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TRAUMATIC BRAIN INJURY

PET imaging detects amyloid deposits after TBI

A study by David Menon and colleagues has demonstrated that ^{11}C-labelled Pittsburgh compound B (PiB)–PET imaging could enable temporal changes in amyloid-β (Aβ) deposits to be evaluated in living patients after traumatic brain injury (TBI). PiB–PET scanning is often used to quantify Aβ deposits in patients with Alzheimer disease (AD), but the method has not been previously validated in TBI.

To assess Aβ aggregation and degradation over 1 year following TBI, Menon and colleagues used PiB–PET to scan the brains of 15 patients with moderate to severe TBI and 11 age-matched controls. The results showed rapid accumulation of Aβ in cortical grey matter and the striatum within hours of the injury, followed by a steady decline suggestive of gradual clearance. Menon's team validated their results using ^{3}H-labelled PiB autoradiography and Aβ-targeted immunocytochemistry in postmortem brain tissue that was obtained from a separate cohort of 16 patients who died after TBI.

Aβ pathology is implicated in the neuropathology of both AD and TBI: amyloid plaques are normally observed only in elderly individuals, but after TBI, large amounts of amyloid precursor protein (APP) are released from injured axons, resulting in accumulation of APP and formation of amyloid plaques in patients of all ages. Although amyloid deposits are gradually cleared during the days and months following TBI, Menon points out that autopsy studies indicate that Aβ plaques (often of the AD-associated form, $A\beta_{42}$) are present in up to 30% of patients with a history of TBI, regardless of age. These findings are in line with epidemiological data suggesting that TBI results in a substantial (2–10-fold) increase in the risk of AD later in life. However, the mechanisms through which TBI might increase susceptibility to AD years or even decades after the initial injury are unknown.

Next, the investigators aim to characterize temporal changes in amyloid. "We plan to undertake imaging at late time points after head injury to see if Aβ deposition recurs, and relate these observations to late life cognitive decline and AD," Menon explains. Another intriguing question is whether single and repeated injuries have different effects on amyloid aggregation. Interestingly, genetic background could affect the risk of AD after TBI. Carriers of *APOE**ε4—a well-established risk allele for AD—are more likely to show amyloid deposits after TBI, and have a higher risk of developing AD following TBI. Menon and collaborators plan to examine the influence of genotype on amyloid binding over time, which could help to identify individuals at particularly high risk of AD.

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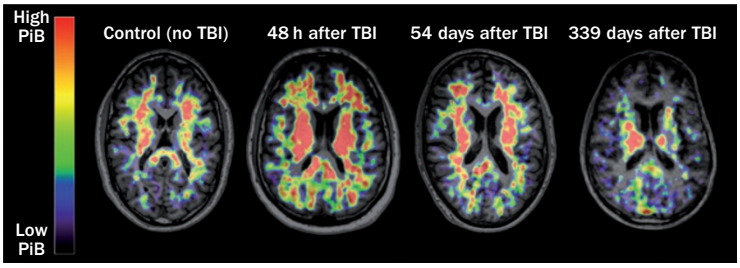

PiB–PET imaging shows accumulation and gradual decline of amyloid-β after TBI. Abbreviations: PiB, Pittsburgh compound B; TBI, traumatic brain injury. Image courtesy of Y. T. Hong and D. K. Menon.

Original article Hong, Y. T. *et al*. Amyloid imaging with carbon 11-labeled Pittsburgh compound B for traumatic brain injury. *JAMA Neurol*. doi:10.1001/jamaneurol.2013.4847