

13. Neural variability in premotor cortex provides a signature of motor preparation

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How does the brain generate rapid and accurate movements of the body? Much work has focused on the role of sensory feedback and internal models in optimizing control signals during movement. Here we explore the possibility that the optimization of control signals begins during motor preparation, before movement begins. Using a delayed reach paradigm, delay-period or 'preparatory' activity can be observed in primary motor cortex (M1), and is even more prevalent in dorsal premotor cortex (PMd). It is often suggested that such activity is related to motor programming. This hypothesis implies that a movement is in large part the product of a motor 'program' latent in the preparatory activity. If so, it would seem critical that the brain optimize preparatory activity, so as to get the desired result when the movement is triggered. Given the presumably non-linear mapping from preparatory activity to movement (and thence to likelihood of reward) one suspects that this optimization is reasonably difficult, and might consume considerable time.

We present evidence, from three sets of experiments, that such optimization does indeed occur during motor preparation. Recordings were made from PMd of two rhesus monkeys. In the first set of experiments, we asked whether trial-by-trial variability in the state of preparatory activity correlates with trial-by-trial variability in the actual movement. Movements made by biological organisms are inherently variable, and this is usually thought to result from noise sources that contribute during the movement. In contrast, we show that a considerable portion of this variability is due to variability in preparatory activity. In particular, delay-period activity was predictive of the natural variability in the peak speed of the upcoming movement ($p < 0.001$ for both monkeys). These data indicate that the state of preparatory activity has consequences for the upcoming movement.

In the second set of experiments, we examined the across-trial variability of firing rates in PMd. Our hypothesis was that, before target onset (before optimization begins) firing rates would likely be variable. However, after optimization is complete, firing rates would be more consistent, assuming that the range of 'optimal' states is limited. We did indeed find that the across-trial variability of PMd firing rates dropped following target onset, with a time-course of 100-200 ms. Variability was assessed by computing the variance, and normalizing by mean firing rate, to exclude the influence of Poisson spiking variability. The time-course of this normalized variance (NV) measurement was found to be consistent with the time-course of motor preparation, inferred behaviorally from reaction time (RT) measurements. We repeated the experiment using three discrete delay period durations (30, 130, 230 ms). Across these conditions, the NV, measured at the time of the go cue, was predictive of the subsequent RT. When we examined the natural distribution of RT's, we found that trials where the NV was lower had shorter RT's. It thus appears that the NV provides a rough signature of the progress of motor preparation. Specifically, we suggest that the NV captures the process by which PMd firing rates travel from a variable initial state to a more consistent, and presumably near-optimal, final state. This application of the NV measurement (which is similar to the Fano-factor) provides a new way of interrogating the function of recorded neurons. Rather than asking under which conditions neurons maximally change their firing rates, the NV asks under which conditions their firing rates become consistent.

The above results suggest that the brain is capable of monitoring the state of motor preparation, and delaying movement if further optimization is necessary. If so, then disrupting preparatory activity ought to delay RT. In the third set of experiments, we used microstimulation to disrupt activity in PMd and M1, either during the delay period or just after the go cue. Microstimulation of PMd just after the go cue caused an increase in mean RT (two monkeys; 30 and 73 sites, mean increase of 26 and 20 ms, $p < 10^{-6}$ for each). In contrast, microstimulation of M1 had almost no effect on RT (12 and 32 sites, mean increase of 4 and 2 ms, $p > 0.1$). Our interpretation is that when motor preparation is disrupted just before it is to be translated into movement, execution is delayed until preparatory activity can be re-optimized. The discrepancy between M1 and PMd is consistent with the greater prevalence of delay-period activity in PMd. Microstimulation appears to selectively disrupt motor preparation related to the reach: there was only a weak effect on saccadic RT (8 and 2 ms, $p < 0.001$ and $p > 0.1$). Microstimulation delivered 100 ms or more before the go cue had only a slight effect on RT (7 and 2 ms), consistent with estimates of the time-course of motor preparation provided by the NV analysis above. Lastly, microstimulation just before the go cue delayed RT, but only if the delay-period was long enough for motor preparation to have been at least partially accomplished (ANOVA interaction, $p < 0.05$ for each).

The above results provide converging evidence that PMd preparatory activity is optimized prior to movement generation. This process appears to take time, possibly explaining why RT's of voluntary movements are longer than expected from conduction delays alone. Optimization also appears to take variable time, possibly explaining why RT's are naturally variable. The end result of this process also appears to be variable, revealing at least one source of movement variability.

Our results are consistent with prior suggestions that a 'forward model' could be used by the brain to optimize motor preparation. In this conception, the forward model would act in concert with a controller, as part of a recurrent circuit that would act to optimize activity. In general, artificial recurrent networks are capable of performing optimizations – typically the optimal solution forms an attractor in the dynamics of the networks. We note that a common property of such models is that activity is variable before optimization is complete, and consistent afterwards, in keeping with our observations that the across-trial variability of PMd neurons drops during motor preparation. Support: Helen Hay Whitney, NIH, BWF, NSF, ONR, Sloan, Whitaker.