

city of Tucson, Arizona, USA, because they depend on sunflower seeds from bird feeders. Several examples of plant and animal species evolving resistance to specific pollutants have also been reported, including killifish tolerating polychlorinated biphenyls (PCBs). Meanwhile, urban variants of white clover gave up on chemical defences against herbivores and gained better freezing tolerance in exchange.

To answer important questions regarding the evolution of species in the rapidly growing urban environment, Johnson and Munshi-Smith call for studies that more systematically make use of the unique, quasi-experimental set-up where new habitat is built in many places across different climate zones. Existing studies have mostly focused on a small number of species in one city or in a few cities in the same geographic region.

The authors call for researchers to “maximize the number of cities studied to test for the generality and convergence of urban evolutionary processes and patterns”. Cities should be studied around the world, with multiple populations sampled along a gradient from the urban to the rural environment, and with planned experiments to elucidate mechanisms of evolutionary change.

The global spread of urbanisation and infrastructure may well be a disaster for what remains of terrestrial wildlife, but it is also an opportunity for researchers to watch evolution in action. Guiding this evolution could even be good for our health. “The trick is that many of the evolutionary changes that occur around us are to our detriment,” says Dunn. “A big challenge moving forward is whether or not we can be smart enough to favour the kinds of evolutionary scenarios that yield species better for our health and well-being rather than worse.”

If we gain an improved understanding of how nature responds to the major disturbances that urbanisation brings, it may help to make cities more compatible with the surrounding landscape, and make them a more suitable and sustainable habitat for both humans and wildlife.

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Profile

Brenda Milner and the origins of cognitive neuroscience

Robert Zatorre

The headlines in the Manchester Guardian on 15 July 1918 were full of news about the gruesome final months of World War I (“British take 260 prisoners near Ypres”), alongside long lists of casualties, and equally long lists of the dead from the influenza epidemic. Also of interest, an article that day defends the controversial proposition that women should be allowed to practice law. It was into this world that the newspaper records the birth of a daughter to Mr and Mrs Samuel Langford. That child was Brenda Milner, one of the most renowned neuroscientists of our day, whose centennial birthday we now celebrate.

The world of neuroscience was also in its infancy at the time, with the Nobels to Pavlov in 1904, and to Ramón y Cajal and Golgi in 1906 establishing some of the first basics of our discipline just a few years before. By the time Brenda matriculated at Cambridge in 1936, initially to study mathematics, and then psychology, some additional progress had been made, but psychology was still part of “moral science” at Cambridge, and the idea of linking it to physiology would have been considered fanciful.

It was the fortuitous move to Canada in 1944—occasioned by a wartime research project for Brenda’s then-husband Peter—that really provided her the opportunity to pursue the work that would make her famous: first, by allowing her to complete her PhD with Donald Hebb, a psychologist at McGill whose classic monograph “The Organization of Behaviour” promoted the idea that complex behavior, and even cognition, could be explained by neural circuitry; and second, because Brenda was subsequently able to work with neurosurgeon Wilder Penfield.

Penfield, the founder of the Montreal Neurological Institute (MNI), had been



Brenda Milner who celebrates her 100th birthday next month. Photographer Meera Paleja; photo courtesy of the Montreal Neurological Institute, McGill University.

performing excisions from epileptic patients’ brains for some years, but was puzzled about the variable consequences on memory and other functions that resulted. Brenda’s mandate was to figure out what was going on, a seemingly impossible task given the lack of knowledge at the time, to the point that Hebb warned her that “No psychologist can survive at the MNI,” as she is fond of reminding everyone with a knowing smile (indeed, she has outlived everyone who was at the MNI in 1950!).

Brenda took a systematic, organized approach to the problem, dissecting behavioral abilities by carefully selecting tasks to probe for specific aspects of function. Much of her work was guided by experimental lesion research in primates and other species, a novelty at the time, and a model which she strongly endorses to this day as a way to gain insight into human brain function. Her first insights came from the application of such careful tests to Penfield’s patients with unilateral excisions of parts of the temporal lobe: she observed that only after removal of medial-temporal structures, rather than neocortex, did memory deficits appear.

But it was her study of patient HM that provided the real breakthrough. Whereas Penfield was too conservative to attempt bilateral medial temporal excisions, an American surgeon had done so in this patient, with devastating results to his memory. Brenda was not only able to document the deep amnesia that HM suffered, but because of her past experience with the other cases, was able to formulate a model about the functional role of the

hippocampal complex in the formation of new memories, information that today is found in every textbook.

In a stroke of inspiration, Brenda decided to try other types of memory task with HM, and found to her enormous surprise and delight that he was able to learn certain skilled tasks, such as drawing in a mirror, while having no explicit memory for ever having learned them. This dissociation became the basis for another foundational aspect of memory theory: that multiple parallel memory circuits can be dissociated depending on the structures involved. Critically, Brenda did not treat HM just as a curiosity to be exhibited, but rather as a kind of Rosetta Stone, a key to understanding, which subsequently led to a series of careful papers with other patients that slowly but clearly uncovered the circuitry underlying memory.

Although Brenda is still today most well-recognized for her work on memory, her contributions in other domains are at least as important. It is hard to appreciate today how little was known in the 1950s and 60s about brain function in relation to cognition: Penfield's famous maps of the cortex are very detailed in the motor regions and a few other areas, but some parts of the brain are labelled vaguely as 'interpretive', while the frontal regions are for the most part just left blank. The frontal lobes became Brenda's playground. She again adapted tasks from experimental studies in monkeys, and began to systematically assay the consequences of lesions, revealing some of the first insights into what today we would call executive functions, such as planning, decision-making, organizing tasks to achieve future goals, modifying ongoing behavior based on updates from the environment, and even emotional and social behaviors. Many of us remember her anecdote about chancing at an airport upon one of the patients with frontal-lobe damage, who was so happy to see her that he inappropriately began to hug and kiss her repeatedly. Far from being appalled, Brenda was delighted to experience this disinhibited behavior, as evidence of the importance of frontal cortex in regulating behavior.

Another domain in which Brenda made major discoveries pertains

to hemispheric specialization. The phenomenon itself had of course been described a century earlier by Broca and others. But Brenda once again was able to improve our understanding by carrying out precise, well-controlled experimental approaches, rather than descriptive case studies, as was still common at the time. An important extension to the concept of lateralization was the observation that memory systems are also lateralized, such that lesions to the left medial temporal lobe result in greater verbal recall difficulties than similar damage to the right, associated with spatial memory deficits. Brenda was also able to definitively quantify hemispheric lateralization patterns in relation to handedness by reporting the relative frequencies of language lateralization for left and right handers who underwent unilateral hemispheric anesthetization via the intracarotid sodium amobarbital test. It was also in her lab that the dichotic listening test was first used as a probe of lateralization. But perhaps her greatest contribution in this domain came with her dogged insistence that the right hemisphere of the brain was not merely 'non-dominant', almost an appendage to the dominant left, as was commonly thought at the time, but rather that it housed its own specialized mechanisms for nonverbal cognition.

One brilliant demonstration of this phenomenon was done in collaboration with Roger Sperry, whose split-brain patients Brenda tested in a tactile recognition task. The results were astounding because, for certain tasks, requiring encoding of complex nonverbalizable shapes, the left hand (controlled by the right hemisphere) far outperformed the right hand, thus demonstrating that the right hemisphere had its own specialization, complementary to language.

Remarkably, Brenda continued to work on many different topics well into her 90s, in particular adapting quickly to new technologies as they became available, especially functional neuroimaging, which she embraced early on, always pursuing the important questions about memory, language and executive function with care and clarity.

It's hard to underestimate Brenda Milner's influence; she provided the impetus for what today is the

well-developed field of cognitive neuroscience. The field could not have achieved any kind of maturity without the foundational discoveries mentioned above. Beyond that, Brenda's lab provided the training ground for a huge number of scientists who went on to found their own groups and who became prominent in their own right. All of us learned from Brenda not only some of the basics of our area, but some broader ways of thinking about science, too. One message we all received was about the importance of honing our experimental questions based on empirical observations. Brenda considers herself a careful observer, not a theoretician; she is fond of saying that theories come and go, but good data always stay, a concept that many of her students have taken to heart. One might argue that contemporary emphasis on brain networks and connectivity patterns renders the older, more localizationist concepts unattractive. But because Brenda was never doctrinaire, she would say that distributed models can certainly be quite powerful, but they still need to explain the behavioral dissociations caused by focal lesions that she reported so clearly.

The other concept that many of us learned from her is to allow students to pursue their own ideas, rather than to give them specific research problems to solve. Brenda always valued creativity and was not afraid to take risks, such as funding the expensive and unproven brain imaging technology in the early days of that domain, from which many of us benefitted. Above all, Brenda always encouraged curiosity, and curiosity-driven research, questioning demands from funding agencies that research have direct applications. Few of her major breakthroughs would have happened had she not had free reign to explore, she likes to point out, despite the fact that most of these did indeed prove to have enormous applications to the clinical domain, and perhaps ironically, have also led to major theoretical insights.

Thank you, Brenda, for everything you've done, and happy birthday!

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