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RESEARCH NEWS

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New Study Finds Similarities Between Brain's Spontaneous and Evoked Activity

For centuries, philosophers have engaged in a rollicking debate over the role the mind plays in processing and comprehending human experiences. Are our thoughts simply a reflection of the world as perceived through our senses? Or does the mind itself construct the features of our experience?

In recent years, as neuroscientists have deployed new techniques to observe the brain in action, they have discovered that the brain is spontaneously active. Their studies have begun to decipher not just how we perceive the world around us, but how the information gathered through our senses trips neural circuits and sets the mind in motion.

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> **— Rafael Yuste**

Now, a new report by a team of Howard Hughes Medical Institute (HHMI) researchers at Columbia University goes a step further in this debate, disputing the idea that our minds are pure reflections of the world. Rather, the new data suggest that our brains might be better defined as a rich dynamical system with internal states that could be the templates of our thoughts or memories.

The cortex is the largest part of our brain and is the site of most mental functions. The cortex receives input from the thalamus, which itself receives inputs from sensory systems. Thus, practically all information about the outside world reaches the cortex through the thalamus. Writing in the December 8, 2005, issue of the journal *Neuron* , a team of researchers working in the laboratory of Rafael Yuste, an HHMI investigator at Columbia University, report that, when the thalamus is stimulated, cortical neurons react in a way that precisely mirrors the patterns of cortical activity that occur

spontaneously, without any kind of input.

“The brain is not a reflex machine. What the thalamus is doing is waking up internal cortical states,” Yuste explained. “The brain is humming along and the world (through the thalamus) appears to be selecting one of those states.”

Since the invention of electroencephalography (EEG) by Hans Berger in the 1920s, scientists have known that the brain is always on. It is a blur of electrochemical activity, even when we are asleep or not gathering information about the world through our senses. This spontaneous activity has traditionally being considered the “noise in the machine” and neuroscientists have mostly ignored it and have instead concentrated on examining how the brain responds to sensory stimulation or how it generates behavior.

However, during the last 20 years it has become clear that the spontaneous activity is very prominent, even during sensory stimulation or motor behavior. Moreover, in earlier studies, Yuste's and other groups have shown that the spontaneous firings of neurons in vitro or in vivo were not random, but instead possessed exquisite spatiotemporal patterns of activity. Nevertheless, it was unclear whether this spontaneous activity was at all important, and the relation between those patterns of spontaneous activity and the sensory inputs remained unknown.

The new work from Yuste, first author Jason MacLean, Brendon O. Watson and Gloster B. Aaron, used calcium imaging techniques to monitor the activity of cortical circuits in brain slices of mouse cortex that were connected to the thalamus. With this optical technique, pioneered by Yuste, they reconstructed with unprecedented resolution the sequential turning on and off of large neuronal populations under different experimental conditions. By stimulating the thalamus, the HHMI team observed that, neuron by neuron, the triggered patterns in the cortex were indistinguishable from those that occur when the cortex is spontaneously active. Moreover, these cortical patterns occurred with great temporal fidelity, suggesting that the cortex can somehow preserve and faithfully replay temporal sequences of activity and that the thalamus can turn this intrinsic program on.

The results of the new experiments from Yuste's group have wide implications. For example, some of the ideas they impact were discussed in Immanuel Kant's philosophical treatises in the 18 th century. Kant was interested in the role of the mind in perception, and he suggested that the brain possesses its own internal categories, such as the sense of space and time, through which the external world is perceived. But the new findings also impinge on modern debates in neuroscience discussing the relative contributions of the thalamus and the cortex in determining patterns of brain activity and the role of recurrent excitatory circuits in sustaining intrinsic states. These intrinsic activity states or “attractors” have long been postulated to exist by theorists as potential mechanisms that implement memories or thoughts.

Yuste said the new work proves that the spontaneous patterns of neural activity that occur in the brain are not random phenomena. “Spontaneous activity, rather than being noise in the machine, is actually engaged by the outside world,” according to Yuste. In other words, the brain seems to harbor its own predefined dynamical states, which are jumpstarted by thalamic activity. Such a notion indicates a dominant role for the cortex in perception, and it flies in the face of a long-held view of the brain that holds that the purpose of the cortex, or brain circuits in general, is more passive, and responds faithfully to sensory inputs in order to generate behavior.

“The results demonstrate that the thalamus is not necessary for the generation of spontaneous cortical activity and it is likely only modulating this intrinsic activity,” Yuste and his colleagues conclude.

Neuroscientists, Yuste predicts, will next attempt to understand the internal logic that governs those intrinsic states and trace the spontaneous internal states of the cortex in behaving animals in an effort to see how they relate to sensory experience and motor planing. Their goal: To understand how internal mental states map out to the world.