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## The first-in-human clinical trial targeting Alzheimer's tau protein

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So far, many of the antibody drugs proposed to treat Alzheimer's disease target only the amyloid plaques. Despite the latest clinical trial that is hailed as our best chance in the quest for treating AD, all later phase trials have failed with many causing severe side effects in the patients, such as abnormal accumulation of fluid and inflammation in the brain. One of the reasons for side effects, many speculate, is due to the antibody directing a reaction towards normal amyloid present in blood vessels or simply releasing beta-amyloid caught in the vessel wall.

The authors of the study have developed a vaccine that stimulates the production of an antibody that specifically targets pathological tau, discovering its "Achilles' heel." It is able to do this because healthy tau undergoes a series of changes to its structure forming a new region that the antibody attacks. This new region (the "Achilles' heel"), while not present in healthy tau, is present in diseased tau early on. Therefore, the antibody tackles all the different varieties of pathological tau. In addition to this important specificity, the antibody is coupled to a carrier molecule that generates a considerable immune response with the added benefit that it is not present in humans, thus avoiding the development of an immune reaction towards the body itself.

Side effects have included a local reaction at the site of injection. This skin reaction is thought to occur due to the aluminum hydroxide, an adjuvant used in vaccines to enhance the body's own antibody production. No other serious secondary effects were directly related to the vaccine. Overall, the safety of the drug and its ability to elicit an immune response were remarkable.

While many trials against Alzheimer's disease stubbornly continue to target amyloid, our study dares to attack the disease from another standpoint. This is the first active vaccination to harness the body's ability to produce antibodies against pathological tau. Even though this study is only a phase 1 trial, its success so far gives the authors confidence that it may be the answer they are looking for to halt the progress of this devastating disease.

