

Exercise for BIO-499: Neural Circuits of Motivated Behaviors

Teachers: Ralf Schneggenburger and Olexiy Kochubey

TAs: Jinyun Wu, Runzhong (Yvonne) Zhang

Unit 7 – Internal Body States: Thirst

(Exercise Session Monday 7.4.2025)

1) Read and discuss the following paper:

Augustine, V., Gokce, S.K., Lee, S., Wang, B., Davidson, T.J., Reimann, F., Gribble, F., Deisseroth, K., Lois, C., and Oka, Y. (2018). Hierarchical neural architecture underlying thirst regulation. *Nature* 555, 204-209.

Please be prepared to show and Discuss all main Figures (Figure 1-5),

plus Extended Data Figure 1, 5 and 7.

2) Physical work, especially in hot ambient temperatures, can lead to strong sweating (up to 2 liters/hour), which causes an imbalance in bodily fluids.

i) How are the **osmolality**, and the **volume** of the blood affected after this challenge?

ii) Name, and explain two regulatory pathways in the body which help to re-establish the **hypovolemic effect** of sweating. Mention the terms Angiotensin II and Arginine-vasopressin (AVP) in your explanation. What is the effect on urine production?

iii) By which mechanism is the **osmolality** of the blood re-balanced? Name two involved pathways, starting from the sensors, and explain the main neuronal / endocrinological pathways involved.

3) Which neurons measure the osmolarity of the the blood plasma? Explain in which two brain structures these neurons are located. Does the blood supply of the neurons involve normal brain arteries? Mention the term "blood brain barrier" in your explanation.

4) Explain how the feeling of "thirst" might be created and represented in the brain. Start with the two brain structures that measure the blood osmolality.

- i) To which further hypothalamic nucleus do the above neurons project?
- ii) In turn, to which further brain areas does the latter hypothalamic nucleus project?
- iii) Where in the brain might the subjective feeling of "thirst" be represented?

5) Following drinking in a water-deprived animal, the activity of neurons in the subfornical organ (SFO) rapidly *decays*.

- i) Explain the neuronal circuits, based on the paper by Augustine et al. 2018 (*Nature*; Mandatory reading), which cause the rapid, anticipatory decay of the SFO neuron activity.
- ii) Speculate what the function of the "anticipatory" quenching of the thirst feeling might be in the regulation of fluid balance.