

# LECTURE

## DR. FRED H. GAGE | NEUROSCIENCE AND ARCHITECTURE

AIA 2003 NATIONAL CONVENTION & EXPO | MAY 8-10 2003 | SAN DIEGO CALIFORNIA | THEME PRESENTATION

It's an honor to be here. I'm here representing members of my discipline - neuroscientists - and in some ways scientists in general. I have what I think will be a straightforward message: neuroscience has reached a degree of understanding about the brain and how it is influenced by the environment such that we might be of help to architects in designing environments that would assist us in our ability to function within those environments.

Before I delve into the facts that lead to this proposition, I'd like to say that I am here in part because of the foresight of John Eberhard, who has been a standard bearer for this proposition of an interaction between neuroscience and architecture, and because of the strength of Norm Koonce and his ideals along these same lines. I'd also like to thank the local committee, Alison Whitelaw and Gil Cooke in particular, who have been influential in helping to bridge this gap between the neurosciences and architecture and create something new.

So first of all, what is neuroscience? Neuroscience is the study of the brain; neuroscientists believe that the brain is the organ that controls behavior. The brain is a complex organ, composed of areas that control vision, other sensory experiences, learning and memory and motor output, as well as areas that help us navigate through novel environments. The intricacies of the brain, however, can be imagined even better in numerical terms. The principle cell of the brain is called a neuron, and we believe that there are approximately a hundred billion neurons in the human brain joined by a hundred trillion connections (see figure 1). I'm not sure I know what that really means, but that represents a lot of connections. In addition to these neurons, the brain is made up of many different types of cells that interact with each other to allow us to perceive and to think.

For many years, the dominant theory of how the adult brain functions encouraged us to think of the brain as a fixed structure, something that was more like a computer in many ways than an organ. The brain, like other tissues, is generated based on a blueprint. Much as you work with blueprints, our body and brain tissues are built on a blueprint, a genetic blueprint, beginning with our DNA. As you know, 2003 marks the 50<sup>th</sup> anniversary of the discovery of DNA's role in the generation of proteins that

make up our body. Within every cell is the DNA complement that can make all the functional proteins that are required for that cell to function. And within every cell in the brain, this genetic material continues to make proteins and continues to function throughout life. Thus the working assumption was that the principle changes that took place in the brain occurred during development and were based on this genetic blueprint. We all started from a single cell. Each of you listening to me this morning started from a single fertilized egg and somehow developed into a full organism; your growth and development followed a specific blueprint.

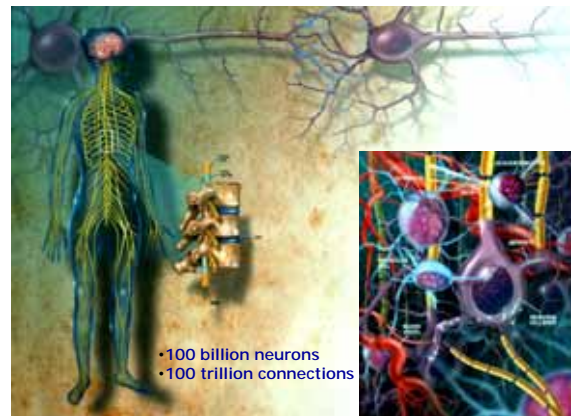


figure 1.

However, we also know that environment dramatically influences brain development, from early stages to a full-grown organ. We have accepted this fact for a long time in the neurosciences - as we grow and develop, the environment can play an important role. While the blueprint is there, defining what the extent of the structure will be, the environment plays a very important role in the final product. At the same time, we believed for many years that, once the mature post-adolescent brain had been formed, it was fixed and immutable. One of the early pioneers, Ramon y Cajal, described it in this way: "Once development was ended, the fonts of growth and regeneration of axons and dendrites, which are the processes of our neurons, dried up irrevocably. In adult centers, the nerve paths are something fixed and immutable; everything may die, nothing may be regenerated."

It was this view of the fixed, immutable structure of the brain that was harnessed and allowed us, or forced us



A publication of:  
**THE ACADEMY OF NEUROSCIENCE FOR ARCHITECTURE**

1249 F STREET SUITE 222 | SAN DIEGO CA 92101 | 619|235-0221  
[WWW.NEUROSCIENCEFORARCHITECTURE.ORG](http://WWW.NEUROSCIENCEFORARCHITECTURE.ORG) | [INFO@NEUROSCIENCEFORARCHITECTURE.ORG](mailto:INFO@NEUROSCIENCEFORARCHITECTURE.ORG)

almost, to think about the brain as a computer. We thought about it so much like a computer that people made jokes that “one fellow has more RAM than another,” suggesting that he has more memory capacity. However, recently, this dogma of the static nature of the brain has been challenged. In our lab, as well as in other labs around the world, we have discovered that the adult brain has a pool of cells, which we call stem cells or immature cells, that persist throughout life, and these cells continue to divide and can give rise to authentic neurons throughout our life. We term this process “neurogenesis,” or the birth of new neurons. Neurogenesis involves a sequence of events that was thought to normally occur only during development; what we have found is that it actually occurs in all mammals throughout life (see figure 2). It doesn’t occur in every area of the brain. It only occurs in a few important structures, and this finding will be important for the point that I would like to make today. Figure 3 shows these dividing cells within the brain at an early stage of cell division. This slide emphasizes the fact that these early dividing cells, even in the adult brain, can grow with extensive processes and extend connections through the appropriate parts of the brain within about a month from the time that they are born.

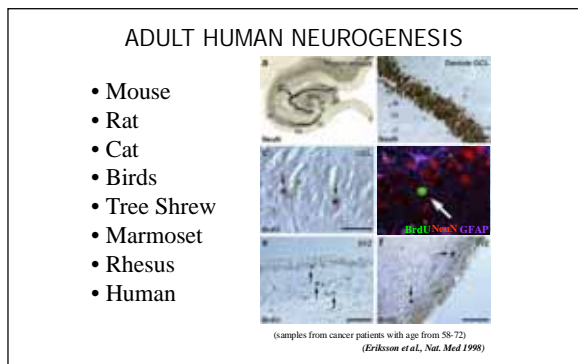


figure 2.

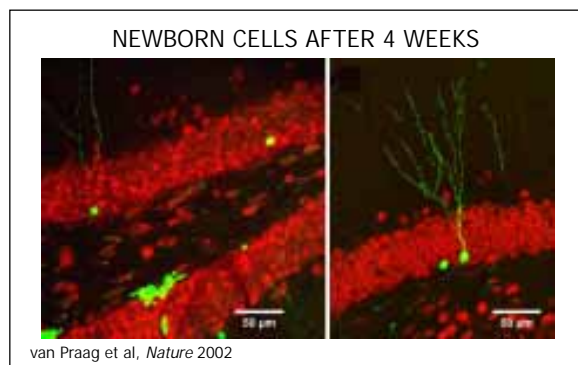


figure 3.

Not only are these cells being born even as we move and interact with our environment: a remarkable aspect of these late dividing cells is that they are affected dramatically by the environment in which they find themselves. Figure 4 provide two rather dramatic examples. These little black dots correspond to the normal complement of newly born cells that are occurring in the adult brain at an early time. At a later time, some cells survive and some differentiate

and become mature cells. By exposing experimental animals to enriched environments, or changing and modifying environments so they contain more stimulation, we can increase dramatically the total number of cells that exists, even within a short period of time. This increase in the division of cells persists in such a way that the animals that survive end up with as many as 50% more neurons that they would have had under other circumstances.

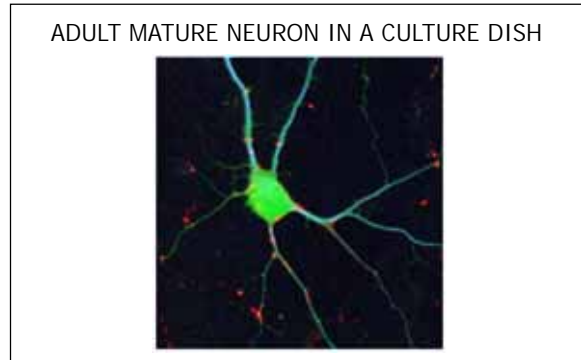


figure 4.

Neuroscience has actually developed to a point where we can now isolate these cells from the adult brain in culture dishes and begin to examine how they function. We’ve isolated these cells and labeled them with a fluorescent marker so we can visualize them in their host environment (see figure 5). What we have developed here are procedures that can allow us to maintain these cells as primitive, non-differentiating stem cells. And the point that I’d like to make here is that these cells have intrinsic systems, or clocks or timers, that tell them when to divide and when to differentiate and mature. Their choice to divide or to mature is entirely dependent on the structural environment that the cells finds themselves in. So, the internal program of the cell that allows it to continue to divide has intrinsic properties. But its ability to differentiate or proliferate exists as a function of the environment that it finds itself in.

The area of the brain where this stem cell division is occurring predominantly is called the hippocampus. It’s embedded within the temporal lobe - these are the cortical areas in this picture. The hippocampus is an important structure because it is the structure of the brain that processes new information. When we sit within an environment and receive new information, that information comes into the cortex and is initially processed as it is acquired. But if that information is going to be stored at all as a memory, it must pass through the hippocampus and then return to the cortex where it’s stored for long-term memory. The hippocampus is not involved in the storage of memories, but in the making of memories. And the hippocampus just happens to be the same area where new cells are born all the time, and our environment is influencing the rate at which those cells are being born.

What this means, in summary, is that while the brain controls our behavior and genes control the blueprint for the design and structure of the brain, the environment can modulate the function of genes and, ultimately, the structure of our brain. Changes in the environment change

the brain, and therefore they change our behavior. In planning the environments in which we live, architectural design changes our brain and our behavior.

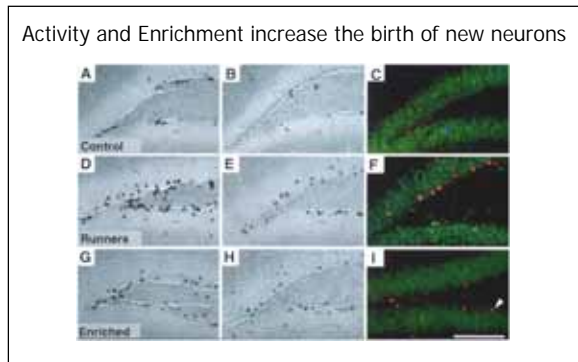


figure 5.

In addition to the basic science that has revealed these secrets about the brain, there are new technologies that are being developed that allow us to look into the living brain and assess what's going on. Functional Magnetic Resonance Imaging can be used to watch a live brain, revealing the structure and function of the cortex. When the brain is activated during a cognitive task or a complex learning task, one can monitor different parts of the cortex which are activated during the task. We can monitor this activation in living individuals. Just to show you how accurate this imaging can be: in the same individual's brain, a simple visual task that has no cognitive task or learning task associated with it will only activate the visual cortex, leaving the parietal cortex alone. With such technologies, we can begin to get at some of the underlying structures that account for our ability to interact with our environment.

There are other techniques that are available to us as we begin to explore the inner workings of the brain, including Positron Emission Tomography, which not only tells us where things in the brain are active but can chemically mark particular systems. For example, an individual in a depressed state, show a dramatic increase in activation of the frontal cortex and amygdala, which are brain areas involved in emotional processing.

So, what does all this information that we are gaining have to do with you as architects? The environment - the structures that we live in, the areas that we play in, the buildings that we work in - affects our brain and our brain affects our behavior. You are designing the structures that we live in. You are affecting our brains. You are changing our brain structures and you are changing our behaviors, and you have been doing so for a long time. And I think it's time that we work together to understand how those brain structures are affected by the designs that you are constructing.

How are we going to do that? How are we going to collect this new information that we can all use to live in an even better, more beautiful, and more effective environment? Well, one way that might be helpful is to develop a kind of empirical architecture, an experimental

architecture based on some of the premises that we use in science. When we design an experiment, the first and most important step is to develop a hypothesis. What do you think might be the best way to design an environment? Many of you know implicitly, in many ways, the correct way to do it. Those ideas, in some sense, can become testable hypotheses.

What I'd like to do is go through with you how you might set up an experiment to test a hypothesis. This proposal is based on a discussion with Thom Penney regarding how one might design an experiment in empirical architecture. First you would have to generate a hypothesis: maybe, "large windows in a school are effective for enhancing academic performance of children." You would then design an experiment with quantifiable outcome measures. This would require identifying comparable schools, with the same age groups and economic status, and yet different in terms of their design and availability of space, of light and volume of stimulation that is coming in through the windows. Then you would conduct an experiment and evaluate the outcome with statistical methods. You would need to do this over a long enough time period and with enough standard tests of outcome performance to be able to accurately assess whether or not these differences were actually reliable. Once you got an answer as to whether or not "large windows in a school are effective for nine year olds of a certain socio-economic status in enhancing their academic performance," you could then generalize this finding to different age groups, even to different school districts, to see whether this principle holds up. So then you would come to the conclusion that, for some reason, having large windows that allow open space with lots of stimulation coming in is not bad, as some school administrators have argued, but is beneficial. The old argument that having large windows was somehow disruptive to children's ability to learn could turn out not to be true.

But why is having large windows beneficial? This question leads to the next, important step. You would ask: "What is it about the stimulation that is occurring externally that is enhancing the students' ability to acquire new information?" And what happens at this point is we begin to work together to obtain some knowledge about the underlying brain mechanisms that might relate to this question. For example, one can imagine that external stimulation, even in a classroom where students are concentrating and learning, could act as a general activator in certain brain areas, which in turn makes the brain more receptive to information coming in from the teacher; merely a hypothesis, but one that I think we might consider testing.

So what are some other experiments that you could consider doing? For my own part, I think about homes for the elderly. It has been shown that, if the elderly are encouraged to move around in their environment and take long walks and if we can enrich their lives by providing more complex environments in homes for the

elderly, they actually perform better on decision-making tasks than they do when not provided these situations. So you could set up experiments to test age-matched, socio-economic matched elderly in different types of homes to see whether or not complex environments are good or bad, in reference to the residents' ability to interact and to survive within their environment.

This final example is one that comes close to my heart. "What is it about an environmental design that makes for an effective research environment?" The two people pictured here represent one of the most effective collaborations between architect and scientist that we know of. The product of that collaboration persists today, and I'm fortunate enough to work in that environment. Figure 6 is of Jonas Salk and Louis Kahn, looking up from the Pacific Ocean at a design of the Salk Institute. Figure 7 is a picture of that same institute taken from the canyon, and here's a little closer view. So, we could ask several questions: "Do aesthetics matter to scientific creativity? Does it make any difference to the effectiveness of my work if I'm working in a beautiful environment?" "Or is there something about the structural design of the building that is more important - less the aesthetics, and more the structure?" I don't know, but these are among the many questions we can seek answers to.



figure 6.

One of the amazing features of this building is shown here: the 65-foot, unimpeded space that exists within the structure, resulting from the trusses being concealed and thus providing this large, unobstructed lab space (see figure 8). What this design does for the scientist is to provide flexibility. All of the cubicles and laboratory spaces that are built within here are supplied with electricity and water from the interstitial spaces. So, if we change our ideas about how we want to do an experiment, we can pull the wires and water up, redesign the rooms, drop everything down and begin the experiment within weeks. This flexibility is another possible hypothesis for why the environment might be effective. This is another clear example of how we can work together to merge your understanding of design with our interest in understanding the elements that are important to the study of the brain.

So I propose to you a merger of disciplines, to form a new discipline that our students will likely populate. It's not likely that we will be the ones who will make the big discoveries, because we first need to begin accumulating

the body of knowledge that can be used in design. One of the arguments against the whole idea of imposing empiricism on architectural design has been that this empirical approach, or the scientific approach, might challenge the intuitive and creative sensibilities of architecture. I argue strongly with that. What we are suggesting is that factual knowledge about how design changes our brain can be, as one of my architectural colleagues and friends said, "an arrow in the quiver of the architect." Rather than stifling creativity, I believe that this added knowledge will actually broaden that creativity.



figure 7.



figure 8.

The environments we live, work and play in are changing our brains and our behavior all the time. I believe it's time that we begin figuring out how they do that, and we can work together on this. I can imagine a time when architectural design will be a subject of study in the clinical sciences and will be used to promote health and to prevent disease by virtue of the knowledge that you can contribute about the structures that you build. I think it's time that we begin, and I look forward to working together with you. Thank you very much.

<sup>fig 1</sup> From "Repairing the damaged spinal cord," by J.W. McDonald et al., 1999, *Scientific American*, p. 64-73. Adapted from original.

<sup>fig 2</sup> From "Neurogenesis in the adult human hippocampus," by P.S. Eriksson et al., 1998, *Nature Medicine*, 4(11), p. 1313-1317. Adapted from original.

<sup>fig 3</sup> From "Functional neurogenesis in the adult hippocampus," by H. van Praag et al., 2002, *Nature*, 415, p. 1030-1034. Adapted from original.

<sup>fig 4</sup> From "Neural stem cells from adult hippocampus develop essential properties of functional CNS neurons," by H.-J. Song et al., 2002, *Nature Neuroscience*, 5(5), p. 438-445. Adapted from original.

<sup>fig 5</sup> From "Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus," by H. van Praag et al., 1999, *Nature Neuroscience*, 2(3), p. 266-270. Adapted from original.

<sup>fig 6,7,8</sup> From *Salk Institute: Louis I. Kahn (Architecture in detail)*, by J. Steele, 1993, New York: Phaidon Press Inc. Courtesy of the Salk Institute.