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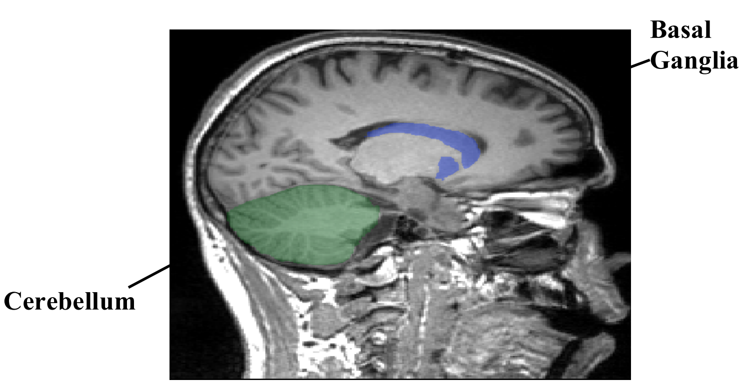
March 3, 2017

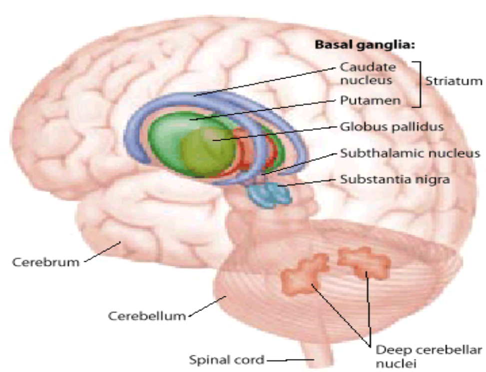
We're just about ready to head off to to San Antonio for the National Ataxia Foundation's Annual Meeting next week. Our team is growing! This year it will include people from three different labs: The Cognition and Action lab at UC Berkeley, the Intelligent Performance and Adaptation Laboratory at Princeton University, and the Speech, Phonetics, and Phonology lab at the University of Delaware. We've joined forces to run a series of new experiments that examine a number of different behaviors that may be affected in ataxia, including arm movements, speech, and attention. Our team will arrive early and stay an extra day after the conference, providing extra opportunities for conference attendees to participate in our studies and, if time allows, allow folks to sample southern Texas hospitality.

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

The research in our lab focuses on how different types of neurological conditions disrupt skilled movement. Our primary studies explore the functions of 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 did require the neural machinery that allowed them 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.





Those of you who have participated in our studies for many years know that we are working on several different projects, which might, at times, seem completely unrelated. Nonetheless, there are a number of central themes that guide our work. Most prominent is our goal 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 he 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. The same holds true for basketball; the professionals can all make shots from just about any place on the court when unguarded in practice. The real challenge is in making that shot when there are nine other—rather large—bodies scattered about the court. 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 Cerebellum and Predictive Control in Speech.

We are continuing with a line of work we started a few years back on speech motor control. Here we are investigating why people with ataxia have slowed speech, and difficulty controlling the pitch and loudness of their voice. 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 that will first cause your arm to first 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 the ideas of feedforward and feedback control in speech. Speech is obviously one of the most amazing of human capabilities, allowing us to communicate about the past, present, and future. The movements of our lips, tongue, and jaw required to produce speech are very fast—some are only 100 ms long! These movements are so fast that they often finish in less time that it takes us to process the sound of our own speech. This means we can't rely on feedback to determine if we produced the right words, but must use some form of predictive, or feedforward control. Our studies have shown that people with ataxia have difficulty in feedforward control. Indeed, one reason they might slow down when speaking is because of this difficulty. A corollary of this idea is that they may be very reliant on feedback control. Indeed, people with ataxia may rely on feedback control to compensate for feedforward control. This would suggest that the cerebellum is not essential for feedback control, a hypothesis we have recently tested and confirmed in our studies of ataxia. We are now taking these ideas and asking if a similar picture holds for arm movements. We will be testing this idea at NAF this year, comparing feedforward and feedback control in reaching. This project involves a collaboration between Ben Parrell, a former post-doc in the lab who is now an assistant professor at the University of Delaware, and researchers at the University of California, San Francisco.

2. The Cerebellum and Temporal Predictions in Perception

Predictive control is important not only over what we do, but also over when we do it. Whether dancing, playing tennis or tying shoelaces, humans are constantly anticipating when an action should be produced or anticipating the movements of other individuals. While quite a few studies have shown that people with ataxia have difficulty in producing well-timed movements or even in judging the passage of time, our new research is focusing on how well individuals with ataxia can make temporal predictions more generally. Here we are comparing two types of temporal predictions. For one type, the temporal prediction is based on a single interval, the sort of thing you might do when waiting for a traffic light or, in baseball, when judging when to swing at a pitched ball. In the other type, the temporal prediction can be based on a rhythmic sequence of events; for example, when listening to music, we can anticipate a particular sound at a particular time because of the rhythm. We have found that individuals with ataxia have difficulty with the interval form of timing, but seem to be fine in using rhythmic information to make temporal predictions. In our ongoing work, we are now exploring this question with a technique called electroencephalography (EEG). For this procedure, we place simple recording devices on the participant's head that can measures electrical activity generated by the brain. Research with neurologically healthy individuals has identified several distinct patterns of brain activity that are relevant to different stages of temporal predictions. Our new research involving people with ataxia will help us understand how the cerebellum contributes to these predictions.

3. How does the cerebellum support the cerebral cortex in learning new motor skills?

Historically the cerebellum has been thought to play a role in the more implicit, or unconscious, aspects of motor learning. In contrast, the cerebral cortex has been associated with more explicit, or conscious aspects of learning. For example, when learning to play tennis, a coach can describe the various steps required to serve. We might internally use this information to explicitly "talk" our way through the serve— "toss ball, swing arm, step forward and follow through." With practice, our movements become more automatic, or implicit. By this view, the cortex plays a critical role in the early stages of learning and the cerebellum takes over as skill progresses.

However, our recent work has revealed that the cerebellum may also be important in the explicit parts of motor learning. To study this, we have been asking people to report what they are doing at various stages when they are learning a new motor task. In this way we not only observe their changes in performance over time, but also have a record of the strategies they are using to modify their movements. The results suggest that this strategic aspect of motor learning may also be compromised in individuals with ataxia. Interestingly, people with ataxia have no difficulty using a strategy if directed by the experimenter. That is, they are capable of modifying their movement commands if given information about how to do this. The problem, though, is in spontaneously coming up with the right strategy. To use our tennis example, our results would suggest that people with ataxia can benefit from coaching—but if they don't have a coach directing them, they have trouble figuring how the right strategy to use.

An unanswered question is whether the difficulty in self-discovery reflects a more "cognitive" problem associated with ataxia or if this is secondary to the motor problems associated with ataxia. It may be that people with ataxia can generate strategies but because of their movement problems, they have trouble deciding if the strategy was appropriate. We are planning new experiments to address this question, part of our ongoing interest in understanding how the cerebellum works with the cerebral cortex to learn new movement patterns, as well as keep learned patterns well coordinated.

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. The biggest news comes from former member, Ryan Morehead, who is now a post-doctoral fellow at Harvard University. Ryan was visiting with his girlfriend this past month and took the opportunity of a return trip to California to propose! In fact, he did the deed on the rooftop right outside our lab. We're now looking forward to his and Mallory's wedding in September.

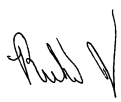
Other past members are doing well. Jordan Taylor is finishing his 6th year as a professor at Princeton University and his lab is doing all sorts of great projects. Some of you may get to work with Sam McDougle, a member of his lab at this year's NAF. Jordan is doing ataxia research around New Jersey/New York through his collaborations with neurologists at Johns Hopkins University in Baltimore and Columbia University in New York City. Be sure to contact him if you are in the area, http://www.princeton.edu/~ipalab/. Ben Parrell is in his second year as a professor at the University of Delaware. He won't be joining us at NAF this year, but we continue to work together on the studies of dysarthria of speech.

Our Berkeley team continues to thrive. Assaf Breska who received his Ph.D. from Hebrew University in Israel will be returning to NAF to coordinate our activities at the conference. He is bringing his EEG equipment to the conference so look for him if you want to see how "alive" your brain is. Assaf will be joined by Hyosub Kim, a post-doc in the lab who received his Ph.D. in rehabilitation sciences from the University of Illinois. This is Hyosub's first trip to NAF and he'll be running a new reaching study. Rounding out our NAF team will be Sam McDougle from Princeton and two undergraduates from Berkeley, Claudia Tischler and Kate Duberg. Ian Greenhouse, a senior post-doc in the lab will be staying home this year, caring for his 6-month old daughter, Lucy.

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 from all of us,



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