The Roles of Borderline Personality Disorder Symptoms and Dispositional Capability for Suicide in Suicidal Ideation and Suicide Attempts: Examination of the COMT Val^158 Met Polymorphism

MATTHEW T. TULL, PH.D.
DEPARTMENT OF PSYCHOLOGY
UNIVERSITY OF TOLEDO

BPD AND SUICIDE

• BPD is characterized by severe instability and dysfunction across interpersonal, emotional, cognitive, and behavioral domains (Gunderson, 2001; Linehan, 1993).

• BPD is associated with high rates of both suicide attempts (>70) (Zanarini et al., 2008) and death by suicide (10%) (Skodol et al., 2002).

• Research is needed to identify the subset of individuals with BPD symptoms who may be at greatest risk for more serious or lethal suicide attempts.
CONTEMPORARY MODELS OF SUICIDE RISK

- Recent suicide risk models have highlighted factors that are necessary for the transition from suicidal ideation to a suicide attempt.
  - Three-Step Model of Suicide (3ST) (Klonsky & May, 2015)
  - Interpersonal Theory of Suicide (ITS) (Joiner, 2005)
  - Both propose that suicide capability is a primary factor necessary for an individual to move from suicidal ideation to a suicide attempt.

3ST and SUICIDE CAPABILITY

- **Acquired capability** develops over time as an individual habituates to pain and develops fearlessness about death through repeated exposure to painful and provocative experiences.
- **Practical capability** encompasses the logistical components that increase the ease with which an individual may employ lethal means.
- **Dispositional capability** is influenced by biological and genetic predispositions to fearlessness about death and pain tolerance.

- Research on dispositional capability is limited.

Klonsky & May (2015)
DISPOSITIONAL CAPABILITY – COMT VAL158Met

• A promising avenue for dispositional capability is examination of gene variation associated with fearlessness and pain tolerance.
• Catechol-o-methyltransferase (COMT) Val158Met polymorphism.

• COMT is involved in the breakdown of estrogen, catecholamines, and the neurotransmitters of dopamine, epinephrine, and norepinephrine.

• Carriers of the homozygous Met/Met variant exhibit 3-4 times lower neurotransmitter catabolic activity than carriers of the Val/Val variant (with Val/Met carriers falling in between).

DISPOSITIONAL CAPABILITY – COMT VAL158MET

• Val/Val carriers exhibit less thermal pain sensitivity than Val/Met and Met/Met carriers (Schmahl et al., 2012).

• The Val/Val variant is associated with lower ratings of both pain and negative affective states associated with pain relative to those with the Met allele (Desmeules et al., 2012; Zubieta et al., 2003).

• The Met/Met variant is associated with greater harm avoidance (Enoch et al., 2008; Hashimoto et al., 2007) and increased startle response (Montag et al., 2008).

• Val/Val carriers may have a greater dispositional capacity for suicide due to decreased pain sensitivity and increased fearlessness.
CURRENT STUDY

• Examine the interactive association of BPD symptoms and the COMT Val<sup>158</sup>Met polymorphism with past-month suicidal ideation and lifetime suicide attempts.

• **Hypotheses**
  • Among Val/Val carriers, higher levels of BPD symptoms would be associated with a greater likelihood of reporting a lifetime suicide attempt, relative to Val/Met and Met/Met carriers.
  • Given that dispositional capability is theorized to increase the risk for serious or lethal suicidal behavior versus suicidal desire, we predicted to only find a main effect of BPD symptoms on suicidal ideation.

PARTICIPANTS

• 59 patients from a residential substance use disorder (SUD) treatment facility.

• 18 to 58 years of age, mean age = 31.59 (SD = 10.09)

• 52.5% men (n = 31),

• 86.4% White (n = 51), 13.6% African-American (n = 8)

• 59.3% high school education or less (n = 25)

• 52.5% annual income of less than $20,000 (n = 31)
CLINICAL CHARACTERISTICS

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>% (n)</th>
</tr>
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<tbody>
<tr>
<td>Borderline Personality Disorder</td>
<td>40.7 (24)</td>
</tr>
<tr>
<td>Posttraumatic Stress Disorder</td>
<td>40.7 (24)</td>
</tr>
<tr>
<td>Major Depressive Disorder</td>
<td>33.9 (20)</td>
</tr>
<tr>
<td>Panic Disorder with/without Agoraphobia</td>
<td>5.1 (3)</td>
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<tr>
<td>Social Anxiety Disorder</td>
<td>22.0 (13)</td>
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<tr>
<td>Obsessive-Compulsive Disorder</td>
<td>16.9 (10)</td>
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<tr>
<td>Generalized Anxiety Disorder</td>
<td>30.5 (18)</td>
</tr>
<tr>
<td>Alcohol Use Disorder</td>
<td>45.8 (27)</td>
</tr>
<tr>
<td>Drug Use Disorder</td>
<td>100 (59)</td>
</tr>
<tr>
<td>Past-month Suicidal Ideation</td>
<td>59.3 (35)</td>
</tr>
<tr>
<td>Lifetime Suicide Attempts</td>
<td>28.8 (17)</td>
</tr>
<tr>
<td>COMT</td>
<td></td>
</tr>
<tr>
<td>Met/Met</td>
<td>20.3 (12)</td>
</tr>
<tr>
<td>Val/Met</td>
<td>44.1 (26)</td>
</tr>
<tr>
<td>Val/Val</td>
<td>35.6 (21)</td>
</tr>
</tbody>
</table>

MEASURES

- BPD was assessed using the Diagnostic Interview for DSM-IV Personality Disorders (DIPD-IV; Zanarini et al., 1996).
  - For each symptom assessed, interviewers provide a score of 0 (absent), 1 (subthreshold), or 2 (threshold).
  - Continuous BPD symptom severity score calculated by summing score for each symptom.

- The suicidality portion of the Mini International Neuropsychiatric Interview, Version 6.0 (MINI; Sheehan et al., 2009) was used to assess suicide outcomes.
  - Items assessing presence/absence of lifetime suicide attempts and past-month suicidal ideation.
PROCEDURES

• Data collected as part of a larger, two-session study examining mechanisms underlying relapse risk among trauma-exposed patients with cocaine use disorders. This study only used data from the first session.

• Eligible participants were recruited for this study no sooner than 72 hours after entry into the facility (to limit interference of withdrawal symptoms).

• Following informed consent, participants were administered diagnostic interviews and provided a saliva sample for genotyping.

• Upon completion of this session, participants were reimbursed $25.

GENOTYPING

• Saliva samples were submitted to the University of Mississippi Medical Center Molecular and Genomics Core Facility for isolation of DNA and genotyping.

• DNA was isolated using Invitrogen™ PureLink™ Genomic DNA Mini Kit.

• All samples generated a single band as visualized on 2% agarose gel stained with ethidium bromide.

• Taqman genotyping was performed using pre-designed Taqman SNP Genotyping Assay for COMT Val158Met (rs4680, Cat#4362691).

• Samples were prepared using iTaq™ Universal Probes Supermix and evaluated on a Bio-Rad CFX96 Real-Time PCR instrument. Allele calls were made using Bio-Rad CFX Manager Software.
RESULTS

- Stata 15.0 was used for all data analyses.

- Firth-type penalized logistic regression models were used to examine the relations of participants’ BPD symptoms, COMT Val^{158}Met polymorphism, and their interaction to each outcome.

- COMT Val^{158}Met genotype was dummy coded to compare the Val/Val group with the Val/Met and Met/Met groups.

- Postestimation commands were used to calculate the probability of each outcome for participants with different levels of BPD symptoms who were Val/Val, Val/Met, or Met/Met carriers.

RESULTS – SUICIDAL IDEATION

- Odds of suicidal ideation increased significantly at higher levels of BPD symptoms (OR = 1.23, 95% CI: [1.08, 1.41], p = .003).

- No effect of COMT (ORs < 0.34, ps > .078).

- The association between BPD symptoms and odds of suicidal ideation did not differ significantly when comparing Val/Val carriers with the Val/Met (OR = 0.98, 95% CI: [0.74, 1.30], p = .902) or Met/Met (OR = 1.02, 95% CI: [0.68, 1.54], p = .919) carriers.
RESULTS – LIFETIME SUICIDE ATTEMPTS

- Odds of lifetime suicide attempt increased significantly at higher levels of BPD symptoms (OR = 1.22, 95% CI: [1.07, 1.38], p = .002).
- No effect of COMT (ORs < 0.50, ps > .140).
- Association between BPD symptoms and odds of lifetime suicide attempt was significantly greater among Val/Val carriers vs. Val/Met (OR = 0.64, 95% CI: [0.42, 1.00], p = .048) or Met/Met (OR = 0.56, 95% CI: [0.34, 0.94], p = .027) carriers.
- More severe BPD symptoms associated with significantly greater odds of a lifetime suicide attempt only among Val/Val carriers, (OR = 1.67, 95% CI: [1.11, 2.51], p = .014).

DISCUSSION

- Participants with more severe BPD symptoms had a greater probability of reporting past-month suicidal ideation, but this relation was not influenced by the Val<sup>158</sup>Met polymorphism.
- However, participants with more severe BPD symptoms who were also Val/Val carriers had a significantly greater probability of reporting a lifetime suicide attempt than all other of participants.
- Finding are consistent with the 3ST (Klonsky & May 2015).
- Findings also provide support for the Val/Val variant as a dispositional factor that may increase suicide attempt risk among individuals with elevated levels of BPD symptoms.
DISCUSSION

• The Val/Val variant was only found to be associated with increased probability of a lifetime suicide attempt among those with higher levels of BPD symptoms.

• Past studies on the relation between the COMT Val^{158}Met polymorphism and suicide have produced inconsistent findings (see González-Castro et al., 2018).

• Our findings suggest that this polymorphism is more likely to be associated with increased probability of having a lifetime suicide attempt in the presence of other risk factors for suicide (BPD).

• BPD associated with a number of other risk factors for suicide attempts, including suicidal desire (Soloff et al., 2000), depression (McGlashan et al., 2000), and nonsuicidal self-injury (Hamza et al., 2012).

LIMITATIONS

• Small sample size

• Unique clinical sample

• Cross-sectional data

• Examination of past suicide attempts

• Candidate gene approach

• Only focused on one dimension of the ITS and 3ST
CONCLUSIONS

• Results add to the literature on suicide risk in BPD by highlighting a potential factor that may represent an inherent elevated capability for suicide within components of this population.

• Findings lend support to the role of dispositional capability in suicide attempt risk, consistent with the 3ST.

• Important to evaluate different dimensions of suicide capability in evaluating suicide risk among patients with BPD and consider those dimensions in BPD treatment.

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