Investigate the Direct Functional Connections Between ipRGCs and AVP Neurons in the SCN

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In mammals, circadian rhythms are regulated by the suprachiasmatic nucleus (SCN) in the hypothalamus, which synchronizes the internal circadian clock with external environment. External light signals are detected by intrinsically photosensitive retinal ganglion cells (ipRGCs) in the eyes, which send signals to the SCN to align circadian rhythms with light-dark cycle. SCN achieves this synchronization through a network of various neurons, including expressing arginine vasopressin (AVP) and vasoactive intestinal peptide (VIP), with VIP neurons being crucial for maintaining circadian rhythms.

While previous studies have focused on the direct connection between ipRGCs and VIP neurons in the SCN, recent research using single ipRGC-tracing techniques has indicated a possible direct connection between ipRGCs and AVP neurons. Additionally, AVP neurons have been shown to be the primary determinant of the circadian rhythm period. These findings suggest a possible pathway for light to influence circadian rhythms through the ipRGC-AVP neuron circuit in the SCN. We hypothesize that AVP neurons can directly receive light signals from ipRGCs, and regulating circadian rhythms.

To investigate the connection between ipRGCs and AVP neurons, we used calcium imaging in acute brain slices from AVP-Cre mice, injecting Cre-dependent GCaMP7f, a calcium sensor, into the SCN region and Channelrhodopsin (ChR) into eyes. With applying TTX and 4AP to block synaptic activation and using optogenetic activation of ChR-labeled ipRGCs, we observed responses of GCaMP-labeled AVP neurons with two-photon microscopy, confirming that AVP neurons were directly activated by ipRGCs. By analyzing variations in responses and cellular subgrouping of AVP neurons, our results suggested that AVP neurons may receive direct ipRGC input from the retina for circadian clock regulation. This approach will reveal new insights into circadian rhythm modulation through the ipRGC-AVP neuron circuit in the SCN.

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