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DEMO Research Proposal: Testing the role of reward in forelimb motor adaptation

Research proposal

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Summary

To perform successful actions, motor commands must be adapted by taking into account the current goal of the animal as well as changes in the environment. The central nervous system has the remarkable ability to adapt to these changes with ease in healthy individuals. For example, we can rapidly adapt to typing on an unfamiliar keyboard or riding a new bicycle. This process called motor adaptation – namely, the ability to learn from environmental perturbations to restore performance – has also been demonstrated in various laboratory tasks such as a physical perturbation to the limb or a task that decouples visual feedback to limb or eye movements [1, 2, 3, 4, 5].

Since the pioneering work of Shadmehr & Mussa-Ivaldi in the 1990's, the use of force field perturbations during forelimb movement has become a powerful way to study the behaviorally observable mechanisms underlying motor adaptation. Despite the successes of these studies, our understanding of neural mechanisms underlying motor adaptation remains elusive. We recently translated these paradigms to a mouse model in order to study neural circuit mechanisms. We found that for forelimb adaptation, the somatosensory cortex (S1) was essential for learning to adapt (Mathis et al, Neuron 2017), but inactivation did not disrupt motor control. The finding suggests a unique role of the cortex for adaptive learning. Yet, how S1 encodes perturbations and systematically adapts to these perturbations remains unclear. **In this proposal, we aim to build on this work to test the role of reward-based learning during motor adaptation.**

1 Background & Introduction

In forelimb reaching tasks in humans, upon introduction of a force field perturbation, reaching movements are initially deviated from the baseline trajectory. Yet with repeated exposure to the same perturbation, one can compensate for the force field and restore performance similar to the baseline level [2]. Motor adaptation was further demonstrated when the perturbation was unexpectedly removed [2, 6], revealing both the trajectory employed to compensate for the perturbation and an 'aftereffect' wherein the subject continued to compensate in the opposite direction of the perturbation. These changes indicate that - behaviorally - the subjects learned a new internal model (representation) that connects motor commands and the resulting movements (or the sensory feedback of the executed movements) in the new environment.

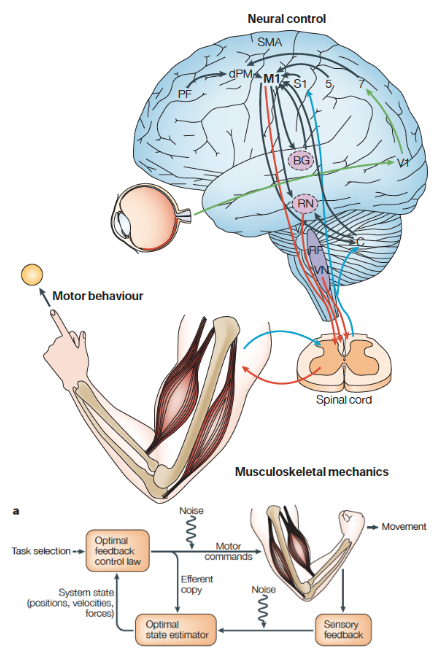

Figure 1: Theory of Adaptive Motor Control: Top: diagram of brain regions likely involved in motor control. Bottom: conceptual diagram of optimal feedback control theory. Adapted from Scott, 2004.

Multiple mechanisms have been proposed for how the brain learns to adapt motor commands to novel environments [7, 8, 9, 10, 11]. Several distinct error signals have been postulated. One proposed mechanism concerns whether an executed movement matches the intended movement. This learning type (supervised learning) is based on sensory feedback about executed actions. For instance, motor adaptation may occur by updating an internal model that relates motor commands and the resulting movements or the sensory feedback about the executed movements (Figure 1). This can be achieved by reducing the **sensory prediction error (SPE)**, the difference between the predicted and actual sensory feedback given a motor command [2, 4, 12, 5].

An alternative hypothesis is that **reinforcement learning** drives adaptation. The brain may choose a particular motor command that results in maximum future rewards (typically given as an explicit correct versus incorrect feedback in an all-or-none fashion in these tasks)[13, 8, 14, 15]. Such learning involves updating predictions about reward associated with different motor commands using reward prediction errors (RPEs)—the discrepancy between the realized and expected reward [16, 17, 11]. Indeed, it has been shown that when sensory feedback is unreliable, reward feedback directly instructs motor adaptation in a force-field adaptation task [18, 19]. Recent evidence from humans performing a visuomotor adaptation task has also suggested that when both reward and sensory feedback signals are available, sensory feedback signals predominate [20].

More generally, it remains to be determined how prediction errors are coordinated to drive behavior—how does the brain weigh different prediction errors in particular conditions?

2 Research Plan

2.1 Scientific Aim(s) & Methods:

Aim:
In this proposal, we aim to determine the factors that facilitate learning from SPEs and RPEs. Using our recently developed head-fixed mouse model of forelimb motor adaptation [5], we will develop a new task that challenges the mice to learn from RPEs and SPEs. In our previous study [5], empirically, adaptation was not correlated with an increased reward rate [5]. Based on modeling with temporal difference learning and a state-space model, these data indicated that reward was not directly driving or instructing motor adaptation, but we did not directly test this. Specifically, here we will test the **hypothesis that reward plays a critical role in defining task-relevant dimensions but not in trial-by-trial feedback that drives adaptation**. To test this idea, we will change the reward zone to examine how this affects motor adaptation.

Methods:
We will develop a **new task that changes the structure of the reward zone to test whether changing the task relevant-dimension affected motor adaptation**. Specifically, we replace the target box with a spatial threshold during the perturbation and washout blocks. This threshold-based reward zone will make lateral deviations task-irrelevant. As a consequence, the hand location at which the animal received reward could be shifted towards the direction of the force field if rewards are relevant to the mouse.

As a control for general effects of reward in this task setting, we will also teach mice to perform the target-shift task where they have to learn from explicit reward feedback, yet perform the same general forelimb/joystick movements. The baseline period will be the same as in all the previous tasks. During the "perturbation" block, however, the reward box is shifted towards the right or left (positive perpendicular displacement) [5]. During the "washout", the box is shifted back to the original baseline location. Here, we expect mice to learn from reward feedback how to modulate their trajectories. *This task serves as an important control to measure the direct effect of reward-based learning on forelimb movements.*

To test whether reward provided trial-by-trial feedback to instruct motor commands we will perform a linear regression analysis. The change in the perpendicular displacement (PD) between the n+1 and n trials (ΔPD_n

= pd_{n+1} - pd_n) during the perturbation block will be fit by a linear regression to the reward history R_n, as follows:

$$\Delta PD_n = C + \beta_1 R_n + \beta_2 R_{n-1} + \beta_3 R_{n-2} + \beta_4 R_{n-3} \tag{1}$$

Where n indexes the trial, and R_n refers to the reward in the n-th trial (0 or 1). This analysis tests if reward obtained on the previous trials (or farther back in history), directly affected the motor command on the current trial. Specifically, this model tests if there are any linear effects.

2.2 Anticipated Results

Given the prior art on the ability of mice to perform this task we do not expect complications in training the mice. In the task where the reward box is shifted to a threshold, we expect, if rewards are equal or more relevant than SPEs, that this reward will shift their behavior such that they do not show within block adaptation – they would continue to let the force field "pull" them to this new reward location. This will also be quantified by the linear regression model, as outlined above. There, one would see that the previous trial would have a strong effect on the subsequent trials lateral displacement.

References

[1] N. Hogan. An organizing principle for a class of voluntary movements. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 4(11):2745–2754, November 1984. PMID: 6502203.

[2] R. Shadmehr and F. A. Mussa-Ivaldi. Adaptive representation of dynamics during learning of a motor task. *The Journal of Neuroscience*, 14(5):3208–3224, May 1994. PMID: 8182467.

[3] J. R. Lackner and P. Dizio. Rapid adaptation to Coriolis force perturbations of arm trajectory. *Journal of Neurophysiology*, 72(1):299–313, July 1994. PMID: 7965013.

[4] C.-S. R. Li, C. Padoa-Schioppa, and E. Bizzi. Neuronal Correlates of Motor Performance and Motor Learning in the Primary Motor Cortex of Monkeys Adapting to an External Force Field. *Neuron*, 30(2):593–607, May 2001.

[5] M. W. Mathis, A. Mathis, and N. Uchida. Somatosensory Cortex Plays an Essential Role in Forelimb Motor Adaptation in Mice. *Neuron*, 93(6):1493–1503.e6, March 2017. PMID: 28334611.

[6] M. S. Fine and K. A. Thoroughman. Motor Adaptation to Single Force Pulses: Sensitive to Direction but Insensitive to Within-Movement Pulse Placement and Magnitude. *Journal of Neurophysiology*, 96(2):710–720, August 2006. PMID: 16707722.

[7] R. Shadmehr and J. W. Krakauer. A computational neuroanatomy for motor control. *Experimental brain research*, 185(3):359–381, March 2008. PMID: 18251019.

[8] J. Izawa and R. Shadmehr. Learning from Sensory and Reward Prediction Errors during Motor Adaptation. *PLoS Comput Biol*, 7(3):e1002012, March 2011.

[9] J. A. Taylor and R. B. Ivry. Cerebellar and prefrontal cortex contributions to adaptation, strategies, and reinforcement learning. *Progress in Brain Research*, 210:217–253, 2014. PMID: 24916295.

[10] A. S. Therrien, D. M. Wolpert, and A. J. Bastian. Effective reinforcement learning following cerebellar damage requires a balance between exploration and motor noise. *Brain*, 139(1):101–114, January 2016.

[11] A. Weinstein and M. M. Botvinick. Structure Learning in Motor Control:A Deep Reinforcement Learning Model. *arXiv:1706.06827 [cs]*, June 2017.

[12] Y.-w. Tseng, J. Diedrichsen, J. W. Krakauer, R. Shadmehr, and A. J. Bastian. Sensory Prediction Errors Drive Cerebellum-Dependent Adaptation of Reaching. *Journal of Neurophysiology*, 98(1):54–62, July 2007.

[13] J. M. Galea, D. Ruge, A. Buijink, S. Bestmann, and J. C. Rothwell. Punishment-Induced Behavioral and Neurophysiological Variability Reveals Dopamine-Dependent Selection of Kinematic Movement Parameters. *The Journal of Neuroscience*, 33(9):3981–3988, February 2013. PMID: 23447607.

[14] V. S. Huang, A. Haith, P. Mazzoni, and J. W. Krakauer. Rethinking motor learning and savings in adaptation paradigms: model-free memory for successful actions combines with internal models. *Neuron*, 70(4):787–801, May 2011. PMID: 21609832.

[15] G. Quattrocchi, R. Greenwood, J. C. Rothwell, J. M. Galea, and S. Bestmann. Reward and punishment enhance motor adaptation in stroke. *Journal of Neurology, Neurosurgery, and Psychiatry*, April 2017. PMID: 28377451.

[16] W. Schultz, P. Dayan, and P. R. Montague. A neural substrate of prediction and reward. *Science (New York, N.Y.)*, 275(5306):1593–1599, March 1997.

[17] R. S. Sutton and A. G. Barto. *Reinforcement learning: An introduction*, volume 1. Cambridge Univ Press, 1998.

[18] S. Y. Schaefer, I. L. Shelly, and K. A. Thoroughman. Beside the point: motor adaptation without feedback-based error correction in task-irrelevant conditions. *Journal of Neurophysiology*, 107(4):1247–1256, February 2012. PMID: 22157120.

[19] I. Kurtzer, P. DiZio, and J. Lackner. Task-dependent motor learning. *Experimental Brain Research*, 153(1):128–132, November 2003. PMID: 14566446.

[20] J. G. A. Cashaback, H. R. McGregor, H. C. H. Pun, G. Buckingham, and P. L. Gribble. Does the sensorimotor system minimize prediction error or select the most likely prediction during object lifting? *Journal of Neurophysiology*, 117(1):260–274, January 2017. PMID: 27760821.