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Injecting instructions into premotor cortex using intracortical microstimulation

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Summary

The premotor cortex (PM) receives inputs from parietal cortical areas representing processed visuospatial information, translates that information into programs for particular movements, and communicates those programs to the primary motor cortex (M1) for execution. Consistent with this general function, intracortical microstimulation (ICMS) in PM of sufficient frequency, amplitude, and duration has been shown to evoke complex movements of the arm and hand that vary systematically depending on the locus of stimulation. Using frequencies and amplitudes too low to evoke muscle activity, however, we found that ICMS in PM can provide instructions to perform specific movements. These instructed actions were not fixed, but rather were learned through associations between the arbitrary stimulation locations and particular movements. Low-amplitude ICMS at different PM locations thus evokes distinguishable experiences that can become associated with specific movements arbitrarily, providing a novel means of injecting information into the nervous system.

Methods

Experimental Setup

We trained two rhesus macaques (L, X) to perform a reach, grasp, manipulate task. Monkeys were instructed to:

- Turn a sphere
- Push a button
- Pull a coaxial cylinder
- Pull a perpendicular cylinder

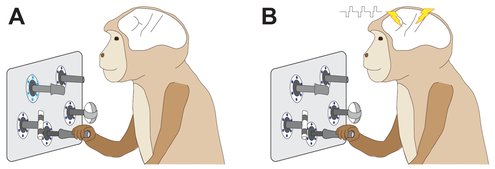

Figure 1. Monkeys had learned to use instructions delivered using (**A**) blue LEDs to perform the task. We then trained each monkey to use (**B**) intracortical microstimulation (ICMS) to perform the same movements.

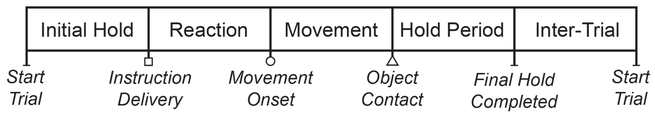

Figure 2. Breakdown of the trial epochs during the reach, grasp, manipulate task.

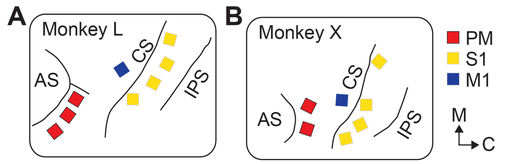

Figure 3. Floating microelectrode arrays (FMAs) implanted in premotor cortex (PM – red), primary motor cortex (M1 – blue), and primary somatosensory cortex (S1 – yellow). AS: Arcuate Sulcus. CS: Central Sulcus. IPS: Intraparietal Sulcus. M: Medial. C: Caudal.

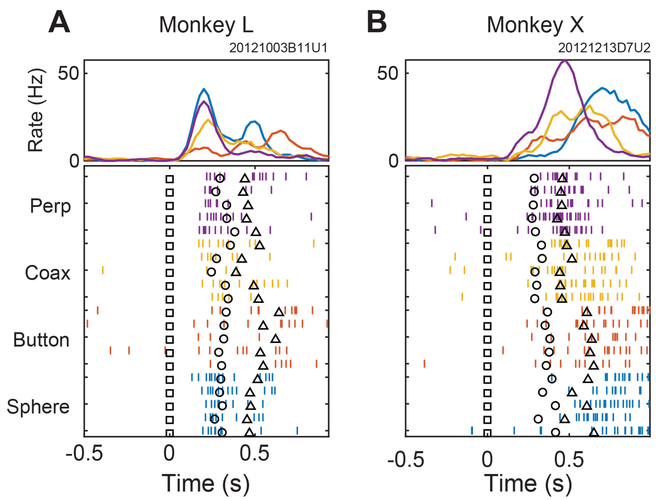

Figure 4. Two example units recorded from premotor electrodes used to deliver ICMS instructions. Perpendicular cylinder (Perp, purple), coaxial cylinder (Coax, yellow), button (red); and sphere (blue). Only five trials shown in the raster display. Trials have been aligned at the instruction onset (Time=0, black squares in the raster trials). Movement onset (black circle) and target object contact (black triangle) also depicted.

Methods

Training to Use Intracortical Microstimulation Instructions

Table 1. Stimulation Parameters

	PM-ICMS	S1-ICMS
Monkey L		
Number of Electrodes	3	4 – 6
Period Frequencies	80, 100, 120, 150 Hz	50, 75, 125, 225 Hz
Amplitudes	18 – 28 µA	20 – 60 µA
Monkey X		
Number of Electrodes	3 – 4	3 – 5
Periodic Frequencies	50, 75, 125, 200 Hz	75, 100, 150, 225 Hz
Amplitudes	20 – 25 µA	25 – 55 µA

PM-ICMS: Instructions delivered in premotor cortex
S1-ICMS: Instructions delivered in primary somatosensory cortex

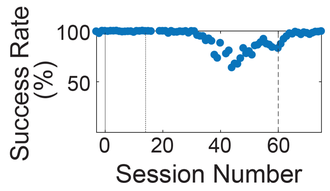

Figure 5: Monkeys first used LED instructions (sessions prior to 0). ICMS instructions then were delivered concurrently (black line, time 0). Gradually, LED intensity was dimmed (dotted line). LED instructions ultimately removed (dashed line). Monkeys progressively learned to use the ICMS instructions as success rate improved.

Results

Training results for both monkeys

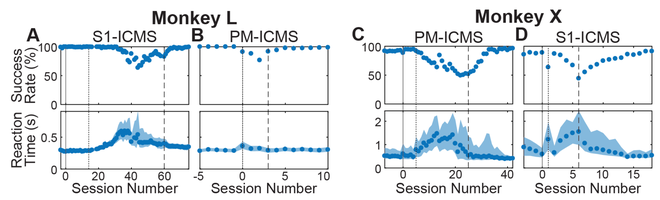

Figure 6: Monkey L first trained to use (**A**) S1-ICMS then (**B**) PM-ICMS. Monkey X first trained to use (**C**) PM-ICMS then (**D**) S1-ICMS.

Sweeping the stimulation parameters for PM-ICMS instructions

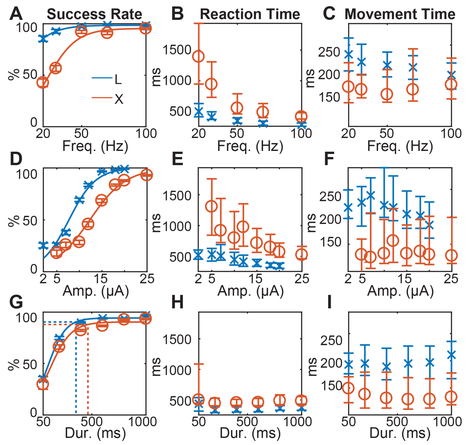

Figure 7:Three parameters of PM-ICMS instructions were varied for each monkey: (**A,B,C**) pulse frequency, (**D,E,F**) current amplitude, and (**G,H,I**) train duration. Success rate (**A,D,G**), reaction time (**B,E,H**), and movement time (**C,F,I**), each have been plotted as a function of the swept parameter. In (**G**) the vertical dotted lines represent the median reaction time across all swept durations for each monkey (**H**), and the corresponding horizontal dotted lines indicate the success rate at this median reaction time, based on the fitted logistic functions.

Table 2: Parameters used during the sweeping experiments. Each instruction delivered through a single electrode in premotor cortex.

	Constant Parameter	Swept Parameter
Monkey L		
Periodic Frequency		20 – 100 Hz
Inter-pulse Interval Range	12.5 – 40 ms	
Amplitude	10 – 28 µA	2 – 20 µA
Train Duration	Until target object contact	50 to 1000 ms
Monkey X		
Periodic Frequency		20 – 100 Hz
Inter-pulse Interval Range	12.5 – 30 ms	
Amplitude	20 – 25 µA	5 – 25 µA
Train Duration	Until target object contact	50 to 1000 ms

Results

Performance using PM-ICMS instructions

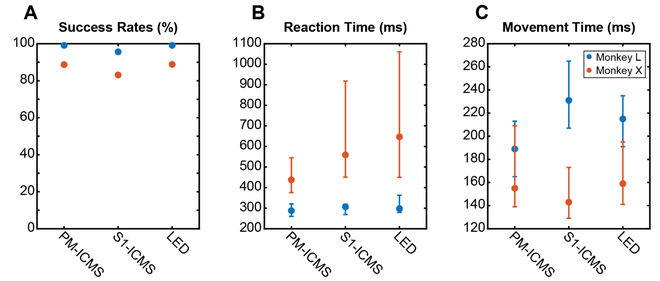

Figure 8:Success rates, reaction times, and movement times were generally similar using PM-ICMS, S1-ICMS, or LED instructions.
A) Both monkeys achieved higher success rates with either PM-ICMS or LED instructions than with S1-ICMS instructions ($p < 0.0001$, X^2 tests, Bonferroni post-hoc tests)
B) Both monkeys also reacted faster to PM-ICMS than to S1-ICMS or LED instructions ($p < 0.0001$, Kruskal-Wallis tests, Tukey post-hoc tests)
C) Monkey L moved faster with PM-ICMS instructions than with either S1-ICMS or LED instructions; Monkey X moved fastest with S1-ICMS instructions ($p < 0.0001$, Kruskal-Wallis tests, Tukey post-hoc tests).

Stimulus-triggered Averaging to detect movements

	PM-ICMS	M1-ICMS
Monkey L		
Number of Sessions	2	
Number of Electrodes	1	1
Amplitudes	20 µA	20 µA
Inter-pulse intervals	12.5 to 40 ms	12.5 to 40 ms
Success Rate	98.2%	22.1%
Monkey X		
Number of Sessions	4	
Number of Electrodes	1	1
Amplitudes	25 µA	25 µA
Inter-pulse intervals	12.5 to 30 ms	12.5 to 30 ms
Success Rate	91.6%	10.6%

Table 3: Parameters used during stimulus-triggered averaging experiments. Each instruction delivered through a single electrode in premotor cortex (PM-ICMS) or primary motor cortex (M1-ICMS).

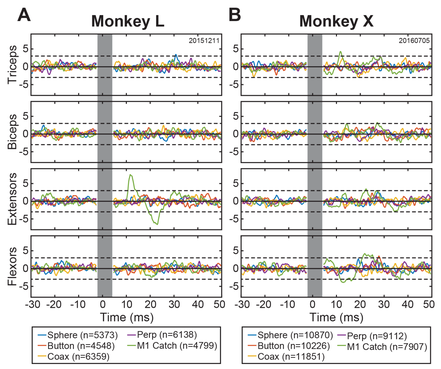

Figure 9:Stimulus-triggered averages of EMG activity. Averages of rectified EMG activity from four upper extremity muscle groups—Triceps, Biceps, forearm Extensors, and forearm Flexors—were compiled for each monkey (**A**, monkey L; **B**, monkey X) using individual ICMS pulses as triggers. ICMS parameters used for these sessions are given in Table 3. Separate averages (colors) were compiled using n pulses delivered through the PM electrode instructing the sphere, button, coaxial cylinder, or perpendicular cylinder, as well as for catch-trial pulses delivered in M1.

Discussion

- Low-amplitude microstimulation in premotor cortex instructed specific actions.
- Association of stimulation at different loci with particular actions was learned.
- Effective microstimulation amplitudes were too low to evoke muscle activation.
- Effective microstimulation patterns did not emulate natural premotor activity.
- Future work will identify other cortical areas where instructions can be delivered using low-amplitude ICMS

Acknowledgments

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