



DEPARTMENT OF PSYCHOLOGY

BERKELEY, CALIFORNIA 94720-1650
2121 Berkeley Way, Room 3302, MC 1650



News from the Cognition and Action Lab at UC Berkeley

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Since our last newsletter, the Cognition and Action lab at UC Berkeley has become a bit of a road show. In addition to attending the past two National Ataxia Foundation's Annual Meetings in Philadelphia and Las Vegas, we've made two trips to Kansas City, Missouri. Stephanie Wilkins, one of the coordinators for the KC support group helped coordinate things so that we could run a few experiments, testing 16 members of the support group over a hectic 3-day period. As you can see from these photos, we do find time to enjoy our time on the road. It's been great meeting everyone and stuffing ourselves with delicious food (thanks Kansas City barbeque!). We plan to attend NAF 2020 in Denver and look forward to seeing many of you there.



Enjoying the barbeque at Q39 in Kansas City



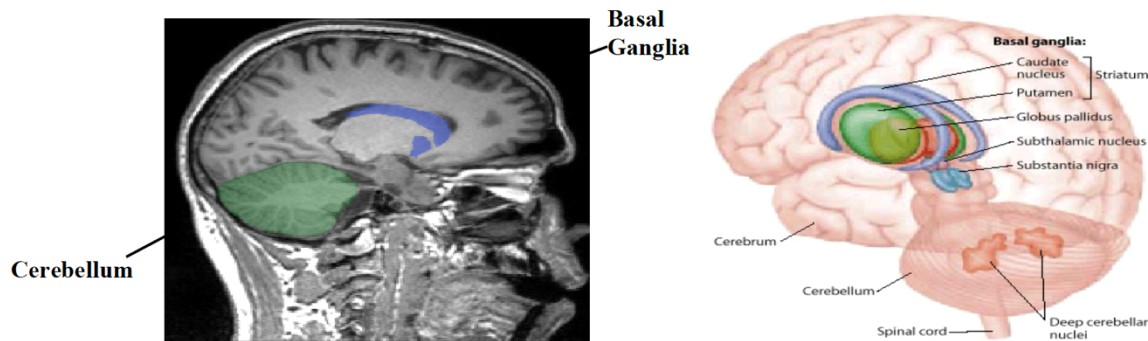
Visiting Vegas for NAF 2019

As always, I'll give an overview of our general mission -- this will be a review for many of you so feel free to skip ahead to the descriptions about our most recent projects.

The main focus of our lab's research is on how different types of neurological conditions disrupt different aspects of human performance and skill. We have focused on what neuroscientists call the "subcortex," the part of the brain that lies under the cerebral cortex, or cerebrum (see the picture). The subcortex is sometimes considered the "ancient" brain, reflecting the fact that the structures that form the subcortex are found in almost all animals, including prehistoric fish, reptiles, birds, as well as mammals. While these animals didn't need to perform complex mental

tasks such as balancing checkbooks and driving cars, they do require the neural machinery to move about and interact with their environment. If a creature couldn't control its movement, it would be at a huge disadvantage in the world. It wouldn't be able to flee from enemies or venture out in search of food and mates. So, it is logical that the systems that control movements are deeply embedded in the brain and that there are numerous similarities in the ways that movements are controlled across a range of species.

We focus on two large structures within the subcortex: the basal ganglia and the cerebellum. If either structure is damaged, a person is likely to have coordination problems. The basal ganglia are the part of the brain that is primarily affected in Parkinson's disease. Many cells in the basal ganglia are dependent on dopamine, one of the chemicals in the brain that allows nerve cells to communicate with each other. Parkinson's disease is caused by a dramatic reduction in the production of dopamine. Cerebellar dysfunction does not result from the loss of a particular brain chemical. Rather, various degenerative disorders, some of which have a known genetic basis,



selectively attack cells in the cerebellum, resulting in ataxia, or a loss of the fine control of skilled movements. In addition, strokes can affect any part of the brain including the basal ganglia and cerebellum.

At any point in time, our lab is involved in several different projects, reflecting our overall mission as well as the specific interests of the lab members. One consistent theme is to understand how the brain produces skilled movements. Note that I talk about how the “brain” produces these actions. Obviously, the muscles are also important; you wouldn't be able to walk, talk or type on a computer if the neural signals were unable to activate the muscles. But much of what determines whether a movement is clumsy or skilled has more to do with the brain than the body. An expert tennis player cannot simply stand in the center of the court and swat at the ball as hard as she can. Rather, much of the expertise involves anticipating where the opponent's shot will land, glancing up to see which part of the court is open, and adjusting the stroke to give the ball just the right spin, speed, and direction. In any sport, or in fact, our everyday activities, skilled action requires accurate perception and memory. Thus, our lab doesn't study motor control in isolation, simply looking at how people activate and control their muscles. Rather, as the name Cognition and Action implies, we study action from a broad perspective, trying to see how skill builds on so many aspects of our mental abilities. Let me now turn to an update of some of the most recent results to emerge from our studies.

1. The Impact of Ataxia and Parkinson's Disease on Cognition

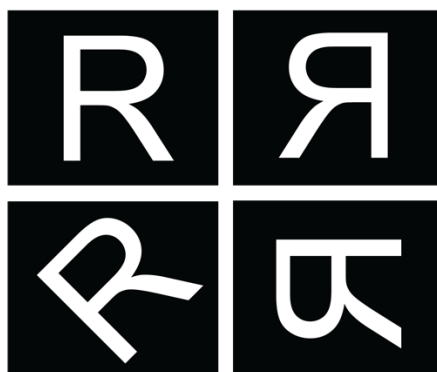
Clinicians who work with individuals with ataxia or Parkinson's disease are very interested in how these degenerative disorders may affect mental abilities as well as motor abilities. Perhaps the basal ganglia and cerebellum are not only important for coordinated movement but are also

essential for coordinated thought. We have been developing a number of experiments to tackle this issue, and test hypotheses about the specific ways in which cognition may be impacted in these disorders. One recent project has involved studies of visual cognition, and in particular, our ability to manipulate visual images in the brain. Look at the two pictures below.



We all readily recognize the toaster on the right. But it's not as obvious to recognize the one on the left—in fact if you didn't see the picture on the right, you might not have recognized the toaster on the left because of the unusual perspective. One way we recognize things from atypical perspectives is to mentally rotate the image, transforming the actual image to see if we get a better match with the images stored in our memory.

To study mental rotation in the lab, we have used a task in which the participant is shown a letter and has to judge if it is written in the normal manner or mirror reversed. The challenge is that the letter is sometimes presented at a tilted orientation and thus, has to be mentally rotated in order to make the normal/mirror-reversed judgment.



By measuring how quickly the participant responds, we can infer how quickly they can mentally rotate the image. Our initial results show that people with ataxia are slower in doing mental rotation, perhaps similar to the difficulty they have in making rapid movements. We will be looking at the performance of people with Parkinson's disease on this task in the coming year.

2. The Role of the Cerebellum in Producing and Understanding Speech

We are continuing our work on speech and language with our collaborators Ben Parrell, a former post-doc in the lab who is now an assistant professor at the University of Wisconsin, and researchers at the University of California, San Francisco. Our studies have been examining two, related issues in speech motor control, feedforward and feedback control, building on ideas developed in the study of arm movements. Consider what happens when you reach and grasp a glass of water. Your brain sends commands down the spinal cord to activate your muscles, causing the arm to move forward and then close your fingers around the glass. The timing between these two events is tightly coordinated. How is this achieved? One idea would be that you use feedback from your arm and eyes to determine when the arm is positioned so that you can grasp the glass. However, feedback takes time—the signals must be transmitted from the arm and eyes to the brain and then processed. If we were solely dependent on using feedback in a continuous manner, our

movements would be much slower. An alternative is that we control movements in a predictive manner, or what is called feedforward control. That is, the brain sends the motor commands to make the arm move forward and predicts, based on those commands, when it will be appropriate to close the fingers around the glass. It is this predictive capability that allows movements to be so fluid and coordinated. By this view, one of the key problems in ataxia is a disruption of predictive control. People with ataxia have difficulty generating accurate predictions and thus either produce errors in their movements or have to slow down, relying on feedback to coordinate their movements.

We have conducted a number of studies over the past two years looking at feedforward and feedback control in speech. Our studies have shown that people with ataxia have a selective problem with feedforward control; their ability to use feedback appears to be intact. The impairment in feedforward control may be one reason why people with ataxia slow down when speaking. By speaking slowly, they are able to take advantage of their ability to use feedback control. Indeed, people with ataxia may rely on feedback control to compensate for feedforward control.

We have also started studying speech perception, examining how the brain adapts to voices that may speak with different accents or intensities, or over devices such as telephones that may distort the sounds. Despite these variations, we are usually able to identify the speech, even though the physical sounds are very different. One idea here is that the brain engages in a very rapid learning process, recalibrating the perceptual system after sampling the current sound environment. To study this, we are running experiments in which we made it very difficult to identify the words, a condition in which this type of learning may be required. We are testing whether this ability is affected by ataxia given that this type of perceptual learning may require generating an accurate prediction of what the speech will sound like.

3. New On-line Testing Program

We have recently launched a new research program, one in which the testing will be conducted on-line. There are a number of advantages to moving some of our experiments on-line. First, it is much more convenient for the participants—they can complete the experiment at home on their own computer and do so whenever it is convenient. Second, we are interested in conducting some studies on learning and to get a real look at learning, it is frequently better to do the testing over multiple days. It would be very difficult to have people come to our UC Berkeley lab over multiple days in a short time period and this kind of research could not be done at the NAF meeting.

Third, by doing the testing on-line, we can increase the number of people we enroll in a given experiment. In our typical laboratory experiments, we test 15-20 individuals in each group (ataxia, Parkinson's, controls). By moving on-line, we expect we can increase this number to 100 or more, recruiting people from all over the country. Considering just our ataxia research program, between the participants we have worked with in California, at the annual NAF meetings, and from our travels to Kansas City, we have now enlisted over 180 people in our studies over the past 10 years. Moreover, we have been in contact with a number of other support groups to recruit new participants. We even have collaborators in Canada, Germany, Norway, and Mexico who would like to join forces to run large-scale, on-line studies. Testing large numbers in a single study is a powerful method for identifying group differences, for example, situations in which individuals with ataxia perform differently than individuals with Parkinson's disease. As important, within each group we can ask how performance changes with age, gender, symptoms, disease duration, and etiology.

There are, of course, limitations with on-line testing. It remains to be seen if we can conduct studies of motor control and motor learning on-line. We need devices to record movements and people use a range of devices to manipulate the cursor on their computer. The way someone moves may be different if they are using a computer mouse compared to a trackpad or joystick. Our initial plans for on-line testing will be limited to experiments in which the responses can be made on your computer keyboard. Some of these may be “motor” based, looking at how people learn to perform typing-like movements. Others will be more “cognitive”, studying different aspects of perception, attention, and memory.

News from CognAC

As always, I want to pass along the latest news about the current and past members of the Cognition and Action Lab. A number of former grads and post-docs have taken up faculty positions and are now busy running their own labs. I mentioned the work of Ben Parrell in the section on our speech program, something that Ben is spearheading from his lab at the University of Wisconsin. Jordan Taylor is settled in at Princeton and in addition to continuing his work on movement disorders, is also now doing research on memory disorders. Makes sense given that learning is not only about acquiring new information, but also about retaining old information. Ian Greenhouse is up at my old alma mater, the University of Oregon. He is involved in a major initiative there on Parkinson’s Disease as part of his work on how the brain not only produces movement, but also inhibits unwanted actions. Hyosub Kim is at the University of Delaware, one of the best research centers for developing and evaluating physical therapy interventions. Ryan Morehead has just landed at the University of Leeds in England where he is going to be involved in developing new methods to study motor control by using advanced virtual reality systems.

The current members of the Cognition and Action lab are a very international group. Many of you have met Assaf Breska, a post-doc from Israel who has been running the EEG studies in the lab to measure brain waves. Two other Israelis have now joined the lab as post-docs, Guy Avraham and Will Saban. Guy is taking a lead role in our new studies on sensorimotor learning and Will’s interests center on how learned movements become automatized. We also have two new grads in the lab who some of you may have already met. Maedbh King hails from Ireland and comes to us following her master’s work in Canada. Her specialty is brain imaging, and in particular, developing detailed maps to show how the cerebellum is engaged in a wide variety of motor and cognitive tasks. JT Tsay comes from that strange land of Chicago. He’s got his hand in a few projects including our new work on cognitive changes observed in ataxia and Parkinson’s disease. The lone Californian in the lab these days is Christina Merrick, a graduate student who has gotten involved in a new project recording brain activity during neurosurgery.

Alas, two other people that are familiar to many of you will be leaving the lab over the next half year. Sam McDougle will be starting a faculty position at Yale University in July and Arohi Saxena is heading off to medical school. They will be missed.

And I don’t want to forget to mention two other new faces of note: Both Ryan and Sam became fathers over the past year! Here’s to hoping Lillian and Leo become members of the UC Berkeley class of 2040!

We hope that this newsletter provides you with a general overview of the research we conduct in lab and, perhaps, some more details about a study in which you may have participated over the past year. We appreciate your willingness to work with us in exploring these research questions and we hope that you can take pride in the fact that you are literally an integral part of the research. The results of our work are published in scientific reports. All of the reports can be found on our

lab website: ivrylab.berkeley.edu. If you prefer, we can send you a copy in the mail. Fair warning: These reports are written at the technical level, so they may not make for the most exciting read...

I want to thank you for dedicating your time and energy to helping with this research. The immediate impact of these studies is not always obvious, but they do help us in understanding how the brain works and learns. We trust that this knowledge will prove useful in the developments of new treatments and rehabilitation protocols.

Best wishes for the new year,



Rich Ivry
Professor of Psychology and Neuroscience

ivry@berkeley.edu
ivrylab.berkeley.edu

