浙江大学
生命演化研究中心

Neural Circuits of Social Needs

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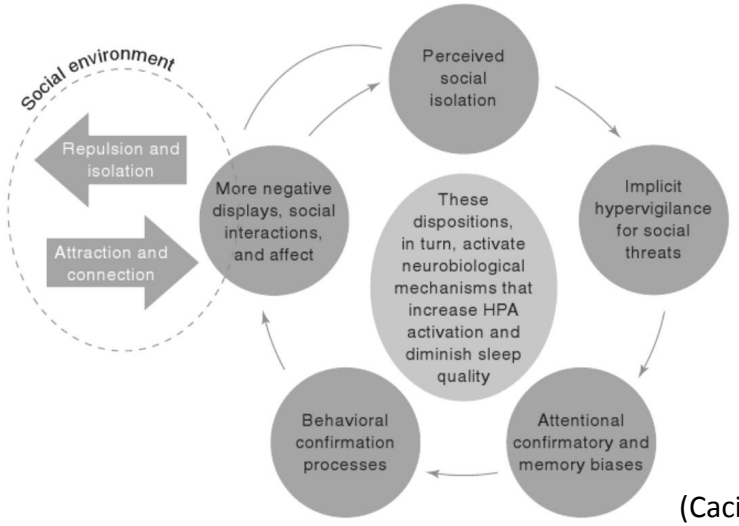
2025/8/15

Social need

Loneliness—Not Just a Matter of Mood!



(Cacioppo and Hawkley, 2009)

Lacking social connection could be as dangerous as smoking up to 15 cigarettes a day

(Holt-Lunstad et al., 2010)

Article

A hypothalamic circuit underlying the dynamic control of social homeostasis

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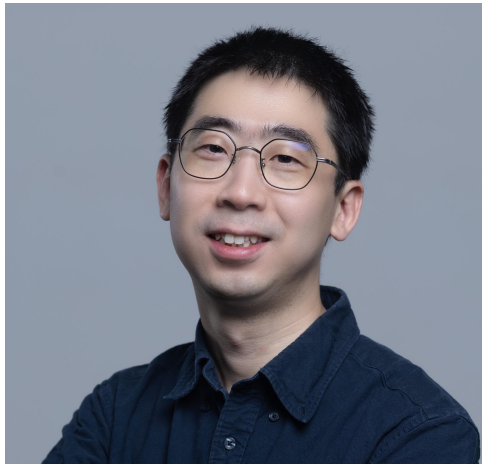
Catherine Dulac
Samuel W. Morris University Professor

Which brain regions and neural circuits encode social need?

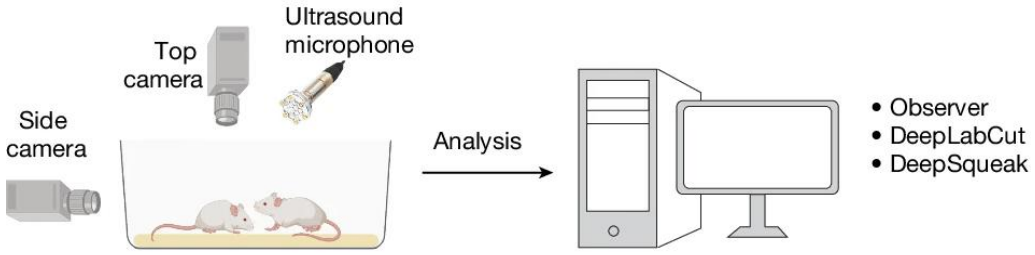
How do animals sense social presence or isolation?

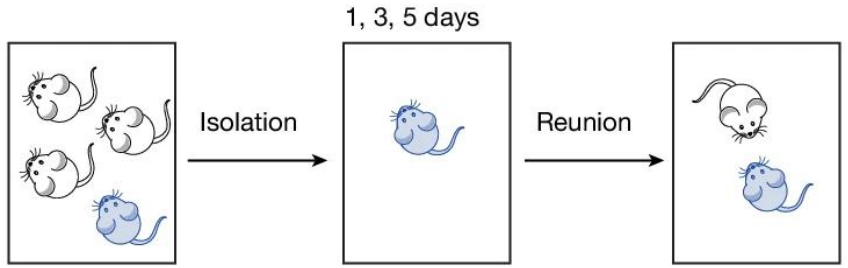
"Understanding the world is to interpret, reconstruct and substitute the world of experience according to one's inner drive. It is like escaping the chaos of the city to view freely from a distant mountain. This is what travelers, artists, poets, and scientists pursue in their own fashion."

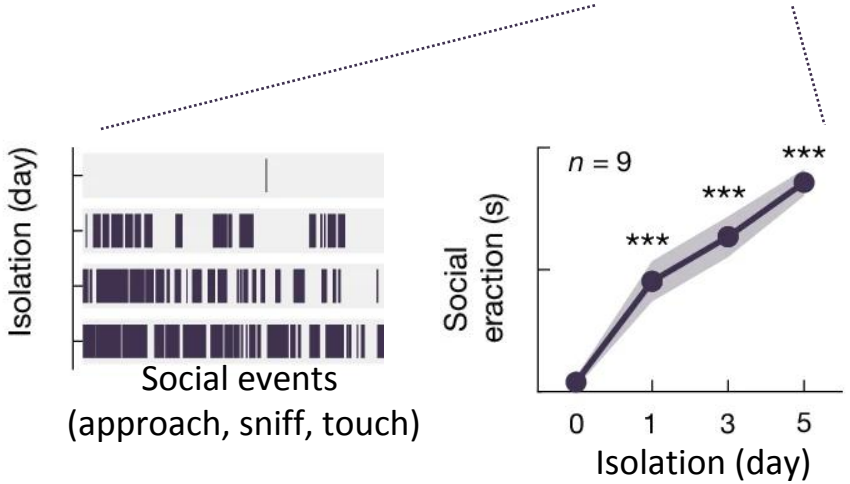


Ding Liu
Westlake University

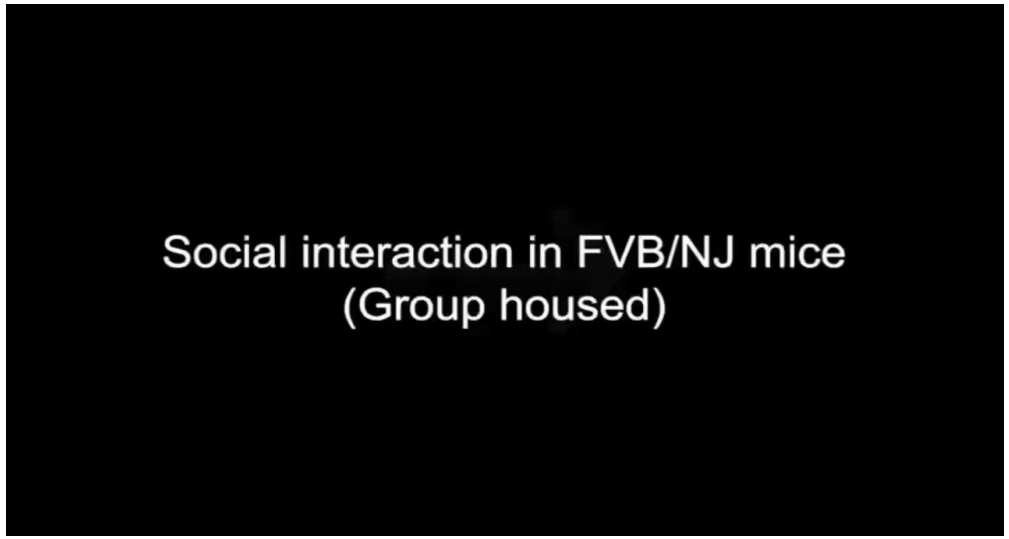
Social rebound

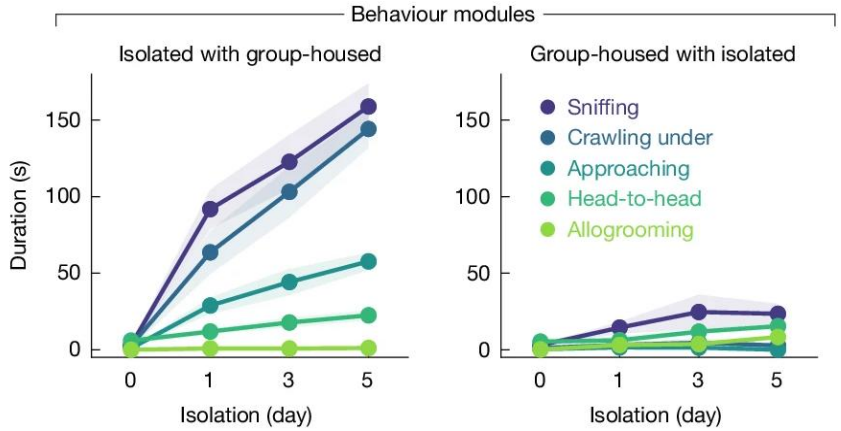






make up (弥补) the lost social time

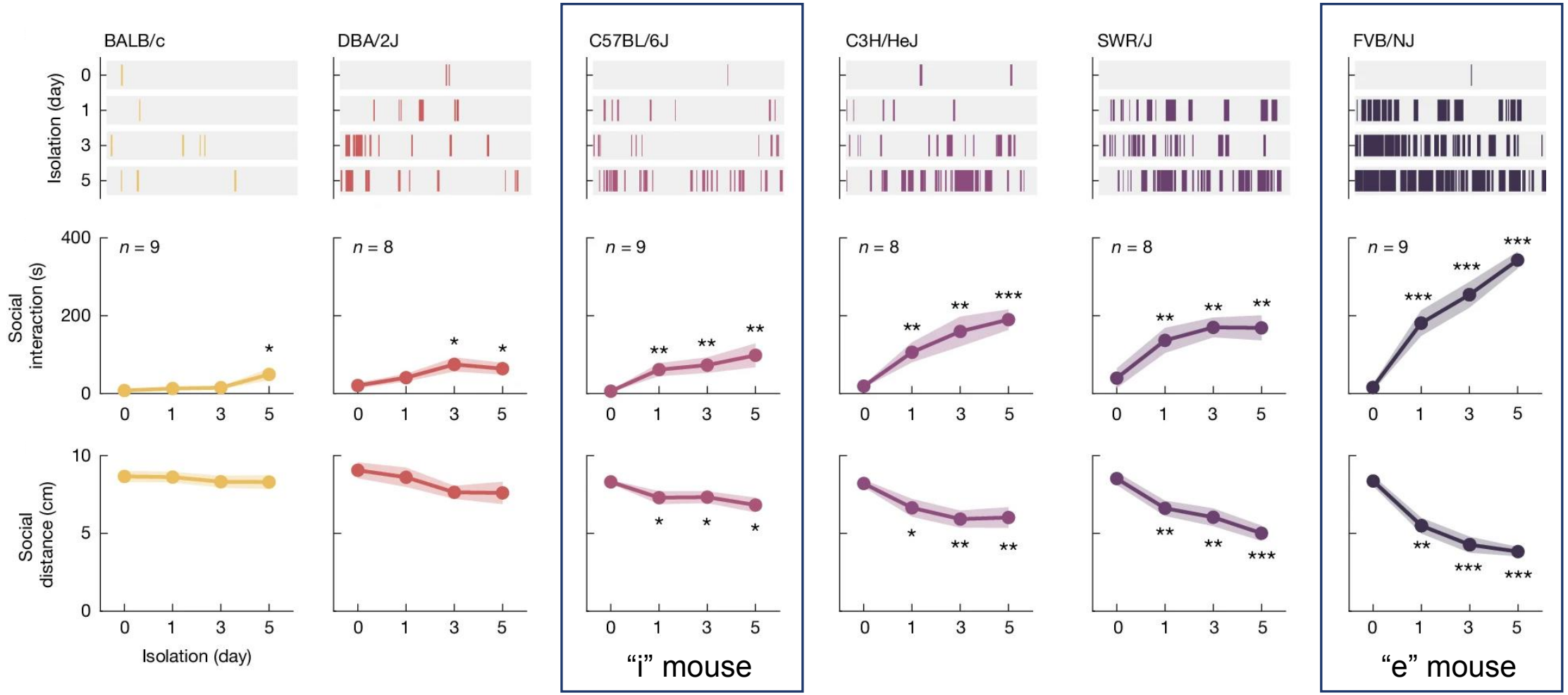




- Social behaviour events initiated mostly by the isolated one.

Social rebound spectrum across mouse strains

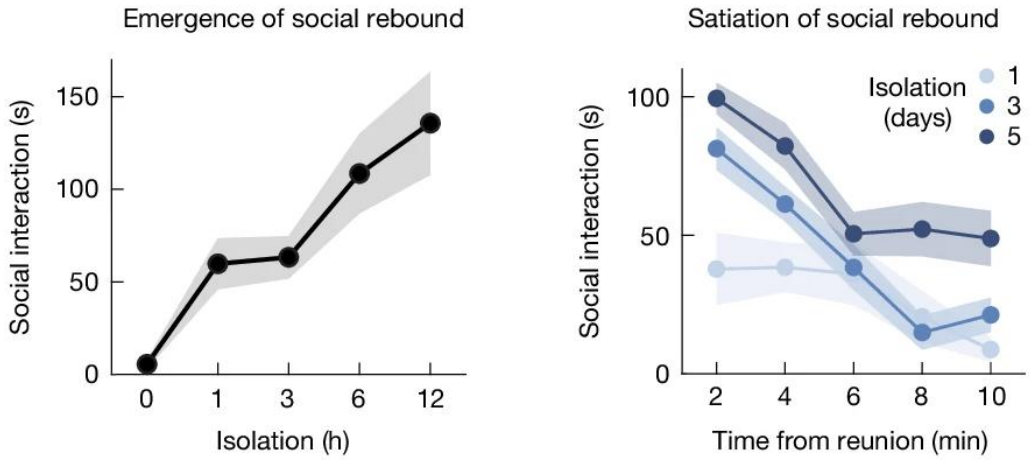
- **<u>Different strains</u> showed highly diverse ranges of social rebound,**
  from weak (BALB/c and DBA) to moderate (C57BL/6J, C3H/HeJ, SWR/J) and strong (FVB/NJ).

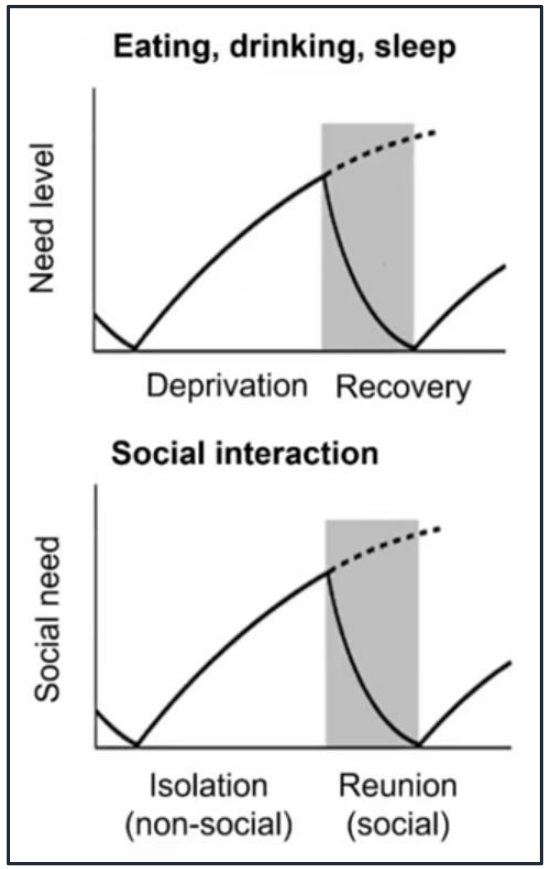


*(female-female) nonsexual affiliative interaction—genetic basis

Social rebound reflects social homeostasis

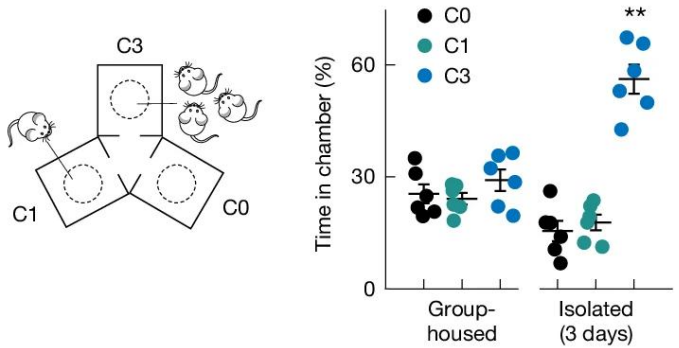
- More intense social rebound with increased isolation time.
- Social rebound behaviour declined over time during reunion.





- starvation
- dehydration
- sleep deprivation
- suicide

- Isolated mice preferred to interact with a group over a single mouse.

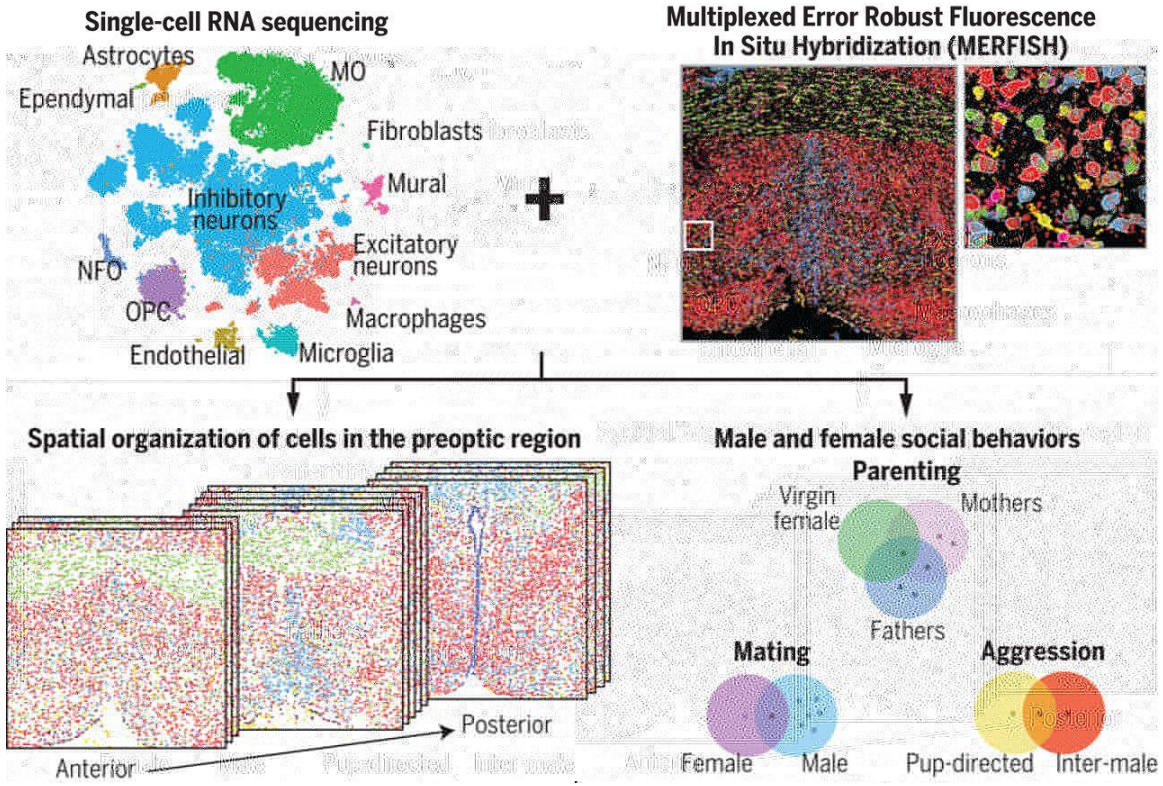


"Social Homeostasis"

Candidate neurons underlying social homeostasis

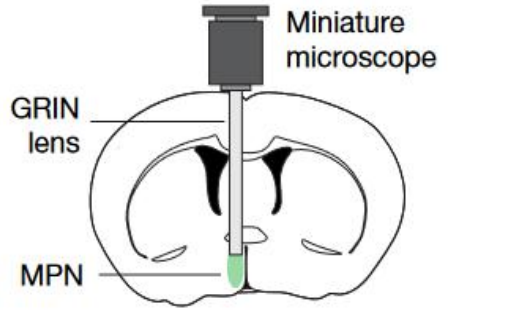
- **The hypothalamic preoptic region is important for sleep, thermoregulation, thirst, and social behavior.**

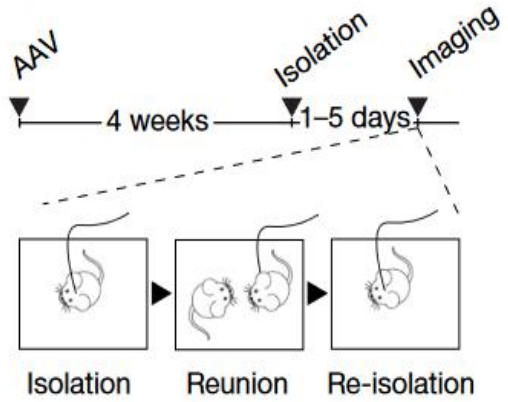
hypothalamic circuits [下丘脑的回路]



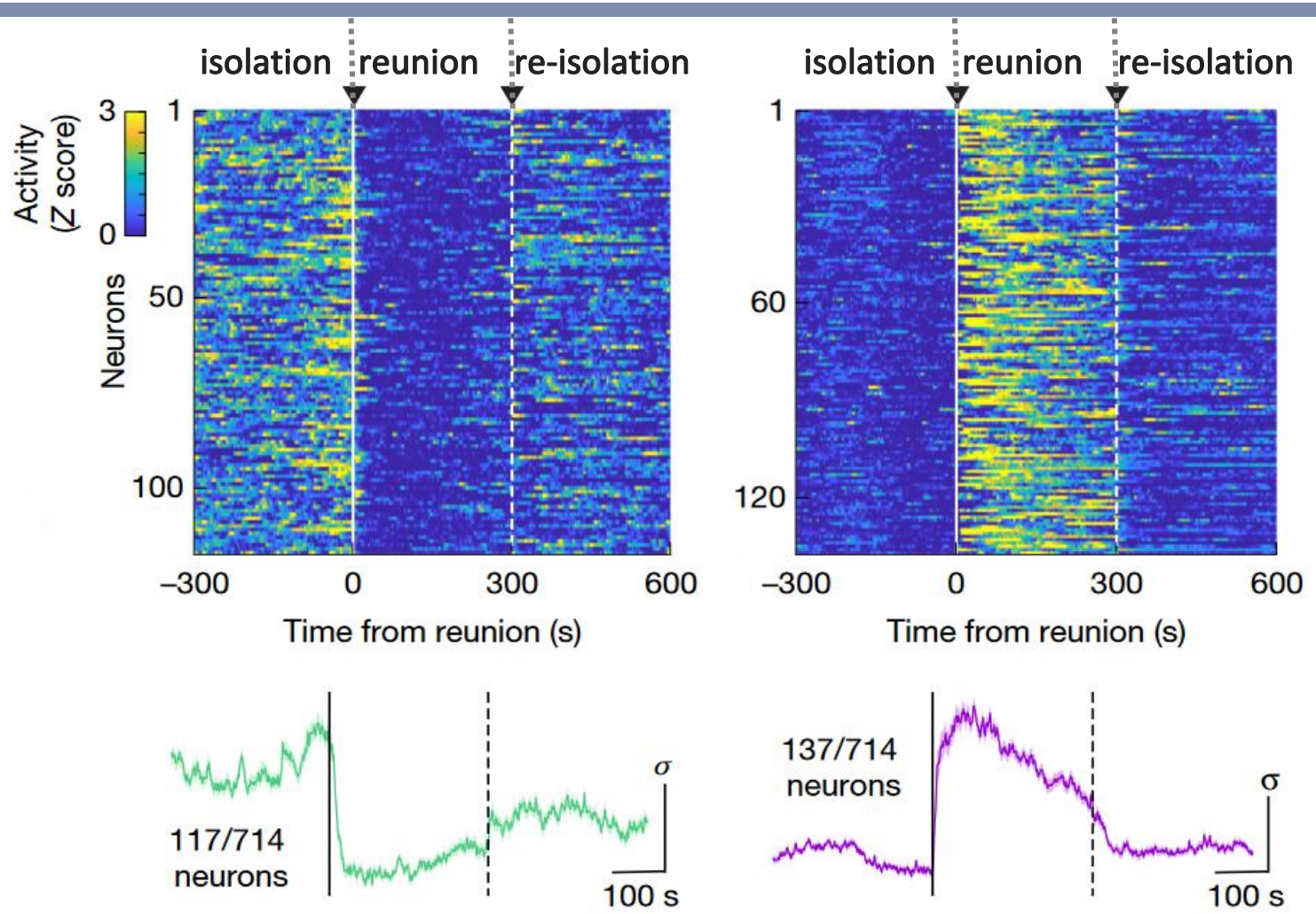
(Moffitt, 2018)

Medial Preoptic Nucleus (MPN)
—a hypothalamic nucleus involved in the control of social behaviours

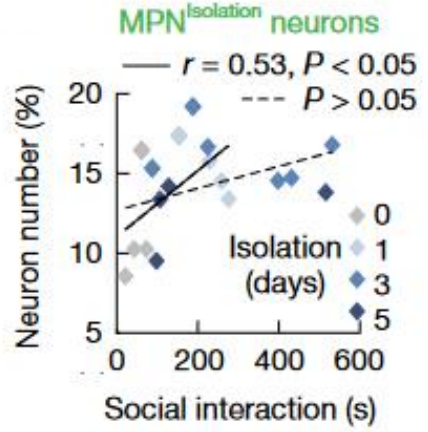




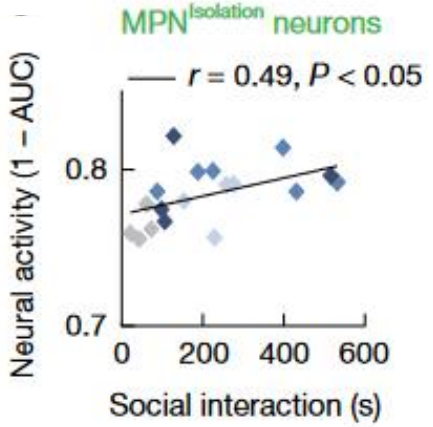
Candidate neurons underlying social homeostasis



- The activity strength of MPN^{Isolation} neurons is correlated significantly with social rebound intensity.



FVB/NJ

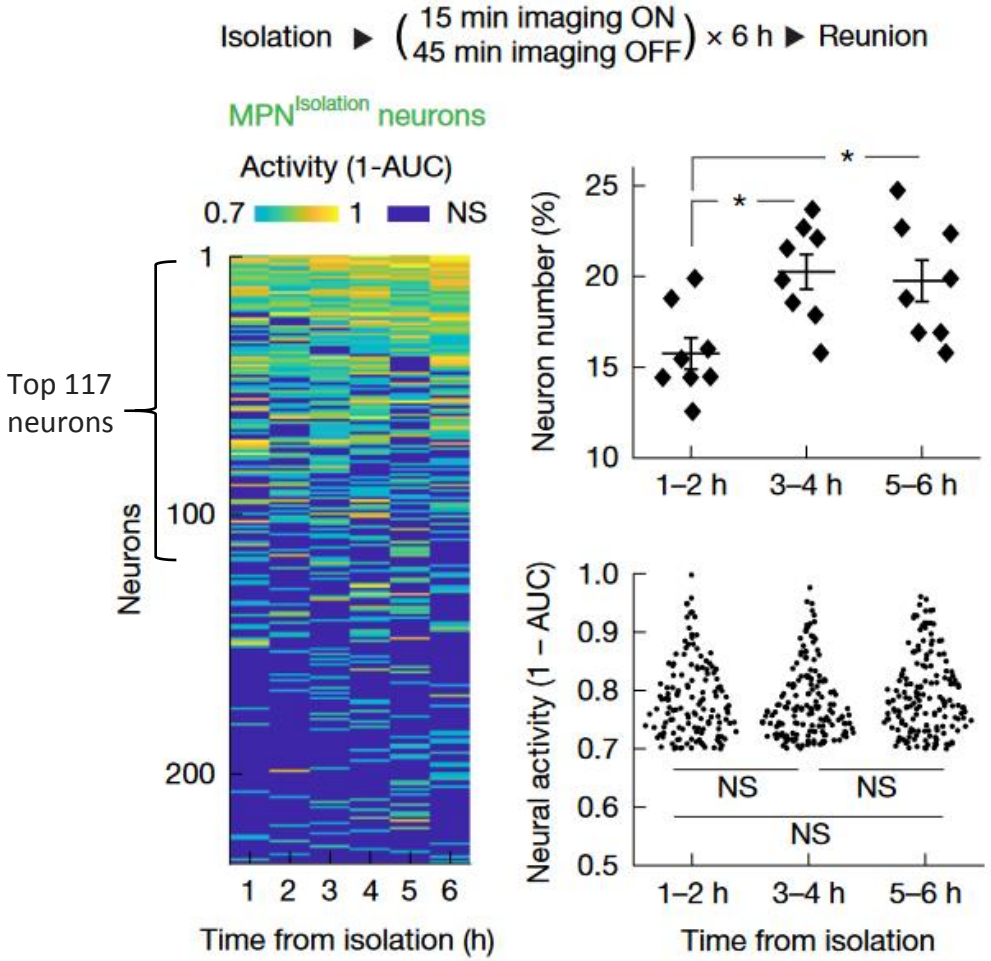


C57BL/6J

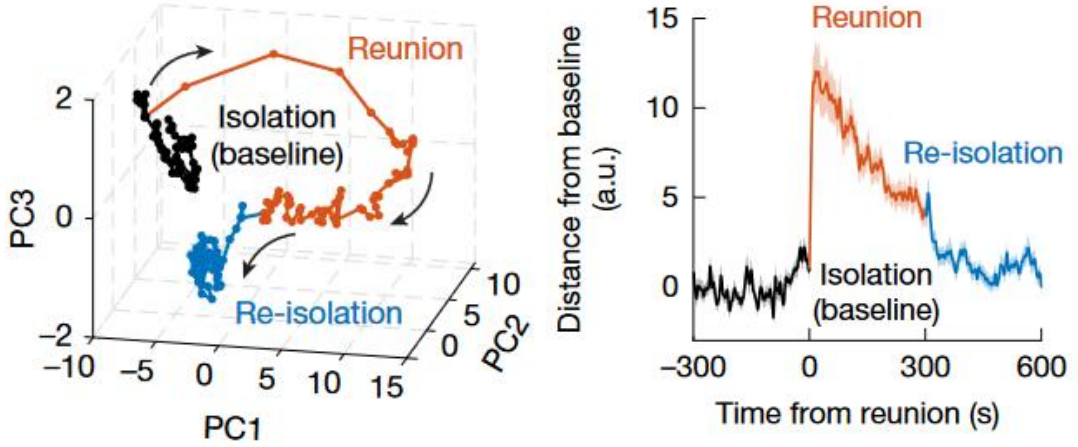
	MPN^{Isolation}	MPN^{Reunion}
When Activated	During social isolation	During social reunion
When Shut Off	Immediately upon reunion	During isolation
What signalling	“Need” singal (negative)	”Reward” signal (positive)

Candidate neurons underlying social homeostasis

- MPNIsolation kept active non-stop during isolation.

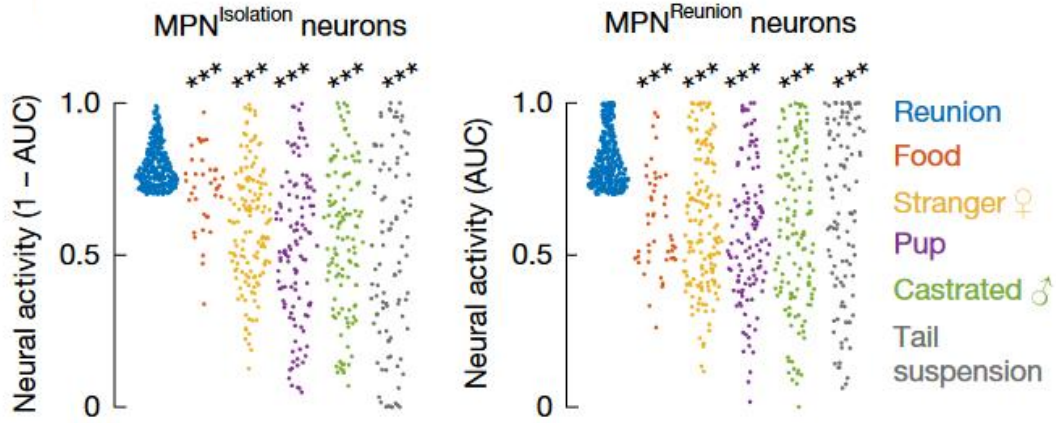


- The PCA trajectory showed distinct neural representations for isolation and reunion states and a rapid state transition upon reunion.

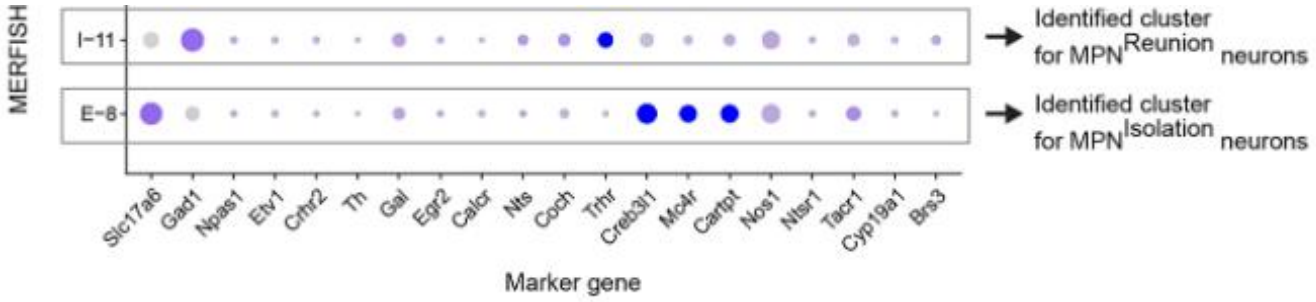


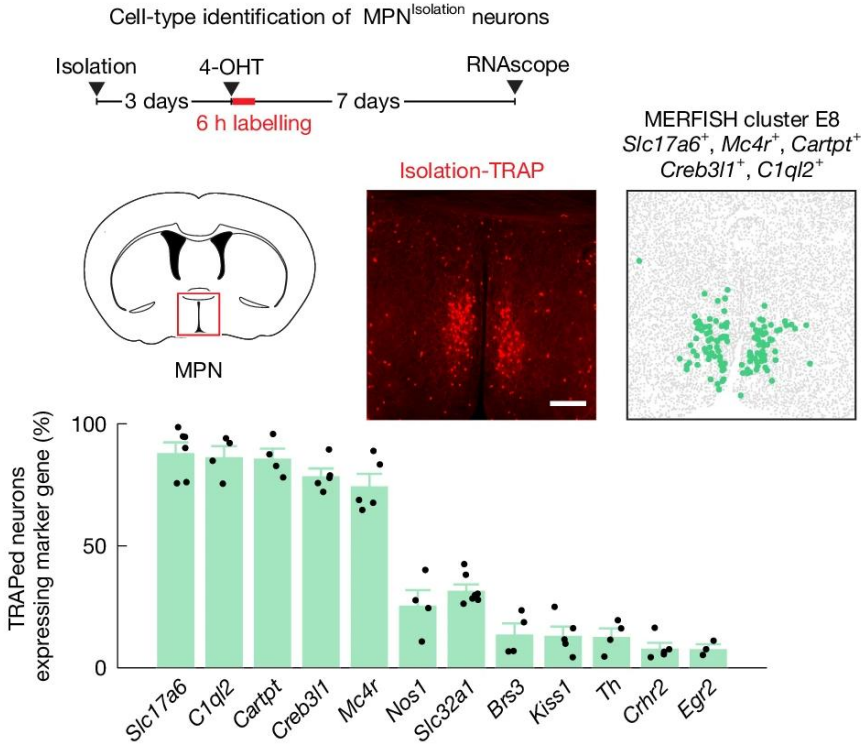
Short-time reunion can also satisfy the social need after isolation.

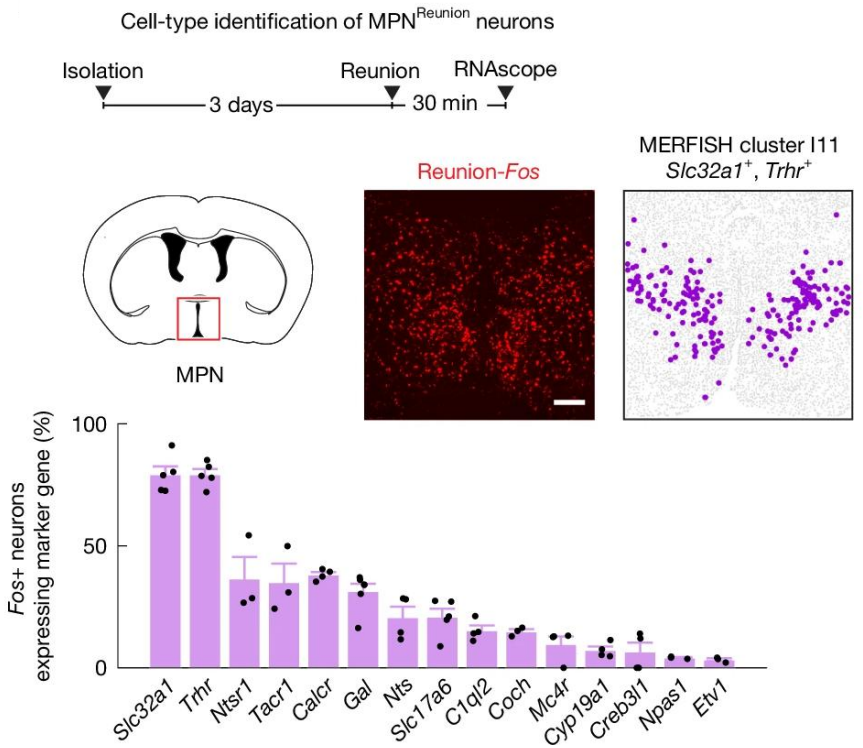
- MPN Isolation and MPN Reunion neurons are uniquely tuned to social isolation.



Molecular identity of activated neuronal populations

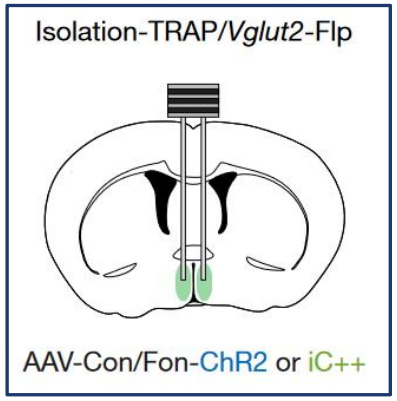


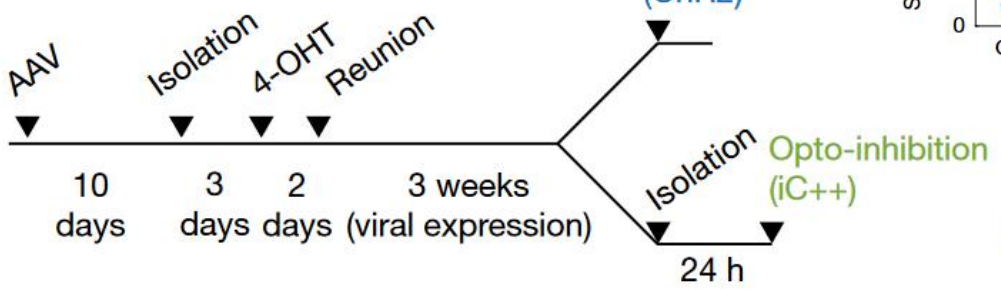


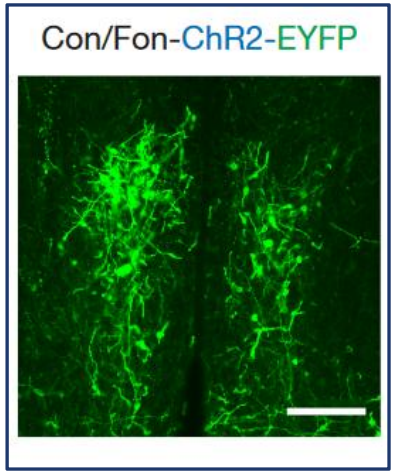


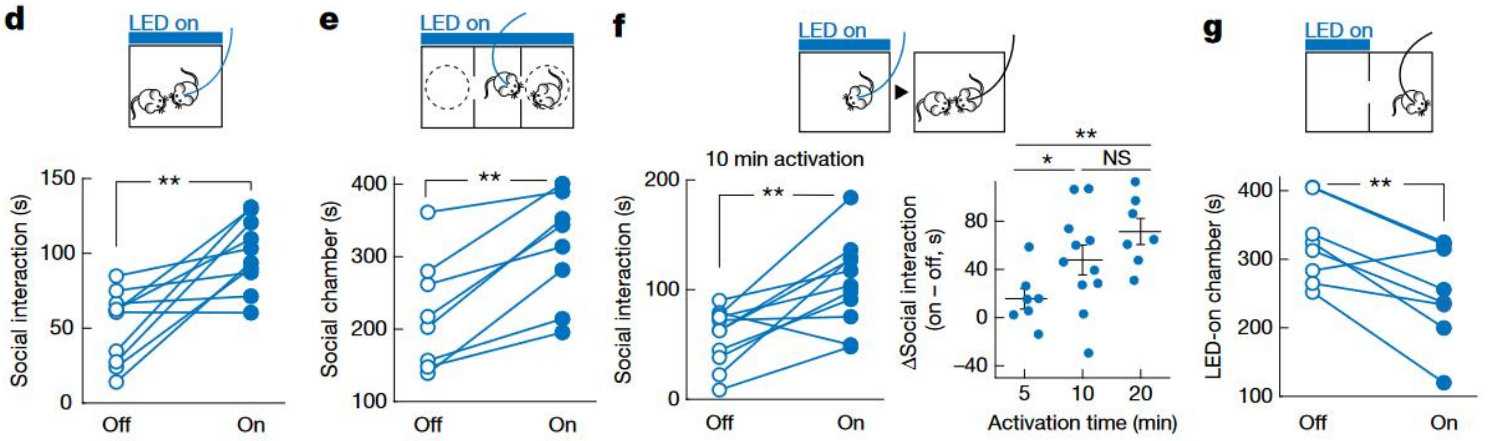
- **MPN^{Isolation} neurons are glutamatergic (谷氨酸能神经元)**
- **MPN^{Reunion} neurons are GABAergic (GABA能神经元)**

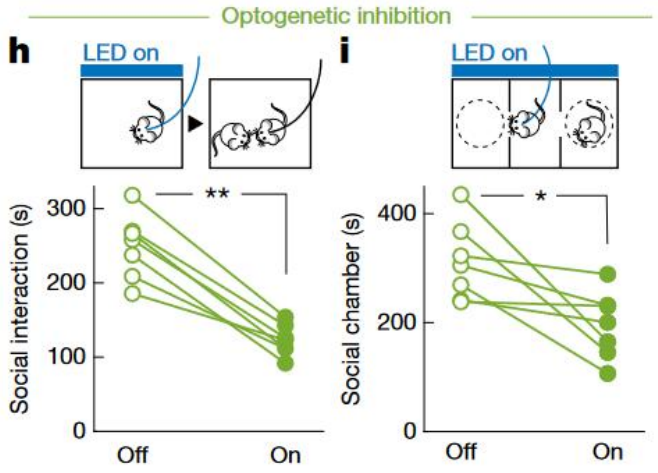
Functional characterization of MPN^{Isolation} neurons





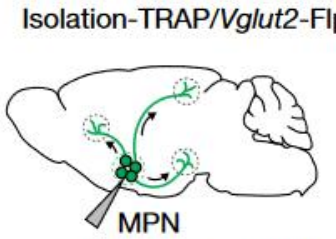




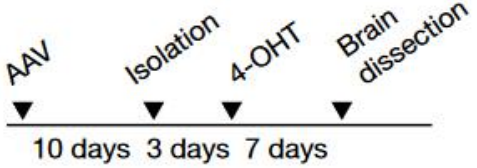


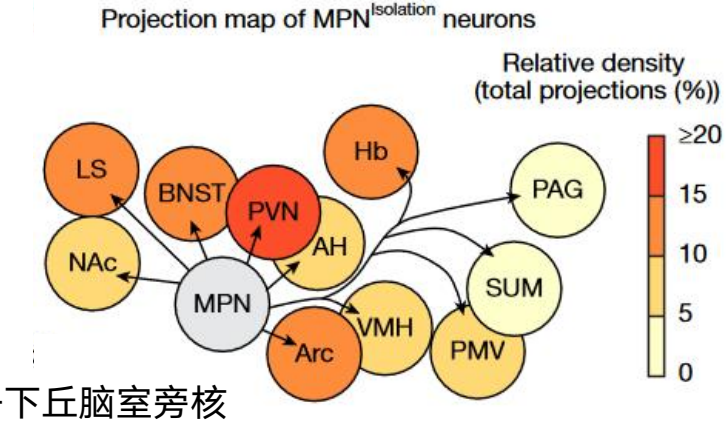
- Altogether, the activity of MPN^{Isolation} neurons seems to be essential to the expression of social need and is sufficient to trigger social interaction in socially satiated mice.

Neural circuits of MPN^{Isolation} neurons



Enhanced Yellow Fluorescent Protein (EYFP)

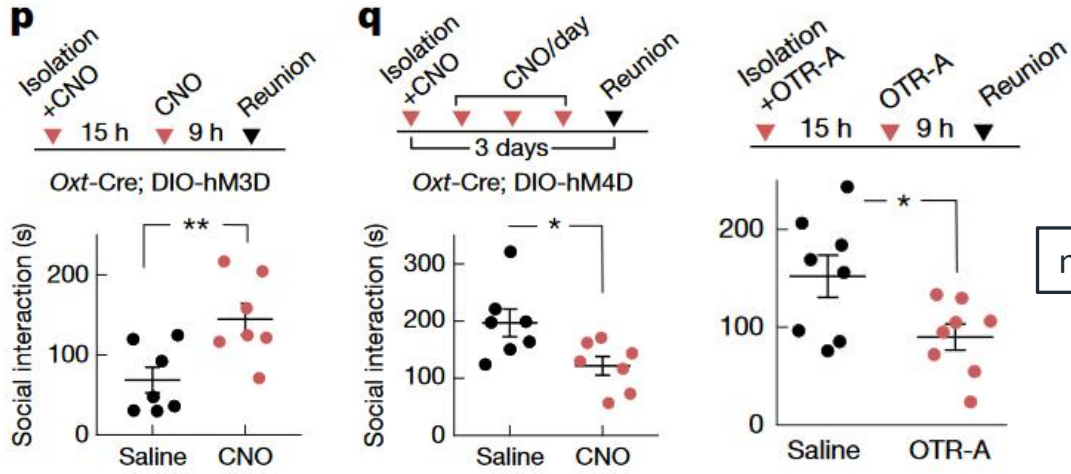




PVN-下丘脑室旁核
Arc-弓状核
VMH-腹内侧下丘脑
SUM-乳头上核
PMV-腹侧预乳头核

- Chemogenetic activation
- Intraperitoneal injection

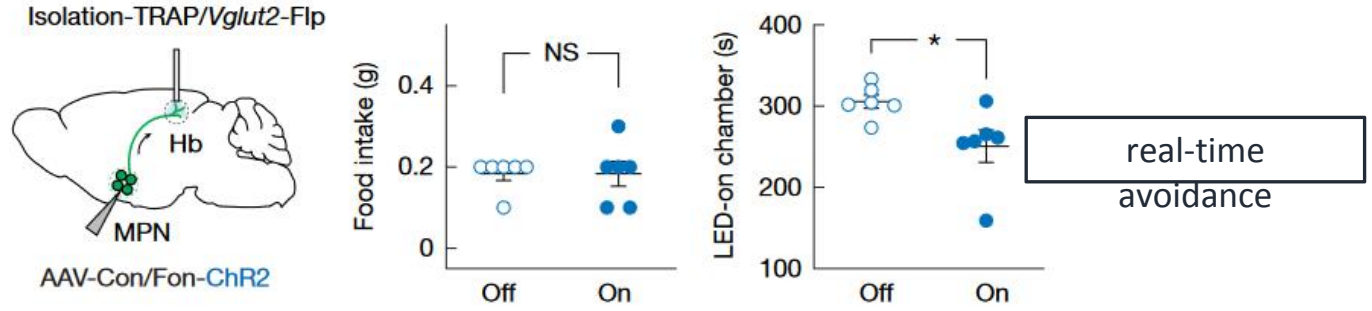
PVN



negative feeling

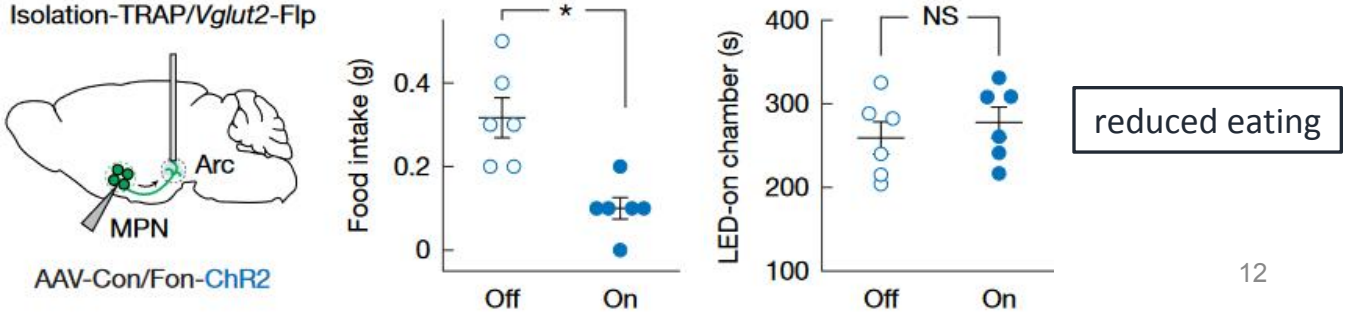
- Optogenetic activation

Hb



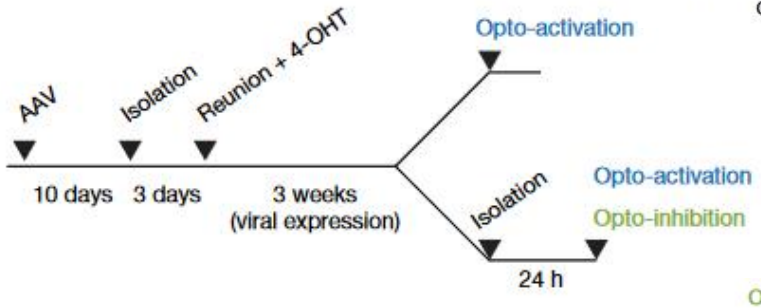
real-time avoidance

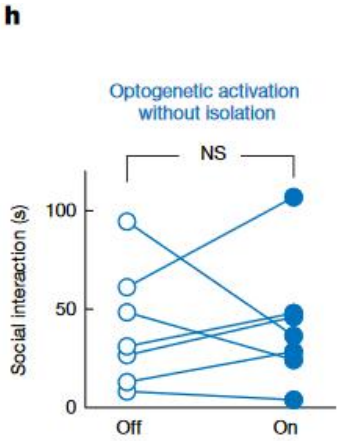
Arc

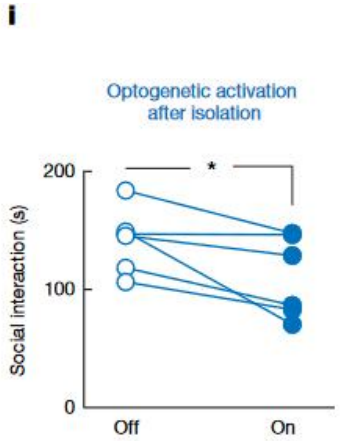


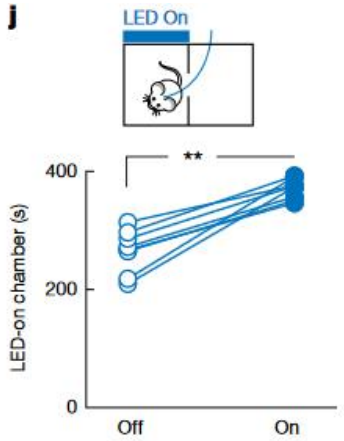
reduced eating

$MPN^{Reunion}$ neurons modulate social satiety

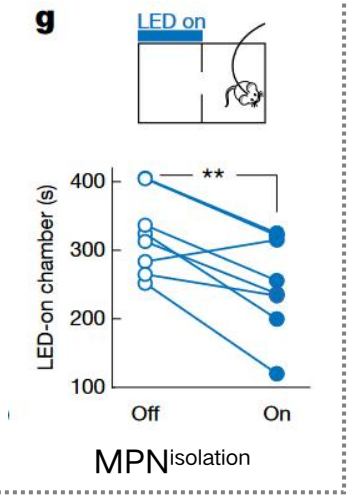


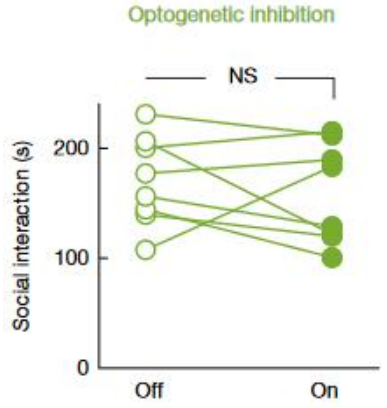




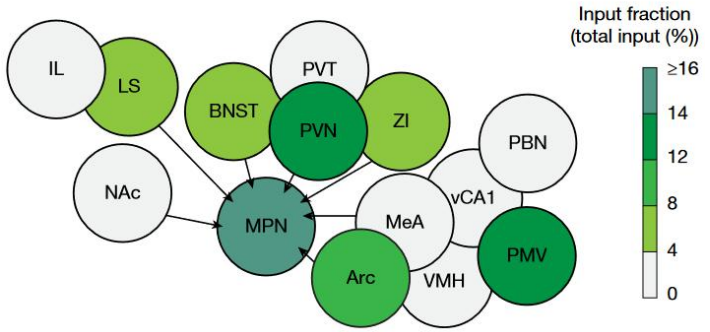


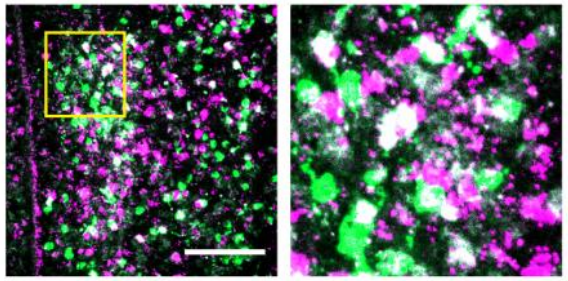
vs.





- $MPN^{Reunion}$ neurons directly synapse onto $MPN^{Isolation}$ neurons.

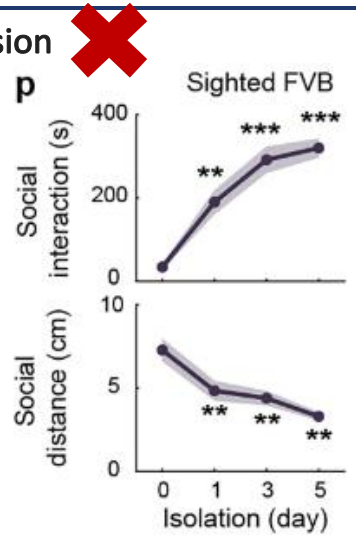


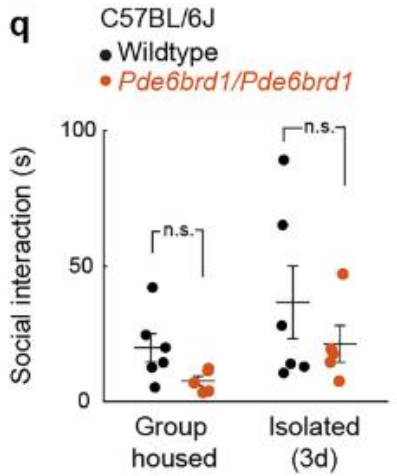


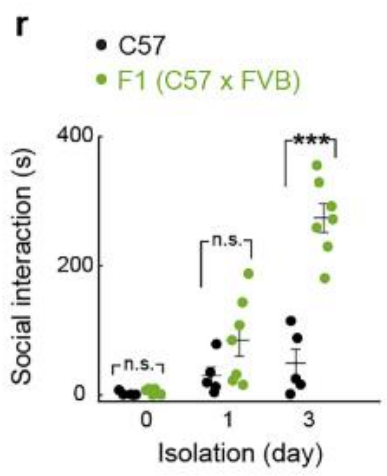
- These connections activate during social reunion.

Sensory basis of social homeostasis

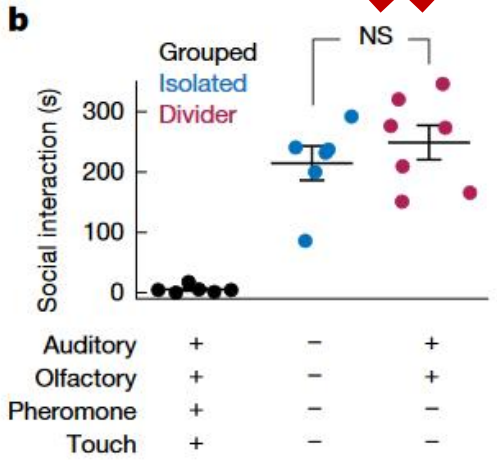
Vision ✖



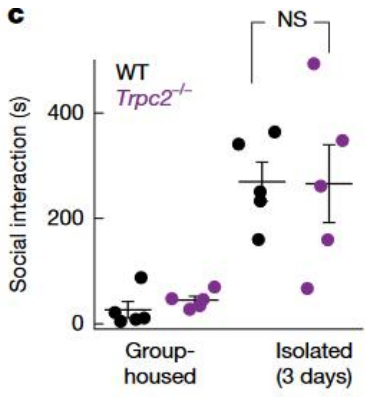


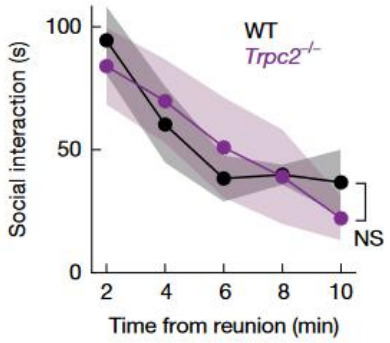


Auditory and Olfactory ✖

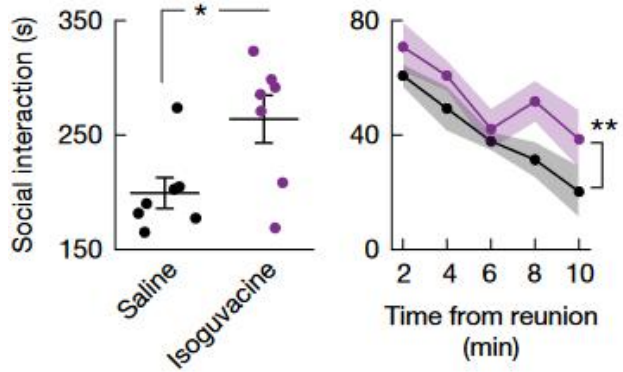


Pheromone sensing ✖

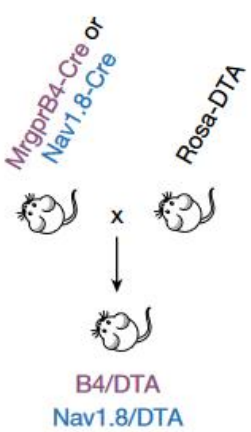


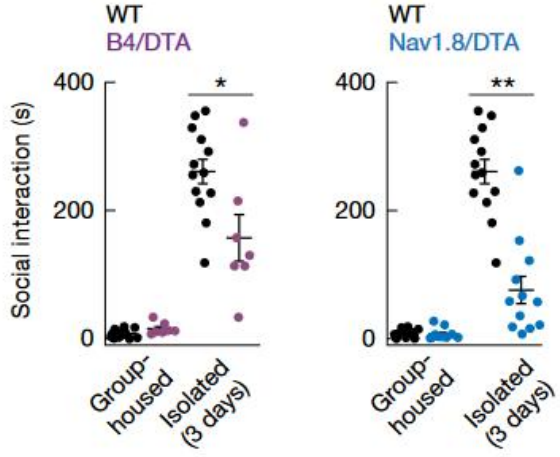


Touch



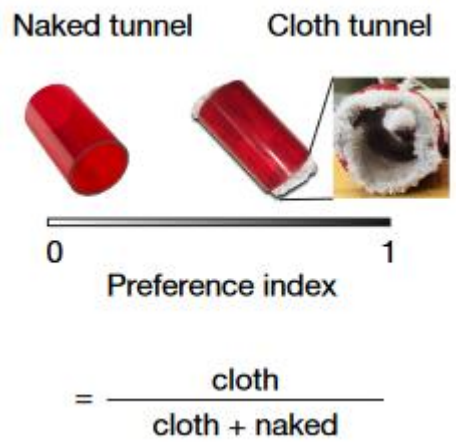
- Prolonged social rebound indicated a delay in the satiation of social need.

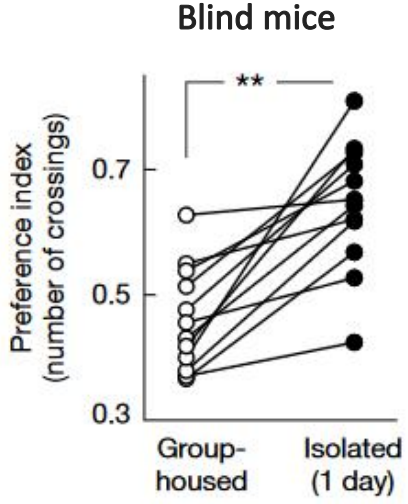


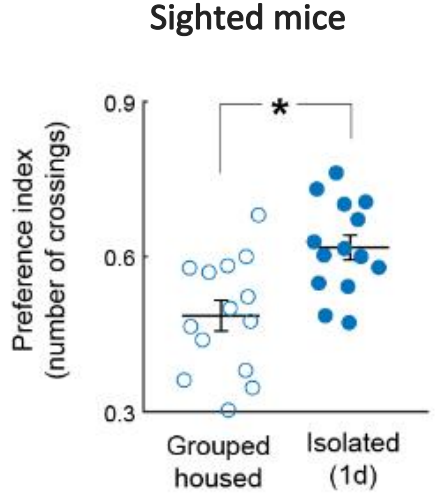


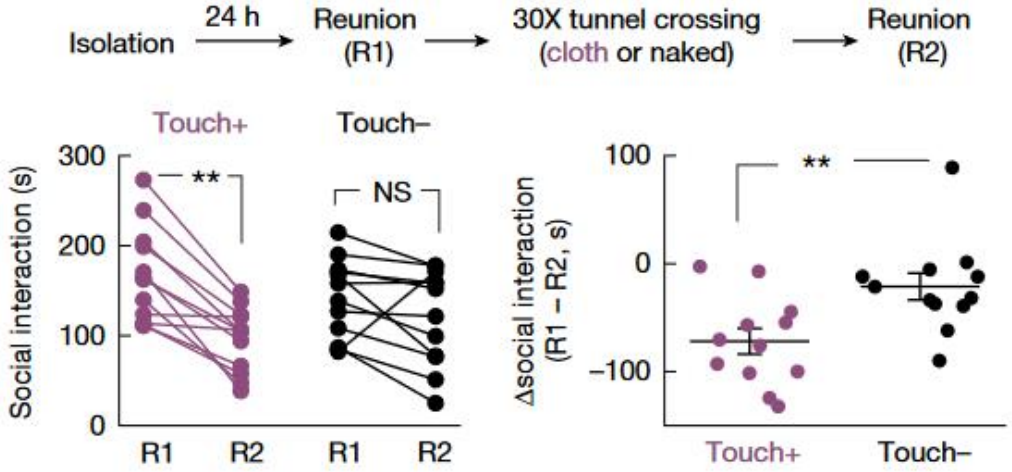
- Loss of mechanosensory neuron reduces sensitivity to social environment and hampers the generation of social drive during isolation.

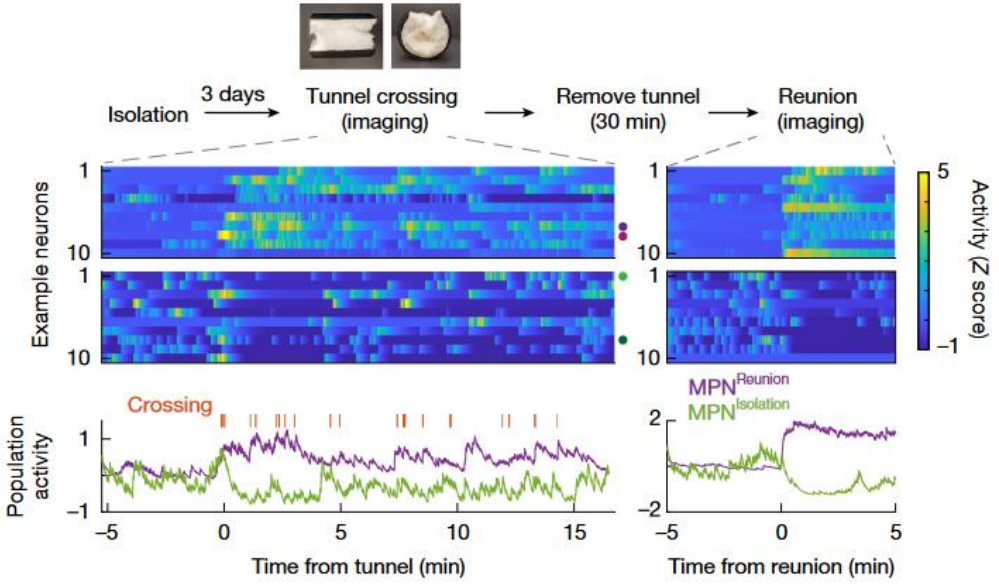
Sensory basis of social homeostasis





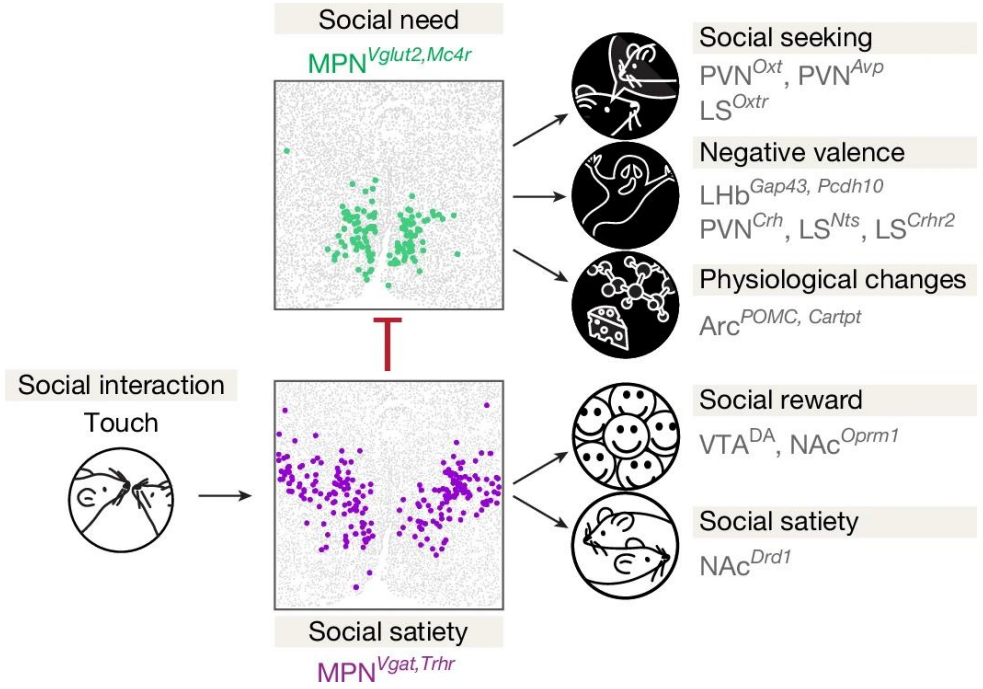






Conclusion

- "Social rebound"occurs after social deprivation, suggesting a homeostatic regulation of social need.
- There are two interconnected hypothalamic neuron types that are activated during either social isolation or social reunion, together orchestrating dynamic switches between "social seeking" and "social satiety".
- Social touch is a key sensory modality for mice to perceive social environment, with lack of touch sensation leading to the emergence of social need, and its presence providing social satiety.
- This project will shed new light into the regulation of social motivation both at the cell-type and circuit-levels.



Future Directions

Direction #1 (social touch)

Context-dependent modulation
Stranger, social crowding

Direction #2 (social need computation)

Natural environment
Need interactions

Direction #3 (evolution)

Parental influence (sugar glider)
Solitary species(hamster)

Direction #4 (sex)

Sex preference

Q & A

Xiaoxu Xu

2025/8/15