

**PRINT EDITION**

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## Dr. Fix-It

**TJOLS**

At first glance, the lobby of Michael Merzenich's headquarters in downtown San Francisco looks like a dentist's office, with couches, a coffee table, some glossy magazines, and a potted orchid. But spend a little time and you may begin to piece together what his business is really all about. Sitting on top of the magazines is a pack of Mensa cards—a deck containing questions to determine whether someone is a genius or merely intelligent. One wall is covered with patents. And another is plastered with news clippings about Merzenich's "brain gym."

Merzenich, a professor in the Keck Center for Integrative Neurosciences at the University of California, San Francisco, is a pioneer in the field of brain plasticity, or the study of the brain's lifelong ability to reorganize itself by forming new neural connections. About 10 years ago, he started Scientific Learning, a company that manufactures software to help children with learning disabilities. Launched on a shoestring, the Oakland, California-based outfit now boasts \$48 million in annual sales. His latest company, Posit Science, makes the Brain Fitness Program, a computer program for older brains designed to sharpen skills and improve memory. Since its founding in 2003, Posit Science has sold tens of thousands of copies of the program at \$395 each.

But colleagues agree that it's never been the money that drives Merzenich. He measures success in a different way. What Merzenich seeks to do is keep peoples' brains as toned and honed as they can be—and changing the brain is possible whether someone is in their early teens or late 90s, he says. Helping people learn something new—a new skill like speaking Italian, say, or dancing salsa—actually alters the brain physically, strengthening neurons and laying down new pathways for neural communication.

"We can use this resource for correction, for assisting somebody that is a little bit or maybe a lot in trouble," says Merzenich, who is Posit Science's chief scientific officer. "So that's what we're trying to do, to marshal this powerful force to help people, to drive their brains correctively."

Merzenich's research, as well as his work at Posit Science, has sharply challenged the view that only very young brains are able to adapt and recover from injury or illness. A recent clinical trial involving users of his Brain Fitness over a period of eight weeks found that participants improved their brain processing speed by more than 131 percent, meaning that the brain was more than twice as fast at taking in and processing information such as speech. What's more, memory improved so much that this function was comparable to that of people 10 years younger.

The program consists of six computer exercises. One includes requiring users to figure out whether the pitch of a tone goes up or down, another is a sound matching game, and yet another asks them to follow directions in order to move objects around on the screen.

randomized and controlled IMPACT study, and Posit Science funded it with a research grant to the two institutions. In the study, half of the 524 participants, aged 65 to 93, did Brain Fitness about an hour a day, five days a week, for eight weeks. Members of the control group watched educational programs and then were quizzed on them. But the gains the controls showed were statistically not as significant as the gains of those who used Brain Fitness.

Nearly half of seniors 85 or older in the United States have full-blown dementia, according to the Alzheimer's Association, and Merzenich says there's no time to waste. "We have the capacity to make almost everybody, every child and adult, stronger, healthier, better from the point of the machinery they are carrying around in their skull," he says. "And what an impact that could have—what tremendous value it would have—to keep people healthier in their brain."

Some researchers are skeptical about what Merzenich says the Brain Fitness program can do. Among the critiques, there's doubt that older people developing cognition problems will have the concentration or the stamina to follow the program for the suggested hour a day for eight weeks.

For others, the notion of a scientist having "clients" is troublesome. Harvard University neurobiology professor John Maunsell says he admires Merzenich's research but feels he is walking a thin line. "It's always a concern when you have scientific reports coming from people who are not completely disinterested in the outcome," he says.

Merzenich brushes aside such criticism, saying that going into the "real world" of commerce, as he calls it, is the way to help real people. As for the rigor of Brain Fitness, Merzenich concedes that changing the brain is hard work, but he says the effort is worth it, and points to his web sites, which are loaded with testimonials from users. "It's like I've walked out of a fog," Ed Steenerson says in one. "Anyone who's known me over the past several years will have seen a real turnaround."

Some of Merzenich's drive to help others stems from his upbringing in rural Lebanon, Oregon. His father, a foreman at a lumber mill, and his mother, a homemaker, both had a strong work ethic, and their six children were expected to give something back to society. Merzenich credits his grandfather, an architect and building contractor who had emigrated from Germany, with fostering his scientific curiosity. His mother's decline from Alzheimer's helped focus his attention on the problems of older people with cognitive impairment.

A kid who built a radio from scratch and served as president of his high school's science club, Merzenich graduated from the University of Portland in 1964 as valedictorian in a class of more than 300 students. He went straight to Johns Hopkins, where he earned his Ph.D. degree in neurophysiology in 1968. After his postdoctoral studies in sensory physiology at the University of Wisconsin, Merzenich headed west to the University of California, San Francisco as an assistant professor of otolaryngology and physiology.

At UCSF, Merzenich quickly made his mark. His work mapping the auditory cortex of different species of animals led him to work with the team that in the mid-1980s developed the commercial version of the cochlear ear implant. The device, which is implanted in a two-hour surgery, restores hearing by stimulating the auditory nerve. It was this work that impressed upon him the incredible power of the brain to remake itself and the profound effect science could have in people's lives.

Since its release more than 20 years ago, the device has been implanted in about 100,000 people worldwide. Its success has given Merzenich a real sense of urgency about the work, says

Posit Science CEO Jeff Zimman. "He's really a man with a mission," Zimman says. "He's in a hurry to get science out into the world."

Brain Fitness has yet to achieve anything like the cochlear implant's level of market penetration, but approximately 150 retirement communities across the United States and Canada now use the program. Meanwhile, one insurance company, Humana, has been offering the \$395-program free or at a reduced price to its Medicare members since 2006.

Charline Truitt, the owner of a company in Orange County, California, that audits mortgage banks, started using the program more than three years ago when she noticed that she was beginning to misplace her keys. "It sounds like a stereotype, but I would find myself in a room and not know why I was there," she says.

Merzenich likens the aging brain to a radio not quite tuned into the right frequency. Doing the program, he claims, will sharpen how you take in and process information, similar to making a signal clearer. Truitt, who started the program in 2004, when she was 60, says she saw dramatic improvement after only a few weeks. "It's amazing really," she says. "The most pronounced was the improvement in my hearing. I had a hard time hearing in noisy rooms, but now I can hear fine. It was phenomenal."

Posit Science has a new project partnering with Easter Seals, the nonprofit organization that works with people with disabilities, to bring the improvements in memory, communications skills, and clarity of thinking seen in older adults to veterans from the wars in Iraq and Afghanistan who have suffered traumatic brain injuries.

When not pursuing his entrepreneurial concerns, Merzenich leads the life of a typical academic scientist. From his 8th floor office at UCSF, he responds to scores of emails he gets from former students and colleagues looking for help with grants and getting papers published. He attends conferences and writes papers, reads up on the latest developments in his field and beyond, and advises the postdoctoral students who work with him.

On a recent morning, he met with Tom Babcock, a research assistant who is doing an experiment to try to ameliorate tinnitus—a persistent ringing in the ears—using himself as a subject. Merzenich reviews the results with him and discusses possible ways to improve them. Gracefully, he segues into a meeting with postdoctoral student Xiao Ming Zhou to talk about his experiment on rats and schizophrenia. Main order of business: Advising him where best to try to publish the results. During this conversation, another postdoctoral student, Linda Wilbrecht, comes in to try to set up a meeting.

"Yeah, Linda, I need to talk to you too about 45 things," he says. "How's life? How's employment?" She responds that she has two jobs. "I need to talk to you about it," she says.

"Only two?" he responds. "Wow, you are so popular."

Wilbrecht, whose research is on the adolescent brain, describes working with Merzenich as a pleasure. "He says taking risks is good even if I don't get grants or publish papers," she says. "Because funding is so tight, a lot of people take fewer risks, so they're not as likely to reach as far or to do something that could fail."

Merzenich has a boldness that is foreign to many scientists, says Henry Mahncke, who studied with Merzenich at UCSF and now works in research and outcomes at Posit Science. "When I first came to UCSF, I thought, 'Here's a man who is thinking thoughts about the brain that 10 years from now will seem new,'" Mahncke says.

Mahncke admires Merzenich's wide reading and broad knowledge, and his ability to absorb and synthesize information from a number of disciplines including molecular biology, psychology, and physiology. "He can look at a set of data and say, 'This is what this means about how the brain works,'" Mahncke says.

Merzenich's broad approach to neurosciences also inspires his colleague, Christoph Schreiner, who came to UCSF in 1981 as a postdoctoral student and returned later as a professor. "He has this ability to integrate information and project out, and that type of synthetic thinking is really quite rare," he says. "He's not just thinking about the next step, but about the next five steps."

On the outside, at least, Merzenich leads a balanced life. He lives in San Francisco but often escapes to a weekend place some 55 miles north of the city in Sonoma County, where he makes wine and olive oil for family and friends. But he never fully relaxes, says his daughter Marghi Merzenich—he's always thinking about science. "He's just very driven to constantly stay in motion," says the younger Merzenich, who is Posit Science's communications director. "He does sometimes have his head in a scientific cloud, but I think that's a good place to be." She says it's often up to her mother, Diane Merzenich, to make sure that Merzenich gets to the right place at the right time.

At the Gerontological Society of America's annual convention last November at San Francisco's Hilton Hotel, participants gathered to celebrate the positive results of the largest study of Brain Fitness. Merzenich showed up late, looking tired and somewhat ruffled, having just flown in from San Diego. One of the guests was James Misko, a neuropsychologist in Dripping Springs, Texas. Misko was so excited about Merzenich's work that he made the trip to San Francisco for this event especially to meet him. One of Misko's patients, a 31-year-old former real estate agent, Ryan Reitmeyer, had suffered a severe brain injury in a boating accident in 2005. Doctors thought he might never talk or feed himself again. "Ryan had very substantial deficits in motor abilities," Misko says. "He had very poor concentration and problem-solving skills and very poor memory."

But Reitmeyer's family didn't give up. One of the therapies they decided to try was Brain Fitness. Reitmeyer first started using it in April 2006. He also consulted nutritionists specializing in the brain, did neurofeedback and physical therapy, and used the Interactive Metronome System, a neurological assessment and treatment tool. Now, a year and a half later, Reitmeyer is doing karate and taking classes in stand-up comedy.

Merzenich's unflagging belief in the brain's enormous potential for recovery makes him a bit of a renegade in the field, says Misko. "It's been very hard to get anybody like the NIH or major scientific journals to pay attention and share the same level of optimism," he says.

Merzenich is used to fighting uphill battles—when he first contended that the adult brain was highly malleable decades ago, he was met with not just skepticism but open hostility. It's natural to be somewhat cautious about making claims about the brain, says Erin Bigler, a psychologist and neuroscientist at Brigham Young University. He says the brain can be very adaptive, including rewiring itself. But since much of the activity occurs on a level too small to see, even with the best of our imaging tools, we can't be sure what is happening at the molecular level. "I tell my students it's like a helicopter over L.A.," Bigler says. "You get a basic idea, but you can't see what's happening unless you're on the ground. You don't know if a water main is blocking traffic or what." Nevertheless, Bigler says Merzenich's research is promising.

Along with programs to ward off cognitive decline, Merzenich and Posit Science are now working on developing programs for people with autism, schizophrenia, and bipolar disorder. And he plans to work on ways to stop disorders in the brain before they start. Strengthening brains that are at risk, he thinks, is the future of neuroscience.

"There's nothing as free as the life of the scientist," he says. "Beyond the findings, to come into the next intuition about what to do next and where it goes or where it leads you, boy, that is open. And that is fun."

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