

Yang Xiang, Ph.D.

University of Illinois at Urbana-Champaign
Urbana, Illinois

Beta-Amyloid Increases AMPAR-mediated Synaptic Activity via b2AR Activation

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Beta-amyloid is a protein fragment that aggregates into amyloid plaque, a characteristic feature of Alzheimer pathology and one that is toxic to nerve cells. Beta-amyloid has been shown to have a number of effects on nerve cells that could explain aspects of its toxicity. Recent studies have found, for example, that nerve cells near amyloid plaques in the brain are abnormally active. The mechanisms that explain this abnormal activity are not known.

Yang Xiang, Ph.D. and colleagues are studying the effects of beta-amyloid on nerve cell activity. They have found evidence that beta-amyloid binds to a receptor known as the beta2-adrenergic receptor. This binding leads to increases in activity of another receptor known as the AMPA receptor. The AMPA receptor is extremely important because it is a receptor for the neurotransmitter glutamate, and glutamate is the major excitatory neurotransmitter in the brain. Increases in AMPA receptor activity in the presence of beta-amyloid could explain the abnormally high activity of nerve cells, which can lead to abnormal brain function and cell death.

Dr. Xiang and colleagues plan to confirm and extend their studies of the effects of beta-amyloid on AMPA receptor activity. They also plan to test drugs that block binding of beta-amyloid to the beta2-adrenergic receptor, to determine if such drugs reduce the toxicity of beta-amyloid. These experiments will advance our understanding of how beta-amyloid is toxic to nerve cells, and may reveal important drug targets for preventing such toxicity.