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Neuronal Receptor Mediating the Disease-causing Effects of A-beta Oligomers

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Beta-amyloid (also called A-beta) is a protein fragment that aggregates into small clusters, called oligomers, and large clusters known as amyloid plaques. Although amyloid plaques were first thought to be the main cause of amyloid toxicity, it is now recognized that beta-amyloid oligomers are also significant toxins in the brain. While the toxic effects of oligomers on nerve cell function have been described, the receptor that binds oligomers and mediates those effects has not been identified. It is believed that such a receptor exists because the effects of oligomers are evident even when they are present at very low levels.

Stephen M. Strittmatter, M.D., Ph.D. and colleagues have identified a protein in the brain that is a candidate receptor for beta-amyloid oligomers. This receptor binds oligomers even at very low concentrations. The researchers have created a strain of mice genetically altered so that the receptor is missing. They observed that some of the detrimental effects of oligomers were absent in these mice.

Dr. Strittmatter's team plans to extend their studies of the receptor using genetic, biochemical, behavioral and electrical techniques. By crossing their mouse strain with another strain that exhibits Alzheimer-like pathology, the researchers will determine if animals lacking the receptor experience fewer Alzheimer-like effects in the brain. They will also use antibodies against the receptor to determine if blocking it can inhibit the detrimental effects of beta-amyloid oligomers. These experiments will advance our understanding of the damaging effects of beta-amyloid oligomers, and may help to identify an important new target for therapies designed to slow or halt the progression of Alzheimer's disease.