Her inquiring mind has a habit of seeing patterns

Neuroscientist Ann Graybiel of MIT studies a region of the brain involved in forming habits and experiencing rewards

By ANDY DWORKIN
THE OREGONIAN

At first, nothing seems to link cocaine, Parkinson's disease and learning to perform tasks almost unconsciously.

But neuroscientist Ann Graybiel found connections among those subjects in a once-neglected area of the brain, the basal ganglia.

The basal ganglia are several masses of gray matter deep inside the cerebrum, the largest part of the brain. Years of research by Graybiel and her colleagues have shown that this acts as a sort of relay center for messages that govern many functions. These include voluntary movements people make without consciously thinking about them, such as tapping the brakes when you see the brake lights of the car in front of you.

The same structures are involved in sending rewarding signals that can relate to both learning and drug use and some movement-related diseases. For instance, many nerve cells in the basal ganglia contain dopamine, a chemical that transmits messages within the brain. These cells are a main target of cocaine. They also are activated to send a "reward" signal when you learn something and are damaged in some nerve diseases, including Parkinson's.

Graybiel's research focuses on figuring out the combination of nerve cells, genes, chemical and electrical signals that occur in the brain to let people turn behaviors into habits or to break bad habits. She conducts research and teaches in the Department of Brain and Cognitive Sciences at the Massachusetts Institute of Technology, the same university where she earned her doctorate in psychology and brain science in 1971.

GRAYBIEL
Studies brain's paths to mastery

Graybiel has won awards for helping unravel some of the complex connections in the brain, including the National Medal of Science, which President Bush awarded her last year. She also won the 2002 Robert S. Dow Neuroscience Award, which Oregon Health & Science University gives each year to a distinguished neuroscientist.

Graybiel, who is in Portland to accept that award, will give a free public lecture on the brain at 7 tonight in the auditorium of the Oregon Museum of Science and Industry. Although no seating or standing room remains for tonight's lecture, Oregon Health & Science University will replay a video of the talk and will have a scientist answer questions at 7 p.m. Oct. 30 in the OHSU Old Library Auditorium.

Here are excerpts of an interview, edited for space and clarity, in which Graybiel discussed the science of the brain.

Q: *How did you become interested in the brain and the basal ganglia?*

A: The brain is so interesting. It controls everything we do and all human history. Everything we like and dislike and strive for and don't. ... It's just so exciting that the study of behavior

Please see **GRAYBIEL,** Page C12

Graybiel: She was swept off her feet by biology of behavior

Continued from Page C11

could be brought down to the level of biology. That there could be a biology of behavior really swept me off my feet. So I got into the field.

I started out looking at vision and movement. And that led me to the basal ganglia. At the time, the basal ganglia were really, really neglected, except by neurologists and a few psychologists (many of whom focused) on extrapyramidal disorders. These are disorders where you aren't paralyzed but nevertheless something is wrong. Like in Parkinson's, you move too little. Or Huntington's, you move too much. Dystonia, you have awkward movements. Catatonia, you don't move at all. Depression, you don't have the get-up-and-go to move. There were disorders that were really overlooked.

So I just started looking around, and we discovered pathways in the basal ganglia that seemed really important. Then we discovered that neurotransmitters in the brain were strongly concentrated in the basal ganglia and highly structured, so they appeared in some areas and not others. Along the way, we happened on the fact that if you give an animal even one little shot of cocaine or amphetamine or some drug that people take, it would turn on the genes in the brain and turn them on in the pattern that we had been studying.

We're trying to study these patterns of turning on genes now in relation to behavior. It turns out these patterns may be related to the kind of obsessive or repetitive behaviors we see in people or animals taking these drugs. We're trying to see if these patterns of gene (expression) appear in human disorders, i.e. schizophrenia or drug addiction.

Q: *What is the connection between motion-related nerve diseases and habits?*

A: We have sensors that record the electrical activity from many, many little neurons at once. We have little hats the rats or mice wear as they perform activities. We can record that (electrical) activity day after day after day, before learning, during learning and after learning, and when they get really, really good at it.

What we found in the very first experiment of that type is there are wholesale changes in the electrical activity of the basal ganglia when an animal learns something. So it looks like what's happening in our head is that patterns of activity are set up in the head when you learn something and when you get in a groove. And when you get in too much of a groove, you have a hell of a time breaking out of it.

Q: *How do the basal ganglia work?*

A: How can the same system that controls how much you move be so involved in Tourette's syndrome? Or ADHD? Or, as is now firmly believed, depression? Somehow this system can reach many areas of brain activity and behavior and thus touch problems from psychiatric problems to movement problems and tics. And probably the way it does this is it talks to a lot of guys, and it broadcasts. It talks to the executive areas of the brain.

Q: *How is the Human Genome Project affecting brain research?*

A: Finding out the genome is really amazing. Now what people do is create animals by knocking in a gene or knocking out a gene or, the newest thing, knocking down a gene (reducing the amount of protein it produces) and see whether the animals have behavior changes.

Q: *Is it hard to discuss the brain with nonscientists?*

A: The brain is hyperforbiddingly complex. It's really complicated. It's got all kinds of systems, feedback, loops within loops within loops. The reason I emphasize the complexity is (to address the question), "If you've got imaging and genes and all this, why don't you just get on with it and solve Parkinson's disease and all that?" But it's so complex. Every time you solve one thing, you open up 100 new areas.

Still, I'm so interested in people and behavior and trying to do something that will help people, I don't have trouble talking about it. In fact, I think it's incredibly important to talk about it. And I love explaining, "What is a neuron?" all the way up to the memory system.

◆

Andy Dworkin: 503-221-8239; andydworkin@news.oregonian.com

The Oregonian, October 23, 2002