Investigating traumatic brain injury as a moderator in the relationship between cortical thickness and volume and mild behavioural impairment.

Background

Mild behavioural impairment (MBI) is a syndrome that captures later-life emergent and persistent neuropsychiatric symptoms to identify a high-risk group for incident dementia [1].

Traumatic brain injury (TBI), a recognized risk factor for dementia, has been linked to MBI in previous studies, although underlying mechanisms remain unknown [2].

Lower grey matter volume in the hippocampal and entorhinal cortex is also linked to MBI [3].

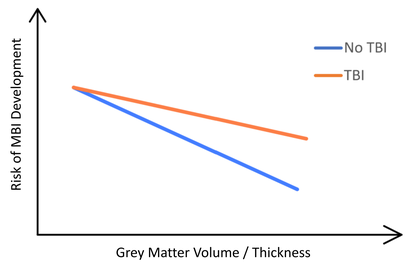
Objective & Hypothesis

Objective

- We investigated the moderation effects of TBI in the relationship between cortical regions implicated in Alzheimer's disease (AD) and MBI.

Hypothesis

- Those with TBI will have a weaker association between AD-specific grey matter volume or thickness and MBI. In other words, TBI will lower the protective effect of greater cortical volume and thickness against MBI onset.



Methods

Participants: The sample included 511 individuals without dementia or neuropsychiatric disorders, aged ≥50 years from the National Alzheimer's Coordinating Center Uniform Data Set, who had available imaging data.

MBI Operationalization: MBI score was derived from Neuropsychiatric Inventory Questionnaire using a published algorithm [4]. Participants were assigned MBI+ status if they had an MBI score ≥ 1 at more than two-thirds of all dementia-free study visits.

AD-specific Cortical Regions included the hippocampal and entorhinal volumes, and thickness of AD meta-region-of-interest (ROI). The ROI included the entorhinal, parahippocampal, fusiform, middle and inferior temporal, and inferior parietal cortices [5].

Moderation Analysis: The associations between cortical measures of AD-specific regions and the development of MBI were analyzed using an accelerated failure time (AFT) model, adjusted for age, sex, education, cognitive status, and a cortical measure*TBI interaction term to assess moderation.

Traumatic brain injury does not lower the protective effect of greater grey matter volume and thickness against the onset of mild behavioural impairment.

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Table 1. Demographic information for the sample.
MBI: Mild Behavioural Impairment, MCI: Mild Cognitive Impairment, TBI: Traumatic Brain Injury

Group	n	M_{age} (SD)	Male (%)	$M_{education}$ (SD)	MBI+ Status (%)	Cognitive Status (% MCI)
TBI -	463	71.6(9.94)	36.7	16.0(7.36)	23.3	21.0
TBI +	48	69.4(11.0)	50.0	15.4(3.69)	27.1	29.2

Results

Longitudinal: Greater hippocampal volume was associated with longer time to MBI development. Entorhinal volume and meta-ROI thickness had a similar direction of effect, but they did not meet statistical significance.

Regions of Interest	TR	95% CI	p-value
Hippocampal volume	1.18	1.04 – 1.33	<0.01
AD-specific composite thickness	1.06	0.95 – 1.17	0.29
Entorhinal volume	1.17	0.99-1.37	0.06

Table 2. Longitudinal associations between cortical regions and development of MBI via accelerated failure time models, adjusted for age, sex, education, and cognitive status. TR: Time ratio.

Moderation: Associations between cortical measures and time to MBI did not differ between TBI+ and TBI- participants, with non-significant interaction effects:

Regions of Interest*TBI	b	95% CI	p-value
Hippocampal volume*TBI	-0.29	-0.62 – 0.05	0.10
AD-specific composite thickness*TBI	-0.10	-0.58 - 0.37	0.67
Entorhinal volume*TBI	-0.37	-0.98 – 0.23	0.23

Table 3. Interaction effects of TBI and cortical regions of interest in accelerated failure time models with time to MBI development as outcome, adjusted for age, sex, education, and cognitive status. TBI: Traumatic Brain Injury, MBI: Mild Behavioural Impairment

Discussion

Key Insights

- Higher cortical thickness and volume is associated with delayed MBI onset, linking morphometrics and behaviour change in advance of dementia.
- Findings suggest that the protective effect of greater grey matter volume and thickness in AD vulnerable regions against development of MBI may be weaker in those with TBI.
- Further research is needed to explore this potential moderation effect.

Limitations

- Low statistical power of the sample
- Using the NPI-Q to derive MBI status, as opposed to the original MBI-C
- Low sensitivity of the TBI variable, which would decrease effect size [6]