Poster
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ACUTE SLEEP DEPRIVATION INDUCES SYSTEMIC ALTERATIONS IN MICE BRAIN: INSIGHTS FROM SPATIAL TRANSCRIPTOMICS

STOmics

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INTRODUCTION

Sleep is crucial for brain homeostasis, emotion regulation, memory consolidation, and spatial orientation. Inadequate sleep can lead to severe physiological disorders, potentially indicating the onset of neurodegenerative diseases. Previous studies have demonstrated that sleep deprivation (SD) results in memory deficits and increased foraging behavior in mice. However, the molecular changes across different brain regions remain to be elucidated due to technical limitations. To investigate the region-specific gene expression and cellular interactions following acute SD, this study utilized six 9-week-old male C57BL/6J mice, with three undergoing 5 hours of SD and three serving as controls. The brains were cryo-embedded and analyzed using the updated Spatially enhanced-resolution omics-sequencing V1.3 (Stereo-seq V1.3) technology.

METHODS

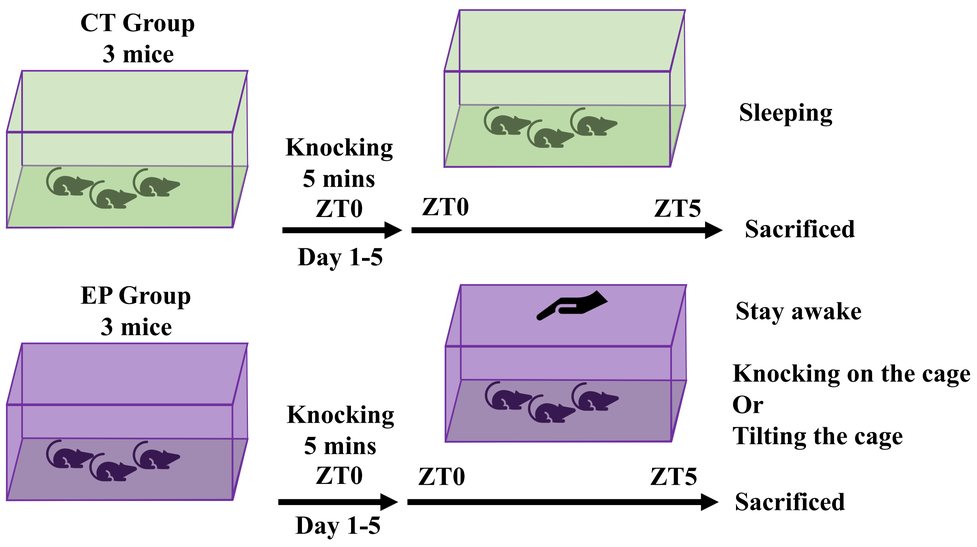

Figure 1. Sleep Deprivation. Six 9-week-old male C57BL/6J mice were maintained on a stable 12-hour light/dark cycle. The experimental group (EP) of three mice underwent 5 hours of sleep deprivation through gentle cage tapping, while the control group (CT) had 5 hours of normal sleep. All mice were subsequently euthanized and dissected. The brains were cryo-embedded using OCT.

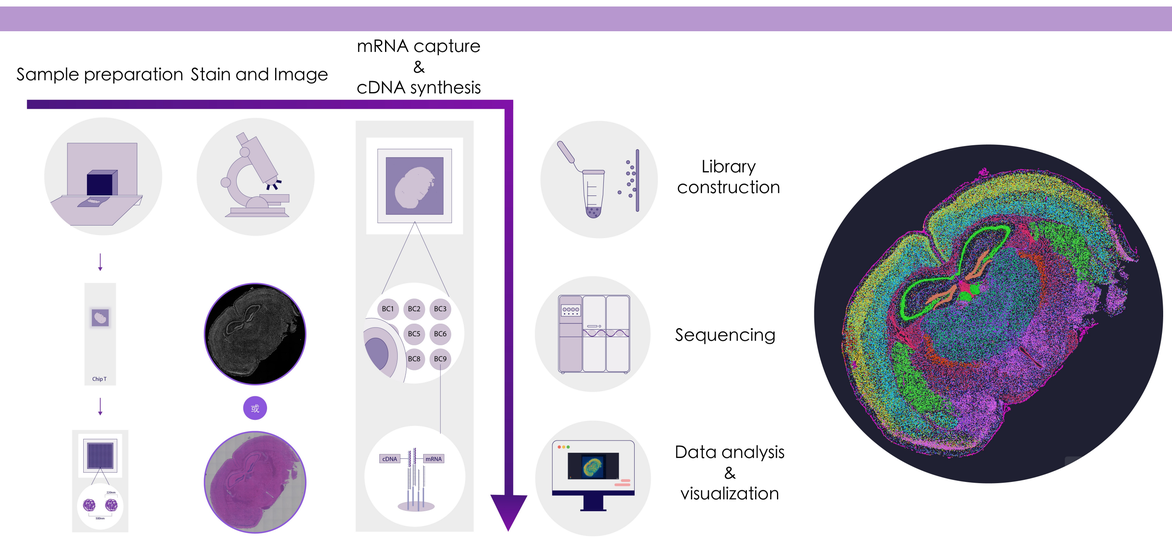

Figure 2. Workflow of Stereo-seq V1.3. The whole workflow includes sample preparation, stain and image, mRNA capture and cDNA synthesis, library construction, Sequencing, and Data analysis and visualization.

RESULTS

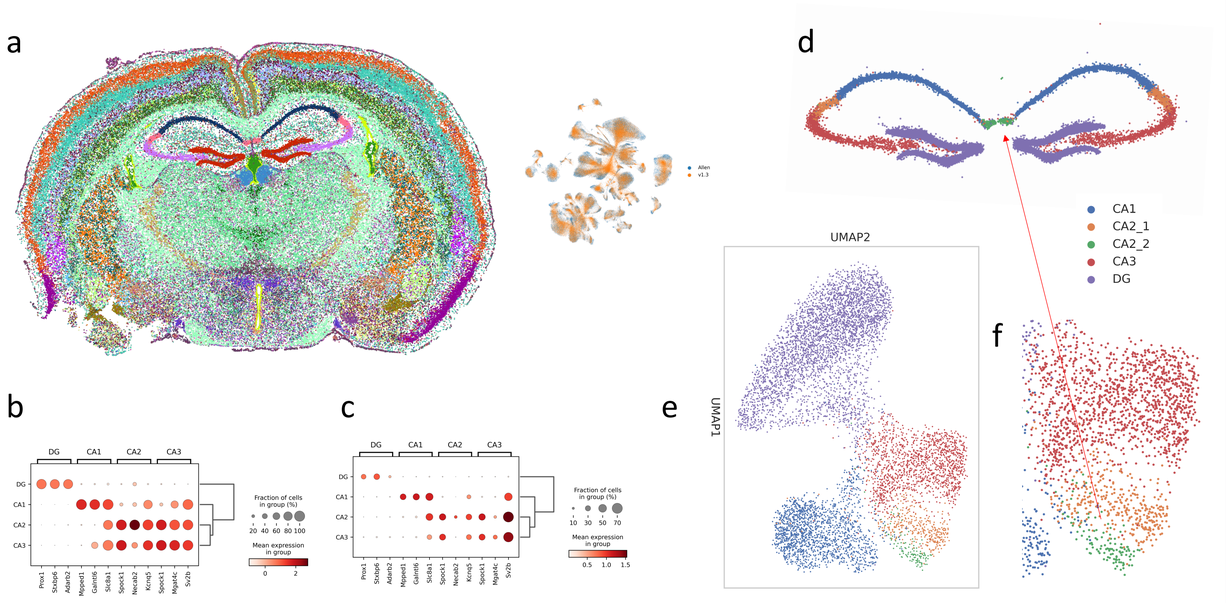

Figure 3. Brain cell clustering and annotation. a. Over 100 million cells per sample were segmented, and 87 subclasses were annotated using the Allen Brain Atlas single-cell dataset. **b.** Dot plot of marker genes for DG, CA1, CA2, and CA3 in the Allen Brain dataset. **c.** Dot plot of marker genes for DG, CA1, CA2, and CA3 in CT2. **d.** Clustering plot of the hippocampus. **e.** UMAP projection of the hippocampus by clustering. f. Detail of the CA2 subclusters.

RESULTS

Table 1. Cell numbers and gene numbers after segmentation with an image-facilitated pipeline.

Groups	Control Group	Control Group	Control Group	Experiment Group	Experiment Group	Experiment Group
Sample Name	CT1	CT2	CT3	EP1	EP2	EP3
Stain type	ssDNA	ssDNA	HE	ssDNA	ssDNA	HE
Cell bin number	145,623	144,180	115,921	166,755	148,913	119,857
Median genes/Cell bin	791	708	1,215	845	691	1,170
Median MID/Cell bin	1,159	1,066	1,820	1,172	1,024	1,719
Saturation	60.10%	65.10%	51.50%	56.41%	62.30%	52.50%

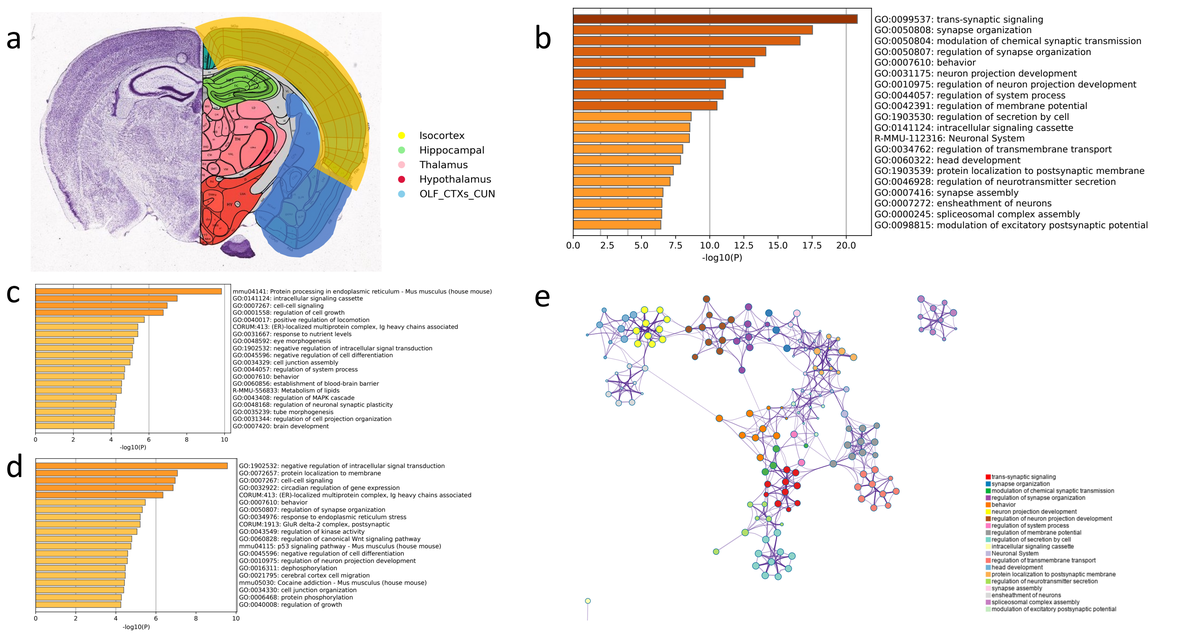

Figure 4. Differential gene expression after sleep deprivation. **a.** Main brain areas. The brain was divided into isocortex, hippocampus, thalamus, hypothalamus, and OLF_CTXs_CUN (olfactory areas, cortical subplate, and cerebral nuclei). **b.** Bar graph of enriched GO terms across differentially expressed genes (DEGs) in the hippocampus. **c.** Bar graph of enriched GO terms across DEGs in the thalamus. **d.** Bar graph of enriched GO terms across DEGs in the isocortex. **e.** Enrichment network for hippocampus with DEGs after sleep deprivation.

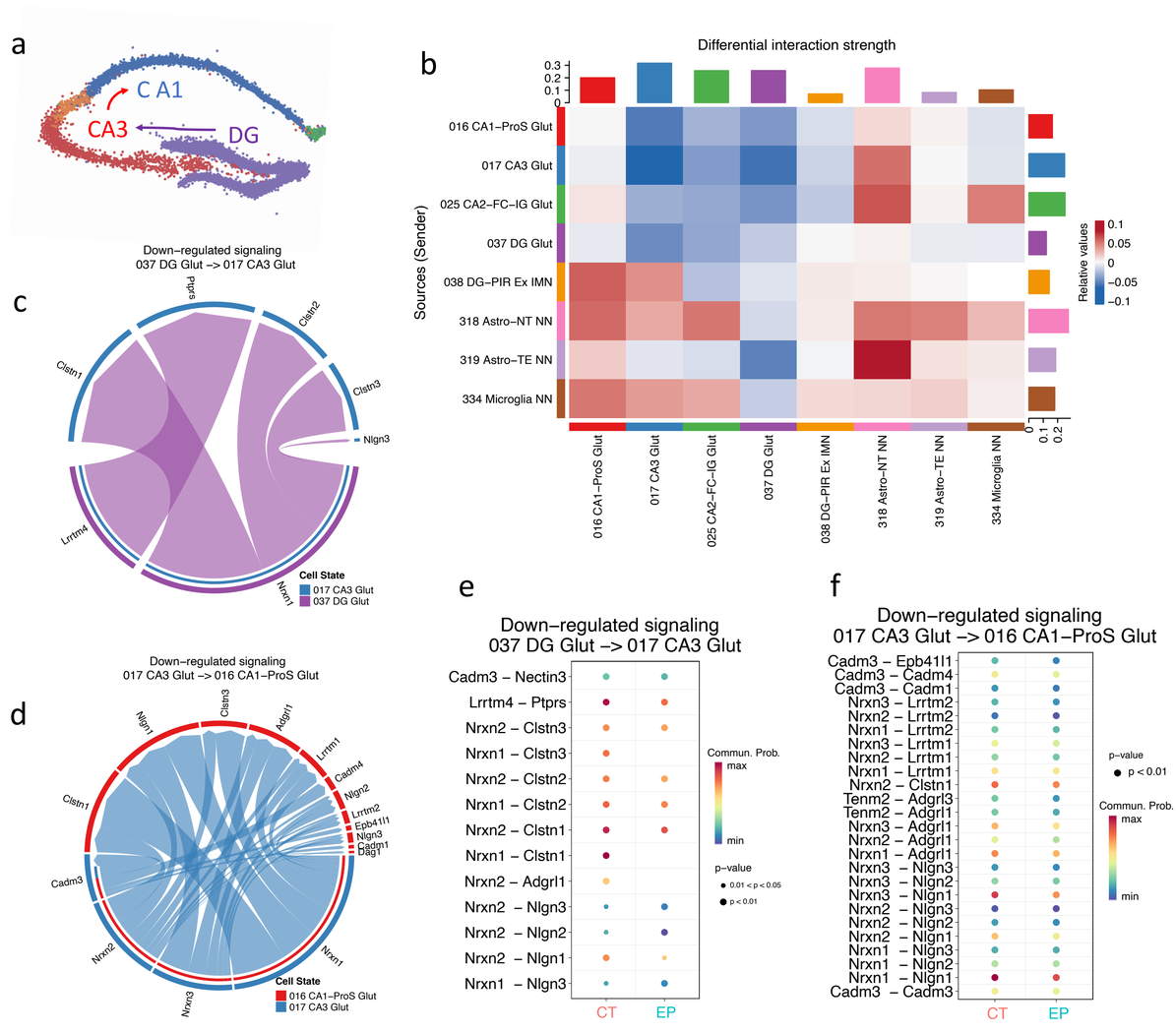

Figure 5. Changes in cell-to-cell interactions after sleep deprivation. a. The classical hippocampal trisynaptic circuit in the hippocampus. b. Differential interaction strength among different cell populations across CT and EP datasets (red/blue colored edges represent increased/decreased signaling in EP samples). c. Down-regulated singling in EP(DG->CA3). d. Down-regulated singling in EP(CA3->CA1). e. Down-regulated signaling ligand-receptor pairs in EP(DG->CA3). f. Down-regulated singling ligand-receptor pairs in EP(DG->CA3).

CONCLUSION

These findings indicate that sleep deprivation affects brain functions, providing insights into the molecular mechanisms underlying the effects of sleep deprivation and offering a high-resolution transcriptomics profiling database and potential directions for future research on related diseases.