Early history and career: Michael Merzenich was born in 1942 in the town of Lebanon in the US state of Oregon, the son of a factory foreman and supervisor and a German-American mother in this small agricultural and lumbering community. Upon graduation from local public schools, he matriculated as a general science major at the University of Portland, where he developed a strong interest in the 'great issues' of philosophy—ultimately coming to the conclusion that the true answers to these greatest of questions about the nature of our humanity must lie in the flesh and blood of the brain. In an initially vaguely organized pursuit of deeper understanding, in his own words, he was "…rather miraculously accepted as a doctoral student in the laboratory of Vernon Mountcastle," an internationally distinguished scientist studying the neurological bases of perception, at The Johns Hopkins University School of Medicine in Baltimore.

Through the course of his graduate education, Merzenich came to the conclusion that the study of neurological processes contributing to listening and language could provide an especially strong entre to an understanding of the brain machinery underlying higher brain function, and to that end, was accepted as a research apprentice in one of the world's strongest auditory neuroscience groups, at the University of Wisconsin, Madison. There, under the mentorship of John Brugge, Jerzy Rose and Clinton Woolsey, he completed initial studies in what was to become a several-decades-long quest to define the fundamental nature of the functional organization of the central auditory and somatosensory nervous systems, initially documented in primate and carnivore animal models.

Upon completion of post-doctoral training, Dr. Merzenich accepted a position as an Assistant Professor—then soon thereafter, Director of the John C. and Edward Coleman Laboratory—In the Departments of Otolaryngology and Physiology at the University of California at San Francisco. In the exceptionally supportive and collaborative UCSF neuroscience research environment—later enriched by the establishment of the Keck Center for integrative Neurosciences—he established a research team that was designed to integrate bioengineering, behavioral science, neurophysiology, and medicine in pursuit of understanding the neurological bases of human ability—and the brain's 'failure modes' generally defined as 'developmental disorders', or psychiatric and neurological 'illness'. Throughout a more-than-40-year career as a research scientist and teacher at UCSF, an over-riding goal was to develop practical tools based on advances in integrative and plasticity-based science, to benefit human populations in need, at all due speed.

Diane Merzenich (nee McCann) officially signed on as his partner in 1966, after her return to the US from undergraduate years at the American University in Beirut. Diane had been a childhood friend. Because his laboratory's research studies commonly extended into the early morning hours, she often had to carry the brunt of raising their three daughters, Elizabeth, Margaret and Karen. She obviously did a wonderful job of it, as evidenced by their life partners and by five wonderful grandchildren, all living nearby our San Francisco home, and by a 50-year-long partnership.

'**Adult' brain plasticity.** Studies undertaken to determine the nature of the functional organization of the great sensory-perceptual systems of the brain were, for Merzenich, a prerequisite for understanding complex brain processes. With a team of bright young research fellows, his research group began to generate detailed reconstructions of the information processing machinery defined at key brainstem, thalamic and cerebral cortical brain levels. The ultimate elusive goal was the derivation of a 'grand model' describing brain operations by rule at every brain level, and describing machine operations as a whole. By the middle of the '70's, his team had shown, beyond question, that the predominant theoretical models of brain systems, almost all derived to explain aspects of visual perception and visual cognition, simply could not apply for audition or language. They struggled to understand how to interpret the functional import or their model system's more-complex organization—understanding intuitively that it *only* made sense if the brain was continuously dynamically organizing itself, on a large scale, throughout life. The often-striking individual variation in auditory and somatosensory system organization also strongly inferred that this individuation reflected differences in neurobehavioral ability. This perspective was at odds with the predominant scientific view in this neuroscience epoch—when scientists, again predominantly studying vision, had come to the conclusion that the brain was hard-wired in early childhood, physically immutable across most of childhood forward to the end of life.

Across this same research period in the 70's and early 80's, Merzenich led a team of neuroscientists, engineers, behavioral scientists and medical doctors that created practical prosthetic device models that evolved into what became a commercial multiple-channel cochlear implant.[1] In his words: "I was hijacked to help with—then lead—these efforts at UCSF, by a wonderful senior otolarygologist, Robin Michelson. As a surgeon, Michelson had inherited a wonderful level of understanding of the physical sciences and a great capacity for invention, perhaps from his great uncle Albert. He had far less understanding of the coding of sound and speech in the inner ear or auditory brain. I helped him make up those and other deficiencies, with crucial assistance from a great collaborative team of surgeons, engineers, anatomists, and behavioral scientists." The medical application of these prosthetic devices has resulted in the restoration of speech reception and language abilities in several hundred thousand profoundly deaf individuals over the subsequent several decades.[2]

The recovery of hearing achieved by cochlear implants again directly challenged the broadly held scientific and medical conclusion that the brain in the older child and adult was 'hard-wired'. To the contrary, a cochlear implant patient of any age quickly adapted functionally to their alternatively- (implant device-) encoded aural speech, progressively recovering speech understanding with surprisingly high fidelity, even when very different sound coding strategies were implemented in model devices.

Serendipitously, in parallel with these medical device development efforts, Merzenich's research team's basic science studies had begun documenting large-scale plasticity in brain "representations" in primate animal models, initially in the somatosensory—then soon afterward, in the auditory—nervous system(s). Initially working in collaboration with Jon Kaas and colleagues at Vanderbilt University, they showed that progressive, large-scale remodeling of the representation of the sensory epithelium of the body followed limited cutaneous denervation. The very different forms of that remodeling with and without peripheral nerve

---

[1] Commercialized by Advanced Bionics, Inc., now a division of Sonova Holding, AG.

[2] In 2014, the US National Academy of Engineering's Russ Prize honored our UCSF team by acknowledging me as a co-inventor of the modern multiple-channel cochlear implant.

repair indicated that this 'adult plasticity' was competitive, and was achieved via temporal-coincident-input-dependent processes.

In the next sequence of studies, laboratory scientists confirmed, beyond argument, that the detailed "maps" of sensory-perceptual inputs in the brain were plasticity-refined, time-based constructs. More specifically, they showed that: a) the primary processing unit of the cerebral cortex, the cortical "mini-column", is a creation of competitive plasticity processes; b) the neuronal memberships and response coherences of neurons within mini-columns are modifiable, on a grand scale, throughout life; and c) to a level of first approximation, that 'adult' cortical plasticity follows a "Hebbian rule", and is expressed as "competitive Hebbian network plasticity".[3] These conclusions led to studies, led by laboratory scientists William Jenkins, Gregg Recanzone, Xiaoqin Wang, Randy Nudo, Christian Xerri and others, in which monkeys were trained to acquire—then progressively improve at skills designed to drive changes in spatial and/or temporal (and integrated spatio-temporal) dimensions of cortical 'representations'. Consistent with a Hebbian plasticity rule, it was easy to drive either 'negative' or 'positive' changes in neurological representations, at will. Specific aspects of physical brain change were invariably strongly correlated with changes in the animal's emergent and improving (or degrading) behavioral performance abilities. By these studies, Merzenich and colleagues demonstrated that the acquisition and experience-driven refinements of any skill or ability is almost certainly a direct product of neurologically lawful, progressive brain remodeling. Physical brain change, through the course of life, is the primary source of operational human abilities and identities.

Translating neuroplasticity science to help neurologically struggling children and adults. At this stage of study progression, circa 1990, the focus of research in Merzenich's laboratory rapidly evolved in two pragmatic directions. First, with the appreciation that they could drive predictable, controlled, positive changes in the brains of neurologically impaired or struggling human populations, his team became committed to more aggressively translating their science out into the world for human benefit. In parallel, with the understanding that these translational efforts would be limited by the efficiency of brain remodeling strategies, they initiated studies designed to further define how to most effectively engage brain mechanisms to most strongly and rapidly enable adult brain plasticity.

In 1992, in collaboration with Rutgers University scientists Paula Tallal and Steven Miller and his UCSF colleagues (especially, William Jenkins), Merzenich's team developed a training strategy designed to restore processing speed and representational accuracy in language-impaired children destined to fail as readers, a large human population shown earlier by Tallal and colleagues to have degraded spectro-temporal speech reception abilities. Following principles established in earlier primate training studies, his team created progressive computerized game-like tasks that rapidly renormalized the aural speech reception and speech

[3] The Canadian psychologist Donald Hebb hypothesized that coincident-dependent changes in synaptic (brain network connection) strengths could provide the basis for 'plastic' organization of brain systems and learning. Theorists later constructed connectionist models with simple excitatory and inhibitory terms that illustrated how these coincident input-dependent processes could more specifically shape cortical circuits ("Hebbian networks"). In studies led by Kamil Grajski, Dean Buonamano, and others, Merzenich's team implemented models of this class, as one strategy for demonstrating that their plasticity-driven phenomenology, to a level of first approximation, was a plastic "Hebbian network".

production abilities of most of these developmentally impaired kids. UCSF Chancellor Joseph Martin supported Merzenich's efforts to establish a company (Scientific Learning Corporation: SLC) to help deliver this science out into the world to help struggling children. SLC has subsequently applied these (and extended) training strategies to improve the language, reading and cognitive abilities of more than 5 million children.

As these practical efforts were growing, Merzenich's UCSF laboratory focused on increasing their understanding of neurological processes controlling brain change, on the path to defining how they could drive the strongest and most-enduring changes with greatest efficiency. Michael Kilgard, Shaowen Bao, Dan Polley and David Blake were especially important contributors. Merzenich's research group also began to more directly model human illness and disease—rapidly showing that there is invariably a major contribution to their expressions resulting from 'negative' plasticity—and initiated studies assessing our ability to overcome these forms of natural negative change expressed in specific clinical indications via intensive, targeted training. Those efforts led to the creation of a second company (established when UCSF generously granted Merzenich a second leave of absence), Posit Science Corporation (PSC), in 2003. PSC's mission has been to translate neuroplasticity science to benefit normally aging individuals, and to drive corrective therapeutic change in individuals of all ages struggling because of a wide variety of clinical indications. Attention and cognitive losses in normal aging or derived from childhood or adult socio-emotional trauma, mild cognitive impairment, schizophrenia, bipolar disorder, major depressive disorder, traumatic brain injury, concussion, stroke, 'chemobrain', brain infections like HIV-AIDS, multiple sclerosis, ADHD, conduct disorders, and addictions—and the delay of onset or prevention of psychotic illnesses and of Parkinson's, Huntington's, Alzheimer's and related neurodegenerative diseases—are among PSC's human medical targets.

The Genie is out of the bottle.[4] The current research and development focus of Dr. Merzenich's team is on delivering these forms of help out into the world, distributed as broadly as possible to promote better brain health in world populations; on that path, to at least often delay and if possible prevent the onsets of psychiatric and neurodegenerative diseases; to help children who struggle because of neurologically damaging earlier childhoods, or because of genetic misfortune; to help millions of individuals amongst us who suffer the vicissitudes of physically injured brains; and to help every individual understand that their brain confers for them the power to improve their abilities and the qualities of their life, almost every day of that life on our planet. The growing understanding of how to apply brain plasticity to guide us to

---

[4] For an overview of Michael Merzenich's scientific contributions and historical perspective, see Merzenich MM (2014) *Soft-Wired*. Parnassus Publ., San Francisco (Amazon). Also see Merzenich MM, Jenkins WM (1993) Reorganization of cortical representations of the hand…. *J Hand Ther 6*; Merzenich MM (2015) Early UCSF contributions to the development of multiple-channel cochlear implants. *Hearing Res 332*; Merzenich MM, et al. (1990) Adaptive mechanisms in cortical networks underlying cortical contributions to learning and non-declarative memory. *Cold Spring Harb Symp Quant Biol 55*; Merzenich MM, Jenkins WM (1995) Cortical plasticity, learning and learning dysfunction. IN*: Maturational Windows and Adult Cortical Plasticity.* Julesz & Kovacs eds, Addison-Wesley:New York; Merzenich MM, de Charms RC (1996) Neural representations, experience and change. IN: *The Mind-Brain Continuum*, Llinas, Churchland, eds., MIT Press; Merzenich et al (1998) Some neurological principles relevant to the origins of—and the cortical plasticity-based remediation of—language-based learning impairments. In: *Neuroplasticity*. Grafman, Cristen, eds., Springer-Verlag, New York; Merzenich MM et al (2014) Brain plasticity-based therapeutics. *Front Hum Neurosci 8*.

better lives IS a revolution that has the potential for transforming human societies on a grand scale.

At the same time, in Merzenich's words "…across the span of my scientific lifetime, neuroscience has transformed our understanding of our true human natures. We are endowed with plastic brains that enable the creation of an interpretable model of the world within each of us in our lives, and that individuate us as an ongoing, life-long work in progress on the basis of the information that we gather from that world and from our external and intra-cranial operations within it, through quadrillions or centillions of change moments. Over the next decades, we shall rapidly grow our understanding of how to exploit this great endowment, for the enrichment of every human life—and by that science, to transform human lives and societies—hopefully very much for the better."

It's team science. In Merzenich's words, "Every scientific, technological and business collaborator has made a significant contribution to this work, as have the tens of thousands of subject volunteers who have helped carry our science out the laboratory door into the world. I accept this Award on behalf of this wonderful research family. Their collective efforts have been acknowledged by the award of this Prize, and by the early award of prizes and awards to me, including the IPSEN Prize, Cortical Discovers Prize, Thomas Alva Edison Prize, Purkinje Medal, Zotterman Prize, Distinguished Scientific Contribution Award (APA), Golden Electrode Award, Russ Prize, and other awards, honorary professorships and distinctions—and by my election to the US National Academies of Science and Medicine. The collective efforts of this research family has resulted in the awarding of more than 60 US patents, in the publication of hundreds of scientific scientific reports—and most important of all, in the provision of help, for millions of children and adults in need."