Catechol-O-Methyltransferase (COMT) and Treatment Response to Meditation and Group Therapy in Veterans with PTSD

Libin Y Said[1], Adam M Lee[1], Seenae Eum[1], Paul D Thuras[2,3], Christopher R Erbes[2,3], Melissa A Polusny[2,3], Gregory J Lamberty[2,3], Kelvin O Lim[2,3], Jeffrey R Bishop[1,2]

1. Department of Experimental and Clinical Pharmacology, University of Minnesota
2. Department of Psychiatry, University of Minnesota
3. Minneapolis Veterans Affairs Health System, Minneapolis MN

CLINICAL AND TRANSLATIONAL SCIENCE INSTITUTE

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Introduction

- Post-traumatic stress disorder is a chronic and debilitating psychiatric disorder that affects 30% of veterans and 8% of the US population.[1]
- Approximately 28-49%[2] of veterans with PTSD display improvement in PTSD symptoms when treated with non-pharmacologic treatment interventions such as:
  - → Mindfulness Based Stress Reduction (MBSR)
  - → Transcendental Meditation (TM)
  - → Present-Centered Group Therapy (PCGT)
- Catechol-O-methyltransferase (COMT) enzyme catabolizes dopamine and norepinephrine, which regulate mood and anxiety.
- The rs4680 (Val158Met) polymorphism alters the enzyme's structure resulting in reduced activity that is only 25% of the wild type.[3]
- The Val158Met polymorphism has been associated with PTSD risk, however its influence on treatment outcome is unknown.
- **Project Aim:** Assess the relationships between the Val158Met polymorphism, symptom severity and treatment response in veterans receiving non-pharmacological treatments.

Methods

Study Population: The study cohort utilized participants (n=120) obtained from a previously conducted randomized clinical trial.[4] Inclusion criteria included: diagnosis of PTSD and on a stable medication regiment for 2 months. Exclusion criteria included no current substance dependence, suicidal ideation, and psychotic disorder.

Genotyping: The *COMT* Val158Met polymorphism genotyping was performed on blood-derived DNA by a TaqMan Genotyping assay analyzed on the Applied Biosystems 7500 Real Time PCR system.

Statistical Analysis: Primary clinical outcomes were PTSD Checklist (PCL) baseline and week nine scores; PCL-Arousal category baseline and week nine scores; and early childhood/lifetime trauma occurrences. ANOVA, T-test, and Chi-Squared tests were used to test for associations between genotype and clinical outcomes.

Figure 1: COMT Val158Met genotyping by allelic discrimination using TaqMan fluorescence probes

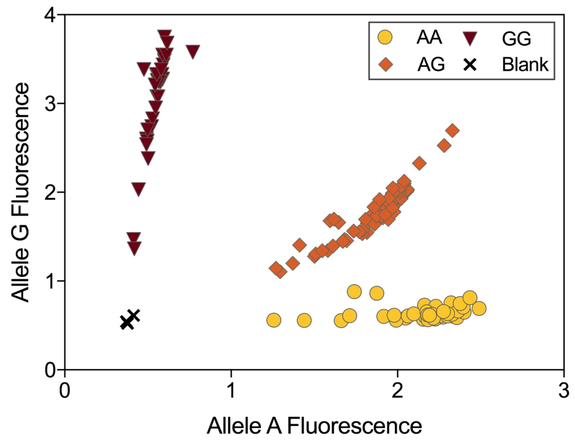


Figure 2: The *COMT* Gene

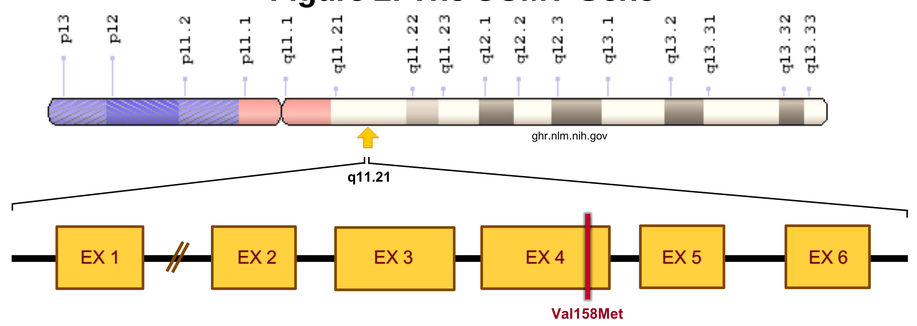
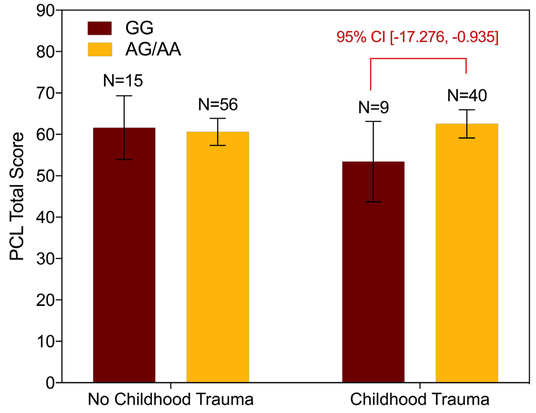


Table 1: Study Cohort Demographics and Summary Data

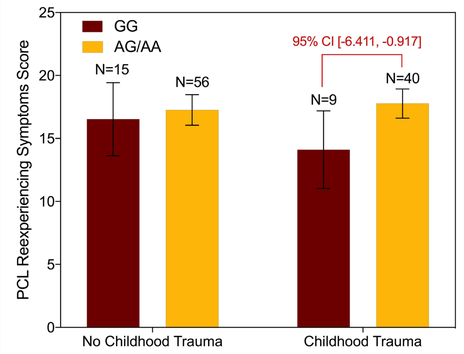
Variable	MBSR &TM N=71		PCGT N=49		Total N=120	
	N	%	N	%	N	%
Male	57	80.2	44	89.8	101	84.2
Race						
Caucasian	59	83.1	43	87.8	102	85.0
Other	12	16.9	6	12.2	18	15.0
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev
Age	59.48	10.87	58.84	9.49	58.78	10.262
PCL Total Score	63.02	10.73	57.43	13.08	60.84	12.03
PCL Total Change (Week 9)	-9.47	12.14	-2.96	10.10	-6.47	11.52
PCL subset scores						
PCL Re-experiencing Baseline	17.81	4.38	15.90	4.25	17.11	4.37
PCL Re-experiencing Change (Week 9)	-2.11	4.47	-0.84	3.72	-1.60	4.11
PCL Arousal Baseline	19.13	3.69	17.96	3.85	18.67	3.89
PCL Arousal Change (Week 9)	-2.52	4.39	-0.75	3.40	-1.60	4.05
PCL Avoidance Baseline	26.09	4.40	23.57	6.02	25.07	5.24
PCL Avoidance Change (Week 9)	-4.85	5.07	-1.37	4.81	-3.27	5.17
	N	%	N	%	N	%
Week 9 Responder	31	43.6	11	22.4	42	35.0
Childhood Trauma	31	43.6	18	42.9	49	40.8

Figure 3: Baseline PCL total scores by COMT genotype across participants with or without evidence of childhood trauma



Prior to the treatment intervention, participants with childhood trauma (n=49) who were Met158 carriers exhibited higher baseline PCL total scores (95%CI [-17.276, -0.935]). No differences in baseline PCL total scores were observed in participants without evidence of childhood trauma (n=71).

Figure 4: Baseline re-experiencing symptoms sub-test scores by COMT genotype across participants with or without evidence of childhood trauma



Prior to the treatment intervention, Met158 carriers with childhood trauma exhibited higher baseline re-experiencing symptom scores (95%CI [-6.411, -0.917]) compared to homozygous Val158 participants. No differences were observed in participants without evidence of childhood trauma (n=71).

Primary Findings

- We identified a significant relationship between the reduced activity 158Met allele and increased PTSD re-experiencing symptoms in patients with childhood trauma.
- This indicates that dysregulated dopamine or norepinephrine signaling may be involved with mechanisms related to specific symptoms related to re-experiencing those events later in life. *COMT* genotypes were not associated with response to the treatments examined herein.

Conclusion/Discussion

Understanding the relationship between how genetics can influence PTSD symptom severity and treatment response to certain interventions can help us discover better more effective genetically-tailored treatment options for people with PTSD.

Strength: Longitudinal data from carefully controlled trials provides a unique opportunity to examine genetic relationships with PTSD treatment outcomes.

Weakness: Future studies in larger cohorts are necessary in order to validate potential gene x environment interactions between *COMT* Val158Met and childhood trauma on PTSD symptom severity.

Translation

Clinical Implication: Identifying potential genetic biomarkers of symptom severity and treatment response may help clinicians improve treatment strategies for patients with PTSD.

Ethical Considerations: lack of representation in study cohort; potential for discrimination; patient privacy

Key Stakeholders: patients with PTSD and their families; clinicians; PTSD treatment centers; and genetic testing companies

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