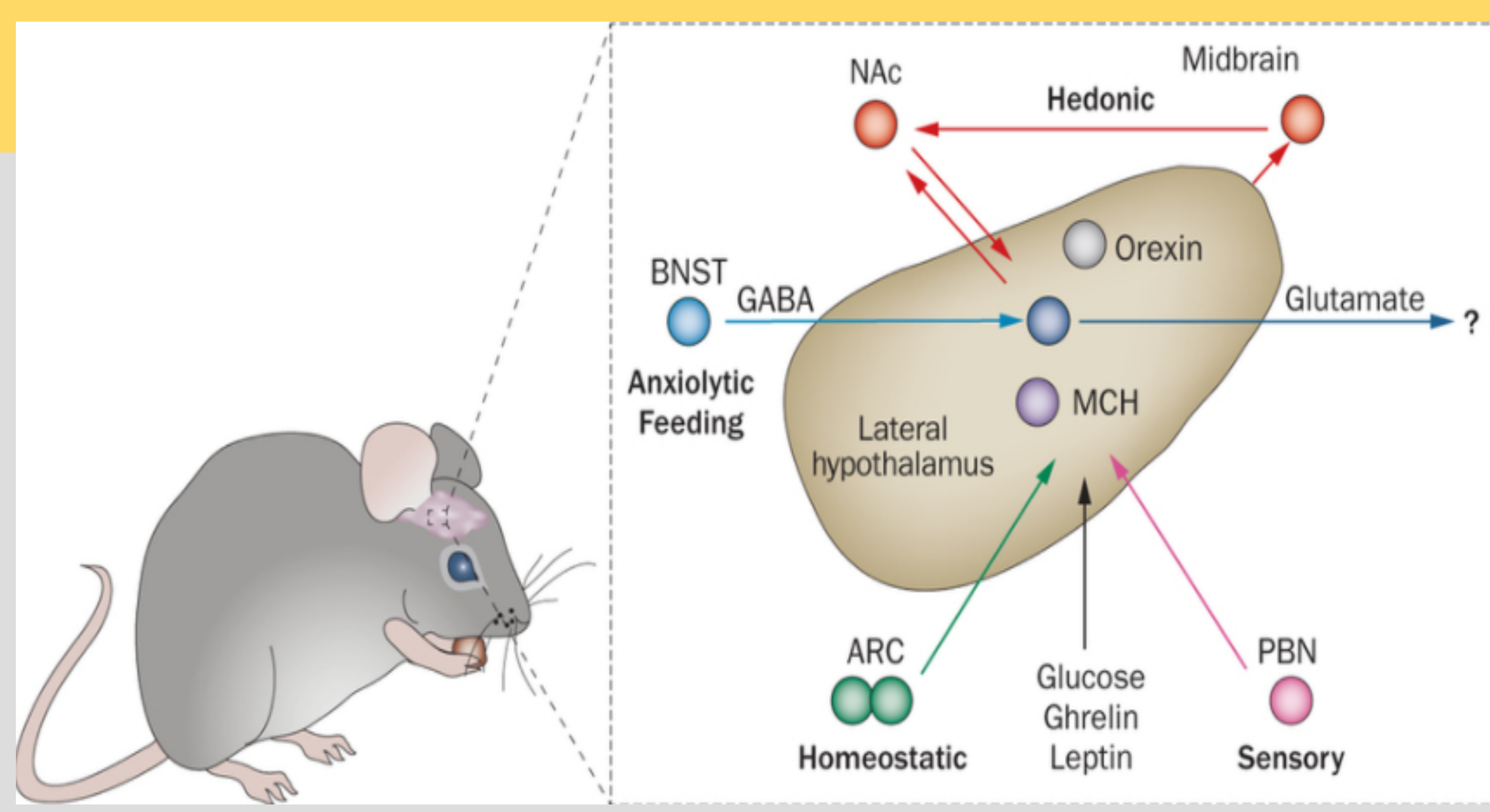
CCK and CRF are both neurotransmitters that are specific to a certain type of cell. GABAergic neurons are neurons that inhibit the production of hypocretin.

Optogenetic stimulation is a process in which light is used to control neurons that have been genetically modified. The cells are modified to have ion channels that are sensitive to light. This technique uses blue light to stimulate Channelrhodopsin-2 channels in neurons.

Understanding the effect of stimulation in the BNST region can further the understanding of the body's sleep system and its reward processing. Sixty million Americans suffer from sleep related disorders annually. Understanding the sleep system is critical in their treatment. Understanding the effects on the hypocretin system can also further explain the process of reward in patients with addiction.

RESEARCH METHODOLOGIES

- I will be working with other post-doc fellows at the lab on this research question. They have looked at how different regions of the brain such as the VTA affect hypocretin cells in the lateral hypothalamus. The previous research mainly focused on how stimuli from other regions of the brain affected the reward centers of the brain. This research will include some aspects of reward, but will extend to the sleep system of the body.
- Essentially, neurons in the BNST region of mice will be stimulated optogenetically, and then the mice will be analyzed through behavioral testing, and cell analysis. The mice will be stimulated, and behavioral testing will be used to analyze whether or not the stimulation was rewarding. After that, the cells in the lateral hypothalamus will be analyzed to see if there is a increase in hypocretin activity. This can show how the stimulation affected the sleep-arousal system.
- I also plan to create a model of this system. I want to simulate the stimulation of these areas of the brain so that it can be used at a template for other experiments. I plan to create a neural network of the connection between the stimulation in the BNST and the reward system in the brain. I hope to apply an adaptive learning algorithm to my neural network to allow it to be more flexible for other modeling.
- The selection of mice used for this experiment will have been modified with a Cre-Virus that allows them to express GCAMP after optogenetic stimulation. This way, the effects of the stimulation can be studied.
- I will be taking the optogenetic data and using that to create the network. Once the network is finished, it should be able to predict given any combination of random data.
- Assuming that a stimulation of a neuron in the BNST is a 1, this will cause a certain stimulation in LH. That stimulation will be based on the percentage of hypocretin neurons stimulated--a number that was found empirically.



DATA ANALYSIS AND RESULTS

I will be using the data collected by my mentor to create a model of my network. However, I will be gathering my own tuning data for my neural network. Since each of the perceptrons need to be weighted and tuned, I will be using a trained neural network system to teach my network. Essentially, I will be giving it inputs and then observing the output. I will then be changing the inputs to get the expected outputs and therefore train my network.

Group	cFos+	Hcrt+	cFos+Hcrt+	cFos+Hcrt-	%Hcrt cFos+	%Hcrt cFos-	%cFos Hcrt+	%cFos Hcrt-
CRF-control	16	63	6	10	9.5238	90.4762	37.5000	62.5000
CRF-control	7	88	1	6	1.1364	98.8636	14.2857	85.7143
CRF-control	9	67	6	3	8.9552	91.0448	66.6667	33.3333
CRF-control	16	85	7	9	8.2353	91.7647	43.7500	56.2500
CRF-control	18	100	12	6	12.0000	88.0000	66.6667	33.3333
CRF-ChR2	32	76	27	5	35.5263	64.4737	84.3750	15.6250
CRF-ChR2	41	111	30	11	27.0270	72.9730	73.1707	26.8293
CRF-ChR2	35	87	19	16	21.8391	78.1609	54.2857	45.7143
CRF-ChR2	32	77	25	7	32.4675	67.5325	78.1250	21.8750
CRF-ChR2	30	62	24	6	38.7097	61.2903	80.0000	20.0000
CRF-ChR2	40	75	29	11	38.6667	61.3333	72.5000	27.5000
CCK-control	11	109	2	9	1.8349	98.1651	18.1818	81.8182
CCK-control	7	94	0	7	0.0000	100.0000	0.0000	100.0000
CCK-control	8	100	0	8	0.0000	100.0000	0.0000	100.0000
CCK-control	16	66	6	10	9.0909	90.9091	37.5000	62.5000
CCK-control	8	47	2	6	4.2553	95.7447	25.0000	75.0000
CCK-control	14	49	3	11	6.1224	93.8776	21.4286	78.5714
CCK-ChR2	44	55	16	28	29.0909	70.9091	36.3636	63.6364
CCK-ChR2	62	75	4	58	5.3333	94.6667	6.4516	93.5484
CCK-ChR2	47	85	24	23	28.2353	71.7647	51.0638	48.9362
CCK-ChR2	22	78	18	4	23.0769	76.9231	81.8182	18.1818
CCK-ChR2	48	68	22	26	32.3529	67.6471	45.8333	54.1667
CCK-ChR2	56	30	9	47	30.0000	70.0000	16.0714	83.9286
CCK-ChR2	70	40	10	60	25.0000	75.0000	14.2857	85.7143

I am modeling this data and putting it into 3 separate networks. As stated before, the CCK control data will be put into a perceptron that outputs a GABA stimulation percentage. That GABA stimulation percentage will then be inputted into another perceptron that will result in a hypocretin stimulation percentage. Similarly the CRF data will be plugged into a perceptron that results in a hypocretin stimulation percentage.

ACKNOWLEDGEMENTS / REFERENCES

Thank you to Dr. William Giardino, The de Lecea Lab for making this project possible.

Works Cited:

By Applying the Firing in Every Column the following Truth Table Is Obtained; X1: 0 0 0 0 1 1 1 1 X2: 0 0 1 1 0 0 1 1 X3: 0 1 0 1 0 1 0 1 OUT: 0 0 0 0/1 0/1 1 1 1 The Difference between the Two Truth Tables Is Called the Generalisation of the Neuron. Ther. "Neural Networks." *Neural Networks*. N.p., n.d. Web. 08 Nov. 2016. <https://www.doc.ic.ac.uk/~nd/surprise_96/journal/vol4/cs11/report.html>.

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