

Songbird Model and Hypothesis

1. How Zebra Finches Help Us Understand Speech Acquisition

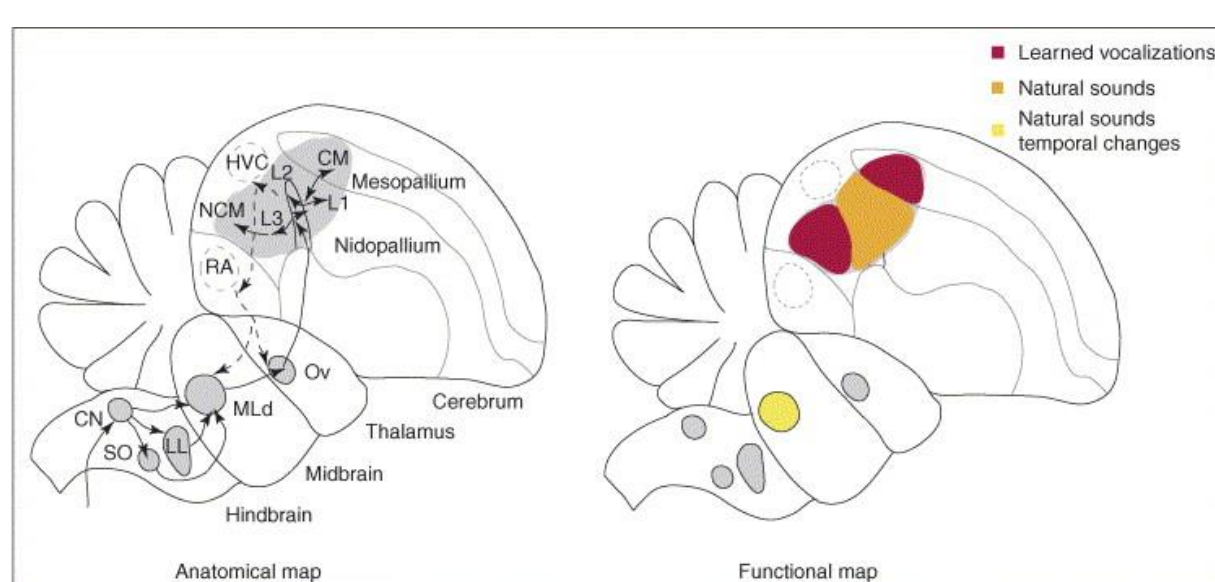


Social animals that heavily rely on auditory system for communication

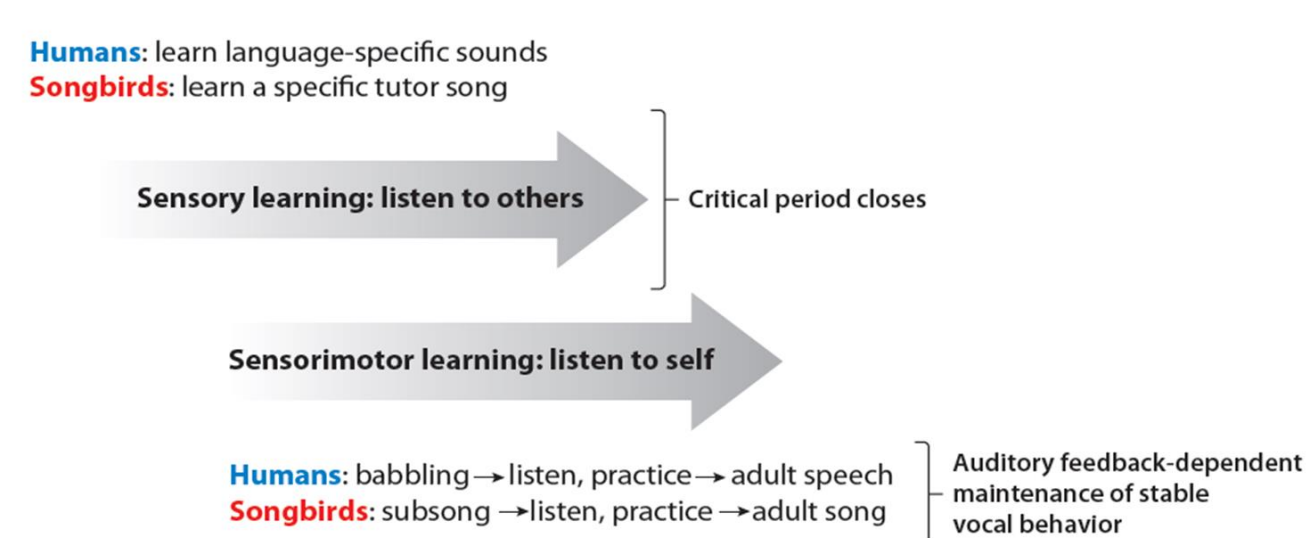
They learn to sing by copying their father, similar to how infants learn to speak by copying parents

They have a higher auditory region similar to secondary auditory cortex in humans

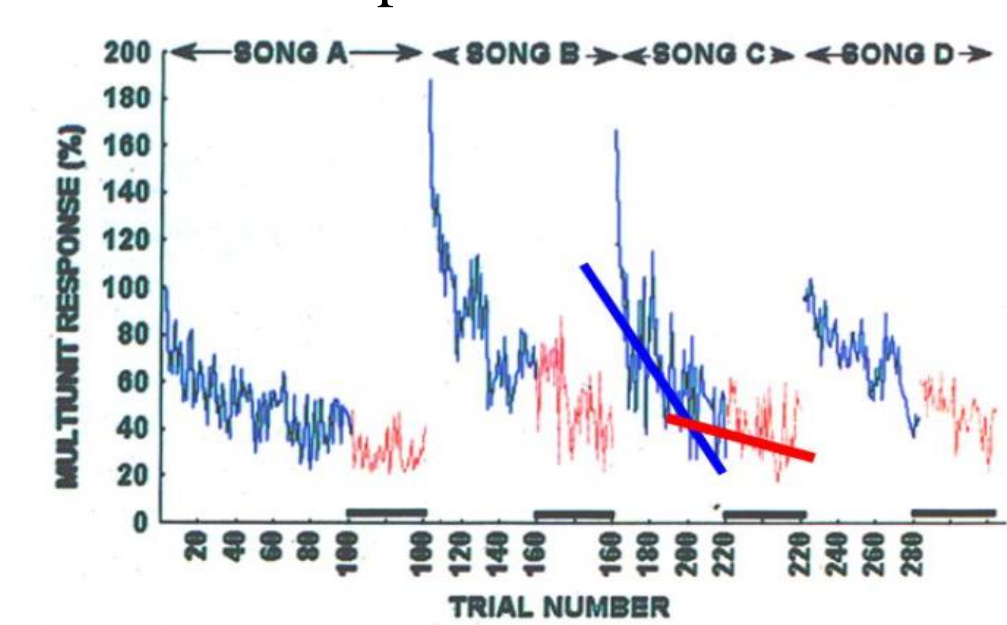
3. Anatomical and Functional Maps of Songbird Brain



2. Song Learning in Zebra Finches

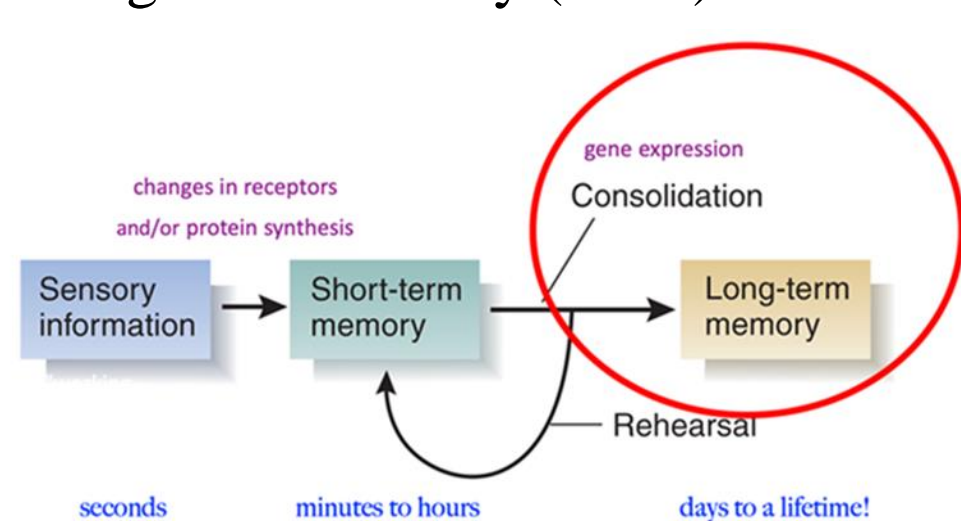


4. Adaptation in NCM

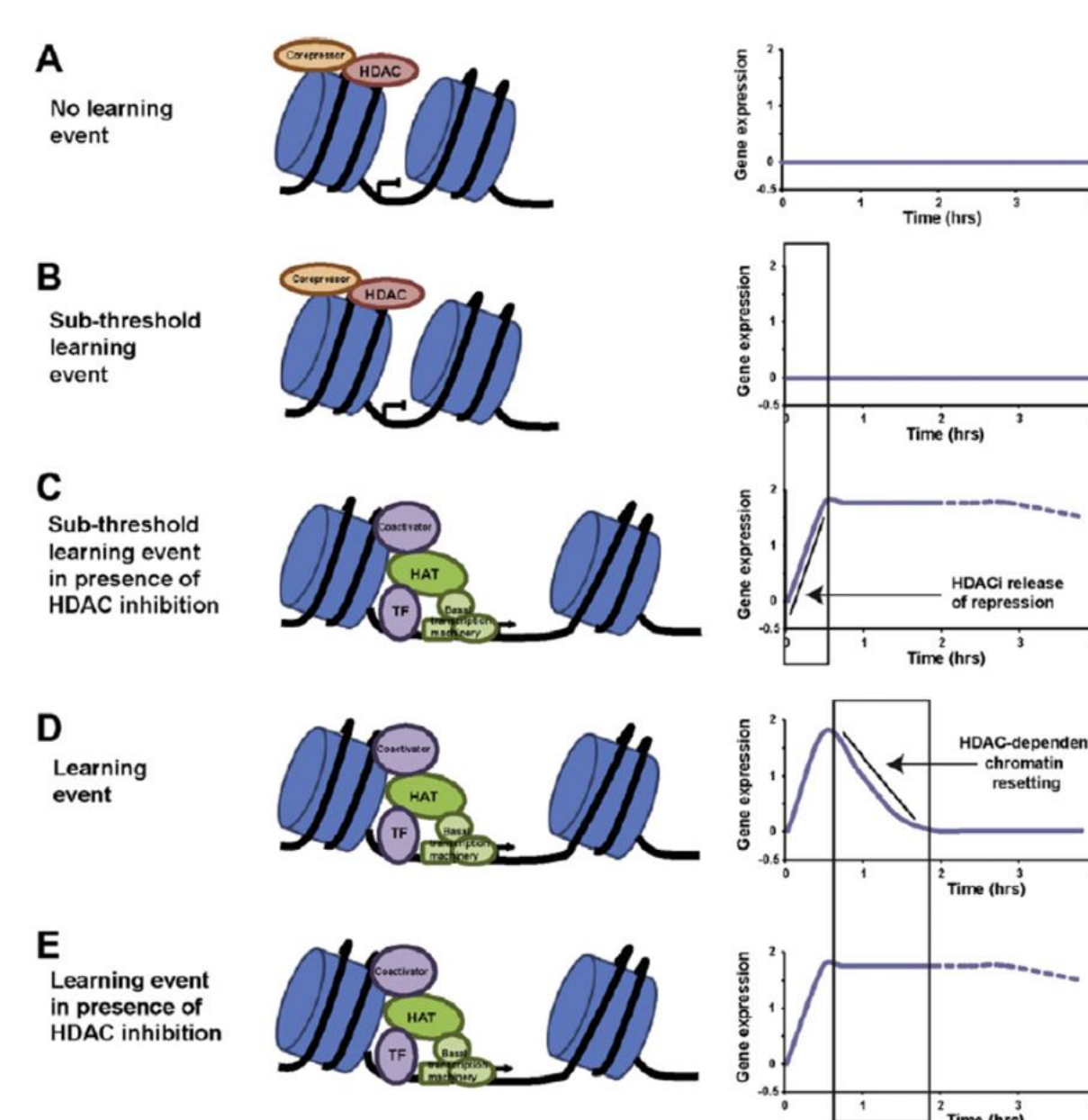


Stimulus Specific Adaptation

5. HDAC3 represses gene expression needed for long-term memory (LTM) formation



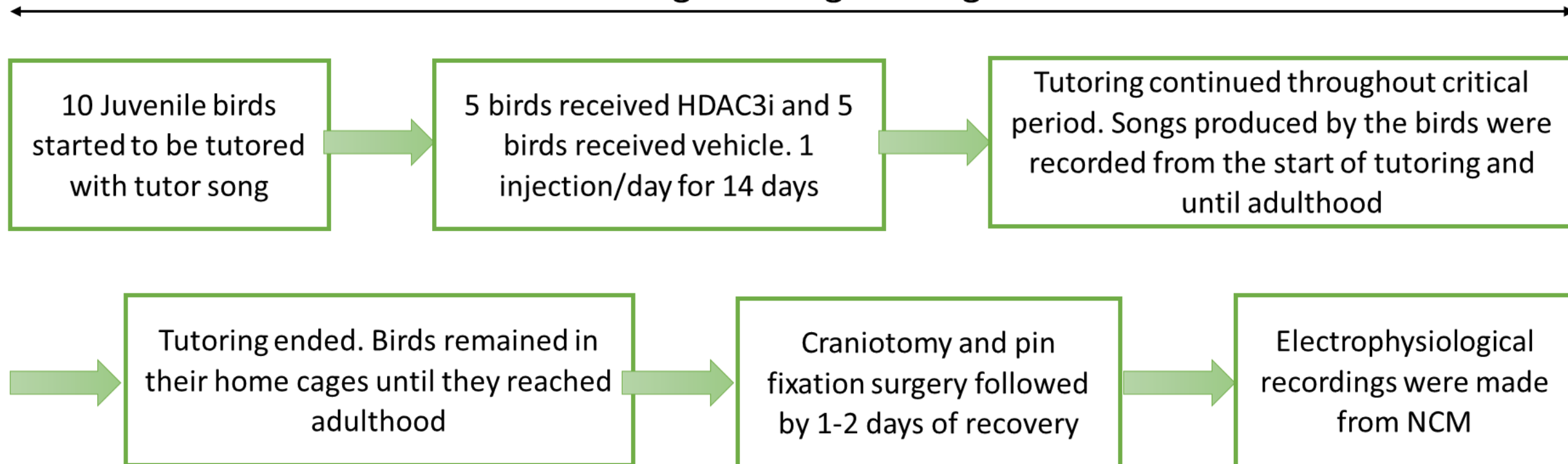
6. By inhibiting the enzyme HDAC3 using HDAC3i long-term memory (LTM) formation can be improved



Hypothesis: Pharmacological intervention using HDAC3i (RGFP966) improves the quality of song imitation and decreases variability in song learning in juvenile zebra finches by strengthening the long-term memory for the tutor song in NCM.

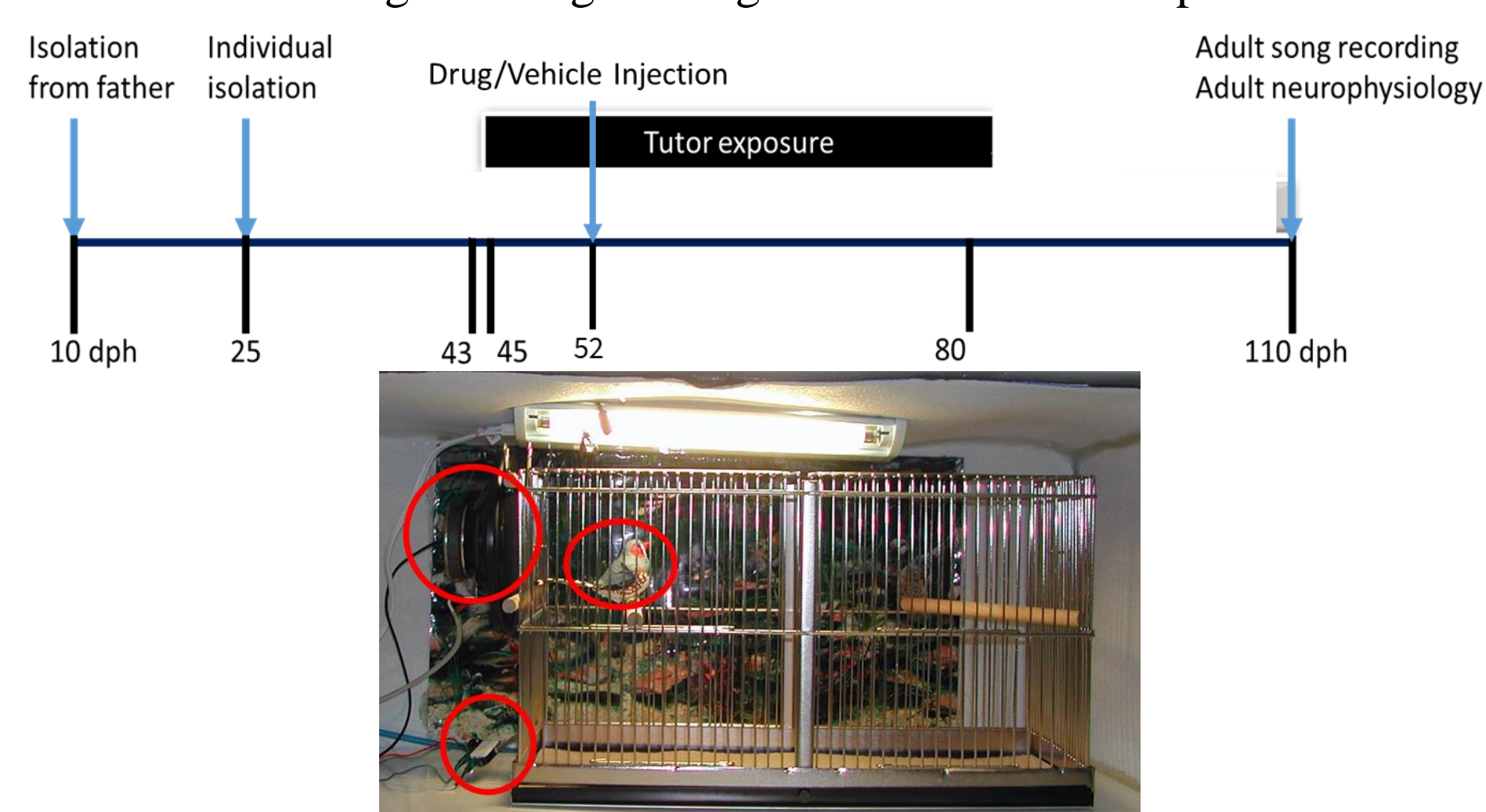
Methods

1. Song Tutoring Paradigm



2. Neurophysiological Recordings

Song Tutoring Paradigm Timeline and Setup

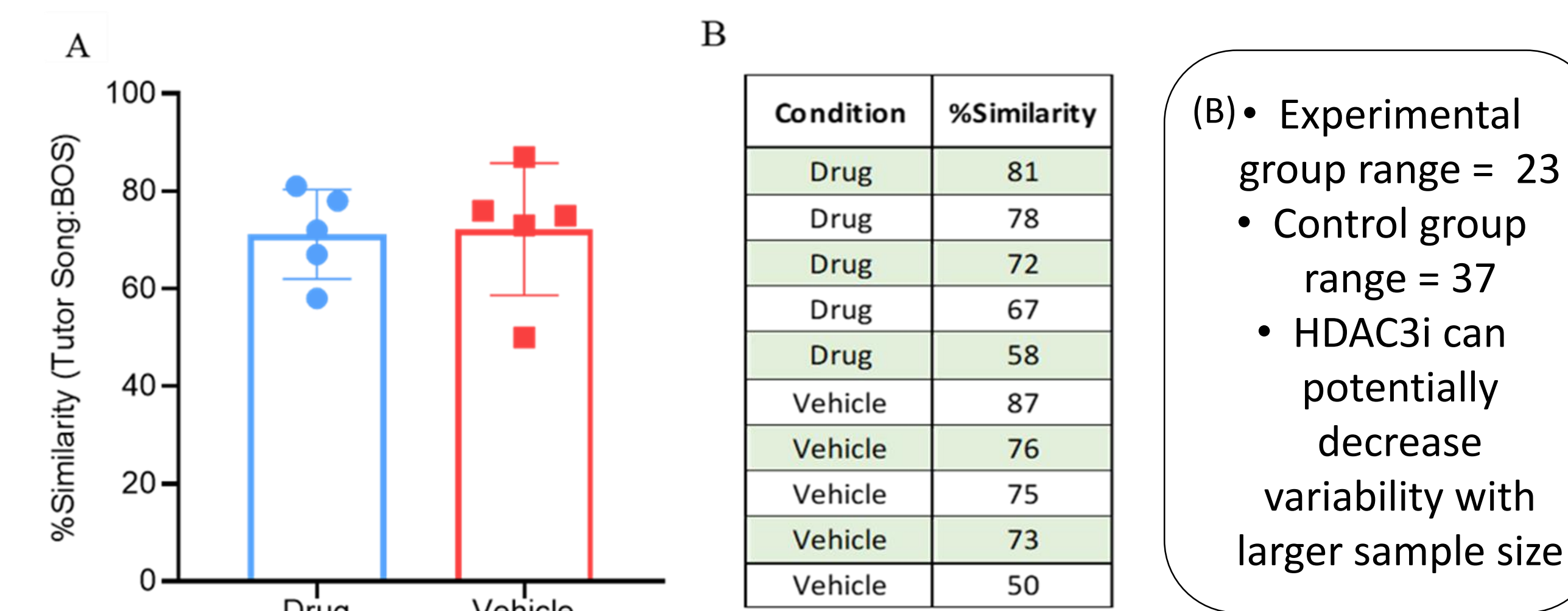


Memory Strength is Quantified Using the Familiarity Index

$$FI = \frac{\text{Rate of Adaptation}_{\text{Novel}}}{\text{Rate of Adaptation}_{\text{Familiar}}}$$

FI near 1 → no memory of tutor song
FI > 1 → memory of tutor song

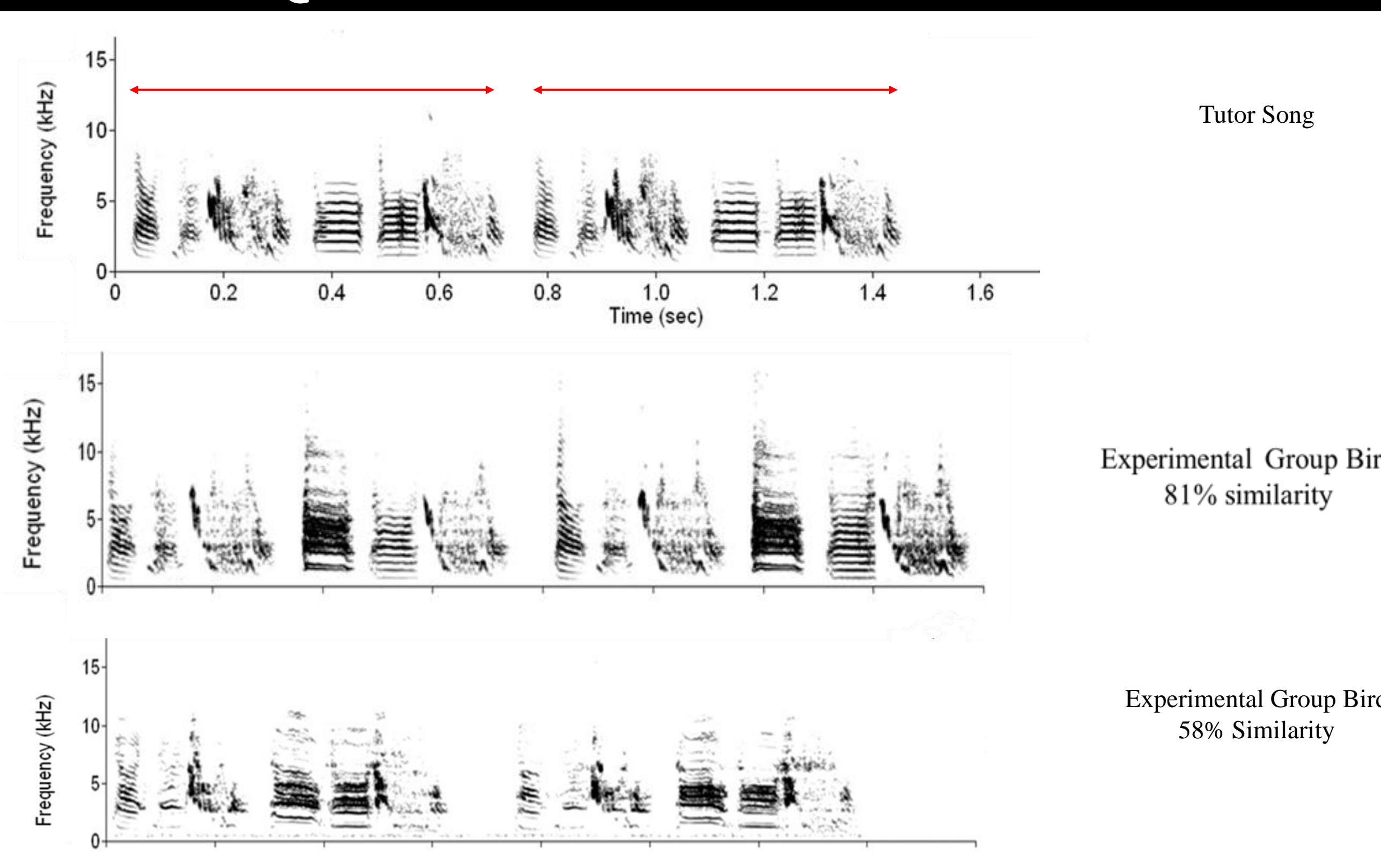
HDAC3i Did Not Improve Song Imitation But It Decreased Learning Variability



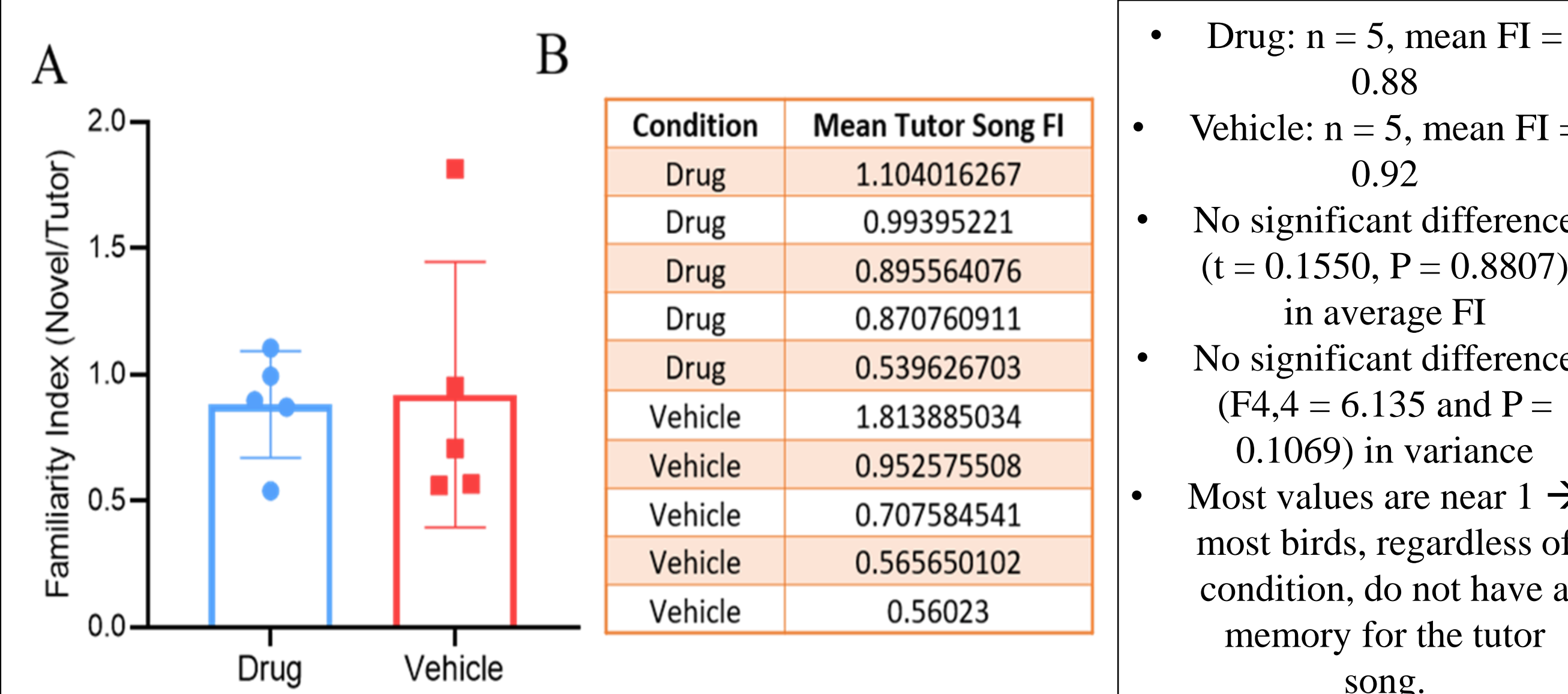
- (A)
- Drug: n = 5, mean SI = 71.2, SD = 9.149
 - Vehicle: n = 5, mean SI = 72.2, SD = 13.55
 - No significant difference in mean SI (t = 0.1367, P = 0.89)
 - No significant difference in variance (F_(4,4) = 2.195, P = 0.65)

- (B)
- Experimental group range = 23
 - Control group range = 37
 - HDAC3i can potentially decrease variability with larger sample size

Qualitative Assessment of Imitation

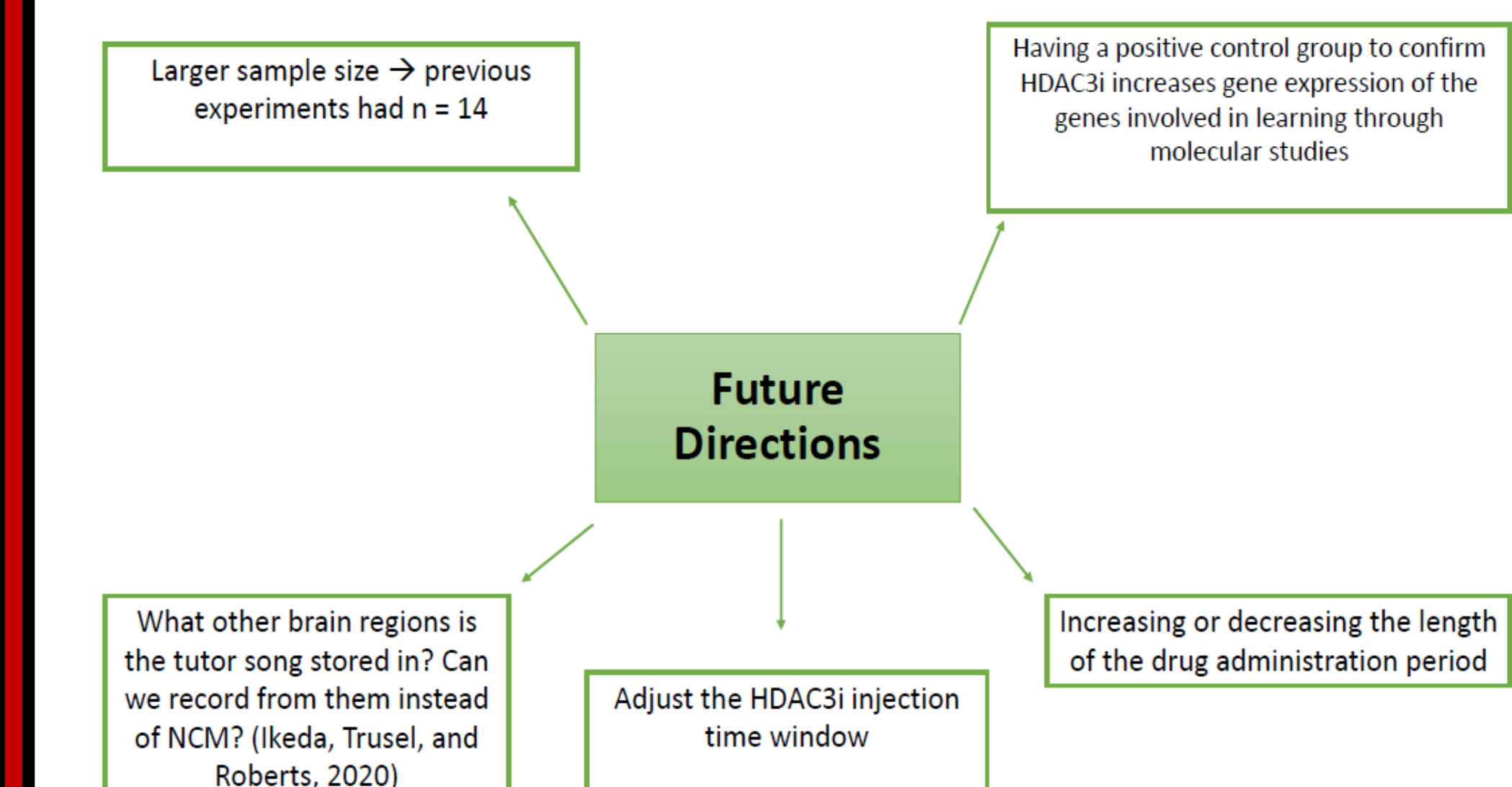


HDAC3i Did Not Strengthen LTM for Tutor Song



Summary and Conclusions

- Observations:
 1. HDAC3i did not improve song imitation.
 2. HDAC3i did not improve memory formation.
 3. There was less variability in imitation among experimental group birds as predicted by our hypothesis, but this result did not reach significance.
- Our project is the first to test the effects of HDAC3 inhibition in juvenile zebra finches.
- Existing literature shows that inhibiting HDAC3 improves LTM in rodents and adult zebra finches.
- Our findings suggest that HDAC3i may not work in the same way in juvenile birds as it did in adult zebra finches.
- However, we are planning to run the experiment on more birds in order to increase the sample size and reassess tutor song memory and imitation.



Significance

Studying neural mechanisms underlying vocalizations and ways to improve them gives us a better understanding of how to enhance speech development and language acquisition in humans. Additionally, the formation of long term memories can be essential for survival and learning; therefore, it is of importance to investigate ways to enhance the process of long-term memory formation. By testing the effects of HDAC3i on the quality of song imitation and the variance in song learning through behavioral and electrophysiological analysis, this experiment is investigating whether it is possible to use epigenetic manipulation to improve a pre-existing system by which zebra finches learn and produce songs.

References and Acknowledgements

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- References:**
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Ikeda, M., Trusel, M., & Roberts, T. (2020). Memory circuits for vocal imitation. *Current Opinion in Neurobiology*, 60, 37–46. <https://doi.org/10.1016/j.conb.2019.11.002>
Phan, M., Pytte, C., & Vicario, D. (2006). Early auditory experience generates long-lasting memories that may subserve vocal learning in songbirds. *Proceedings of the National Academy of Sciences*, 1088–1093.
Theunissen, F., & Shaevitz, S. (2006). Auditory processing of vocal sounds in birds. *Current Opinion in Neurobiology*, 16(4), 400–407. <https://doi.org/10.1016/j.conb.2006.07.003>