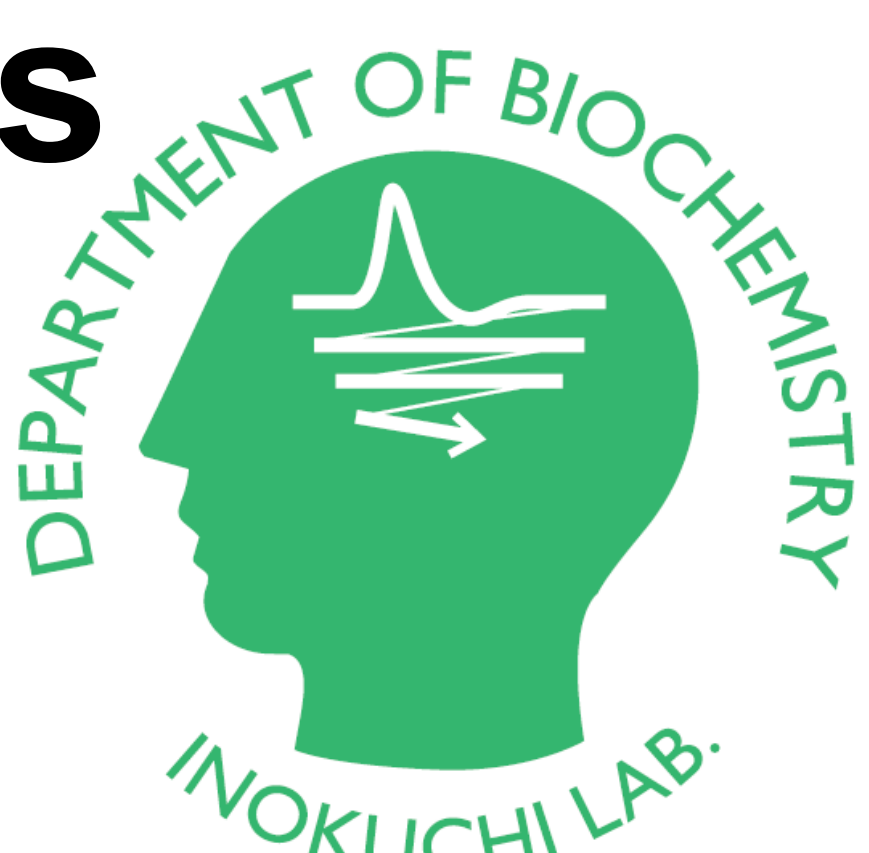


Neuronal ensemble orchestrated intersection of two distinct emotional memory traces

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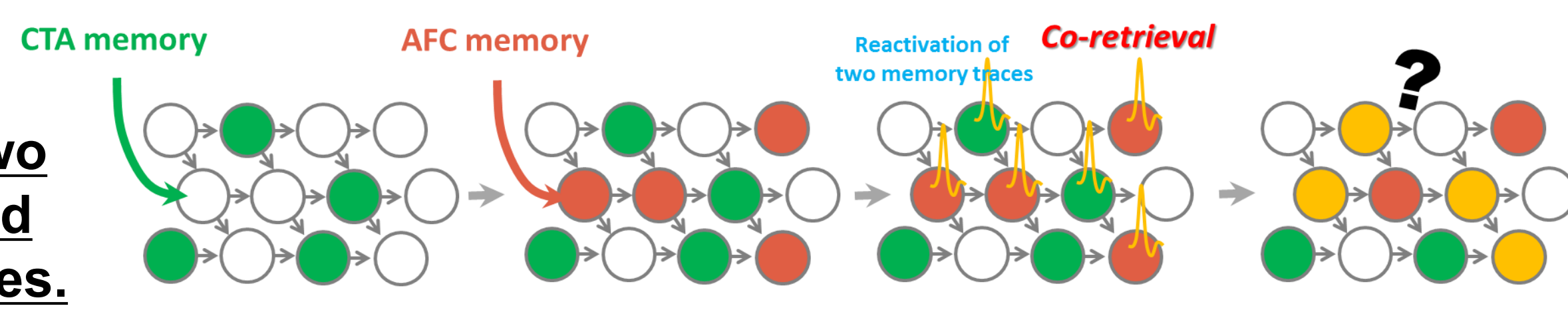
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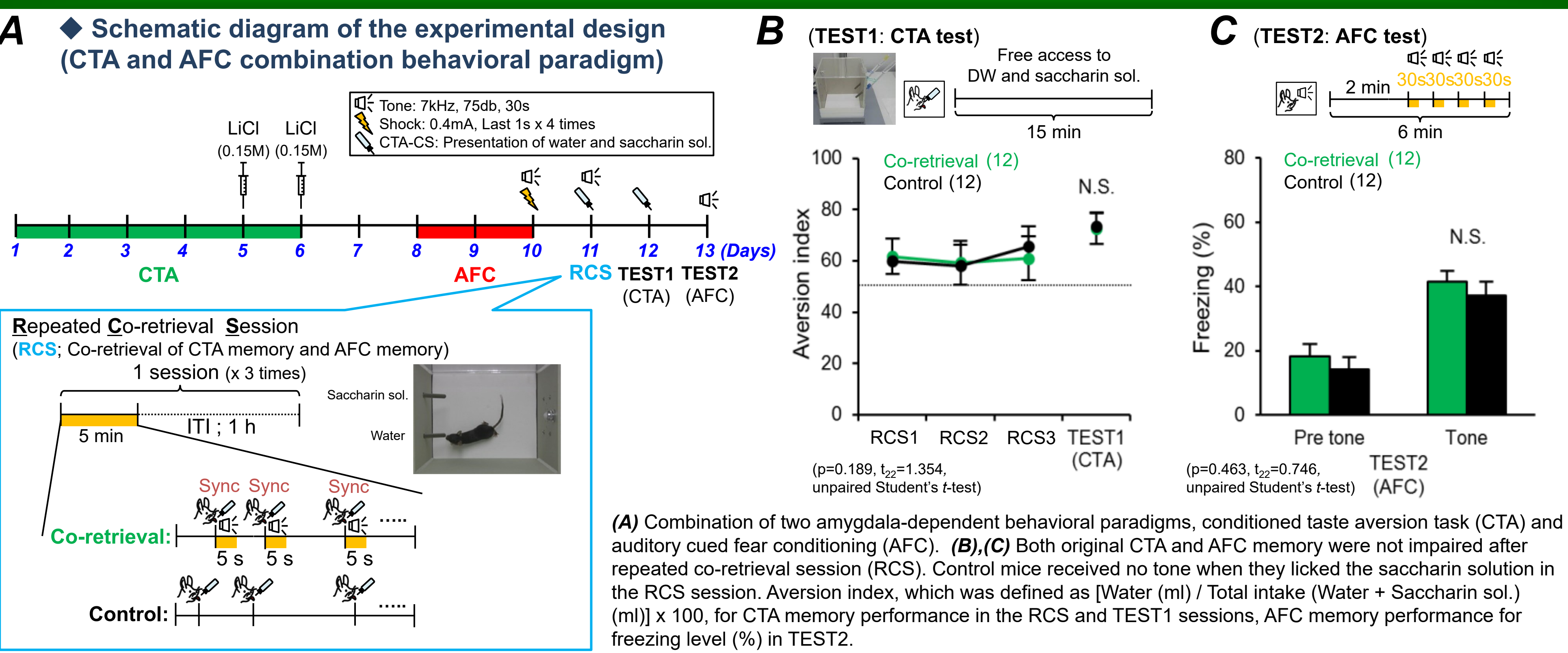
Summary

Memories are not stored in isolation from other memories but are integrated into associative networks^{1,2}. Although recent progresses reveal that a specific neuronal ensemble represents a given memory³⁻⁵, mechanisms underlying the memory association remains elusive. Using two amygdala-dependent behavioural paradigms, conditioned taste aversion (CTA) and auditory-cued fear conditioning (AFC) in mice, we find that presenting the conditioned stimulus used for the CTA task triggers the conditioned response of the AFC task, that is, freezing behaviour, after natural co-reactivation of their memory retrievals, which is accompanied by an increase in the ratio of the co-shared neuronal subpopulation, an overlapping ensemble, in the basolateral amygdala. Optical silencing of the overlapping ensemble suppresses CTA retrieval-induced freezing. However, retrieval of the original CTA or AFC memory is not affected. These results indicate the existence of a small population of co-shared neurons that mediates the link between memories but is unnecessary for recalling individual memories.

Our findings provide new insights into the shared neuronal ensemble is indispensable for the association of two emotional memories but is not required for the retrieval of the original memories.

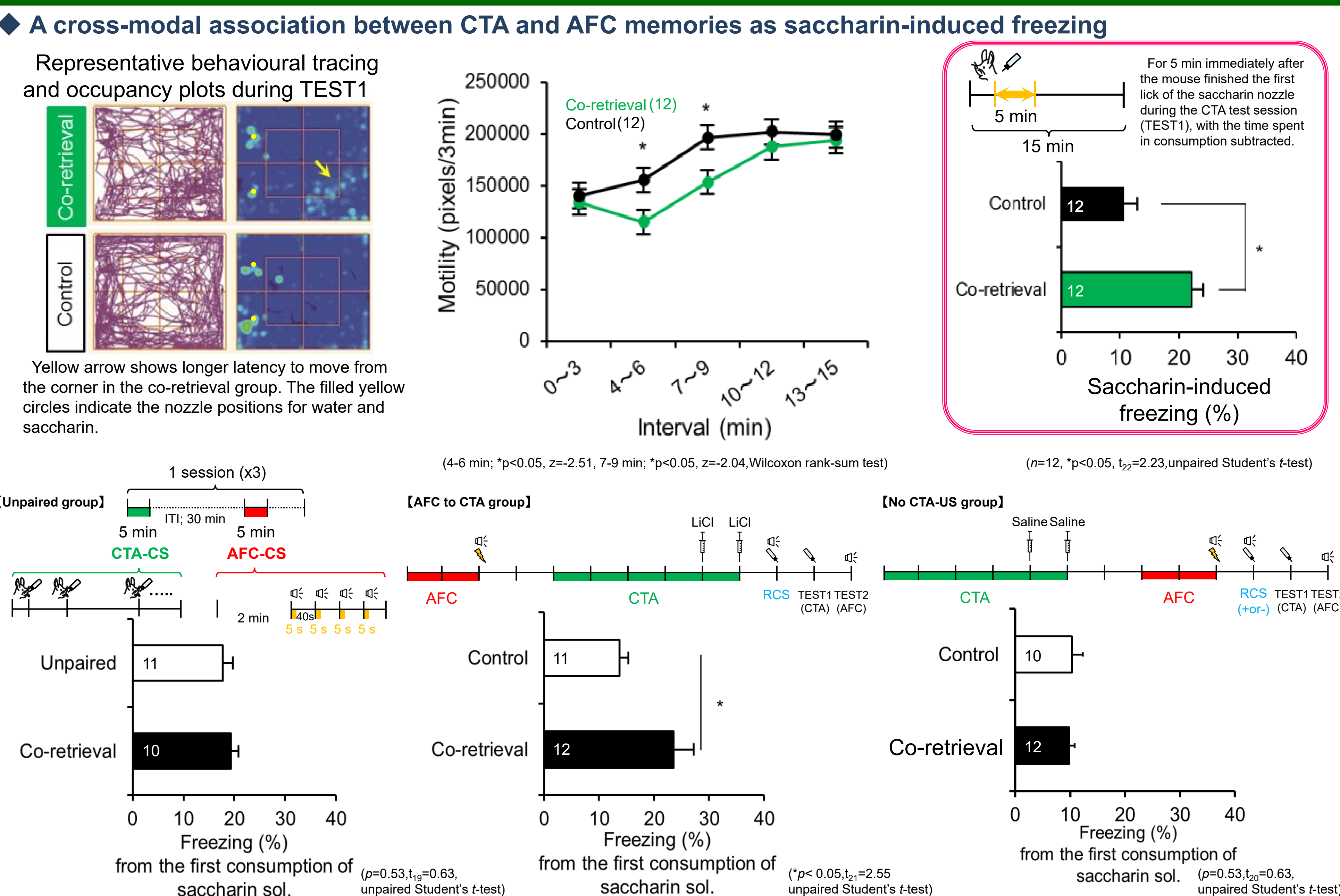


Methodology



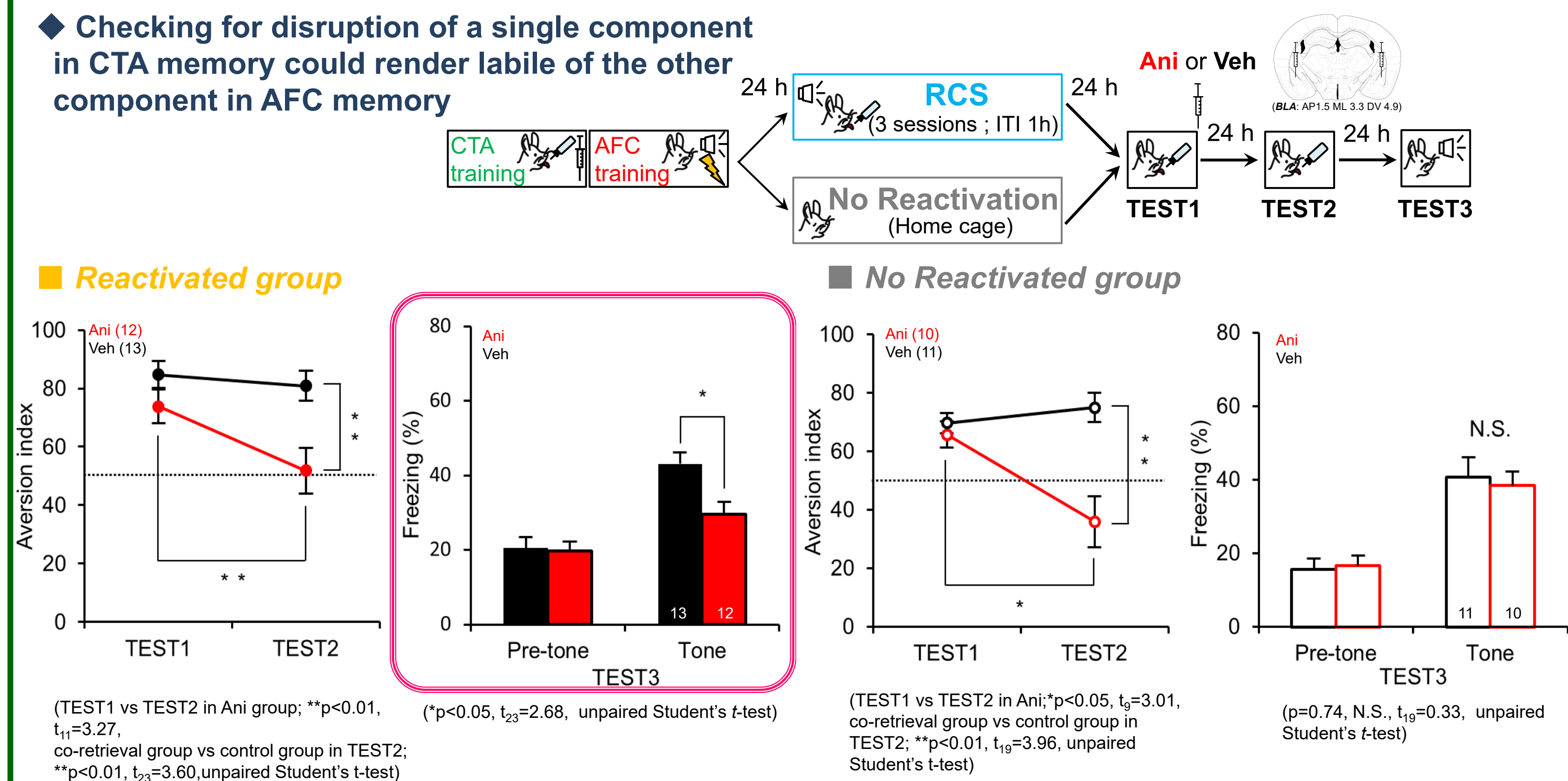
Result 1

Saccharin-induced freezing is generated through repetitive memory retrieval



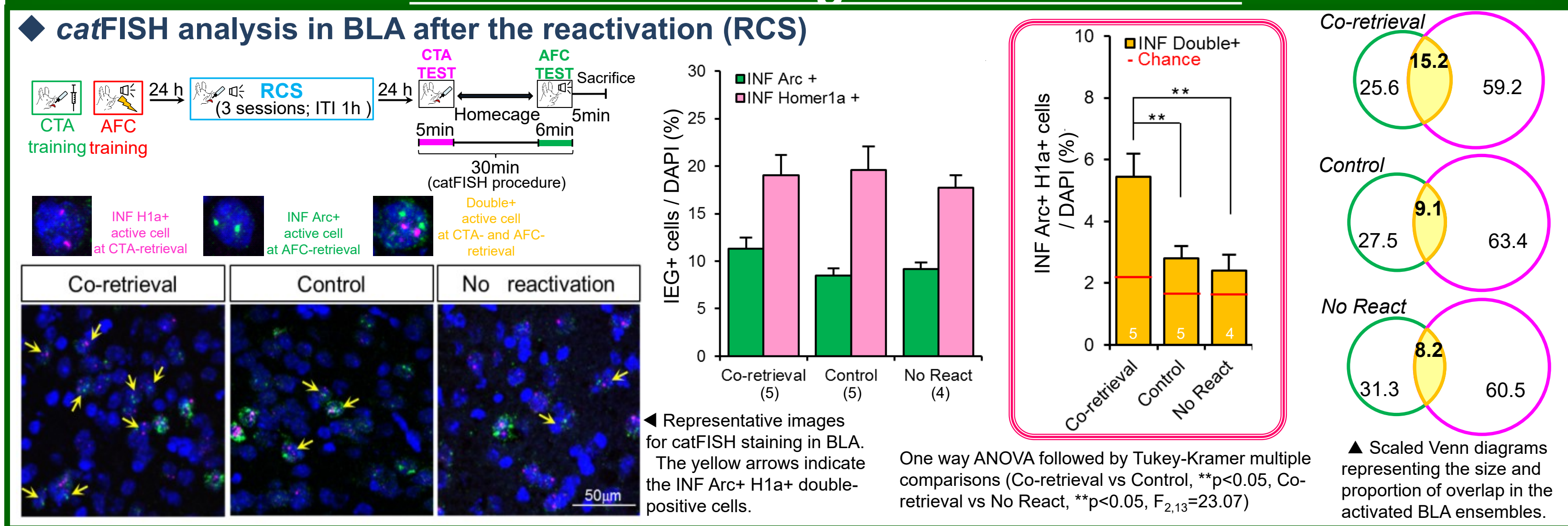
Result 2

Disruption of CTA memory retrieval by blockade of protein synthesis in BLA impairs original AFC memory



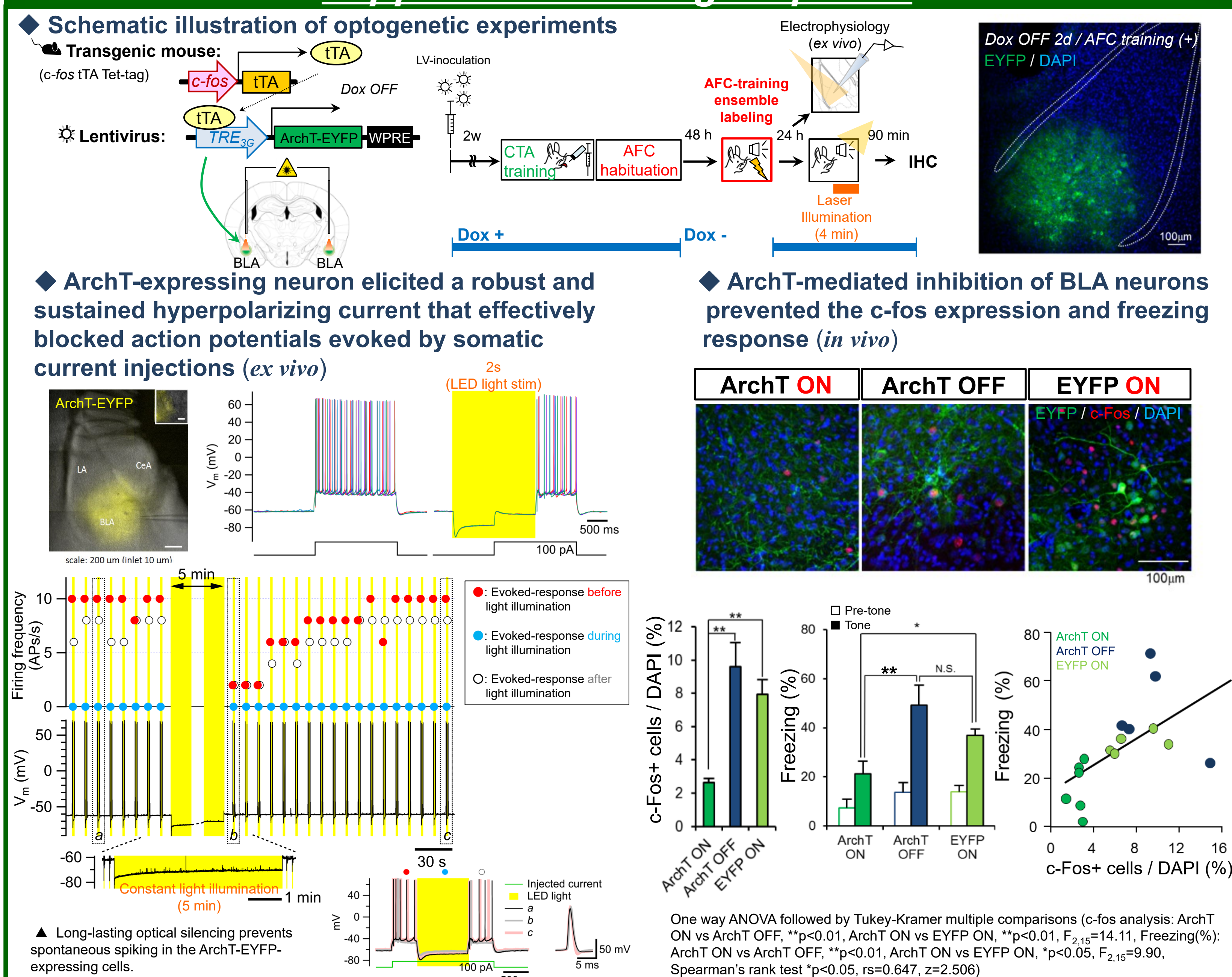
Result 3

Repetitive retrieval-induced plasticity triggers neuronal convergence in the BLA



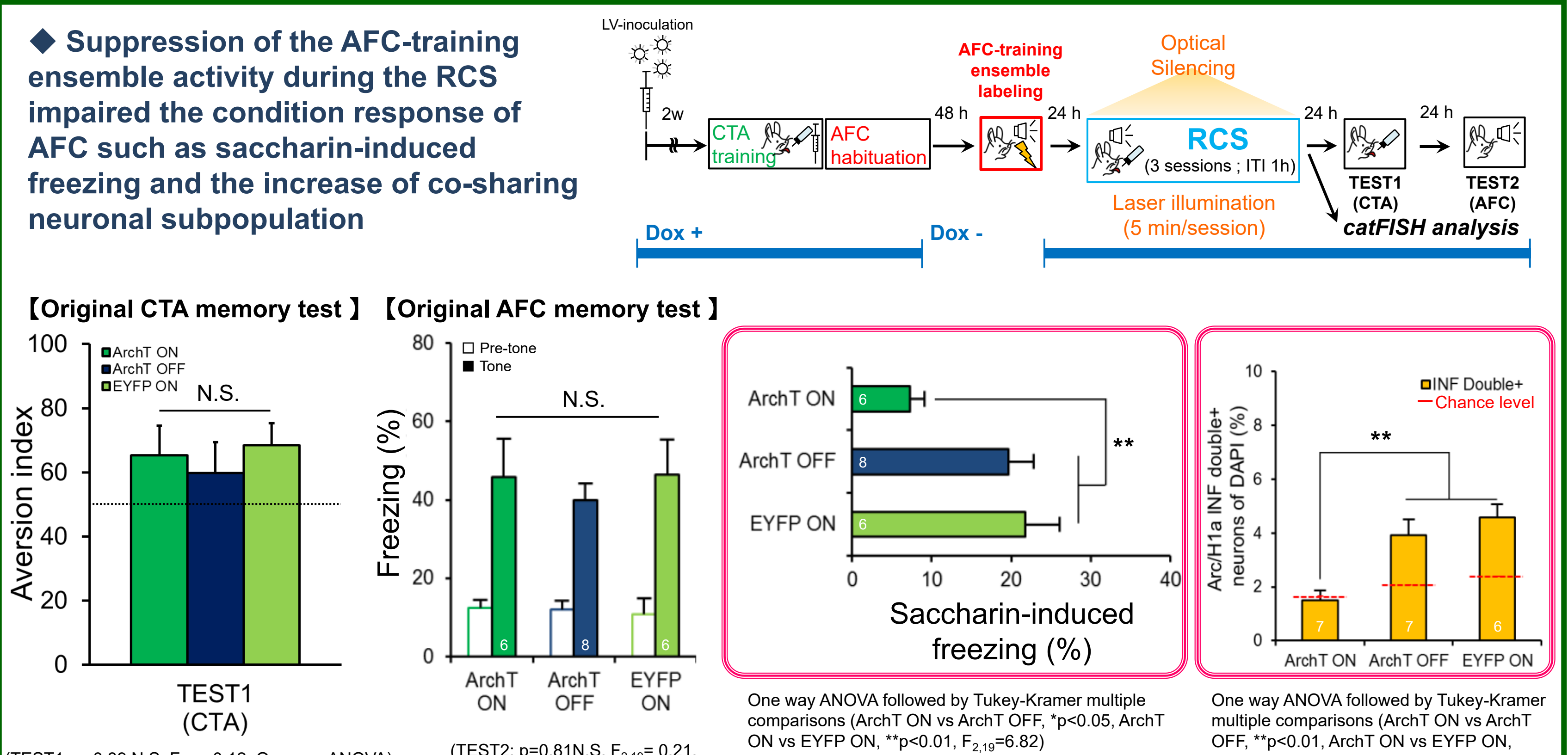
Result 4

Optical silencing of AFC-training ensemble suppresses freezing response



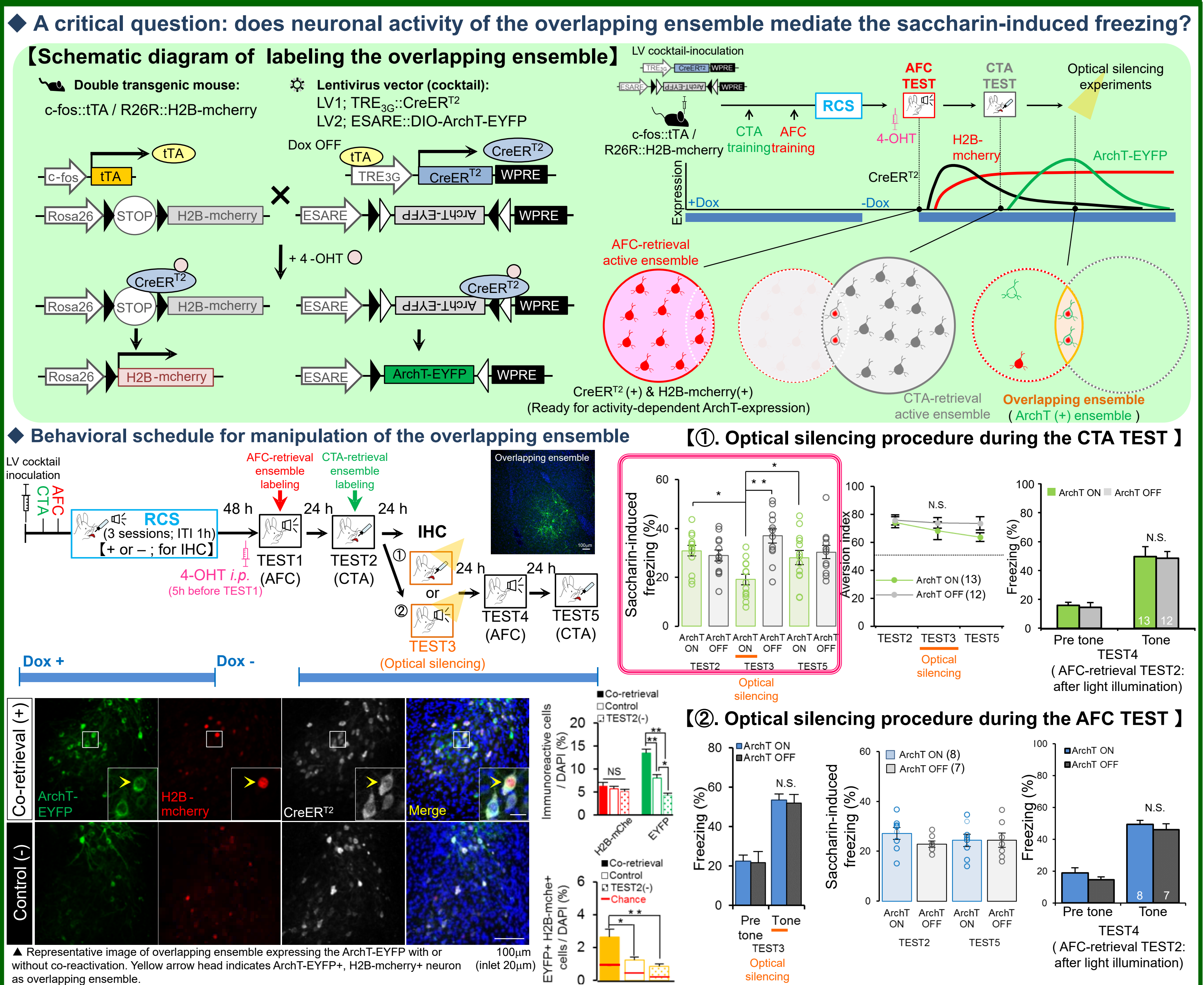
Result 5

Synchronous activity of distinct neuronal ensembles during the RCS generates a link between CTA and AFC memory



Result 6

Overlapping ensemble links two distinct emotional memories



Conclusions

- We show a pronounced property of the shared ensemble. We provide evidence that its neuronal activity is indispensable for the association of two emotional memories but is not required for the retrieval of the original memories.
- Generation of the shared ensemble is not restricted to the memory acquisition, as shown in the aforementioned studies, but is also formed by synchronous and repeated retrieval of once-consolidated memories.
- Our findings provide a fundamental principle for the basis of dissociating unwanted connected memories without affecting the individual original memories.

Reference: 1. D. O. Hebb, *The Organization of Behavior: A Neuropsychological approach* (John Wiley and Sons, New York, 1949). 2. J. R. Anderson, G. H. Bower, *Human Associative Memory*. (Wiley, New York, 1973). 3. X. Liu et al., *Nature* 484, 381-385 (2012). 4. S. A. Josselyn, S. Kohler, P. W. Frankland, *Nat. Rev. Neurosci.* 16, 521-534 (2015). 5. S. Tonegawa, X. Liu, S. Ramirez, R. Redondo, *Neuron* 87, 918-931 (2015).

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