Peter Huttenlocher

(1931–2013)

Neurologist who showed formation and pruning of synapses in child development.

Peter Richard Huttenlocher, a wonderfully kind and quietly driven neurologist, showed that billions of synapses — the connections between brain cells that mediate learning and memory — are generated in the human cerebral cortex during the first months of life. He also made the more surprising discovery that many of these synapses are eliminated during subsequent years, just when children achieve the most important developmental milestones, such as walking and speaking.

This idea — that the elimination, or 'pruning', of synapses is as much a part of learning as their formation — has come to influence fields as diverse as developmental neuroscience, child development, early education and native language learning.

Huttenlocher, who died of pneumonia on 15 August after a long struggle with Parkinson's disease, was born in Oberlahnstein bei Koblenz, Germany, in 1931. His mother, an opera singer, refused to join the Nazi party and fled to the United States in 1937, leaving the young Peter and his brothers to be raised by their father, a chemist. Huttenlocher's experiences as a child witness of Nazism during the Second World War, and of the starvation and suffering of German survivors in the Russian and French zones in post-war Germany, contributed to his lifelong interest in ethics, morals and human behaviour.

In 1949, aged 18, he travelled to the United States with his older brother Dieter to visit his mother, and decided to stay. Soon after Peter arrived, he attended the University of Buffalo in New York where he met his future wife, Janellen Burns, who would go on to become a successful cognitive psychologist.

Peter graduated *summa cum laude* in philosophy in 1953, and he and Janellen married a year later. Together, they moved to Harvard University in Massachusetts, where she obtained her PhD in Psychology, and he his doctor of medicine at Harvard Medical School, graduating *magna cum laude* in 1957. After medical residency training and two research fellowships, Huttenlocher spent a couple of years as an instructor at Harvard, followed by eight years as an assistant and then associate professor of paediatrics and neurology at the Yale School of Medicine in New Haven, Connecticut. In 1974, he and Janellen moved to the University of Chicago in Illinois, where he remained for the rest of his career. There, he was a professor of paediatrics and neurology and the founding head of child neurology.

JAMES BALLARD/UNIV. CHICAGO MEDICINE

In the mid-1970s, Huttenlocher began to study the formation of synapses in the brains of healthy children and young adults who had died from various causes. Using an electron microscope, and doing much of the work himself, he mapped the developmental trajectory of synaptogenesis in the cerebral cortex from around the time of birth to early adulthood. He originally planned to compare the brains of children with intellectual disabilities to those without, but, as he later wrote in an essay on the subject, he soon discovered that "the findings in the normal population were more interesting than the abnormal population".

Huttenlocher found that the number of synapses increases more than tenfold during the first year after birth. This made sense, given the need for synaptic connections to form the neuronal circuits that underlie new abilities and memories in the first year of a child's life. Surprisingly, however, sometime during the second year of life, the total number of synapses drops drastically. Huttenlocher showed that synaptic pruning continues over several years — just when children are acquiring language, learning to run and starting school, with total synaptic counts stabilizing in adolescence.

Huttenlocher's discovery that synapses are overproduced and then pruned was 20 years or more ahead of its time. Today, most ideas about human brain development, from the microscopic to the macroscopic to the societal, draw on his work. For instance, researchers are now investigating the mechanisms that control pruning, the possibilities that this synaptic plasticity provides, and how to use an understanding of synaptic development to optimize early educational intervention, language learning or music instruction. Moreover, in the past decade, most models of autism spectrum disorder have suggested that people with autism might not have fewer synapses in their brains than people without, but, instead, that they show defects in the removal of synapses that are usually eliminated.

Huttenlocher continued his work on synapses throughout the 1970s. He was among the first to observe that the brains of individuals with intellectual disability have the same number of synapses as those without, but that the synapses tend to be different in shape. This discovery of the relationship between synaptic shape and function is another key element in our understanding of brain plasticity and learning. He also made numerous other contributions; for example, he discovered that an inherited form of epilepsy is associated with a mild brain malformation, and he advanced the understanding and treatment of various childhood neurological conditions such as tuberous sclerosis.

Peter's greatest passions were teaching, his research and caring for the innumerable children with brain conditions who came to him for treatment. But he also enjoyed classical music, playing the flute, gardening and baking. And he took great pleasure in his three children (all of whom have pursued impressive careers) and four grandchildren. He will be remembered for his pioneering and visionary work on human synaptic development, and also by the many patients whose lives he made better and the many physicians and students whom he trained in his years at Yale and at the University of Chicago. ■

Christopher A. Walsh *is a Howard Hughes Medical Institute investigator, chief of genetics and genomics at Boston Children's Hospital and professor of paediatrics at Harvard Medical School in Boston, Massachusetts. He was a student under Peter Huttenlocher at the University of Chicago in Illinois.*
e-mail: christopher.walsh@childrens.harvard.edu