

Alzheimer's disease biomarkers can predict postoperative delirium

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Clinical studies have demonstrated a strong association between Alzheimer's disease (AD) and delirium. A change to the Tau protein, which can lead to the formation of tangles in brain, is one of the

hallmarks of AD pathology, and Tau phosphorylation at threonine 217 (Tau-PT217) and threonine 181 (Tau-PT181) are new plasma biomarkers that can detect early-stage AD. A clinical study led by investigators at Massachusetts General Hospital (MGH) has shown that plasma Tau-PT217 and Tau-PT181 are associated with incidence and severity of postoperative delirium. The findings are published in *Annals of Surgery*.

Early studies from the same research group at MGH have shown that the ratio of beta amyloid (which causes AD's signature plaques) to Tau in cerebrospinal fluid is associated with [postoperative delirium](#). Recent studies in other labs have reported that plasma Tau-PT181 concentration distinguishes AD dementia from other neurological disorders. Plasma levels of Tau-PT217 are associated with the changes in [cerebrospinal fluid](#) levels of Tau-PT217 and AD development.

In this current study, the team at MGH developed a novel method to measure Tau-PT217 and Tau-PT181 concentrations in plasma of patients, called nanoneedle technology, in collaboration with NanoMosaic (Woburn, MA). "The nanoneedle technology is ultrasensitive, requires a small volume, and can measure low concentrations of molecules, including Tau-PT217 and Tau-PT181," says lead author Feng Liang, MD, Ph.D., in the Department of Anesthesia, Critical Care and Pain Medicine at MGH. "More than 20,000 nanoneedles are integrated on a silicon substrate assigned to detect one analyte. Each nanoneedle is a single molecule biosensor functionalized with antibodies," says Liang.

The group conducted experiments in 139 patients who had a knee replacement, hip replacement, or laminectomy (a type of back surgery) at MGH. They have discovered that preoperative plasma concentrations of Tau-PT217 and Tau-PT181 are associated with postoperative [delirium](#). Moreover, Tau-PT217 is a stronger indicator of postoperative

delirium than Tau-PT181. "These outcomes help diagnosis of postoperative delirium; identify intermediate outcomes that could facilitate [clinical studies](#); and elucidate the insight into potential mechanisms of postoperative delirium, ultimately leading to better and safer postoperative outcomes in patients," says senior author Zhongcong Xie, MD, Ph.D., the director of the Geriatric Anesthesia Research Unit in the MGH Department of Anesthesia, Critical Care and Pain Medicine. Xie is also Henry K. Beecher Professor of Anesthesia at Harvard Medical School. "These data also suggest that Tau phosphorylation, contributes, at least partly, to the development of postoperative delirium," says Xie.

Adds co-author Oluwaseun Akeju, MD, chair of the Department of Anesthesia, Critical Care and Pain Medicine: "Postoperative delirium could be a clinical manifestation of preclinical AD and might serve as a useful early warning sign to patients."

High preoperative plasma concentrations of Tau-PT217 or Tau-PT181 can predict the presence and severity of postoperative delirium, with Tau-PT217 being the more strongly associated with these outcomes. "We hope this work will promote more research to confirm these associations and to understand further the mechanisms underlying the interaction of delirium and AD, ultimately leading to better interventions for both," says study co-author Edward R. Marcantonio, MD, SM, from the Department of Medicine at Beth Israel Deaconess Medical Center.

More information: Feng Liang et al, Preoperative Plasma Tau-PT217 and Tau-PT181 Are Associated With Postoperative Delirium, *Annals of Surgery* (2022). [DOI: 10.1097/SLA.0000000000005487](https://doi.org/10.1097/SLA.0000000000005487)

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