

How Does the Brain Keep Track of Time?



Ann M. Graybiel, PhD

For decades, scientists have wondered, how does the brain keep track of time? Encoding time is universally required for learning how to perform daily tasks such as walking up and down stairs or more complicated tasks like playing the piano. Neuroscientists have theorized that the brain “time stamps” events as they happen; however, they couldn’t find any evidence that such time stamps existed. In 2009, a group of neuroscientists at the Massachusetts Institute of Technology (MIT) uncovered

some important evidence about how primate brain cells actually keep track of time.

The team was led by Professor Ann Graybiel of MIT’s McGovern Institute for Brain Research, a NPF-supported scientist who has dedicated her career to uncovering the brain circuitry underlying medical issues such as Parkinson’s disease, and included Dr. Naotaka Fujii of the RIKEN Brain Institute in Japan, and Dr. Dezhe Jin of Penn State.

Why is timing important in Parkinson’s disease?

Most people’s brains seem to provide timing information that is used in purely cognitive activities such as learning and also providing rhythm in motion. Playing a musical instrument or even clapping in time with music take advantage of this timing circuit in the brain. Simple reward-based learning—if you put a piece of chocolate in your mouth, you experience a pleasurable taste—is believed to be intuitively connected by the brain properly attributing the reward to the activity that generated it. For some things, like eating chocolate, people know the connection between activity and reward, but in some more complex situations, this intuitive circuit plays a role. It is believed that this timing function is impaired in some people with Parkinson’s disease. In addition, actions that are normally managed by timing a sequence of actions, like walking, can require much more conscious thought when the timing does not occur naturally.

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Postdoctoral Fellow Ledia Hernandez with Professor Graybiel in the MIT lab.

How did Professor Graybiel investigate timing?

The MIT team reasoned that, by using a set of complex electrodes they had developed, they could be able to detect neurons that didn't do any thinking but just provided a regular "tick" for other neurons to listen to in order to track time. Researchers taught two macaque monkeys to perform a simple eye-movement task in which they took direction from visual signals on a computer screen. After receiving a "go" signal, the monkeys were free to perform the task at their own speed. After filtering out the neurons whose activity was associated with the action of the task, there remained a set of neurons that just consistently fired at specific intervals—100 milliseconds, 110 milliseconds, 120 milliseconds, and so on. These cells in the monkeys' brains coded time with great precision.

Professor Graybiel's revolutionary tools allowed, for the first time, the observation of the activity of individual neurons in the brain. These observations were aggregated to give a clear picture of the function of the basal ganglia as a whole, rather than one specific area as had been done previously. This method, focused on the area of the brain associated with Parkinson's disease, offers a powerful tool that can be leveraged to develop new insight into how the brain works and also understanding of how therapies for Parkinson's actually affect neuron function.

"The results raise the possibility that the representation of time may reflect an inherent tendency for the brain to represent time as part of ongoing task-specific information processing. If so, neural circuits might build time representations as an infrastructure to use when needed,"

explains Professor Graybiel. "Such encoding would have major advantages for neural processing related to learning how to control actions, because all of the elements needed to form on demand new associations between events and precisely timed actions would be available. This may help to target DBS-type therapies to the actual moment of initiation, for example, or to the right loop."

What does this mean for the future of Parkinson's treatment?

Methodology developed by Professor Graybiel opens a powerful new pathway to understanding the inner workings of the brain. These techniques offer a way to do direct measurement of neurons and neuron function, with the ability to detect neuronal activity as fast as it occurs. These findings may facilitate the development of neural prosthetic devices or drugs for conditions such as Parkinson's disease.

"The relevance to PD is potentially tremendous, as the last several decades of clinical research experience have revealed that much of the PD disability results from issues in timing. Therefore, some of the next generation of treatment paradigms and technological advances could be directed toward brain cell time stamps," said Dr. Michael S. Okun, NPF's National Medical Director.

Professor Ann M. Graybiel has been researching Parkinson's disease since 1986. She received a 3-year grant from the National Parkinson Foundation entitled, "Analysis of Cortico-Basal Ganglia Loop Function in Macaque." Dr. Graybiel served on the National Parkinson Foundation Scientific Advisory Board from 1997-2008.

The results of her research were published in the Proceedings of National Academy of Sciences of the U.S.A. in October 2009.