RETROSPECTIVE

Leslie Ungerleider, 1946–2020: Who, what, and where

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Leslie Ungerleider, a pioneering neuroscientist who profoundly shaped our understanding of the visual system, died unexpectedly but peacefully at her home on December 11, 2020, at the age of 74. She was the Chief of the Laboratory of Brain and Cognition at the National Institute of Mental Health and an NIH Distinguished Investigator. Despite struggling with health issues in recent years, she remained vibrant and fully engaged in science until her abrupt passing, leaving many colleagues, collaborators, and mentees in shock. Leslie's intellectual legacy runs both deep and broad, as she made major contributions to our understanding of the functional organization of the visual cortex in humans and nonhuman primates using a combination of neuroanatomical, neurophysiological, neuroimaging, and behavioral methods. Leslie is best known for demonstrating that the primate visual cortex contains separate neural systems for perceiving "what" things are and "where" they are located.

Leslie was an ardent supporter of women in neuroscience and was a highly inspirational role model, starting at a time when there were far fewer female senior neuroscientists than in the present day. In her many leadership positions across multiple scientific organizations, she was a passionate advocate for women. More broadly, the depth to which she influenced those she mentored, collaborated, or interacted closely with revealed itself in the outpouring of sentiment in the days immediately following her passing (1). Leslie was not only a brilliant and influential scientist, but equally notably, she deeply cared about all of her laboratory members as well as the community, and was gifted in communicating at all levels. She fully engaged with whomever she was talking with and suffered the details to get all aspects of doing science right, from the experimental design to the final write-up. While kind, Leslie was also blunt, direct, and honest. Under her mentorship, her laboratory members thrived.

Leslie Ungerleider. Image credit: Michael Beauchamp (Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA).

Leslie received her undergraduate degree in psychology from Harper College (later renamed the State University of New York) in Binghamton, New York. Intrigued by animal behavior, she entered graduate school at New York University and in 1970 received a doctorate in experimental psychology by studying hypothalamic stimulation effects on rat behavior; her first peer-reviewed publication was in *Science* (2). After a brief period at the University of Oklahoma, Leslie joined the laboratory of Karl Pribram at Stanford in order to study the effects of brain lesions on visual perception in macaque monkeys. Mortimer Mishkin, a leading neuroscientist at the NIH, having heard Leslie talk about her work at the 1974 Society for Neuroscience meeting, initiated a conversation with her to discuss seemingly conflicting findings from his own laboratory, then invited her to the NIH to "sort things

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Author contributions: D.C.V.E., S.K., and P.B. wrote the paper.

The authors declare no competing interest statement.

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Published March 12, 2021.

out." Leslie arrived at the NIH in 1975 and remained there for the rest of her career.

In collaboration with Mishkin, Leslie carried out a seminal set of experiments showing that lesions to the inferior temporal cortex impaired perception of object identity ("what it is"), whereas lesions to the posterior parietal cortex impaired perception of spatial relationships ("where it is"). They also showed that spatial localization and object identification both required an intact striate cortex (V1, or primary visual cortex), but were preserved after superior colliculus lesions in monkeys (3, 4). This pointed to a dramatic difference in visual system functional organization in primates vs. rodents, given that previous studies in the hamster by Gerald Schneider had implicated the superior colliculus in the analysis of spatial relationships. Leslie's "what" vs. "where" model provided an elegant and intuitively attractive division of labor for thinking about higher visual functions, because the information needed to ascertain object identity (e.g., stimulus features within the part of the visual field occupied by an attended object) is very different from that needed to assess object location and spatial relationships across a broad expanse of the visual field. Additionally, information about object identity vs. location is used in very different ways to mediate behavior.

Such findings led naturally to questions of the neural circuitry that underlies the flow of visual information from the V1 through extrastriate visual areas to the posterior parietal and inferotemporal cortices. Soon after arriving at the NIH, Leslie began an extensive set of anatomical studies of connectivity among cortical areas and subcortical nuclei in the macaque visual system. Many of these studies also included mapping of visual topographic organization, which Leslie carried out in collaboration with neurophysiologist Bob Desimone, who came to the NIH in 1980. Our understanding of the functional organization of the primate extrastriate visual cortex has been reshaped in three fundamental ways by their discoveries along with those from a handful of other laboratories, including those of Zeki, Van Essen, Gross, Hubel, and Livingstone in the macaque, and Allman and Kaas in New World monkeys. The first way was the identification of dozens of distinct visual areas in the occipital, parietal, and temporal cortices, rather than the much smaller number of areas anticipated from classic architectonic studies from a century earlier. The second way was the realization that anatomical connectivity patterns were surprisingly complex, involving hundreds of pathways among the dozens of cortical areas, but could nonetheless be arranged in a distributed hierarchical configuration. The third way was the identification of multiple processing streams at each level, including the splitting at high levels into the ventral (what) stream that feeds into the inferotemporal cortex and the dorsal (where) stream that feeds into the posterior parietal cortex.

Lesion studies in humans had suggested that the human visual system contains what and where systems similar to those in the macaque. Once noninvasive human neuroimaging became feasible using positron emission tomography, Leslie collaborated with Jim Haxby in early studies that provided functional localization data in support of distinct dorsal and ventral streams in the human brain. With the advent of functional MRI, with its higher spatial resolution and greater ease of use, Leslie's research shifted even more strongly to human neuroimaging, while still vigorously pursuing monkey studies. She became chief of the Laboratory of Brain and Cognition and was joined by Alex Martin and Jim Haxby, and later by Peter Bandettini and Chris Baker.

Leslie soon became an international leader in studying the neural basis of human cognition. Her approach to pursuing imaging studies with hypotheses derived from monkey neurophysiology provided important grounding for the fledgling fields of cognitive neuroscience and human neuroimaging. The breadth of Leslie's contributions is truly impressive. Her studies included object and face perception, visual awareness and imagery, working memory, selective attention, perceptual decision making, emotional behavior, motor- and value-based learning, initially in humans and later in monkeys using imaging as well. Leslie's pioneering studies laid the foundation for many of these cognitive subfields and often supplied textbook material right away. Her approach was characterized by her fearlessness in taking new directions, while still applying the same rigor and depth that were typical for all her work. Leslie's studies included both healthy individuals and those with disorders of visual function. Her laboratory helped pioneer a cross-species approach, and the translational nature of her research provided an early and convincing demonstration of the power of functional neuroimaging.

Leslie was an extraordinarily clear communicator. She understood the importance of effective written and spoken scientific communication. Her papers were written with a clear logic and flow, building one idea on the next like fitting pieces into a puzzle and offering an irresistible interpretation of the bigger picture that could be taken from it. The same was true for her lectures. Leslie was known for preparing them with meticulous attention to detail and with an easy-to-follow story line; her slides were simple and clear, with the verbal content perfectly aligned. Leslie made sure that her trainees acquired these important skills. Many of them remember sitting next to Leslie and going through a paper draft sentence by sentence, while Leslie gave a tutorial in scientific writing, in supportive and encouraging ways. The number of practice talks that were held before major conference presentations were infamous. Leslie would work tirelessly to make sure that all issues with the slides and their presentations were completely resolved before sending her trainees off! The same was true for preparing the principal investigators (PI) in her laboratory for upcoming quadrennial reviews before the NIH Board of Scientific Councilors. Each PI would take turns sharing their talks with Leslie as she dissected every slide and persisted until a clear narrative emerged. Her deep and unwavering engagement, clear and insightful thinking, and gift for communicating and motivating

was fundamental in forging the cohesion and success of the Laboratory of Brain and Cognition. Among her many awards, including election to the National Academy of Sciences, one that was especially meaningful to her was the 2020 Glass Brain Award, the highest award of the Organization for Human Brain Mapping (5).

Growing up in science without a role model, Leslie was acutely mindful of the vulnerabilities of her female mentees. Leslie had unwavering trust in the talents of her female mentees and taught them many things: How to boost self-confidence, how to negotiate a fair start-up package, and how to balance the demands of a scientific career with having a family and raising kids. If a mentee showed a moment of self-doubt, Leslie would put a little smile on her face and say with a firm voice "I know you can do it!" Having Leslie as a role model shaped the careers and personal growth of many young female scientists, who emulated her supportive leadership style in their own laboratories. In her later years, as she became more physically frail, Leslie's resiliency revealed itself all the more clearly. We will all miss her greatly, but her passion and nurturing example will live on in all whose careers she touched.

1 Kudoboard, "Dr. Leslie G. Ungerleider (1946–2020)." *Kudoboard* (2020). https://www.kudoboard.com/boards/xTXTsGrh. Accessed 02 February 2020.

2 L. G. Ungerleider, E. E. Coons, A behavioral measure of homosynaptic and heterosynaptic temporal summation in the self-stimulation system of rats. *Science* **169**, 785–787 (1970).

3 L. G. Ungerleider, M. Mishkin, "Two cortical visual systems" in *Analysis of Visual Behavior*, M. Goodale, D. J. Ingle, R. J. W. Mansfield, Eds. (The MIT Press, Cambridge, MA, 1982), pp. 549–586.

4 M. Mishkin, L. G. Ungerleider, K. A. Macko, Object vision and spatial vision: Two cortical pathways. *Trends Neurosci*. **6**, 414–417 (1983).

5 A. Puce, "Leslie Ungerleider is interviewed by Aina Puce" (video recording, 2020). https://www.youtube.com/watch?v=zt4i71bXrcw. Accessed 2 February 2020.