Inter-region interactions encode real-time adaptive biasing of performance during motor skill learning

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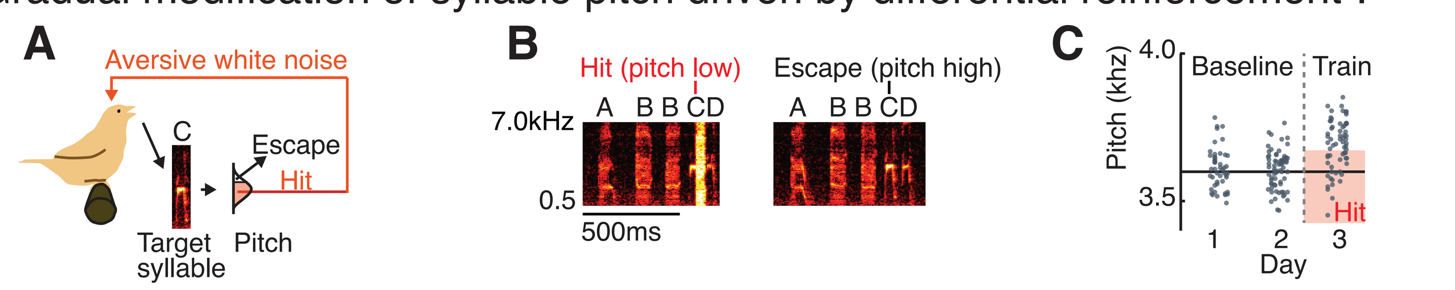
Background

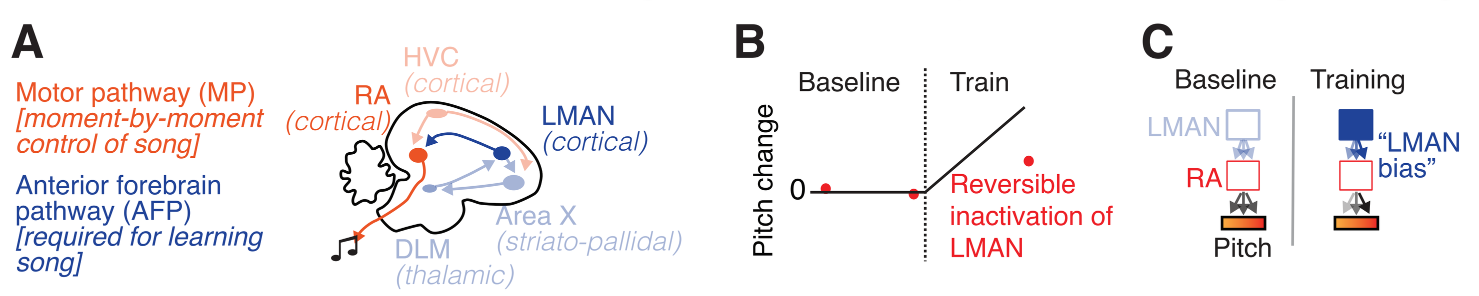
Motor skills flexibly adapt to environmental changes or to cognitive demands[1]. Neural recordings and perturbations suggest an important role for top-down input from higher-order motor areas, likely by biasing activity in primary motor areas[2]. How does this biasing input drive behavioral adaptation?

A behavioral paradigm to study motor skill adaptation.
Gradual modification of syllable pitch driven by differential reinforcement[3].



(N.B. both up and down shifts are possible)

A neural circuit for learning pitch modifications.
LMAN activity adaptively biases pitch, presumably mediated through RA. This is inferred from studies inactivating LMAN[4] or its inputs to RA[5] during learning.



Three alternative models for how this bias is implemented:
(1) LMAN conveys **real-time, or moment-by-moment, motor instruction** specific to the the motor features being modified (i.e., syllable, context, and pitch).
(2) LMAN conveys a **slow modulatory signal**, which lacks specificity for the timing and context of the motor features being modified. This is analogous to anticipatory attentional and motor biasing that alters the baseline activity of superior collicular motor fields for saccades[6].
(3) LMAN activity is **permissive** for the expression of plasticity that occurs downstream in the *motor pathway*.

Methods

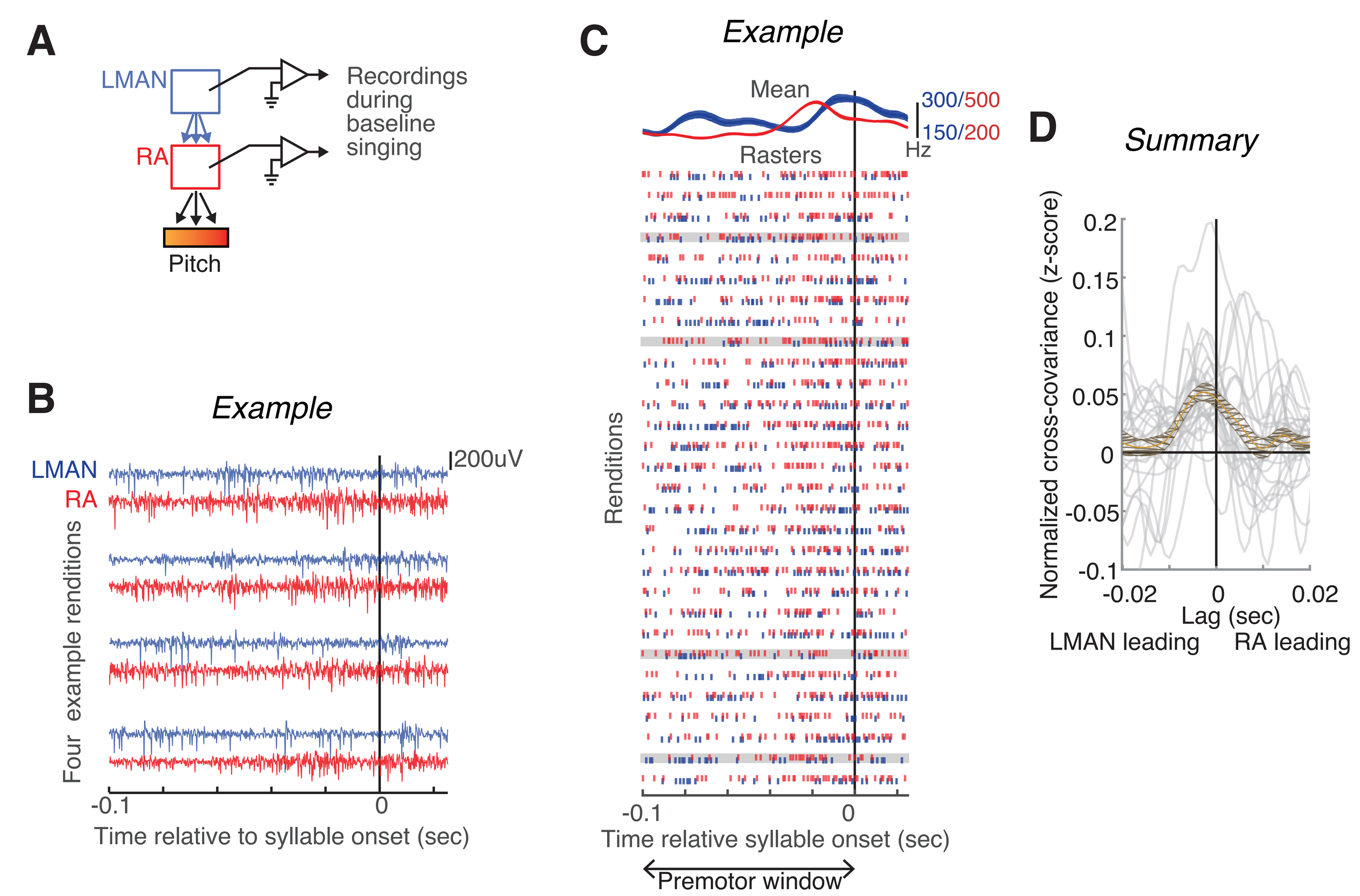
We developed an approach to identify a neural correlate of LMAN bias during learning. We recorded multi-unit activity concurrently in LMAN and RA in Bengalese finches during learning, with arrays of 4-6 tungsten electrodes attached to movable microdrives in LMAN and RA.

We computed the cross-covariance of spike patterns in LMAN and RA (2.5 ms spike bins), separately for each syllable's premotor window (100 ms) and at different timepoints during learning. Cross-covariance was normalized by z-scoring against trial-shuffled data, which removes the influence of the similarity of across-rendition means of LMAN and RA activity.

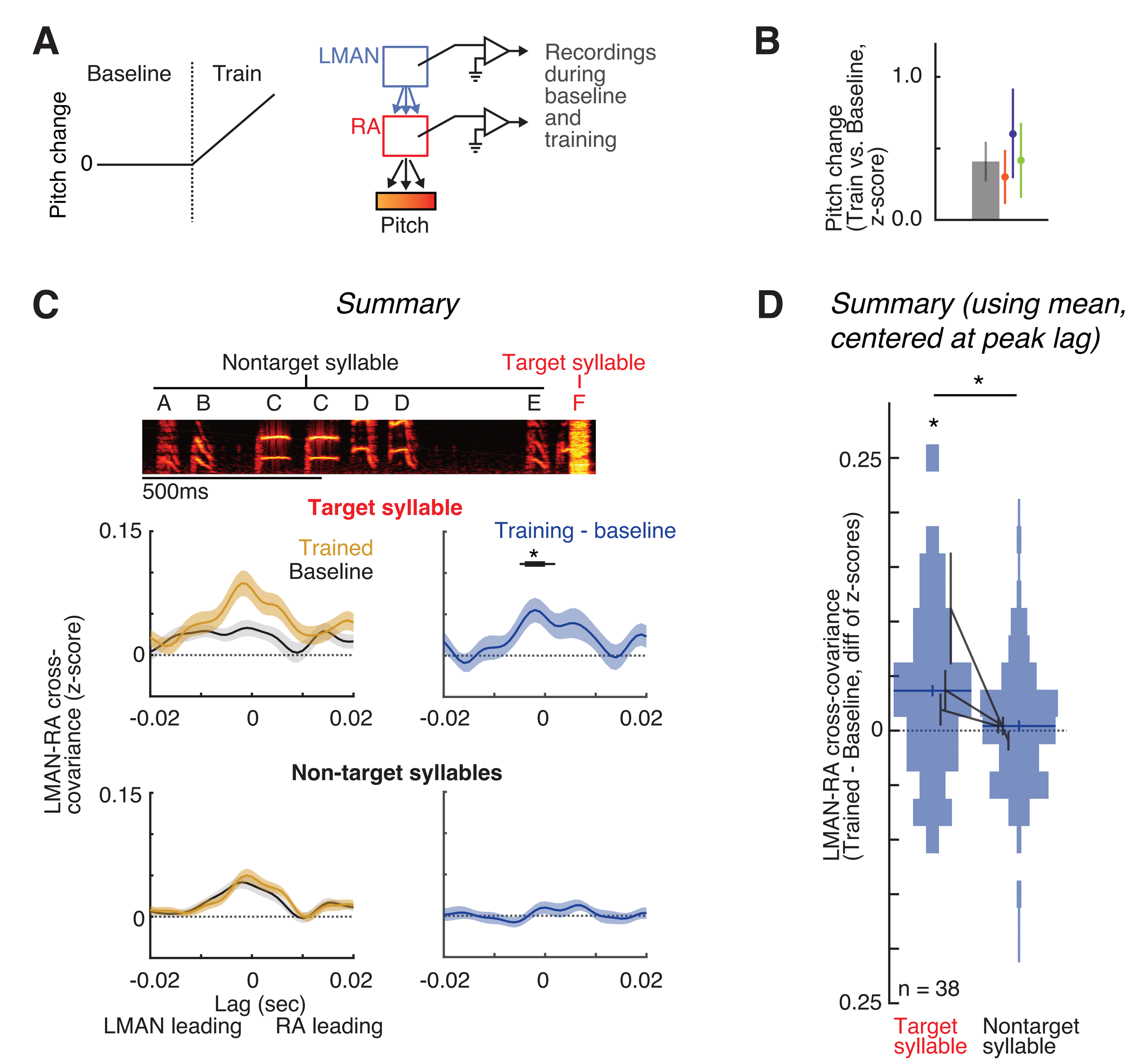
Prior studies in sleeping and anesthetized birds indicate that LMAN-RA cross-covariance reflects synaptic input from LMAN to RA[7]. This causal interpretation is also supported by the lack of direct feedback from RA to LMAN and the lack of obvious common input that could account for the short-lag timing of the cross-covariance peak.

We tested whether LMAN-RA cross-covariance changes during learning, and how those changes relate to behavioral features.

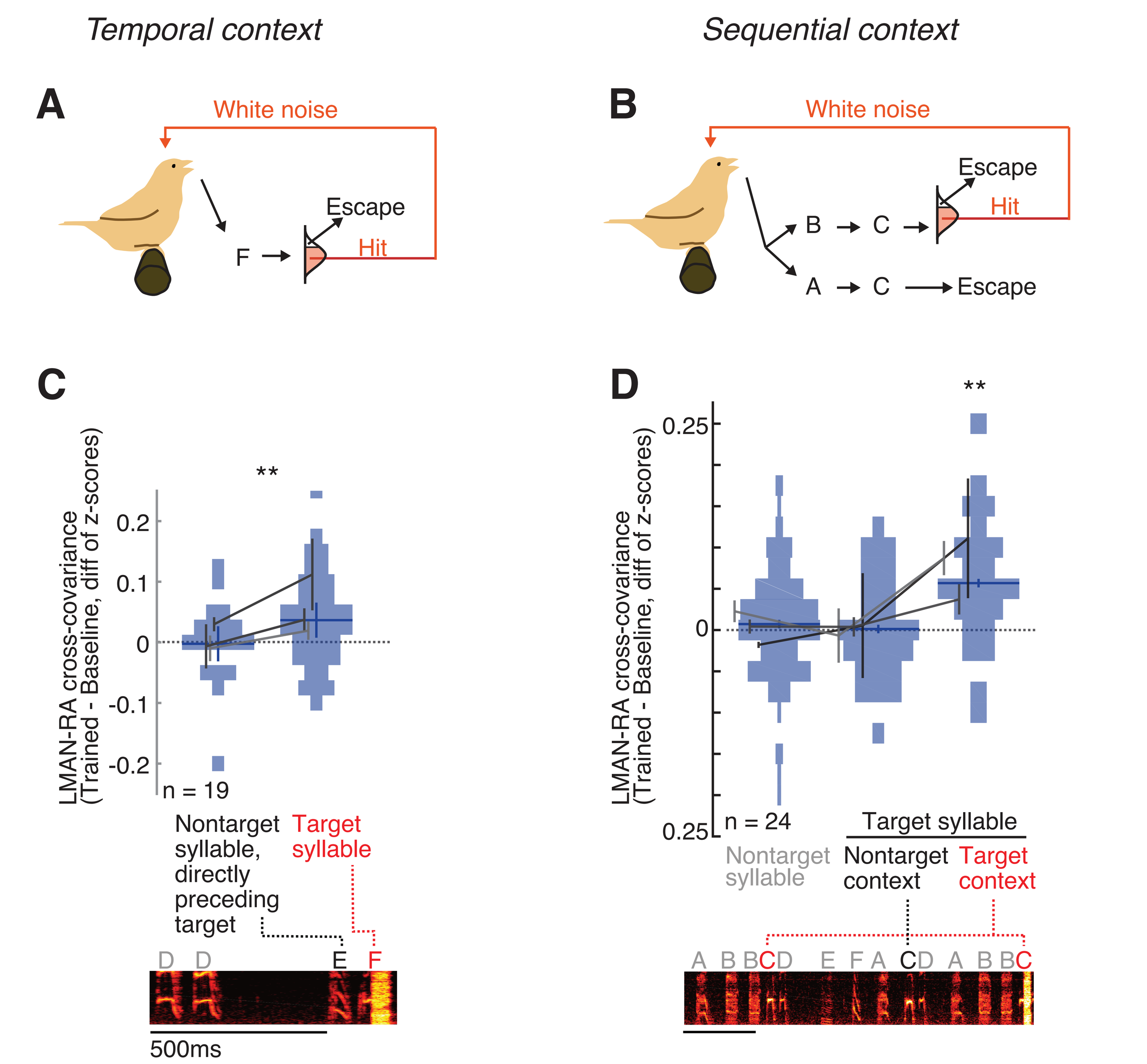
Result 1: A neural signature of LMAN-RA interaction during baseline singing.



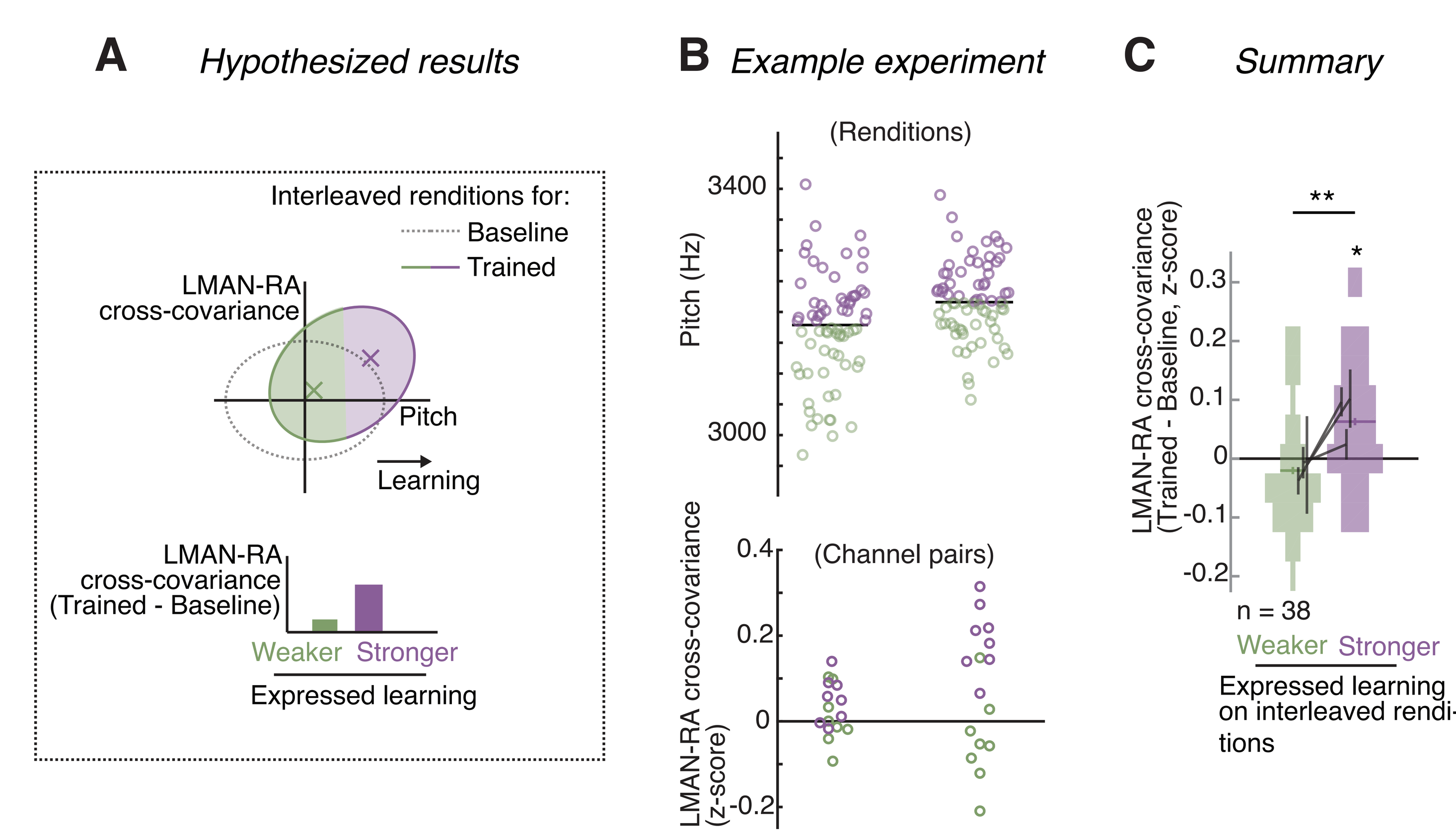
Result 2: LMAN-RA interaction strengthens specifically for the syllable targeted for learning.



Result 3: The strengthening of LMAN-RA interaction is context-specific.



Result 4: Rendition-by-rendition variation in LMAN-RA interaction predicts rendition-by-rendition variation in expression of learning.



Conclusions

We identified a neural signature of LMAN bias: LMAN-RA cross-covariance (Results 1, 2). The increase in LMAN-RA cross-covariance was specific to temporal and contextual features targeted for learning (Result 3) and was correlated on a rendition-by-rendition basis with the expression of learning (Result 4). **These data suggest that LMAN bias is real-time motor instruction (Model 1).**

LMAN may learn instructive signals through plasticity that integrates context, motor state and performance feedback.

More generally, real-time top-down motor instruction may contribute to other motor skills that demand temporal- and context-specific control, and those known to involve inter-area interactions[8], including in cortical-basal ganglia circuits[9].

We speculate that instructive bias may gradually "train" downstream motor circuits, leading to lasting, adaptive updates to motor skills encoded in primary motor areas.

References

1. e.g., **Wolpert, D. M., Ghahramani, Z., & Flanagan, J. R.** (2001). Trends in cognitive sciences, 5:487-494; **Taylor, J. A., & Ivry, R. B.** (2014). In Progress in Brain Research 210:217-253).
2. **Doyon, J., Ungerleider, L. G., Squire, L., & Schacter, D.** (2002). Neuropsychology of memory, 3:225-238; **Shadmehr, R., & Holcomb, H. H.** (1997). Science, 277:821-825; **Makino, H., et al.,** (2017). Neuron, 94:880-890; **Hikosaka, O., Nakamura, K., Sakai, K., & Nakahara, H.** (2002). Current opinion in neurobiology, 12:217-222; **Dayan, E., & Cohen, L. G.** (2011). Neuron, 72:443-454; **Perich, M. G., Gallego, J. A., & Miller, L. E.** (2018). Neuron, 100:964-976.
3. **Tumer, E. C., & Brainard, M. S.** (2007). Nature, 450:1240-1244.
4. **Andalman, A. S., & Fee, M. S.** (2009). Proceedings of the National Academy of Sciences, 106:12518-12523;
5. **Warren, T. L., Tumer, E. C., Charlesworth, J. D., & Brainard, M. S.** (2011). Journal of neurophysiology, 106:1806-1821.
6. **Moore, T.** (2006). Current opinion in neurobiology, 16:159-165; **Lauwereyns, J., Watanabe, K., Coe, B., & Hikosaka, O.** (2002). Nature, 418:413-417; **Ikeda, T., & Hikosaka, O.** (2003). Neuron, 39:693-700.
7. **Kimpo, R. R., Theunissen, F. E., & Doupe, A. J.** (2003). Journal of Neuroscience, 23:5750-5761; **Hahnloser, R. H., Kozhevnikov, A. A., & Fee, M. S.** (2006). Journal of neurophysiology, 96:794-812.
8. **Narayanan, N. S., & Laubach, M.** (2006). Neuron, 52(5), 921-931; **Makino, H., et al.,** (2017). Neuron, 94:880-890;
9. **Lemke, S. M., Ramanathan, D. S., Guo, L., Won, S. J., & Ganguly, K.** (2019). Nature neuroscience, 22:1122.

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