Catechol O-Methyltransferase Haplotype Predicts Posttraumatic Stress Disorder Symptom Severity Six Weeks after Sexual Assault

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Trauma RecoverY: Understanding Mechanisms & Promoting Healing

Background:

- 1 in 5 US women experience sexual assault (SA) during their lifetime.[1]
- Posttraumatic Stress Disorder (PTSD) is a common sequelae of SA.[2]
- Catechol-O-Methyltransferase (COMT) is the primary enzyme that degrades catecholamines, including epinephrine, norepinephrine, and dopamine.
- A recent study identified an association between a single nucleotide polymorphism (SNP) in the gene encoding the COMT enzyme, *COMT*, and PTSD outcomes.[3]
- To date the association between *COMT* haplotype and posttraumatic psychological outcomes has not been assessed. This may be useful, because when multiple disease susceptibility variants occur in the same gene, the overall functional state of the gene may not be easily deduced from information regarding an individual SNP.[4] This has been shown to be the case for *COMT*.[4]
- In this study, we assessed the association between *COMT* haplotype and PTSD and depressive symptoms after SA.

Methods:

- Women ≥ 18 years of age presenting within 48 hours of sexual assault to one of 11 Sexual Assault Nurse Examiner (SANE) programs were recruited (Figure 1).
- Study evaluations included interview assessments performed one and six weeks after assault. One week evaluation included an assessment of participant age and ethnicity (European American or African American) and DNA collection (Oragene DNA Self-Collection Kit).
- Six week evaluation included an assessment of PTSD symptoms (PTSD Symptom Scale-Interview (PSS-I)), and depression (Depression Anxiety Stress Scales).
- Genotyping (rs4633, rs4680, rs4818, and rs6269) was performed using the Sequenom platform. These SNPs were used to identify 3 common *COMT* haplotypes, which based on their association with sensitivity to pain stimuli have been termed the average pain sensitivity (APS) haplotype (A_T_C_A), the high pain sensitivity (HPS) haplotype (A_C_C_G), and the low pain sensitivity (LPS) haplotype (G_C_G_G)[5].

Figure 1. Study Network

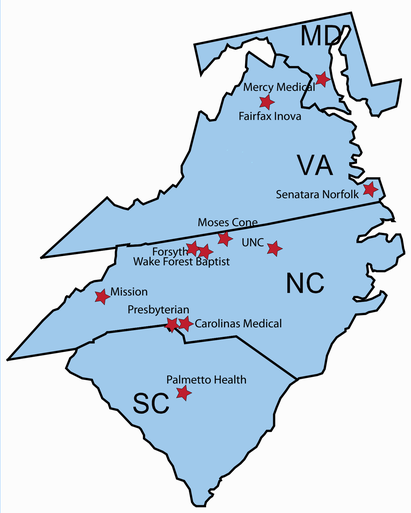

Table 1. Patient Characteristics

Characteristics	SANE Evaluation N=83
Age (mean, SD)	26 (8.2)
Ethnicity (n, %)	
African American	30 (36)
European American	53 (64)
Employment (n, %)	
Work full time	23 (28)
Work part time	21 (25)
Student	39 (47)
Not working	18 (22)
Highest level of education completed (n, %)	
8-11 years	11 (13)
12 years or completed high school	16 (20)
Some college or post high school training	44 (53)
College graduate or beyond	12 (14)
Annual family income (n, %)	
$0 - $19,999	25 (30)
$20,000 - $39,999	16 (20)
$40,000 - $59,999	6 (7)
$60,000 - $99,999	10 (12)
$100,000 or Higher	9 (11)
Refused to Answer	17 (20)
Relationship status (n, %)	
Not in a serious relationship	40 (48)
Serious relationship, not living together	10 (12)
Serious relationship, living together/married	13 (16)
Separated/Divorced/Widowed	11 (13)
Refused	9 (11)
Number of children (n, %)	
None	47 (57)
2 or less	22 (27)
3 or more	11 (13)
Refused	3 (4)

Figure 2. Patient flow through study

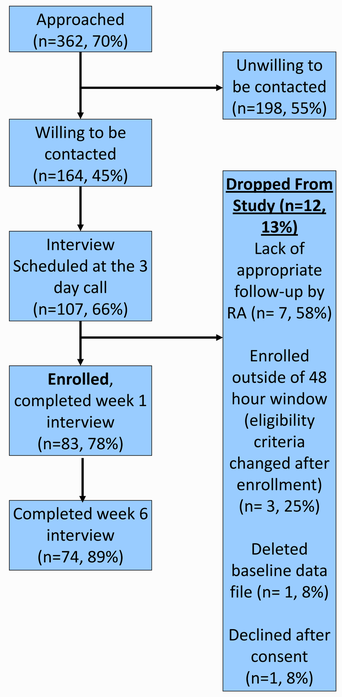

Table 2. Linear regression models assessing influence of COMT LPS copy number on PTSD severity (PSS-I score) and Depression (DASS score) six weeks after sexual assault

	PTSD Severity Score β	t	p-value		*Depression Score* β	t	p-value
Intercept	18.392	3.076	0.003	Intercept	8.774	2.912	0.005
Race	-1.026	-0.374	0.710	Race	-1.764	-1.274	0.207
Age	0.570	3.798	<0.001	Age	0.155	2.042	0.046
LPS Haplotype ≥1 Copy	-7.530	-2.730	0.008	LPS Haplotype ≥1 Copy	-3.377	-2.430	0.018
Model R^2	0.252			Model R^2	0.139		

Figure 3. Mean PTSD score 6 weeks after SA

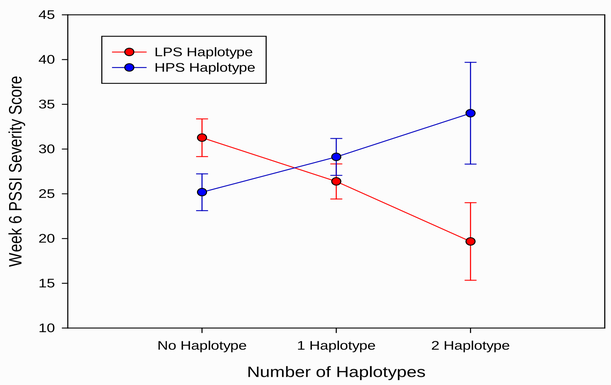

Figure 4. Mean depressive symptom score 6 weeks after SA

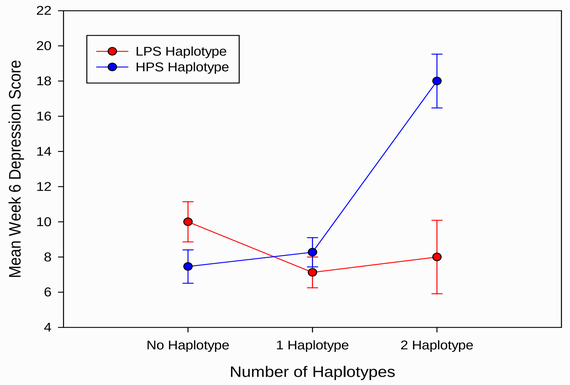

Table 3. Linear regression models assessing influence of COMT HPS copy number on PTSD severity (PSS-I score) and Depression (DASS score) six weeks after sexual assault

	PTSD Severity Score β	t	p-value		*Depression Score* β	t	p-value
Intercept	10.476	1.842	0.070	Intercept	5.239	1.835	0.072
Race	-0.452	-0.161	0.872	Race	-1.493	-1.061	0.293
Age	0.564	3.655	0.001	Age	0.151	1.954	0.055
HPS Haplotype ≥1 Copy	5.493	2.023	0.048	HPS Haplotype ≥1 Copy	2.408	1.767	0.082
Model R^2	0.213			Model R^2	0.101		

Women's Health Study

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Methods (Continued):

The association between *COMT* LPS and HPS haplotype presence or absence and PTSD symptom severity and depression were assessed via linear regression analysis adjusted for age and ethnicity.

Results:

- Participant flow through the study is shown in Figure 2. Eighty-three women agreed to an informational telephone call and subsequently consented to a one week interview.
- Most women were European American (53/83), < 30 years of age (59/83), and did not have children (47/83) (Table 1). Six week follow-up was obtained in 74 patients (89%).
- In linear regression analysis adjusted for age and ethnicity, the presence of one or more LPS haplotypes was associated with reduced PTSD symptoms (Table 2). Those with one or more LPS haplotypes also had reduced depressive symptoms at the 6 week interview (Table 2).
- In contrast, the presence of one or more HPS haplotypes was associated with increased PTSD symptoms (Table 3). Women with one or more HPS haplotypes also showed a trend towards higher depresive symptoms at 6 weeks (Table 3).
- The effect of HPS and LPS copy number on PTSD and depressive symptoms are displayed in Figures 3 and 4, respectively.

Conclusions:

- These findings provide preliminary evidence that *COMT* haplotype is associated with PTSD and depressive symptom vulnerability after SA.

References

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