What Makes The Brain Tick, Tick, Tick...

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The brain is a "time machine," assert Duke neuroscientists Catalin Buhusi and Warren Meck. And understanding how the brain tracks time is essential to understanding all its functions. The brain's internal clocks coordinate a vast array of activities from communicating, to orchestrating movement, to getting food, they said.

In a review article in the October 2005 Nature Reviews Neuroscience, Buhusi and Meck discuss the current state of understanding of one of the brain's most important, and mysterious, clocks -- the one governing timing intervals in the seconds to minutes range. Such interval timing occupies the middle neurological ground between two other clocks -- the circadian clock that operates over the 24-hour light-dark cycle, and the millisecond clock that is crucial for such functions as motor control and speech generation and recognition. Meck is a professor and Buhusi is an assistant research professor in the Department of Psychological and Brain Sciences.

Interval timing is central to broader coordination of tasks such as walking, manipulating objects, carrying on a conversation and tracking objects in the environment, they said.

"Interval timing is necessary for us to understand temporal order of events, for example when carrying on a conversation," said Meck. "To understand speech, I not only have to process the millisecond intervals involved in voice onset time, but also the duration of vowels and consonants. Also, to respond, I need to process the pacing of speech, to organize my thoughts coherently and to respond back to you in a timely manner. That's all interval timing, and in fact it's hard to find any complex behavioral process that timing isn't involved in."

Deciphering the neural mechanisms of such clocks may be even more fundamental to understanding the brain than figuring out, for example, neural processing of spatial position and movement, they said.

Said Buhusi, "I would argue that time is more fundamental than space, because one can just close one’s eyes and relive memories, going back in time; or prospectively go forward in time to predict something, without actually changing your position in space."

Understanding the machinery of interval timing is profoundly difficult because it is "amodal," said Buhusi and Meck. That is, the interval timing clock is independent of any sense -- touch, sight, hearing, taste or smell. Thus, it cannot be localized in a discrete brain area, as can the circadian clock, which has clear inputs from the visual system and outputs that control the cyclic release of circadian hormones.

“So, this process has to be distributed so it can integrate information from all the senses,” said Meck. “But more importantly, because it’s involved in learning and memory, you could argue that time isn’t directly perceived, but that we make temporal discriminations relative to memories of previous durations. Such features have made the machinery of interval timing more elusive, and some even questioned whether an internal clock of this sort even exists.”

In the 1980s Meck and his colleagues at Brown and Columbia Universities proposed what became the traditional theory for explaining interval timing which involved a “pacemaker-accumulator” model. This model holds that somewhere in the brain lurks an independent biological pacemaker that regularly emits neural timing pulses or "ticks." However, more recent research by Meck and his colleagues at Duke, has led to the development of a "striatal beat frequency" model of interval timing involving the “coincidence detection” of oscillatory patterns of neural activity. The striatum is a part of the brain structure known as the basal ganglia, which control basic body functions such as movement.

In this model, explained Buhusi, “each structure in the brain contributes its own resonance, and all these oscillations are monitored and integrated by the basal ganglia or striatal circuits. It’s like a conductor who listens to the orchestra, which is composed of individual musicians. Then, with the beat of his baton, the conductor synchronizes the orchestra so that listeners hear a coordinated sound.”

Thus, in essence, the entire brain is an intricate interval timing machine, in which individual structures busy with their own neural tasks, generate resonances that integrate to become ticks of the neural clock.

Meck, Buhusi and their clockwork colleagues are using an array of experimental techniques to try to identify this “baton” timing signal and to refine the theory. These include studies using genetically modified mice, pharmacological tools, recording of electrical brain signals in ensembles of brain cells and functional magnetic resonance imaging of the brain.

For example, they are studying how the clock’s ticking changes in Parkinson’s patients as they change levels of their medication, which effects the amount of dopamine in their brains. Dopamine has been implicated as a key signaling molecule in the neuronal circuitry of the timing machinery.

“When Parkinson’s patients are on their medication, they time quite normally,” said Meck. “But as their medication wears off, we can see their clock slow down by recording their brain signals.”

Said Meck of their research, “We’re addressing two challenges. One is to find the molecular processes that underlie this internal clock. And the second challenge is to build more realistic models of how this timing process works, with constant, parallel input from throughout the brain.” In such studies, the researchers face the daunting process of trying to monitor the intricate swirling of neural activity throughout the entire brain, said Meck.

“Looking at only one place in the brain for the interval clock is like the blind man feeling just the toe of the elephant and trying to describe how it works,” he said. “While we’re very excited about our success so far, we want to be modest about our capabilities. We are blind men touching just one part of this elephant that is time.

“And our new review paper, to the best of our knowledge, is the first to try to integrate the different fields and levels of analysis that contribute to understanding timing and time perception, to help advance this exciting field.”

Source: Duke University

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