

As an undergraduate I devoted my time during the academic year primarily to coursework. During the summers (2000, 2001, and 2002), I worked on a research project in the University of Chicago's Brain Research Imaging Center, a new suite of functional magnetic resonance imaging scanners (fMRI), where my research advisor was the BRIC's director, Dr. Steven Small. I was interested in sensorimotor systems, which matched the Center's focus on recovery from stroke.

The cortical correlates of movement have been known for many years: when a part of the body moves or is stimulated, a set of corresponding regions of cortex become active (e.g. Penfield et al 1950). The cortical patches are known as representations, and they are found in several cortical areas. I was interested in the regions with the most robust response, primary motor cortex (M1) and primary somatosensory cortex (S1). In these regions, the topology of representations resemble the topology of the body (e.g. neighboring fingers have neighboring representations).

Representations can change over time as a function of usage patterns (e.g. Recanzone et al 1992). For example, it was found in monkeys that if two neighboring fingers are bound together, their S1 representations fuse. If a finger is amputated, the nearby fingers encroach on its former territory. If a finger is used extensively for a task, its representation enlarges and encroaches upon neighboring representations. These changes were observed in the relatively short term, periods of a few months, and the tasks were relatively simple. To get a broader understanding of cortex's capabilities, I wanted to know how the sensory and motor systems change under conditions on the opposite end of the spectrum: for a very complex task, learned over the course of decades.

A musician's training is well-suited to a study of long term motor and sensory learning. Professional musicians play their instruments for many hours each day, actively attending to and modifying their performance. When I looked at the fMRI literature on motor studies of musicians, however, I found it consisted of essentially one kind of experiment (e.g. Hund-Georgiadis et al 1999 and Krings et al 2000): musicians and nonmusicians performed a difficult finger movement task while in the scanner, and the researchers looked for differences in brain activation to describe how the musician's motor system differs from a nonmusician's.

The problem with such an experiment is that the two groups are not performing the same task. Nonmusicians make significantly more mistakes and can't perform the task as quickly as musicians. Moreover, musicians have experience training themselves to learn complex movements, so they probably use a different learning algorithm than the nonmusicians. Since the two groups performed different tasks, we can not directly compare the corresponding brain activation.

This problem is not just an isolated technical flaw. It arises in the study of any "expert" system: the experts can do things which nonexperts can't, and if the nonexperts are trained on a complicated task, they are no longer nonexperts. Therefore experts have no control group for direct comparison. This logic led me to realize that a better question to ask is whether becoming an expert changes the performance of simple tasks. In the case of musicians, does learning to play an instrument alter the sensory and motor pathways that underlie everyday movements?

For short term learning of a simple task, we know that a finger's representation grows when the finger learns a complex task. In the case of musicians, there are two additional factors. The first is that the musician's training is long term. There might be an additional consolidation of the learning in cortex. The second factor is that the same representations are probably used for widely different tasks. For the musician, executing a precisely timed trill and dialing a telephone number use the same muscles and mechanoreceptors, and, presumably, the two tasks correlate with activity in the same regions of M1 and S1.

I wanted to find out whether the cortical changes associated with long term learning were similar to the patterns of short term learning. My plan was to make a null hypothesis that long term cortical changes would be identical to short term changes, and then test whether the data refuted the null hypothesis.

I settled on the following task: subjects in the scanner receive visual cues (a number or letter on the right or left side of the screen) and respond by tapping the corresponding finger. At rest, the hands are in a relaxed, palm down position, and the fingers are slightly curved. Tapping a finger means picking it up, moving it forwards about an inch and tapping down, then returning to rest. The task was very easy to learn, and no subject took more than a couple minutes to master it.

I planned to begin the study by scanning intermediate musicians from the University of Chicago's Chamber Orchestra and comparing them to subjects who had never played an instrument or learned any fine motor skills. When I left Chicago to attend graduate school in fall of 2002, I had scanned and analyzed the performance of 3 musicians and 4 control subjects. Such a small population did not provide enough data to adequately test my hypothesis. However, my protocol and analysis are documented and I expect another student will scan the remaining necessary subjects within the next few years. If none does, I will most likely return to Chicago for a summer to finish the study.

My work in the BRIC was largely independent. Once I became familiar with the kinds of experiments made possible by fMRI, I read the literature and developed the question mostly on my own, though I discussed my ideas with Dr. Small and other lab members frequently. To develop the experimental design, I worked with Dr. Small and his postdocs. Once I learned the data analysis methods, I performed them myself and wrote my own scripts to execute them. I was also responsible for training and testing subjects.

In graduate school, I've completed four research rotations, quarter-long projects in prospective thesis labs. The most meaningful for me was the rotation with David Kleinfeld. In his lab, my goal was to make a computational model of ion channel dynamics which could be related to experimental findings in the Kleinfeld lab.

The finding was that motor neurons in young rats begin to show a physiological property known as subthreshold resonance (which I don't describe here) at just about the same time as they incorporate a new ion channel into their membranes. My goal was to discover whether the new ion channel alone could induce subthreshold resonance in a normal neuron. My method was to model a single-compartment neuron using Hodgkin-Huxley style equations, and then add in a term describing the ion channel's dynamics.

I found that the new ion channel was sufficient to induce subthreshold resonance. But this finding wasn't the end of my study. Since the phenomenon could be modeled, I could explore its mechanism in extremely fine detail. I examined the state of the cell as it

began to show subthreshold resonance, going so far as to follow the ion channels' internal variables at submillisecond resolution. Through such a close study, I was able to make conclusions about the mechanism of subthreshold resonance.

This rotation taught me an important and effective use for computational models in empirical research. Of course, my model might have reproduced the phenomenon through a different mechanism than neurons actually use. But the model suggested a plausible mechanism, and my work led to new physiological experiments that tested my predictions. Through further elaboration of the model, and further experiments, each playing off the other, we gain a deeper understanding of the biological system.

References

- Hund-Georgiadis, et al. (1999) "Motor-learning-related changes in piano players and non-musicians revealed by functional magnetic-resonance signals" *Experimental Brain Research* (1999) 125:417-425
- Krings, et al. (2000) "Cortical activation patterns during complex motor tasks in piano players and control subjects. A functional magnetic resonance imaging study" *Neuroscience Letters* 278 (2000): 189-193
- Penfield W, Rasmussen T (1950) *The Cerebral Cortex of Man. A Clinical Study of Localization of Function*. New York: Macmillan.
- Recanzone GH, Merzenich MM, Jenkins WM, Grajski KA, Dinse HR (1992) "Topographic reorganization of the hand representation in cortical area 3b of owl monkeys trained in a frequency discrimination task" *Journal of Neurophysiology* 67: 1031-1056