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In memoriam: Dr. George Bartzokis, neuroscientis who developed the 'myelin model' of brain diseas

Mark Wheeler/UCLA Health Sciences | September 10, 2014

Dr. George Bartzokis, a neuroscientist who originated the theory that the degeneration of the brain's myelin contributed to many developmental and degenerative diseases, such as schizophrenia and Alzheimer's, died of pancreatic cancer on August 22. He was 58.

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A professor of psychiatry at the UCLA Semel Institute for Neuroscience and Human Behavior and the David Geffen School of Medicine, Bartzokis was born in a Greek refugee camp in Romania in 1956. When he was 14, his family immigrated to Boston, where he quickly learned English by using a Greek dictionary while watching television. His parents purchased a pizza shop in Newton, Massachusetts, where he worked throughout high school, college and his first two years of medical school. He graduated cum laude from Harvard College and earned his medical degree at the Yale University School of Medicine.

In 1983, he moved to California to begin his psychiatry residency at UCLA, where he completed his internship and residency at the NeuroPsychiatric Institute (now the Semel Institute) and a research fellowship in brain imaging. Prior to becoming a professor of psychiatry, he was a professor in the UCLA Department of Neurology, as well as the clinical core director of the UCLA Alzheimer's Disease Research Center and the Memory Disorders and Alzheimer's Disease Clinic.

"This was a man of quiet demeanor, but of great compassion and unusual talent, devoted to his family and meticulous in his science," said Dr. Peter Whybrow, director of the Jane and Terry Semel Institute for Neuroscience and Human Behavior, the Judson Braun Distinguished Professor and the executive chair of the Department of Psychiatry and Biobehavioral Sciences. "Over the past decade, I have been privileged to sample some of this fine character firsthand. George would appear in my office every few months, bringing with him the excitement of his latest ideas and his most recent publications. He was resolute in his vision, and I looked forward to our meetings. I learned much from George."

As a professor in the department of psychiatry, Bartzokis was an early investigator into the damaging effects of iron in the brain. He invented and patented a method for measuring brain iron levels in vivo using magnetic resonance imaging.

Bartzokis also conceived a novel developmental model for neuropsychiatric diseases based upon what makes the human brain most unique: its high myelin content. Myelin is a fatty sheath that coats nerve axons, allowing for efficient conduction of nerve impulses. It is key to the fast processing speeds that underlie our higher cognitive functions and the encoding of memories. "The pervasive myelination of our brain is the single most unique aspect in which the human brain differs from other species," he noted.

In 2001, Bartzokis demonstrated that myelination follows an inverted, U-shaped growth trajectory in the brain that peaks in middle age and falls off with continued aging. The myelin that is deposited in adulthood covers increasing numbers of axons with smaller axon diameters and so spreads itself thinner and thinner, he found. As a result, he argued, the myelin becomes more susceptible to the ravages of age in the form of environmental and genetic insults, and it slowly begins to break down faster than it can be repaired.

His myelin model cut across the current symptom-based classification of neuropsychiatric disorders, emphasizing instead that dysregulations in myelination drive various neuropsychiatric disorders across the life cycle. His model proposed that disruptions in myelin metabolism at defined developmental phases cause specific types of mental illness by undermining the synchrony of neurotransmission. He most intensively studied this in schizophrenia, where he found the white matter volume trajectory across the lifespan in schizophrenic people was lower than in normal people, and that some of the antipsychotic medications could correct white matter volume loss.

The steady cognitive decline with aging and the development of dementia was another major area of focus for Bartzokis. Most scientists have focused on the accumulation of the amyloid beta peptide, since it is found in the brains of Alzheimer’s sufferers. That is understandable, Bartzokis said, since the same genes and enzymes involved in controlling myelination and myelin repair are, ironically, also involved in the production of amyloid-beta proteins. Bartzokis' point was that the amyloid beta may actually develop as a result of the natural process of the repair and maintenance of myelin. Most drugs that have been developed for Alzheimer's targeted amyloid beta, but little if any clinical improvement has been seen. Targeting amyloid beta, he said, is "similar to cleaning up a house that's been flooded by water but never repairing the actual pipe that created the flood.” He believed that drug development should focus on the targets much farther upstream, earlier in the process before the amyloid beta plaques develop. With modern brain imaging technology, clinicians could track the dynamic changes taking place in the brain and intercede well before any signs of Alzheimer's are seen.

"The greatest promise of the myelin model of the human brain is its application to the development of new therapeutic approaches," Bartzokis said.

Bartzokis always credited the excellent mentors he had in his early research years. They included Drs. William Oldendorf, Ted Van Putten and Michael Goldstein. Bartzokis went on to mentor over 50 individuals who have developed their own careers through graduate or medical school.

"He was a remarkably innovative thinker," said Dr. Lori Altshuler, director of the UCLA Mood Disorders Research Center, of which Bartzokis was a member. "He never let dogma define his thinking. He was incredibly well-read in a wide range of fields, including physics, biology and genetics. His main driving passion was to discover medications that could change the trajectory of psychiatric illness. He felt drug development in the arena of myelin repair had a solid theoretical rationale for being able to be effective if not curative for some disorders. The field has lost a deep thinker who will be sorely missed."

Bartzokis was also known for his sly sense of humor. His family carried that forward in the program for his funeral by listing as one of his academic mentors "Leonard McCoy," the ship's surgeon in the original "Star Trek" series. Bartzokis always joked that McCoy was how he became so intrigued with Magnetic Resonance Imaging (MRI), because he thought the futuristic device the doctor used to instantly diagnose medical conditions would most likely have been based on Nuclear Magnetic Resonance (NMR) Spectroscopy, just as MRI is.

Bartzokis is survived by his wife, Kelly Phelan, and two daughters, Katherine and Christina. His funeral was held on Sept. 1 at St. Sophia Greek Orthodox Cathedral in Los Angeles. Donations in his memory may be made to the UCLA Foundation for the George Bartzokis Innovative Research Fund. Please send to Alan Han, director of development, neuroscience, UCLA Health Sciences, 10945 Le Conte Avenue, Suite 3132, Los Angeles, CA 90095-1784.

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