

Brain Age Gap

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1. The difference between **predicted brain age** and **chronological age**.

1. **Positive BAG:** Brain appears older than the person's chronological age, potentially linked to neurological or systemic health risks.
2. **Negative BAG:** Brain appears younger, possibly indicating better resilience or health.

Exploratory Observational Studies

In a Exploratory Observational Study Coetzee et al. analyzed data from 85 TBI patients and 22 healthy controls (HCs). High-resolution T1W images were processed using FreeSurfer 7.0. pBAs were calculated from T1s. Differences between the two groups were tested using the Mann-Whitney U. Associations between the BAG and other factors were tested using partial Pearson's r within groups, controlling for CA, followed by construction of regression models.

After correcting for multiple comparisons, TBI patients and HCs differed on PCL score (higher for TBI patients) and cortical thickness (CT) in both hemispheres (higher for HCs). Among women TBI patients, BAG was correlated with pBA and hippocampal volume (HV), and among men TBI patients, BAG was correlated with pBA and CT. Among both men and women HCs, BAG was correlated only with CA. Four hierarchical regression models were constructed to predict BAG in each group, which controlled for CA and excluded pBA for multicollinearity. These models showed that HV predicted BAG among women with TBI, while CT predicted BAG among men with TBI, while only CA predicted BAG among HCs.

These results offer tentative support to the view the factors associated with BAG among individuals with TBI differ from factors associated with BAG among HCs, and between men and women. Specifically, BAG among individuals with TBI is predicted by neuroanatomical factors, while among HCs it is predicted only by CA. This may reflect features of the algorithm, an underlying biological process, or both ¹⁾.

This study is a conceptually interesting and methodologically promising exploration of brain aging in TBI. However, the small sample, lack of external validation, and limited clinical relevance of the results undermine its translational value. Future studies should focus on:

Prospective, longitudinal designs

Larger, more diverse cohorts

Integration of cognitive, behavioral, and functional outcomes

Transparent ML methodology with external performance benchmarks

1)

Coetzee JP, Kang X, Liou-Johnson V, Luttenbacher I, Seenivasan S, Eshghi E, Grewal D, Shah S, Hillary F, Dennis EL, Adamson MM. Predicting brain age for veterans with traumatic brain injuries and healthy controls: an exploratory analysis. *Front Aging Neurosci.* 2025 May 15;17:1472207. doi: 10.3389/fnagi.2025.1472207. PMID: 40443792; PMCID: PMC12119580.

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