

Associations Between Head Injury and Mild Behavioral Impairment Across the Cognitive Spectrum

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Background

- The sequelae of traumatic brain injury may contribute additional complexity to the clinical picture of mild cognitive impairment (MCI) and dementia progression
- Due to shared underlying neural circuit disruption, the construct of mild behavioral impairment (MBI) may have utility in relating neuropsychiatric symptoms (NPS) to traumatic brain injury in the context of neurodegenerative processes

MBI Domains	Neuropsychiatric Inventory Symptoms
Decreased Motivation	Apathy/Indifference Depression/Dysphoria
Affective Dysregulation	Anxiety Elation/Euphoria
Impulse Dyscontrol	Agitation/Aggression Irritability/Lability Aberrant Motor Behavior
Social Inappropriateness	Disinhibition
Abnormal Perception or Thought Content	Delusions Hallucinations

Study Objective

- To investigate the cross-sectional associations of prior head injury with MBI prevalence by cognitive status and to examine the prospective associations of prior head injury and MBI domain positivity with risk of dementia

Methods

Design	• Cross-sectional analysis of prospective cohort
Setting	• Atherosclerosis Risk in Communities (ARIC) Study
Participants/ Enrollment	• 2,246 community-dwelling adult patients • Age 18 or older • ARIC visit 5 baseline (2011-2013)
Exposure	• Cognitive status – algorithmic diagnosis • Head injury - combination of self-reported data and ICD-9/10 code data from hospitalizations and ED visits
Outcomes	• Neuropsychiatric symptoms (NPI-Q) • MBI subdomains
Analyses	• Association between head injury prior to baseline (history of head injury versus no head injury) and baseline cognitive status (MCI or normal) with MBI domain positivity • Association of head injury and MBI domain positivity with risk of developing dementia in the time period between baseline (ARIC visit 5) and ARIC visit 7

Results

Table 1 – Weighted participant characteristics, ARIC Visit 5 (2011 – 2013), Unweighted N = 2,246

	Normal Cognition			Mild Cognitive Impairment		
	No History of Head Injury (n=907)	History of Head Injury (n=391)	P Value	No History of Head Injury (n=636)	History of Head Injury (n=312)	P Value
Age (years), mean (SE)	75.1 (0.2)	75.5 (0.3)	0.148	76.6 (0.3)	76.7 (0.4)	0.686
Female, % (SE)	65.9 (1.9)	52.4 (3.0)	<0.001	54.6 (2.5)	41.9 (3.1)	0.002
Race/center, % (SE)			0.015			<0.001
Minnesota Whites	32.4 (1.9)	37.3 (3.0)		23.8 (1.8)	34.4 (3.2)	
Maryland Whites	29.5 (1.6)	24.6 (2.2)		25.8 (1.9)	27.7 (2.7)	
North Carolina Whites	17.1 (1.6)	23.8 (2.8)		18.5 (1.6)	22.1 (2.6)	
North Carolina Blacks	1.7 (0.5)	2.2 (1.0)		0.5 (0.3)	0.3 (0.3)	
Mississippi Blacks	19.2 (1.8)	11.9 (2.2)		31.4 (2.7)	15.6 (2.2)	

Table 2 - Weighted Adjusted Odds Ratios (95% Confidence Intervals) for the Cross-sectional Association of Head Injury and Cognitive Status with Mild Behavioral Impairment Domains

	Normal Cognition and No History of Head Injury (n=907)	Normal Cognition and History of Head Injury (n=391)	MCI and No History of Head Injury (n=636)	MCI and History of Head Injury (n=312)
Decreased Motivation	1 (Reference)	1.34 (0.63, 2.85)	2.02 (1.13, 3.61)	3.33 (1.80, 6.16)
Affective Dysregulation	1 (Reference)	1.11 (0.73, 1.70)	1.81 (1.28, 2.56)	2.21 (1.44, 3.38)
Impulse Dyscontrol	1 (Reference)	1.10 (0.72, 1.68)	1.53 (1.09, 2.16)	1.68 (1.12, 2.51)
Social Inappropriateness	1 (Reference)	1.31 (0.56, 3.08)	1.48 (0.70, 3.12)	3.12 (1.44, 6.77)
Abnormal Perception or Thought Content	1 (Reference)	2.17 (0.64, 7.39)	3.64 (1.55, 8.54)	2.55 (0.91, 7.15)
Impairment in Any 1+ MBI Domain(s)	1 (Reference)	1.11 (0.79, 1.57)	1.60 (1.20, 2.14)	2.04 (1.44, 2.88)

Table 3 - Weighted Adjusted Hazard Ratios (95% Confidence Intervals) for the Prospective Association of Head Injury and Mild Behavioral Impairment Domain Positivity with Dementia Risk

	No Head Injury, 0 Positive MBI Domains (n=1,160)	No Head Injury, 1+ Positive MBI Domains (n=383)	Head Injury, 0 Positive MBI Domains (n=481)	Head Injury, 1+ Positive MBI Domains (n=222)
Overall	1 (Reference)	2.15 (1.55, 2.99)	1.30 (0.93, 1.81)	2.62 (1.81, 3.80)
Stratified by Visit 5 Cognitive Status				
Normal Cognition	1 (Reference)	2.42 (1.36, 4.33)	1.68 (0.96, 2.93)	2.50 (1.28, 4.86)
MCI	1 (Reference)	1.57 (1.12, 2.20)	0.89 (0.63, 1.25)	1.93 (1.31, 2.86)

Conclusions

- Baseline MCI without head injury was associated with increased odds of impairment in the MBI domains of decreased motivation, affective dysregulation, impulse dyscontrol, and abnormal perception/thought content, as well as impairment in any one or more MBI domain(s)
- Baseline MCI and a history of head injury were associated with increased odds of impairment in the MBI domains of decreased motivation, affective dysregulation, impulse dyscontrol, and social inappropriateness, as well as impairment in any one or more MBI domain(s)
- Compared to participants with no head injury and no MBI symptoms, having 1+ positive MBI Domains significantly increased the risk of developing dementia between baseline (ARIC visit 5) and follow up (ARIC visit 7) regardless of head injury history or absence thereof
- History of head injury but not MBI domain positivity did not result in significantly increased risk of developing dementia
- The association of MBI with MCI represents a strong priority for ongoing research and may help elucidate distinct patterns of progression to dementia

Limitations

- Small sample size in prospective analyses
- MBI-C was not originally collected in the ARIC study (Established, published algorithm for converting NPI-Q data to MBI domains utilized)
- Head injury defined by self-report and ICD codes

Implications

- The association of MBI with MCI represents a strong priority for ongoing research and may help elucidate distinct patterns of progression to dementia
- The potential influence of remote head injury on the progression from normal cognition to dementia has yielded mixed results, necessitating further mechanistic study