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Alzheimer's Disease (AD) is the most common neurodegenerative disease in humans, affecting approximately 11% of people aged 65 years and older. While AD pathology is characterized by amyloid-beta (Aβ) peptide aggregation into insoluble plaques, numerous studies have implicated water-soluble Aβ oligomers as the most toxic form of Aβ. To date, the structure and mechanism of toxicity of soluble Aβ oligomers remains unclear due to an inability to accurately purify and quantify soluble Aβ oligomers from human AD patient and animal model brains. In particular, several methods utilize the interaction between biotin and streptavidin to purify and quantify Aβoligomers. However, studies have shown endogenous biotin-containing molecules occur in many regions of the central nervous system. Thus, the reliability of these techniques may be compromised if any proteins—including Aβ oligomers—are endogenously biotinylated.

In this experiment, soluble lysates from the forebrains of triple transgenic AD (3xTg-AD) mouse models were prepared and treated with streptavidin-conjugated agarose beads and free avidin protein, followed by streptavidin-conjugated agarose beads. Samples were separated using size-exclusion chromatography (SEC), and the abundance of biotinylated molecules and Aβ species—both monomeric and oligomeric—were assessed through direct and indirect enzymelinked immunosorbent assays (ELISA) for all groups. We found that treatment with streptavidinconjugated agarose beads resulted in the complete loss of immunoreactivity previously attributed to Aβ oligomers. Therefore, it raises the intriguing possibility that Aβ oligomers derived from the 3xTg-AD mouse model are endogenously biotinylated. Additional analysis via mass spectrometry will be performed to confirm the biotinylation of Aβ oligomers in 3xTg-AD mouse model and human AD patient brains.