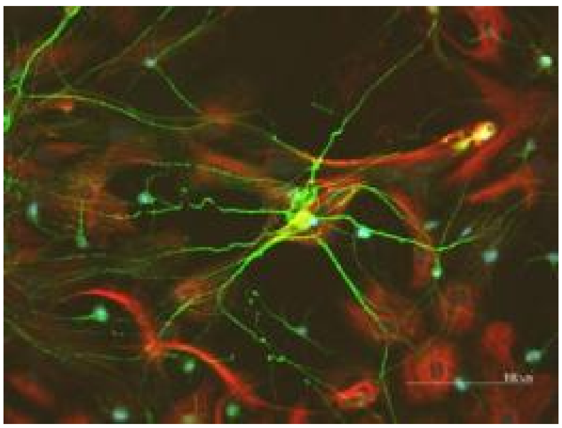
Catching calcium waves could provide Alzheimer's insights (w/ Video)

February 12 2010



This photo shows neurons (green) and astrocytes (red) grown in culture. Astrocytes have become a hot research topic as evidence mounts suggesting that astrocytes in the brain’s cortex do more than provide support to neurons. UC San Diego bioengineers recently found that amyloid beta peptides (Aβ) spontaneously trigger calcium waves in purified cultures of astrocyte cells extracted from the cortex region of rat brains and grown in the lab. These calcium waves could be relevant for understanding the origin of Alzheimer's disease. Photo credit: Chris MacDonald

New insights on what causes Alzheimer's disease could arise from a recent discovery made by bioengineers from the University of California, San Diego. The finding concerns the infamous amyloid beta peptides (Aβ)—fragments of which form plaques thought to play a role in Alzheimer's disease. The bioengineers found that amyloid beta peptides (Aβ) spontaneously trigger calcium waves in purified cultures of astrocyte cells extracted from the cortex region of rat brains and grown in the lab. These calcium waves could be relevant for understanding the origin of Alzheimer's disease. The accumulation of Amyloid beta fragments and sustained disruption of the calcium balance within cells are leading hypotheses for what causes Alzheimer's disease.

The work also adds to researchers' understanding of a class of cells found in the brain called astrocytes, which have become a hot research topic as evidence mounts suggesting that astrocytes in the brain's cortex do more than provide support to neurons.

The UC San Diego bioengineers published the new findings in the January 25, 2010 issue of the journal *ASN NEURO*. "We didn't generate these waves artificially. Amyloid beta fragments induced the waves spontaneously, and that raises some interesting questions about the pathophysiology of Alzheimer's disease and how astrocytes may be involved," said bioengineering professor Gabriel Silva from the UC San Diego Jacobs School of Engineering and the senior author on the paper.

The calcium waves Silva and his team observed have not been reported in astrocyte networks in healthy brain cortex tissue, but they have been seen in the cortexes of rats with Alzheimer's disease. "The fact that amyloid beta peptides—independent of any other cell type—are able to induce calcium waves in astrocyte networks is one of the major findings of the paper," said Silva, who is also affiliated with UC San Diego's Department of Ophthalmology, Neurosciences Program, and Institute of Engineering in Medicine. The new UC San Diego finding that amyloid beta peptides spontaneously trigger the formation of calcium waves in networks of purified astrocytes from the rat brain cortex could prove useful for determining the role that astrocytes play in Alzheimer's disease. This, in turn, could help to clarify what causes Alzheimer's disease and could suggest new drug targets to either slow down or reverse the widespread neuronal death associated with Alzheimer's disease, the bioengineers conclude. There is currently no cure for Alzheimer's disease, the most common form of dementia.

Waves of Calcium

Using fluorescence imaging of purified astrocyte cells extracted from rat cortex tissue, the researchers imaged calcium signals rising and falling across networks of astrocytes. The calcium waves arose only after the researchers added Amyloid beta peptides to the astrocyte cultures.

"In the cultures of astrocytes where we have applied the amyloid beta, we see these huge scale calcium transients and changes spreading throughout the network. One cell will light up, and then all the cells around it will start lighting up—a wave that maybe takes up 150 or 200 cells. That is an intercellular calcium wave and its propagation," explained bioengineering Ph.D. student Chris MacDonald from the UC San Diego Jacobs School of Engineering. MacDonald and Siu-Kei Chow (MS bioengineering, 2009) and Diana Yu (Ph.D., bioengineering 2009) share the first author position on the paper and contributed equally to this work.

"I look at the mechanistic interpretations of the data through mathematical modeling. We see what is happening, but the question is why. And to do that, we need to probe a little bit deeper. Why does amyloid beta cause these waves? We know it does, but why?," asked MacDonald. Answering this "why question" could help researchers finally understand what causes Alzheimer's disease.

Deep Neuroscience Questions

By tracking calcium waves in networks of brain cells, researchers can see changes in membrane voltage, which offers insights into how neurons and other brains cells, including astrocytes, communicate. A better understanding of how the brain works from this bottom-up perspective could lead researchers closer to answering some of the deepest questions in neuroscience. Calcium imaging is emerging as the primary method for interrogating the activity of cellular neural networks, explained Silva, whose Cellular Neural Engineering laboratory focuses, in part, on how information flows through networks of brain cells. According to Silva, answering some of the deepest questions in neuroscience—like What are the origins of creativity, logical reasoning, consciousness and emotions?—will require a better understanding of how information is processed by functional networks in the brains of humans and other species.

"We are just getting to the point where the math and engineering methods are starting to be developed to allow one to study brain networks at the scale of individual cells," said Silva. His lab collaborates with Henry Abarbanel's group in the Department of Physics at UC San Diego on mathematical modeling of neurophysiological systems and computational neuroscience.

In the *ASN NEURO* paper, the researchers used calcium imaging to study a purified astrocyte network. Meanwhile, novel complementary techniques, including "two photon optical microscopy" are raising the possibility of experimental tools capable of testing and validating new theories about how the brain functions from the perspective of cellular networks. This technology could also help researchers uncover how individual brain cells behave as signals propagate through a given network. The Silva lab collaborates with Anna Devor's Neurovascular Imaging Laboratory in the Department of Neuroscience at UC San Diego on experimental cellular imaging and neurophysiology.

Today's fMRI (functional magnetic resonance imaging) tools are useful for studying the brain, but their spatial resolution is far too course to provide insights at the cellular level. "With fMRI, you have no information on what is happening at the individual circuit and network level," said Silva. With technologies such as two photon optical microscopy, researchers are aiming to uncover how the brain works in much finer detail.

Mapping Brain Networks is Just the Start

While mapping the activity of cell networks is "a fantastically interesting problem" according to Silva, it is just the beginning. A more difficult problem involves determining how the brain uses that information. "Pushing the envelope of understanding for these types of problems requires breakthroughs in engineering, math and physics. That is the interesting part for us," said Silva.

Provided by University of California - San Diego

Citation: Catching calcium waves could provide Alzheimer's insights (w/ Video) (2010, February 12) retrieved 19 April 2024 from https://medicalxpress.com/news/2010-02-calcium-alzheimer-insights-video.html