tell the difference." Even Blackwood's high lod score may be misleading, he continues. "Results like these have been presented before using the same approach" and did not hold up. "So until the research is replicated, I can't jump up and down about these scores." Moreover, the sample sizes are small enough to warrant caution. Finally, Risch and Botstein note that some of Freimer's markers don't seem strongly associated with the illness, and they fault him for not performing a formal statistical analysis that might indicate whether the haplotype frequency in patients with the disease was merely the result of chance.

"I just wonder how many times you can cry wolf without damaging the public's perception of this research," says Risch. At least 14 different chromosomal regions (including the five new ones, as well as one that Botstein's own group recently announced) have now been reported to contain manic-depression genes, he says. "We have four genes for Alzheimer's, two for breast cancer, yet not one for manic depression despite all of these intensive searches. Why is that? Now we have five more loci being claimed to harbor genes. Given the past history of the field, it's not clear to me which if any of these is real."

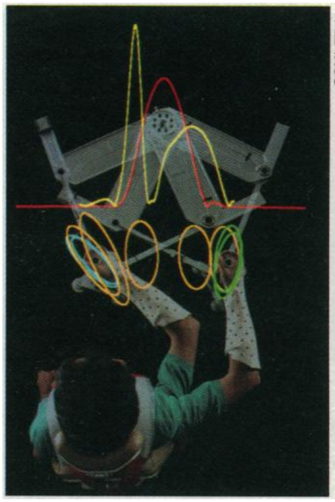
The three researchers counter that Risch and Botstein are far too pessimistic. Their emphasis on lod scores is misleading, Blackwood says. "It's only part of the picture. We use it to pinpoint interesting regions, then go to these sites to see if there's something going on, such as chromosomal rearrangement" that might account for the genetic malfunction. "What we've done is put forward a testable hypothesis," says Freimer, "which we are now testing." That test, via the independent Costa Rican sample, should reveal the statistical significance of the inheritance of the haplotypes his team discovered. Ginns, too, is pushing ahead. And Schork thinks these papers do the field a service by "pointing out the need to develop statistical methods for assessing complex disease traits. They shouldn't be chided because these tools don't yet exist."

One area that all the researchers do agree on is that pooling data—both positive and negative—would speed the process along. "One of the biggest problems is that these studies and others only publish their positive findings," says Risch. "Maybe these studies have turned up some genes that seem to be only of modest effect, but if we merged our data, we'd see they are significant." Blackwood says he would be happy to provide data which did not appear in *Nature Genetics* because of space limitations to anyone who asks, while Freimer says his are under review at another journal. The Amish cell lines are available at a National Institute of General Medical Sciences repository in New Jersey. Such sharing might smooth out these research ups and downs.

–**Virginia Morell**

NEUROSCIENCE

Tilting Against a Major Theory Of Movement Control



Out of sync. The ellipses show the subject's arm movements, with the predicted velocity profile in yellow and the actual profile in red.

GOMI ET AL

At first glance, Hiroaki Gomi and Mitsuo Kawato's invention at the ATR Human Information Processing Research Labs in Kyoto, Japan, looks like a computer setup for arm-wrestling. But it's not. They use their apparatus—a semicircular steel table with a complex system of levers and shafts supporting an armrest above the mirror-smooth surface—to test the strength of the reigning theory about how the brain controls voluntary movements of the arm and other limbs. And as Gomi and Kawato report on page 117, the theory, known as the equilibrium point hypothesis, seems to have lost a round.

The hypothesis implies that the brain does not compute all the forces required to move a limb from one place to another, but simply launches the limb, depending on reflexes and the intrinsic elasticity of the muscles to get it to its destination. That's possible, the theory holds, because that intrinsic springiness makes opposing muscles seek an equilibrium, or balance, whenever the brain perturbs the system by setting the limb in motion—hence the name equilibrium point hypothesis. But by tracking a moving arm and measuring its stiffness along the way with their invention, Gomi and Kawato have undermined the hypothesis, providing evidence that the brain is in fact in control throughout a movement, doing all the calculations necessary to figure out what muscles to move and when.

The Japanese findings join an earlier challenge to the equilibrium point hypothesis, reported in the October *Journal of Neurophysiology* by James Lackner's team at Brandeis University in Waltham, Massachusetts. If the U.S. and Japanese work is right—and not everyone agrees that it is—the researchers will have overcome an idea so entrenched that "it's becoming the folklore of motor-control science," says neuroscientist Gerald Gottlieb of Boston University.

Gomi and Kawato's experiment focused on a variant of the equilibrium point hypothesis that implies that the brain picks the endpoint for a movement and then specifies the trajectory the arm will follow by triggering a sequence of muscle contractions that ensure it reaches that final position. Based on their calculations, Gomi and Kawato predicted that an arm following an equilibrium point trajectory should accelerate rapidly, slow down, and then speed up again before coming to its final destination. Previous work by other scientists had also indicated that the arm should remain stiff throughout the movement.

Designing an apparatus to test those predictions was not easy. "It's a major technical problem to measure stiffness during movement without disrupting the movement," says neurophysiologist Allan Smith of the University of Montreal. It requires a lightweight apparatus that can move as fast as the human arm while being strong and rigid enough to measure the arm's stiffness and movement. To achieve this, Gomi and Kawato designed a setup consisting of an arm brace linked to a motor-driven spindle controlled by a computer, all suspended above the table by flowing air to minimize the effects of extraneous forces on the arm. Even Emilio Bizzi of the Massachusetts Institute of Technology (MIT), who helped develop the version of the equilibrium point hypothesis Gomi and Kawato tested, describes their apparatus as "ingenious."

For the experiments now being reported, three people performed a series of arm movements that each repeated eight times. The subject sat in the chair and extended his or her right arm over the chest-high table, setting it into the arm brace and grasping a handle. The subject then moved the arm to a target displayed on a computer screen at the end of the table as sensors in the brace and handle relayed position and force data back to the computer, which plots the actual trajectory of the arm.

Sometimes, the computer allowed the limb to proceed unimpeded. But at other times, it caused the apparatus to push on the arm a little, too quickly for the brain to adjust for the perturbation. Such perturbations check whether the arm is indeed following the trajectory calculated by Gomi and Kawato.

As the researchers soon learned, the actual trajectories differed from what they predicted. Instead of rapid acceleration, followed by a slowdown and subsequent speeding up, Gomi and Kawato found that the arm moved more smoothly, gradually accelerating and then decelerating as it came close to the final position. And the stiffness was not maintained, but decreased in the middle of the movement after an initial increase. "The brain does not send a signal that is a reproduction of the actual trajectory," Gottlieb notes.

Indeed, Gomi and Kawato think their results put the brain in full control of a movement. They propose that it works backward from visual information about the location of the target to figure out the final angle joints and muscle lengths in the arm once it reaches it target. Then it determines the timing and types of commands it needs to send those muscles to achieve those angles and lengths. "We believe that the brain possesses and utilizes an internal model of the arm for determining the motor command," Kawato says. Gottlieb agrees: "The brain knows enough physics to tell [the muscles] what to do; it doesn't rely on reflexes."

Lackner came to similar conclusions using a very different experimental apparatus, a round rotating room. Subjects placed in the center of this room lose the ability to tell whether or not it's spinning, and so can't rely on sensory clues to correct their movements for external forces, Lackner says. If the equilibrium point hypothesis is valid, subjects should be able to touch a target whether or not the room is spinning, because their movements should follow a set trajectory without undergoing corrections along the way. But that's not what Lackner found. When subjects first tried this task while rotating, they were way off. After several tries, however, their accuracy improved. Then, when the room stopped, the subjects missed the target again.

To Lackner, that "learning" indicates the brain gets a lot of feedback and makes adjustments in the course of a movement, something it shouldn't be able to do if it is simply launching the arm toward an endpoint. "There's a very detailed, ongoing monitoring [by the brain] in anticipation of ongoing movements," Lackner concludes. "We've demolished the hypothesis."

Not everyone agrees. MIT's Bizzi thinks the body may sense the room's rotation, even without conscious perception of it, and thus some unrecognized compensation may account for Lackner's results. And he and Tamar Flash of the Weizmann Institute in Rehovot, Israel, whose own work supports the equilibrium point hypothesis, argue that the Japanese workers used too simple a method for estimating the trajectory the arm should take, making their comparisons meaningless.

The situation is further complicated, however, by a split between Bizzi and others within the pro–equilibrium point hypothesis camp. Anatol Feldman, a Russian-born physicist turned neuroscientist who now works at the University of Montreal, first proposed the equilibrium point hypothesis in 1965. He doesn't think the brain picks an endpoint or has preset trajectories as Bizzi suggested. "It's a dynamic process that does not require a specific program [of action]," Feldman explains. Still, he concedes that even if the brain relies on the springlike properties of the musculoskeletal system to simplify motor control, it might nonetheless have some kind of internal model, albeit not like the one Kawato suggests.

Kawato, too, acknowledges the complexities of how the brain controls movements. "It's not so easy to do these experiments, and it's not so easy to analyze or interpret these data," he says. "They are good starting points for discussion, but I think the dispute will continue."

–Elizabeth Pennisi

EARTH SCIENCE

Impact Craters All in a Row?

After Jupiter got machine-gunned by the pieces of a shattered comet two summers ago, geologists naturally wondered whether the same thing had ever happened to Earth. At last month's Lunar and Planetary Science Conference in Houston, planetary geologist Adriana Ocampo of the Jet Propulsion Laboratory in Pasadena, California, and geologist Kevin Pope of Geo Eco Arc Research in La Cañada, California, announced they had found what look like the scars of a similar rapid-fire impact: a string of three 12-kilometer impact craters in the Sahara of northern Chad.

If Pope and Ocampo are right—and for now they face plenty of skepticism—geologists would have more evidence of the cosmic hazards menacing Earth. They would also have another indication that the Late Devonian period, a time of mass extinctions roughly 365 million years ago, was a particularly hazardous time. Geologists had already identified debris around the world from several impacts in the Late Devonian. And that's also when Ocampo and Pope think the debris of a dismembered 1- to 3-kilometer object slammed into the Chad site.

Neither Ocampo nor Pope has ever set foot in Chad, however. Geologists on the ground had already confirmed that an impact created one crater, but Ocampo and Pope are inferring the same origin for its two fainter companions based only on 1994 radar images from the Space Shuttle. That was not enough to convince cratering specialists at the meeting. In the absence of rock samples, says John McHone of Arizona State University, "I'm just not happy with the Chad site being a chain." Adds cratering specialist Richard Grieve of the Geological Survey of Canada, "There's no geological evidence that they're craters" rather than eroded traces of buried volcanoes.

Clinching evidence is available only for the 12.6-kilometer Aorounga, at one end of the chain. In 1992, a French group including Jean-François Becq-Giraudon of the French Geological Survey and Bureau of Mines in Orléans, France, visited the site and established that the flat-lying rock beds around the feature had indeed been turned upward by a great blast. They also collected quartz grains scarred by the shock of an impact.

Until they can match that kind of evidence, says Pope, "we do want to be careful not to say these are confirmed as two more impact craters." But he thinks that the circumstantial evidence is strong. "It's not only that they are circular features; they also exhibit a pattern similar to Aorounga's—circular depressions with a central peaklike structure." And he sees no signs of volcanic activity.

If he and Ocampo are right, the Late Devonian was a dangerous time indeed. Microscopic spherules of glass scattered across Belgium and China point to two sizable impacts

JPL/NASA

Convincing likeness? Faint companions to the impact crater visible at left in this Shuttle radar image may record a string of impacts.

1.5 million years apart (*Science*, 8 January 1993, p. 175). And in January's *GSA Today*, geologist John Warme of the Colorado School of Mines and paleontologist Charles Sandberg proposed that still another impact triggered a huge underwater landslide in Nevada about 3 million years earlier.

The spherules had already provoked speculations that a shower of comets, dislodged from the comet cloud surrounding the solar system by a passing star, pelted Earth and triggered the Late Devonian mass extinction, when 70% of all invertebrate species in the oceans died out. But for the Aorounga chain to be confirmed as part of an impact shower, someone will have to mount an expedition to northern Chad, where both the climate and the politics are unwelcoming. Watching the show on Jupiter, it seems, was easier than understanding the home planet.

–Richard A. Kerr