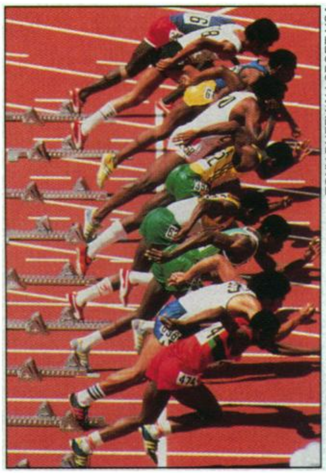
NEUROSCIENCE

Neurons Put the Uncertainty Into Reaction Times

Sprinters on the starting blocks waiting for the gun want to maximize every aspect of their performance. But there is one aspect they can't control, no matter how hard they try. Reactions to a stimulus—even one as anticipated as the starter's gun—can vary randomly by a tenth of a second or more. "You are not in control," says neuroscientist Jeffrey Schall of Vanderbilt University in Nashville, Tennessee. "Sometimes you go fast and sometimes you go slow." Too fast, and you may be disqualified for starting too soon after the gun, as British sprinter Linford Christie was in this summer's Olympics. Too slow and you may lose the race.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Hidden handicap. Sprinters leaving the blocks are at the mercy of randomly varying reaction times.

Schall may not be able to help sprinters solve their dilemma, but he and graduate student Doug Hanes report on page 427 that they have taken a step toward understanding this variability, which shows up in all tests of reaction times. Recording from brain neurons that trigger eye movements in monkeys in response to a visual signal, they found a variation from trial to trial in the rate at which the activity of the controlling neurons ramps up to a threshold, which then triggers the movement. It is as if a bucket must be filled to the brim for the response to occur, says Schall, but the water flow is different every time you turn on the tap.

Mathematical analyses of human reaction times and measurements of neural activity with electrodes placed on the scalps of human subjects had already suggested this general idea. But Schall and Hanes provided the first insight into what's happening in individual neurons to produce the effect. "To see it at a single-cell level is really incredible," says Gordon Logan, a psychologist who studies reaction time at the University of Illinois, Urbana-Champaign. Besides adding to the understanding of normal brain function, the work could provide insights into neurological conditions ranging from attention-deficit hyperactivity disorder (ADHD) to Parkinson's disease.

The variability of reaction times has been a puzzle since psychologists first began measuring them more than 100 years ago. The travel times of nerve impulses, for example, should produce an unvarying (and much shorter) delay than what actually occurs. Instead, explains physiologist Roger Carpenter of the University of Cambridge, U.K., "[with] a mean reaction time of say 200 milliseconds, you might have as much as 100 milliseconds of variability" between consecutive identical trials with the same subject. And this variability appears to be a "deliberate randomization," he says, like "dice-throwing going on in the brain."

A mathematical analysis that Carpenter performed in the early 1980s of reaction times in human subjects pointed to a possible explanation: random variation in the time it takes for the movement-triggering neuronal signals to reach some threshold. Further support for the idea came from experiments done in the mid-1980s by Michael Coles, Gabriele Gratton, Emanuel Donchin, and their colleagues at the University of Illinois, Urbana-Champaign. They asked human subjects to respond to symbols flashed on a computer screen by squeezing their right or left hand. Meanwhile, using scalp-mounted electrodes, the researchers measured electrical activity in the part of the cerebral cortex that directs movement. The electrodes registered a variable rate of increase in neural activity, up to a fixed threshold level associated with the response.

Schall and Hanes wanted to see whether they could detect similar thresholds and the varying buildup in individual neurons. To do this, they trained monkeys to do a reaction-time task in which the animals first fix their eyes on a dot in the middle of a blank computer screen and then, when that dot disappears and another appears to the right or the left, shift their gaze to the new dot. As the animals performed the task, the researchers used electrodes inserted into the monkeys' brains to record the activity of single neurons in a part of the brain called the frontal eye field (FEF), which controls eye movements.

In hundreds of trials, the monkeys' reaction times varied from roughly 150 to 400 milliseconds, and the length of the response time depended on how fast the FEF neurons increased their firing rate to a level that seemed to trigger the eye movement. "Each cell has a certain threshold," says Schall, "and if you reach that threshold, 20 milliseconds later the eyes are going to move." For each neuron the threshold remained constant, but the time to reach it varied. Additional experiments confirmed that the thresholds are real: When the monkeys were given a "stop" signal after the signal to move, they were unable to prevent the eye movement if the FEF neurons had reached the threshold.

Hanes and Schall do not yet know what accounts for the trial-to-trial variation in the time it takes for the FEF neurons to reach their thresholds. But their picture of a neural threshold for reactions might just improve the understanding of certain neurological conditions.

For example, Parkinson's patients have slowed reaction times in eye-movement tests, something that could arise, says Schall, if "the threshold has been raised to a higher level, or the cells accumulate activity abnormally slowly." And Logan notes that children with ADHD do poorly in stop-signal trials—they are less able than normal children are to stop a reaction once it has been triggered—and that their performance is improved by Ritalin, a drug used to relieve the behavioral problems of ADHD. That suggests that ADHD involves an abnormality in the neural mechanisms that control reaction time, says Logan, and Schall and Hanes's work provides "an animal model to look at the neural basis of this."

While the Vanderbilt workers looked only at visual reaction times, Carpenter has analyzed humans and animals in a variety of situations in which they must respond to sounds, lights, even touch. He has found that the distribution of reaction times is similar in all cases, suggesting that they share a common underlying neural mechanism.

But why does this dice-throwing in the brain occur at all? While it may be distinctly disadvantageous to the sprinter waiting for the gun, Carpenter theorizes that it may have evolved because of the advantage it could sometimes provide. In the real world, there is often choice between responses, he notes, and random variation in an animal's reaction time may cause the animal's choices to vary also in a random way. In some cases, that can have a survival advantage. When a predator is trying to figure out what its prey will do, for example, the prey may benefit by behaving randomly—just what the sprinter in the blocks would like to avoid.

–Marcia Barinaga