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In Memoriam

Lessons from Leslie: A Tribute to an Extraordinary Scientist and Mentor

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The scientific community has lost one of its giants, Leslie G. Ungerleider, who, for many years, was chief of the Laboratory of Brain and Cognition at the National Institute of Mental Health (NIMH) and an National Institutes of Health (NIH) Distinguished Investigator. It is difficult to put into words what this loss means. Leslie was a deeply respected and admired leader across the neuroscience community and beyond. Those who met her at conferences or attended some of her brilliant lectures were often left with an indelible impression from the interaction. Researchers who were fortunate enough to collaborate with Leslie experienced her unique mark on their scientific thought. In addition, for those trained by her (such as the authors of this tribute), Leslie profoundly contributed to shaping their career paths as well as their personal growth. Leslie was an extraordinary scientist, mentor, and friend.

Leslie Ungerleider in 2002. Photo courtesy of Michael Beauchamp, Baylor College of Medicine.

In addition to her fundamental scientific contributions, the exceptional mentorship she offered to all working in her lab is an inextricable part of Leslie's legacy. Here, we reflect on some of Leslie's most notable scientific achievements and how her perspectives on science, career building, and mentorship influenced our own paths.

A Visionary Scientist

Born in 1946 in Queens, New York, Leslie discovered her love for brain science through experimental psychology as an undergraduate at Harper College in Binghamton and then as a graduate student at New York University. Yet, her work that ultimately changed the course of neuroscience began at Stanford University with Karl Pribram, where Leslie studied primate visually guided behavior and how it is affected by brain lesions. She then continued this work at the NIMH in Mortimer Mishkin's lab, which she joined in 1975. Leslie's perspective integrated multiple disciplines, and the rich knowledge that comes with each. This deeply cross-disciplinary approach was one of the contributors to Leslie's remarkable insights as a scientist. She often sought several different scientific pursuits (and sometimes career paths) in parallel: as a neuroanatomist, her work provided the bedrock for an understanding of structural connectivity within the visual system and beyond; as a neurophysiologist, her studies (many of them with Robert Desimone) laid the foundation for an understanding of the functions of the visual system; and as a neuroimager, she translated her rich knowledge of the primate brain to the exploration of structure–function relationships in human cognition. We believe that Leslie's career and approach to neuroscience offer an important insight for future scientists. The two pillars of outstanding science that Leslie epitomized were 'depth' and 'breadth'. She taught us not only that mastery of one or two research methods is indispensable, but also that strong, solid (not superficial) knowledge of multiple areas of research is a requirement for good science; a key to asking profound questions. Leslie's research grew from clear hypothesis-driven inquiry, informed by broad and deep theoretical frameworks. To many of us who worked closely with her, her 'So what?' interjections were always a reminder that research should be an undertaking aiming at meaningful answers. We should strive to test fundamental questions by integrating knowledge across research areas and fields. It feels that, perhaps more than ever, models of profound and scholarly scientific pursuits are needed for invigorating future generations of scientists; Leslie embodied one that was both inspiring and productive during her long and distinguished career.

A Unique Thinker

One of the most important things Leslie taught us was how to go about thinking out our research. Her way of thinking about neuroscience was uniquely logical and integrative. Each experimental result was a puzzle piece that had to fit into the broader framework of what was known about anatomy, physiology, neuroimaging data, and behavior. Breadth and depth of expertise were necessary prerequisites for this type of thinking, but were not sufficient. Leslie was able to draw knowledge from data, in that she saw connected patterns and systems, rather than disjointed lists of facts. When faced with seemingly conflicting results, she was intrigued, not disappointed. She taught us to consider how a current experiment's results fit together with other results and theories all the way from sensation to perception, and then to attention, memory, and behavior. She pointed out the trap of becoming too invested in a particular theory, or worse, a rivalry between advocates of opposing theories. She made clear that data were as important as their interpretation. However tenacious she was in laying all the puzzle pieces until they fit, she was even more decisive in starting from scratch if a new puzzle piece showed up that did not fit.

Leslie's ability to extract fundamental principles from a multitude of findings is what gave rise to her earliest, and most well-known concept: the organization of the visual system into parallel pathways. At a time when the organization of extrastriate cortex was largely an enigma, Leslie, together with Mort Mishkin [1], proposed that the multitude of visual areas were organized into two largely separated projection pathways, both originating in primary visual cortex: an occipitotemporal (or ventral) pathway, which processes information about the identity of an object (or what it is), and an occipitoparietal (or dorsal) pathway, which processes information about the location of an object (or where it is). This simple dichotomy has become a defining framework for conceptualizing the organization of sensory systems more generally, and has inspired thousands of studies since. It is part of almost every neuroscience textbook and sets the stage in many lectures on the visual system. The functional distinction between the 'what' and 'where' pathways was not based only on the double dissociation found in studies of the behavioral results of lesions in the temporal versus parietal cortices. Leslie considered the logic of the overall neuroanatomical organization, including the source and destination of the information, and the nature of its processing along those pathways. What was the behavioral purpose of the information being extracted and represented? The question, 'What does it mean?' guided her work and, not surprisingly, was frequently posed to everyone in her lab.

This way of thinking about how disparate pieces in a puzzle had to fit together in a meaningful way (with a clear logic) also meant that Leslie had a deep interest in other people's research. She listened intently to others' results and ideas, to be stored in her mind as additional pieces to the puzzle, even if it was not immediately obvious where each piece might fit.

Asking Big Questions

Equipped with the breadth and depth of knowledge from a multidisciplinary background, Leslie was able to pursue big, impactful questions, a way to conduct science that inspired all of us. For example, her research over the years has helped define our current understanding of the neurobiology of working memory, bottom-up and top-down attentional systems, affective and social processing, object and face perception, visual imagery, perceptual decision-making, as well as plasticity in the motor system. Although all these research domains are now well-established subfields of cognitive neuroscience, several of them were hard to envision as full-fledged research programs when Leslie's career began. She had a broad vision for the nascent field of cognitive neuroscience and a keen sense for identifying opportunities to tackle questions about the biological basis of psychological processes through innovative ideas as well as incorporating novel technologies, methods, and approaches from the moment they became available.

Leslie's enthusiasm for the scientific question appeared to enable a certain fearlessness that, combined with creativity and intellectual ingenuity, characterized her work. Throughout her career, Leslie objected to the idea of seeing her work as defined by a specific approach, methodology, or brain function. She was not bounded by disciplines or levels of analysis. Moving across subfields and adopting new methodologies can be challenging, and sometimes criticized, but Leslie accomplished this successfully at various points in her career. Indeed, her wide-ranging contributions to neuroscience are testament to the success this scientific mindset can bring.

A Generous Mentor

Leslie's knack for identifying and cultivating scientific talent was as impressive as her intellectual gifts. It is no accident that her laboratory was a wonderful home for the many trainees and collaborators that came from near and far, both scientifically and geographically. She had her own vision, but was a world-class listener, intellectually generous, and unfailingly supportive. She forged a scientific family that brought the best out of trainees and collaborators. You might have to share a tiny office, but you were welcome to a part of the magic that Leslie created.

Leslie was keenly aware of the value and importance of clear scientific communication, and a tremendous amount of her mentoring efforts was spent on teaching these skills. Her papers were written in a crystal-clear manner and followed a rigorous logic. Different paragraphs presenting carefully built arguments would lead to theoretically or empirically grounded conclusions or hypotheses with an almost mathematical rigor. Rather intimidating at first, she held us all against her high standards of scientific writing. Many of those who worked with her can probably identify with the experience of sitting side-by-side with Leslie to work on a paper. She would carefully read through a piece of text, then frown a bit and turn to you with the question: 'Okay, now, how about you just tell me what it is you want to say?'. However, then even very clear answers were often followed by: 'And do you think this is what you have written down here?'. In the ensuing mentoring process, she would insist on breaking down thoughts into a logical progression of statements that built upon each other and led to an inescapable conclusion or summary statement for that paragraph as well as an opening for the next one. Leslie's knowledge of the literature was striking, and she shared it to inform our reasoning. Remarkably, she was simultaneously insistent on us reaching her quality standards, and encouraging as well as patient while sending us back to work on the next iteration.

Leslie's talks were always as clear as her writing. Being shy and uncomfortable in public speaking at the time she joined the NIH, Leslie was encouraged by colleagues and mentors, in particular Patricia Goldman (later Goldman-Rakic), who was among the first female scientists Leslie met in her field. Pat told Leslie that it was important to 'get out there as much as possible'. Leslie's strategy to overcome her stage fright was to prepare her talks meticulously. Everyone who has attended one of Leslie's lectures admired her perfect slides, their logical progression, and the perfect match between verbal delivery and content on the slide. Here too, we benefited from Leslie's coaching. When it comes to presentations, Leslie taught us three principles: decide on a clear story line and a set of logically congruent statements as the backbone of the talk; use sparse (and legible!) slides showing no more than necessary, with graphs and illustrations to be preferred over words; and then of course: 'practice, practice, practice'. Even after (what seemed like) a near-infinite number of practice sessions, Leslie sometimes teased us with the good-natured threat that she would call us at a random moment at night, to test our readiness to deliver the talk at any time and under any circumstance. Leslie's mentorship still guides how we approach writing our papers or put together our talks, and how we teach these essential skills to our trainees.

A Female Role Model

Leslie was one of the most influential neuroscientists of her time, which was no small feat in an era dominated by male colleagues. Leslie knew all too well about the challenges facing her female mentees, and she did everything she could to prepare them for the next stages of their careers. She taught her female trainees how to negotiate. Having been part of a fight to rectify gender-based salary disparities at NIH, Leslie checked on us when we were applying for faculty jobs; she would ask directly what salary was offered to us. If this was left for a later part of the negotiation process, she encouraged us to stand up for ourselves. Her support was unwavering; with empathy if a talk we gave did not go that well, and strong support and cheering ahead of a major challenge. The 'You can do it!' that we would hear while leaving her office still rings in our ears when we face occasional self-doubt.

Leslie has left us much too soon, but she left us with an enduring vision of what is important in science. She taught us that good teamwork, trust, and communication are critical for excellent science. She showed us that science moves forward when ideas are freely shared and respectfully debated, when contributions are appreciated and acknowledged, and when women and men are treated equally. Leslie embraced respect for everyone's strengths and weaknesses, promoted inclusivity and team spirit, and showed how this leads to the highest-quality science. Leslie is no longer among us, but still looking over us, encouraging us to carry forward the beautiful vision of science that she unlocked for us. Leslie, thank you for everything, we will miss you.

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Spotlight

A Novel Role for Hypothalamic AgRP Neurons in Mediating Depressive Behavior

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A recent paper by Fang *et al*. examined the role of Agouti-Related Peptide (AgRP)-expressing neurons in the arcuate nucleus of the hypothalamus in mediating depressive-like behavior in mice. Chronic, but not acute stress, led to changes in neuronal excitability in AgRP neurons concomitant with the display of depressive-like behaviors, which were bidirectionally modulated using AgRP-selective chemogenetic