Data for Brain Reference Architecture of SK25LHbDepressionModel

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Abstract

This dataset offers structural information (Brain Information Flow - BIF) about brain areas linked to Major Depressive Disorder (MDD), specifically focusing on the lateral habenula (LHN). Drawing from studies on stress circuits and neuron-glia interactions , the data defines several components: prelimbic cortex layer 6 neurons (PL.L6), LHN glutamatergic neurons (_LHN), locus coeruleus neurons (_LC), and LHN astrocytes (LHN_astrocyte). It outlines connections within the PL.L6 → _LHN → _LC → LHN_astrocyte → _LHN circuit. Presented in the brain reference architecture (BRA) format, this dataset provides a framework for models looking into LHN circuit issues and their possible connection to depression symptoms.

Keywords: Brain Reference Architecture; Lateral Habenula; Major Depressive Disorder; Astrocyte

Author roles:

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1 Context

Brain Reference Architecture (BRA) is the reference architecture for software that realizes cognitive and behavioral functions in a brain-like manner. The architecture primarily consists of the mesoscopic-level anatomical data of the brain and the data of one or more functional mechanisms that are consistent with that knowledge(Yamakawa, 2021). BRA consists of Brain Information Flow (BIF), which represents structural knowledge of the brain, and Hypothetical Component Diagram (HCD)/Funciton Realization Graph (FRG), which represent brain functionality.

This BRA dataset summarizes brain regions implicated in Major Depressive Disorder (MDD). Recently, the lateral habenula (LHN) has received particular attention due to its strong association with MDD (Cameron, Weston-Green, & Newell, 2024; Hu, Cui, & Yang, 2020; Proulx, Hikosaka, & Malinow, 2014). The LHN is reciprocally connected with numerous subcortical regions (Groos & Helmchen, 2024; Zhang, Wu, Cui, & Peng, 2022) and is known to receive projections from the frontal cortex, particularly from the medial prefrontal cortex (mPFC) in mice (Mathis, Williams, Fillinger, & Kenny, 2021). In depressive mouse models, burst firing specific to LHN neurons has been observed (Corona & Kenny, 2025; Yang et al., 2018), and there is growing evidence suggesting astrocytic involvement in depressive pathology (Arjmand et al., 2022; Xin et al., 2025). Based on these findings, this BRA dataset organizes connectivity information centered on LHN neuronal populations and astrocytes. The Regions of Interest (ROIs) include LHN glutamatergic neurons, LHN astrocytes, and LC (locus coeruleus) neurons. As an input to these ROIs, the prelimbic cortex (PL)—a part of the medial prefrontal cortex projecting to the LHN—is provided.

2 Method

Sampling strategy Based on the relationship between neuro-glia (astrocyte) interactions within the LHN and Major Depressive Disorder (MDD), we constructed a Brain Information Flow (BIF) centered on the LHN–LC–LHN astrocyte circuit. The connectivity information was extracted from neurophysiological studies describing stress-related circuits involving the LHN.

Projection from mPFC to LHN LHN projects to numerous subcortical regions, including the locus coeruleus (LC) (Groos & Helmchen, 2024; Xin et al., 2025; Zhang et al., 2022), and LC provides positive feedback to LHN astrocytes (Xin et al., 2025). Inputs to the LHN arise not only from subcortical structures but also from the deep layers of the neocortex, particularly from the medial prefrontal cortex (mPFC) in mice (Mathis et al., 2021). A study by Mathis et al. demonstrated that deep-layer neurons of the mPFC projecting to the paraventricular nucleus of the thalamus (PVT) also co-project to the LHN, and noted that this projection pattern resembles the thalamic connectivity reported in previous work (Gabbott, Warner, Jays, Salway, & Busby, 2005). In the study (Gabbott et al., 2005), layer VI neurons of the infralimbic cortex (IL), prelimbic cortex (PL), and dorsal anterior cingulate cortex (ACd) were shown to project to the mediodorsal thalamus (MD), a subdivision of the thalamus. Although the MD and PVT are anatomically adjacent, they are distinct nuclei. Meanwhile, projections from the PL to the PVT mainly originate from layer VI pyramidal neurons[1], and it has been suggested that both a direct pathway from PL to PVT and an indirect pathway via the anteroventral sector of the thalamic reticular nucleus (avTRN) exist (Ma et al., 2024). Integrating these findings, we infer that layer VI pyramidal neurons in the PL project to LHN neurons. Fig.1 shows the BIF image.

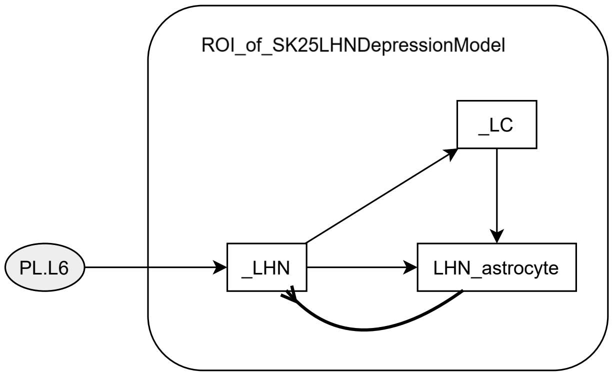

Figure 1: BIF Images. *Abb. LHN*: lateral habenular nucleus, *LC*: locus coeruleus, *LHN_astrocyte*: astrocyte in LHN, *PL_L6*: layer 6 pyramidal neurons of prelimbic cortex.

Circuit ID and graph order The Circuit ID of each Uniform Circuit registered in the dataset is assigned as follows:

(1) If the nucleus to be registered already exists in the WholeBIF (based on the Allen Institute's Human Brain Atlas (DHBA)[2]), its pre-registered ID is used.

(2) If it is not pre-registered, the Circuit ID is assigned according to the naming convention of the BRA dataset.

Although LHN and LC were pre-registered, they were initially registered with "uniform = False." Therefore, we re-registered them with "uniform = True" by adding a prefix "_". Both LHN_astrocyte and PL.L6 were registered following the Circuit ID naming convention. The graph order of LHN and LC follows that defined in the DHBA. LHN_astrocyte is considered a substructure of the LHN, and its graph order is assigned accordingly. For PL (in mice), homologous to the human dorsal anterior cingulate cortex (dACC; graph order = 1383) (Fenton et al., 2014), the graph order of the dACC was used.

3 Dataset Description

Repository location BRA Editorial System (BRAES) https://sites.google.com/wba-initiative.org/braes/data

Object name and versions Please refer to the "Project" sheet in the BRA data for the more detail of data summary.

Table 1: BRA DATA SUMMARY

BRA Data			
Object Name	Template	Including Content(s)	
		BIF	HCD/FRG
ProjectID.bra	*version 2.2*	√	-

[1]Projections from layer V of the PL to the PVT are reported to be scarce.
[2]Adult Human (Modified Brodmann): https://atlas.brain-map.org/

Table 2: BRA IMAGE SUMMARY

Graphic Files: BIF Image	
File Type	Object Name
BIF Image	SK25LHbDepressionModelBIF.xml
HCD Image	-
FRG Image	-

Creation dates The start and end dates of when the data was created (2025-09-15 to 2025-10-19).

Language English.

License The open license under which the data has been deposited (CC-BY 4.0).

Publication date The date in which the dataset was published in the repository (2025-11).

4 Caveats for Data Usage

In this dataset, layer VI pyramidal neurons of the prelimbic cortex (PL) are defined as inputs to the ROI, and the connectivity information is based on findings from mouse studies. For data consistency and to assign a hierarchical structure according to the Allen DHBA, the PL is mapped to the human dorsal anterior cingulate cortex (dACC). However, it should be noted that the dataset does not imply or specify any direct correspondence or replacement of connections between the PL and dACC.

Funding Statement

Not applicable

Competing interests

Not appliable

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