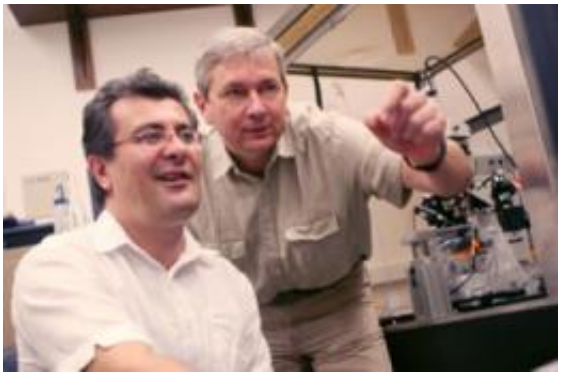
New findings about brain proteins suggest possible way to fight Alzheimer's

October 6 2009



Here are Drs. Joachim Herz (right), Murat Durakoglugil of UT Southwestern Medical Center. Credit: UT Southwestern Medical Center

The action of a small protein that is a major villain in Alzheimer's disease can be counterbalanced with another brain protein, researchers at UT Southwestern Medical Center have found in an animal study.

The findings, available online in the journal Proceedings of the National Academy of Sciences, suggest a promising new tactic against the devastating illness, the researchers said.

The harmful protein, called beta-amyloid, is found in the brain and, when functioning properly, suppresses nerve activity involved with memory and learning. Its normal function can be likened to a red traffic light, restraining nerve cells from getting overexcited when they receive

stimulating signals from neighboring cells. People with Alzheimer's disease, however, accumulate too much beta-amyloid - the traffic light gets stuck on "red" and nerve cells become less responsive.

Another brain protein, called Reelin, acts as a "green light," stimulating nerve cells to respond more strongly to their neighbors' signals.

The new study shows that applying Reelin directly to brain slices from mice prevents excess beta-amyloid from completely silencing nerves.

"If we can identify a mechanism to keep the nerve cells functioning strongly, that might provide a way to fight Alzheimer's disease," said Dr. Joachim Herz, professor of molecular genetics and neuroscience at UT Southwestern and the study's senior author.

In the study, the researchers recorded electrical currents in the mouse hippocampus, an area of the brain associated with learning and memory. From their experiments they determined that Reelin and beta-amyloid interact with the same protein complex, called an NMDA receptor, which plays an important role in coordinating chemical signals between adjacent nerve cells.

They found that Reelin activates and strengthens the response of the NMDA receptor. In the presence of too much beta-amyloid, the receptor migrates into the cell, reducing the cell's sensitivity to incoming signals. By contrast, in strong concentrations of Reelin, the receptor remains active and the cell has the green light to continue receiving normally.

Dr. Herz said the study is especially important because this mechanism involves another protein involved in Alzheimer's called ApoE4, which is the primary risk factor for the most frequent late-onset form of the disease. The receptor that binds to ApeE molecules also binds to Reelin, and is part of the red-light/green-light complex that controls the

sensitivity of the NMDA receptors.

"These results imply that Reelin, ApoE and beta-amyloid converge on the same molecular mechanism, which is critical in the Alzheimer's disease process, and Reelin may be a common factor to fight both beta-amyloid and mutated ApoE," Dr. Herz said. "This study establishes a rationale that ApoE receptors have an action that can keep the Alzheimer's disease process at bay by preventing damage in the first place."

The researchers are currently studying the role of ApoE4 in this mechanism. Mimicking or preserving normal Reelin function to stimulate the ApoE receptors might provide a path to stave off the disease, Dr. Herz said.

Source: UT Southwestern Medical Center (news : web)