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Research report

Interaction between genetic variants and exposure to Hurricane Katrina on post-traumatic stress and post-traumatic growth: A prospective analysis of low income adults

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ABSTRACT

Background: There is considerable variation in psychological reactions to natural disasters, with responses ranging from relatively mild and transitory symptoms to severe and persistent posttraumatic stress (PTS). Some survivors also report post-traumatic growth (PTG), or positive psychological changes due to the experience and processing of the disaster and its aftermath. Gene–environment interaction (GxE) studies could offer new insight into the factors underlying variability in post-disaster psychological responses. However, few studies have explored GxE in a disaster context.

Methods: We examined whether ten common variants in seven genes (*BDNF*, *CACNA1C*, *CRHR1*, *FKBP5*, *OXTR*, *RGS2*, *SLC6A4*) modified associations between Hurricane Katrina exposure and PTS and PTG. Data were from a prospective study of 205 low-income non-Hispanic Black parents residing in New Orleans prior to and following Hurricane Katrina.

Results: We found a significant association (after correction) between *RGS2* (rs4606; $p=0.0044$) and PTG, which was mainly driven by a cross-over GxE ($p=0.006$), rather than a main genetic effect ($p=0.071$). The G (minor allele) was associated with *lower* PTG scores for low levels of Hurricane exposure and *higher* PTG scores for moderate and high levels of exposure. We also found a nominally significant association between variation in *FKBP5* (rs1306780, $p=0.0113$) and PTG, though this result did not survive correction for multiple testing.

Limitations: Although the inclusion of low-income non-Hispanic Black parents allowed us to examine GxE among a highly vulnerable group, our findings may not generalize to other populations or groups experiencing other natural disasters. Moreover, not all participants invited to participate in the genetic study provided saliva.

Conclusions: To our knowledge, this is the first study to identify GxE in the context of post-traumatic growth. Future studies are needed to clarify the role of GxE in PTS and PTG and post-disaster psychological responses, especially among vulnerable populations.

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1. Introduction

Each year, an estimated 500 events throughout the world meet the Red Cross definition of a natural disaster (Norris et al., 2005). People exposed to natural disasters have a greater risk of experiencing mental health problems, including post-traumatic stress disorder (PTSD; Galea et al., 2007; Neria et al., 2008). PTSD is a debilitating condition characterized by re-experiencing, avoidance and numbing, and hyperarousal symptoms (American Psychiatric Association, 1994). One-fifth to one-third of natural disaster survivors experience PTSD (Galea et al., 2007, 2008). Women, African Americans, and low-income populations have been found in some studies to have at least two times the odds of experiencing disaster-related PTSD relative to their counterparts (e.g., males,

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Whites, and those with higher income; Galea et al., 2008; Brewin et al., 2000; Norris et al., 2002).

However, there is considerable variation in levels of posttraumatic stress (PTS), or symptoms of PTSD, in the aftermath of disasters. Even among vulnerable groups, survivors' responses range from relatively mild, acute, and transitory to severe and persistent PTS symptoms that meet diagnostic criteria for PTSD (Galea et al., 2008). Greater exposure to disaster-related stressors and lower social support have been shown to predict more severe PTS and PTSD (Norris et al., 2002). In addition, some survivors also experience positive responses following exposure to traumatic events (Bonanno, 2004), including posttraumatic growth (PTG), or self-reported positive psychological changes induced by the experience and processing of a traumatic event and its aftermath (Tedeschi and Calhoun, 1995). These positive changes, which often co-occur with PTSD (Lowe et al., 2013), include improved interpersonal relationships, a greater sense of new possibilities, increased personal strength, heightened spirituality, and an enhanced appreciation for life. Although less is known about PTG, recent studies suggest that upwards of 50% of survivors of natural disasters experience some degree of PTG (Tang, 2006; Xu and Liao, 2011; Yu et al., 2010), with PTG being more common among older adults, non-Hispanic Blacks, and those exposed to a greater number of stressors (Lowe et al., 2013).

Although genetic factors contribute to variation in response to trauma (Dunn et al., 2011; Koenen et al., 2009a), only a handful of studies have examined gene–environment interaction (GxE) as a determinant of PTSD and anxiety-related outcomes in the context of a natural disaster (Kilpatrick et al., 2007; Koenen et al., 2009b; Amstadter et al., 2009; Pietrzak et al., 2013). Kilpatrick and colleagues found a three-way interaction between *5-HTTLPR* genotype, hurricane exposure, and social support, with the highest levels of PTSD detected among those with the short/short (s/s) genotype, low social support, and high hurricane exposure (Kilpatrick et al., 2007). A similar finding was observed in the same study for *RGS2*, a gene that encodes the regulator of G-protein signaling 2; here, the highest levels of post-hurricane PTSD were observed among people with two copies of the *RGS2* C (major) allele, low social support, and high exposure to the hurricane as well as other potentially traumatic events (Amstadter et al., 2009).

Although this literature suggests that GxE may play a role in the etiology of post-disaster PTSD, these studies have several limitations. First, most were cross-sectional and unable to examine GxE at different time points post-disaster. Second, all lacked pre-disaster data, even though prior studies have shown that pre-disaster factors (e.g., mental health status, degree of social support) are among the strongest predictors of post-disaster psychological responses (Ginexi et al., 2000; Norris et al., 2002; Sullivan et al., 2013). As a result, it remains unclear to what extent GxE predicts psychopathology beyond pre-disaster factors. Third, most examined only one gene, rather than multiple potentially important genes. Finally, no studies to our knowledge examined GxE for PTG.

The current study overcomes these limitations by examining whether ten common variants in seven genes (*BDNF*, *CACNA1C*, *CRHR1*, *FKBP5*, *OXTR*, *RGS2*, *SLC6A4*), identified as related to psychiatric phenotypes, modified the association between level of exposure to Hurricane Katrina ("Katrina") and degree of PTS and PTG. We used data from an on-going prospective study of 1019 (259 genotyped) low-income non-Hispanic Black parents who resided in New Orleans prior to Katrina, which made landfall as a Category 3 storm on August 29, 2005 and led to extensive property damage and population displacement (Knabb et al., 2005; U.S. Department of Commerce, 2006). Being part of an ongoing study uniquely positioned us to prospectively examine the relationship between exposure to Katrina and subsequent outcomes, after adjusting for pre-storm characteristics. Because of our modest sample size, we restricted our investigation to genetic loci previously associated with PTSD (*BDNF*, *FKBP5*, *RGS2*, *SLC6A4*) or an associated mood and anxiety disorder (*CACNA1C*, *CRHR1*, *OXTR*), either alone or in interaction with an environmental insult. We hypothesized that the highest levels of PTS would be observed among individuals with both high-risk genetic variants and higher hurricane exposure, after adjusting for pre-disaster factors. Given the lack of research on PTG, we made no a priori hypotheses for this outcome.

2. Methods

2.1. Sample and procedures

Data were from a sample of participants (Lowe et al., 2010; Rhodes et al., 2010) in the New Orleans site of the Opening Doors Study, a multi-site national study designed to examine whether modest performance-based scholarships promoted academic achievement, health, and well-being of low income parents attending community college (Richburg-Hayes and Brock, 2009). To be eligible for the study, students had to be between the ages of 18 and 34, be a parent of at least one dependent child under 19, have a household income under 200% of the federal poverty level, and have a high school diploma or equivalent. In 2004 and 2005 (Time1, or T1), 1019 participants completed a brief survey, which assessed demographic, physical, and mental health information. Prior to Katrina, 492 participants had been enrolled long enough to complete a more extensive 12-month pre-disaster follow-up survey (T2). Between May 2006 and March 2007 (T3), 402 (81.7%) participants who completed the T2 survey were successfully located and completed a post-disaster interview by phone with a trained interviewer. The T3 interview was similar to T2, but also included an inventory of hurricane exposure and a measure of PTS. Between April 2009 and March 2010, trained researchers administered an additional post-disaster survey by phone (T4) to 409 participants (83.1% of the T2 sample; 348 of these respondents also completed the T3 survey). The T4 survey included the same measures as T3 plus a measure of PTG.

All T4 participants were invited to provide a saliva sample for the purpose of genomic analysis; 259 of these respondents did so. There were no significant differences between respondents who provided a sample and those who did not with respect to nearly all social-demographic characteristics. However, respondents in the genetic sample had slightly higher levels of T1 social support (genetic sample mean=3.25; SD=0.46; non-genetic sample mean=3.17; SD=0.44; $p=0.032$).

2.2. Measures

2.2.1. Predictors: Severity of exposure to Hurricane Katrina

Exposure to Katrina was measured at T3 using an 8-item scale jointly designed by the Washington Post, the Kaiser Family Foundation, and the Harvard School of Public Health (Brodie et al., 2006). Participants indicated whether they experienced any of the following conditions in the immediate aftermath of the storm: (1) no fresh water to drink, (2) no food to eat, (3) felt their life was in danger, (4) lacked necessary medicine, (5) lacked necessary medical care, (6) had a family member who lacked necessary medical care, (7) lacked knowledge of safety of their children, and (8) lacked knowledge of safety of their other families members. Exposures were summed to create a total score. For the 101 individuals missing data on Hurricane Katrina exposure at T3, we used their responses to this scale at T4. Exposure reports were modestly correlated ($r=0.43$) among the 104 participants with data at both T3 and T4; although some respondents over-reported ($n=38$) (i.e., reported higher levels of exposure at T4 compared to T3) or under-reported exposure ($n=38$), the average difference between the two reports of exposure was small (mean difference=0.119; SD=2.26).