COMT Val158Met Polymorphism is Associated with Post-traumatic Stress Disorder and Functional Outcome Following Mild Traumatic Brain Injury

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Introduction

Mild traumatic brain injury (mTBI) results in variable clinical trajectories and outcomes. The source of variability remains unclear, but may involve genetic variations, such as single nucleotide polymorphisms (SNPs). A SNP in catechol-o-methyltransferase (COMT) is suggested to influence development of post-traumatic stress disorder (PTSD), but its role in TBI remains unclear.

Methods

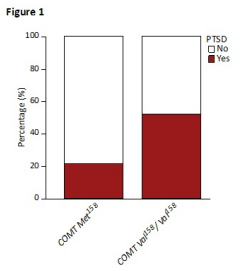
A retrospective analysis was conducted of the Transforming Research and Clinical Knowledge in Traumatic Brain Injury Pilot (TRACK-TBI Pilot) study to determine whether the COMT Val158Met polymorphism is associated with PTSD and global functional outcome as measured by the PTSD Checklist – Civilian Version and Glasgow Outcome Scale Extended (GOSE), respectively.

Table 1. Demographic and clinical information of included subjects with mild traumatic brain injury.

Variable	*Met*^{158} (N=70)	*Val*^{158}/*Val*^{158} (N=23)	Sig. (p)
Age (y)			
Mean ± SD	40 ± 17	42 ± 14	0.682
Gender			
Male	42 (60%)	14 (61%)	0.941
Female	28 (40%)	9 (39%)	
Race			
Caucasian	52 (80%)	13 (20%)	
African-American/African	6 (46%)	7 (54%)	0.032
Other races	12 (80%)	3 (20%)	
Pre-existing Psychiatric Disorder			
No	47 (67%)	10 (44%)	0.043
Yes	23 (33%)	13 (56%)	
Substance Abuse			
No	56 (80%)	15 (65%)	0.148
Yes	14 (20%)	8 (35%)	
Mechanism of Injury			
Motor vehicle crash	22 (31%)	2 (9%)	
Cyclist/pedestrian hit	15 (21%)	6 (26%)	
Fall	21 (30%)	8 (35%)	0.140
Assault	8 (11%)	6 (26%)	
Struck by/against object	4 (6%)	1 (4%)	
ED Arrival GCS			
13	1 (1%)	0 (0%)	
14	12 (17%)	5 (22%)	0.817
15	57 (81%)	18 (78%)	

Results

Figure 1. The COMT Val158Met polymorphism is associated with lower prevalence of qualifying for screening criteria for post-traumatic stress disorder (PTSD) at 6-months following mild traumatic brain injury.



Univariate analysis

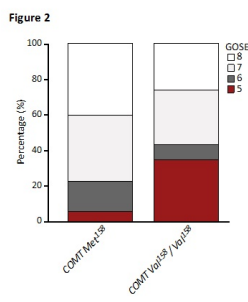
Predictor	Odds Ratio (OR) [95% CI]	Predictor Sig. (p)	Nagelkerke Pseudo-R^2	Model Sig. (p)
COMT Met^{158}	0.25 [0.09-0.69]	0.006	11.0%	----------
Preexisting psychiatric disorder	6.85 [2.54-18.49]	6.3×10^{-5}	22.6%	----------
Substance abuse	3.44 [1.26-9.38]	0.016	8.6%	----------

Multivariable analysis

Predictor	Odds Ratio (OR) [95% CI]	Predictor Sig. (p)	Nagelkerke Pseudo-R^2	Model Sig. (p)
COMT Met^{158}	0.32 [0.11-0.97]	0.044	29.5%	8.1×10^{-5}
Preexisting psychiatric disorder	5.17 [1.80-14.89]	0.002	----------	----------
Substance abuse	1.88 [0.60-5.88]	0.281		

White, did not meet PTSD qualification on screening criteria; red, met PTSD qualification on screening criteria. COMT = Catechol-O-Methyltransferase.

Figure 2. The COMT Val158Met polymorphism is associated with greater global functional outcome as measured by the Glasgow Outcome Scale Extended (GOSE) at 6-months following mild traumatic brain injury.



Univariate analysis

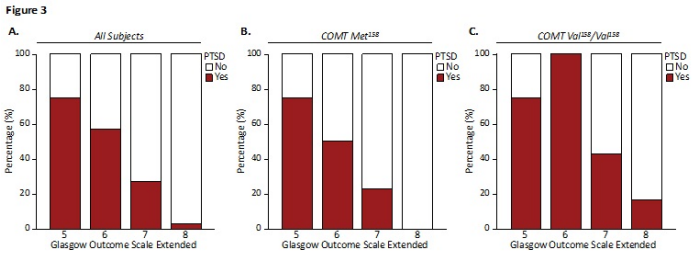
Predictor	Odds Ratio (OR) [95% CI]	Predictor Sig. (p)	Nagelkerke Pseudo-R^2	Model Sig. (p)
COMT Met^{158}	2.87 (1.20-6.86)	0.018	5.9%	----------
PTSD	0.08 [0.03-0.21]	3.62×10^{-7}	30.6%	----------
Age (y)	0.99 [0.97-1.02]	0.499	0.5%	----------
No GCS deficit	2.55 [1.00-6.57]	0.051	3.9%	----------

Multivariable analysis

Predictor	Odds Ratio (OR) [95% CI]	Predictor Sig. (p)	Nagelkerke Pseudo-R^2	Model Sig. (p)
COMT Met^{158}	1.73 [0.69-4.35]	0.243	32.8%	9.06×10^{-7}
PTSD	0.09 [0.03-0.26]	5.0×10^{-6}	----------	----------
Age (y)	1.00 [0.98-1.03]	0.723		
No GCS deficit	1.86 [0.69-5.01]	0.218		

White, GOSE score of 8; light gray, GOSE score of 7; dark gray, GOSE score of 5; red, GOSE score of 5. COMT = Catechol-O-Methyltransferase.

Figure 3. Global functional outcome is negatively associated with the presence of concomitant post-traumatic stress disorder at 6-months post-injury.



COMT = Catechol-O-Methyltransferase.

Learning Objectives

By the conclusion of the session, participants should be able to:

1. Understand the incidence and relevance of PTSD following mild TBI

2. Describe the known risk factors with an emphasis on the COMT single nucleotide polymorphism that are associated with development of PTSD following mild TBI

3. Describe the importance of a potential underlying relationship between PTSD and functional outcome following TBI

Conclusions

The COMT Val158Met polymorphism (rs4680) is associated with incidence of PTSD and functional outcome following isolated, uncomplicated mTBI, and may exert a protective effect. Larger studies in more diverse populations are needed to confirm the role of COMT Val158Met in psychological health following mTBI. Whether COMT Val158/Val158 homozygotes would benefit from heightened clinical surveillance and/or pharmacologic and behavioral therapy targeted towards symptomatic manifestations of PTSD remain to be determined.