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Anxiety sensitivity mediates gender differences in post-concussive symptoms in a clinical sample

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ABSTRACT

Traumatic brain injury (TBI) is both prevalent and potentially disabling. Extant literature has demonstrated women to report greater post-concussive symptoms (PCS) compared to men, highlighting the necessity of investigations into malleable, gender-linked risk factors for PCS that hold promise for reducing this gender disparity. Anxiety Sensitivity (AS) and Distress Tolerance (DT) are gender-linked risk factors that may be related to PCS. Despite a breadth of research supporting elevated AS and reduced DT in women, no study to date has investigated whether AS and DT mediate gender differences in PCS. The current sample was composed of 59 participants selected from a larger study based on their report of a past TBI. Findings indicated that AS, but not DT, significantly mediated gender differences in PCS. The present results suggest that AS is a cognitive risk factor that can partially account for the gender disparity in the expression of PCS. AS may influence an individual's interpretation of PCS as dangerous, thereby amplifying the perception of PCS severity. This suggests that efforts to reduce the burden of TBI may benefit from targeting AS in prevention and treatment paradigms, especially among women.

1. Introduction

Traumatic Brain Injury (TBI) is an important health concern warranting further attention. Each year, 1.4 million Americans seek medical attention for a TBI, with 1.1 million receiving emergency department treatment, 235,000 being hospitalized, and 50,000 people dying as a result of their injury (Langlois et al., 2006). In addition, a substantial number of brain injured individuals do not present for treatment (Setnik and Bazarian, 2007). Coronado et al. (2012) estimated that, including treatment seeking and non-treatment seeking individuals, 3.5 million Americans sustained a TBI in 2009 alone. Moreover, TBI often results in a broad range of disability including both acute and chronic personal, familial, and occupational impairment (Langlois et al., 2006). This is partially related to a myriad of potentially chronic TBI-related post-concussive symptoms (PCS), including memory loss, attentional control impairment, and difficulty concentrating (Ryan and Warden, 2003).

It appears that women report elevated PCS compared to men (Colvin et al., 2009; Dick, 2009; Farace and Alves, 2000). Farace and Alves (2000) conducted a meta-analysis of gender differences in TBI outcomes and demonstrated that men were more likely to receive a TBI, but women reported greater PCS following a TBI. In concert with these findings, a review of sport-related TBIs found that males were more likely to receive a TBI but females reported greater PCS (Dick, 2009). These findings, coupled with the demonstrated distress and impairment associated with TBI and PCS (Langlois et al., 2006; Ryan and Warden, 2003) underscore the elevated TBI-related dysfunction experienced by female patients. Despite this evidence, little is known regarding factors influencing the gender difference in self-reported PCS. Therefore, it is critical to evaluate gender-linked factors associated with PCS, particularly factors with demonstrated malleability that may serve as future treatment targets to mitigate this discrepancy.

Some evidence suggests that PCS may be amplified by psychological factors (Bryant and Harvey, 1999; Cicerone and Kalmar, 1995; Garden and Sullivan, 2010; Hoge et al., 2008; Iverson, 2006; Schneiderman et al., 2008). Research suggests that brain injured individuals with comorbid Major Depressive Disorder (MDD; Cicerone and Kalmar, 1995; Garden and Sullivan, 2010; Iverson, 2006) or post-traumatic stress disorder (PTSD; Bryant and Harvey, 1999; Hoge et al., 2008; Schneiderman et al., 2008) report greater PCS when compared to psychologically healthy brain injured individuals. Given research suggesting that cognitive risk factors (i.e., individual differences in interpretations that place an individual at risk for psychopathology) contribute to MDD and PTSD (Leyro et al., 2010; Naragon-Gainey, 2010; Olatunji and Wolitzky-Taylor, 2009; Taylor, 2003), it is plausible that gender-linked cognitive risk factors may partially explain gender

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differences in PCS. Two risk factors that may elucidate gender differences in PCS include Anxiety Sensitivity (AS; Reiss and McNally, 1985) and Distress Tolerance (DT; Leyro et al., 2010).

AS, commonly referred to as the "fear of fear," is a risk factor characterized by a tendency to interpret benign arousal-related sensations as indicative of harm or danger (Reiss and McNally, 1985). For instance, an individual with high AS may interpret sensations of cognitive dyscontrol as indicative of harm rather than as a benign symptom of anxious arousal. A breadth of literature has demonstrated higher AS scores among women in both nonclinical (Deacon et al., 2003; Stewart et al., 1997; Zvolensky et al., 2001) and clinical samples (Schmidt and Koselka, 2000). Among undergraduate students, Deacon et al. (2003) found females to have significantly higher AS scores in one sample and marginally higher AS in another sample. Schmidt and Koselka (2000) investigated gender differences in AS among those with a panic disorder diagnosis and found women to have higher AS when compared to men. Moreover, this gender difference has been shown to begin in childhood and adolescence and continue through adulthood (Armstrong and Khawaja, 2002; Walsh et al., 2004).

In the context of TBI, high AS may exacerbate distress associated with PCS through the perception of these symptoms as indicative of harm or danger. An individual with high AS may interpret PCS-related symptoms in an exaggerated or catastrophic way (e.g., difficulties concentrating may be misinterpreted as being indicative of mental illness or catastrophic injury-related brain damage). The perception of PCS as catastrophically dangerous or harmful may then amplify the perception of PCS severity, resulting in greater distress and subsequently greater PCS through a positive feedback loop (Bryant and Harvey, 1999; Coronado et al., 2012; Hoge et al., 2008; Iverson, 2006; Karzmark et al., 1995; Schneiderman et al., 2008; Stewart et al., 1997). Consistent with this, two studies of TBI patients on emergency units indicated that AS was significantly associated with self-reported PCS (Wood et al., 2011, 2014).

DT is another risk factor that may partially account for gender differences in PCS. DT has been conceptualized as an individual difference variable reflective of the capacity to tolerate aversive emotions/sensations, and has been assessed via self-report and behaviorally via persistence on discomfort/stress-inducing tasks (Leyro et al., 2010). Like AS, gender differences have been observed in DT, with females reporting lower DT than males (Gratz et al., 2011; Simons and Gaher, 2005). Although research on DT and PCS is lacking, low DT may exacerbate PCS via greater sensitivity to distressing sensations and emotions associated with PCS. Individuals with low DT may find PCS to be more intolerable when compared to individuals with high DT, resulting in elevated distress and associated salience of these symptoms. Finally, recent literature suggests that DT and AS are related subfactors of an overarching affect sensitivity/tolerance factor (Allan et al., 2015), and so it is important to determine if any observed relationships between AS/DT and PCS are common or specific.

The current study sought to address gaps in the extant TBI literature by examining if AS, a gender-linked cognitive risk factor, mediates the effect of gender on PCS when controlling for MDD and PTSD diagnoses. Based on previous findings, we predicted that AS would significantly mediate the effect of gender on PCS, such that women would report greater AS and subsequently report greater PCS. We also explored if DT significantly mediated the effect of gender on PCS. Based on results of related work with DT (Gratz et al., 2011; Simons and Gaher, 2005), we also predicted that DT would significantly mediate the effect of gender on PCS.

2. Methods

2.1. Participants

Participants included 59 individuals selected from a larger investigation examining the effects of a brief, computerized intervention designed to reduce AS (Schmidt et al., 2014). All data were collected at baseline prior to randomization and intervention. To be eligible, participants had to be 18 years or older and speak English. Participants were also over-sampled for self-reported AS at or above the community mean (Taylor et al., 2007), though not all participants reported elevations. Exclusionary criteria for the parent study included a significant medical illness that would prevent completion of interoceptive exercises included in the brief intervention (i.e., respiratory disorder, cardiovascular disease, uncontrolled hypertension). Participants were also excluded if they reported current or past psychotic spectrum disorders, current bipolar spectrum disorders not stabilized on medications, or significant suicidal intent requiring immediate hospitalization. No participants in the present sample endorsed a history of psychotic and/or bipolar spectrum disorders. Participants for the current study were selected based on their indication of a history of TBI. The sample was roughly evenly distributed by gender (females=30, 50.8%). The majority of participants identified as White (67.8%) followed by African-American (22.0%), Hispanic/Latino (1.7%), and Other (e.g., biracial; 8.5%). Age ranged from 18 to 87 (M=42.10, SD=16.34).

2.2. Procedure

Individuals meeting initial eligibility criteria completed a baseline battery of self-report questionnaires and a semi-structured diagnostic interview for the DSM-IV-TR (SCID/NP; First et al., 1994) prior to randomization to treatment or control groups. The study was approved by the university's Institutional Review Board and informed consent was obtained from all participants prior to the collection of data.

2.3. Measures

2.3.1. Anxiety sensitivity index – 3 (ASI-3)

The ASI- 3 (Taylor et al., 2007) is an 18-item self-report measure used to assess an individual's tendency to interpret benign anxiety-related arousal symptoms as potentially harmful or dangerous. The ASI-3 was adapted from the original ASI (Reiss and McNally, 1985) to improve its psychometrics. Respondents indicate the extent to which each item reflects their typical experience on a 5-point Likert scale ranging from 0 (*very little*) to 4 (*very much*). Previous research has demonstrated the ASI-3 to have strong psychometrics, such as good to excellent internal consistency, factor stability, test-retest reliability, and convergent, discriminant, and predictive validity (Farris et al., 2015; Taylor et al., 2007). In the current study, the ASI-3 demonstrated excellent internal reliability (α=0.95).

2.3.2. Distress tolerance scale (DTS)

The DTS (Simons and Gaher, 2005) is a 15-item self-report measure used to assess individual differences in the ability to experience and withstand negative psychological states. Respondents are asked to indicate the extent to which they agree with statements regarding times they experienced negative psychological states on a 5-point Likert type scale ranging from 1 (*strongly agree*) to 5 (*strongly disagree*). Lower scores on the DTS reflect greater difficulty tolerating negative psychological states. In the current study, the DTS demonstrated excellent internal reliability (α=0.94).

2.3.3. Neurobehavioral symptom inventory (NSI)

The NSI (Cicerone and Kalmar, 1995) is a 22-item self-report measure used to assess an individual's experience of PCS. The NSI is composed of four subscales: vestibular symptoms, somatic symptoms, cognitive symptoms, and affective symptoms. Respondents indicate the extent to which each item reflects their typical experience in the past 2 weeks on a 5-point Likert scale ranging from 0 (None) to 4 (Very Severe). Previous research has demonstrated the NSI to have strong psychometrics (Cicerone and Kalmar, 1995; King et al., 2012). For