

Insights from Neuroscience

Bullying Research Network Think Tank
University of Nebraska Lincoln
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- Bullying causes health problems.
 - “environmentally mediated causal risk factor”

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Gene–environment interaction between peer victimization and child aggression

“Genetic modeling showed that peer victimization is an environmentally driven variable that is unrelated to children’s genetic disposition.”

Abstract

Although peer victimization places children at serious risk for aggressive behavior, not all victimized children are aggressive. The diathesis-stress hypothesis of disease proposes that an environmental stressor such as peer victimization should lead to maladjustment mostly in those individuals with preexisting genetic vulnerabilities. Accordingly, this study examined whether the link between peer victimization and child aggression is moderated by children’s genetic risk for such behavior. Using a sample of 500 6-year-old twins, peer victimization was assessed through peer nomination and aggressive behavior was assessed through peer and teacher reports. Children’s genetic risk for aggression was estimated as a function of their co-twin’s aggression and the pair’s zygosity. Genetic modeling showed that peer victimization is an environmentally driven variable that is unrelated to children’s genetic disposition. Results also provided support for the notion of a gene–environment interaction between peer victimization and child’s genetic risk for aggressive behavior, albeit only in girls. For boys, peer victimization was related to aggression regardless of the child’s genetic risk for such behavior. Different socialization experiences in girls’ compared to boys’ peer groups may explain the different pattern of results for girls and boys.

The Need to Belong

- Need to belong is a fundamental human motivator
- Wired to belong



Need to belong is so strong that...

- Being rejected by a deplorable, loathed group like the Klu Klux Klan is perceived as hurtful to people who are not part of, nor condone, such a group
 - Gonsalkorale & Williams, 2007

- Studies show that people can relive and re-experience social pain more easily than physical pain and the emotions they feel are more intense and painful.
 - Chen, Williams, Fitness, Newton, 2008
- It seems that physical pain is often short lived whereas social pain can last a life time.

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Neural correlates of social exclusion during adolescence: understanding the distress of peer rejection

Recent neuroimaging studies have shown that parts of the cortical physical pain network are also activated when a person is socially excluded

Physical and social pain share similar neural structures
Linked to evolution
↑ survival among mammalian species

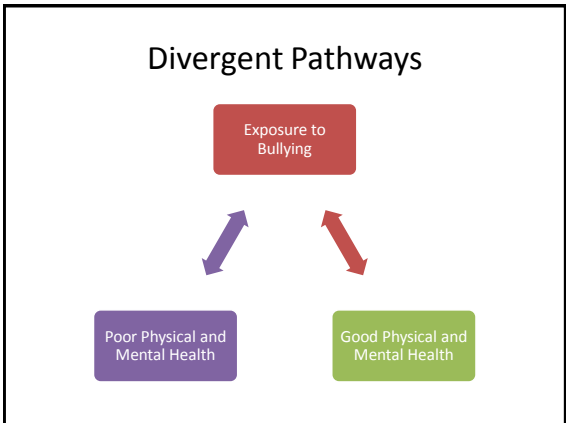
Individuals with higher rejection sensitivity and interpersonal competence scores displayed greater neural evidence of emotional distress, and adolescents with higher interpersonal competence scores also displayed greater neural evidence of rejection, perhaps suggesting that adolescents who are vigilant regarding peer acceptance may be most sensitive to rejection experiences.

Keywords: peer rejection; adolescence; functional magnetic resonance imaging

Pain Network

- dACC
 - unpleasantness associated with physical pain
- Insula
 - negative affect and visceral pain
- Periaqueductal gray
 - pain processing and attachment behaviours
- Right ventral prefrontal cortex (RVPPFC)
 - linked with regulation of distress associated with physical pain and negative emotional

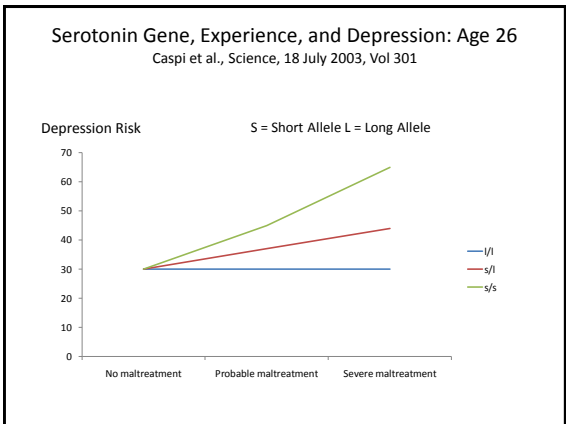
	dACC	insula	RVPPFC
Eisenberger, et al. (2003)	☑	☑	☑
Burklund, et al., (2007)	☑		☑
Masten et al. (2009)		☑	☑



Influence of Life Stress on Depression: Moderation by a Polymorphism in the 5-HTT Gene

Avshalom Caspi,^{1,2} Karen Sugden,¹ Terrie E. Moffitt,^{1,2*} Alan Taylor,¹ Ian W. Craig,¹ Honalee Harrington,² Joseph McClay,¹ Jonathan Mill,¹ Judy Martin,³ Antony Braithwaite,⁴ Richie Poulton³

In a prospective-longitudinal study of a representative birth cohort, we tested why stressful experiences lead to depression in some people but not in others. A functional polymorphism in the promoter region of the serotonin transporter (5-HTT) gene was found to moderate the influence of stressful life events on depression. Individuals with one or two copies of the short allele of the 5-HTT promoter polymorphism exhibited more depressive symptoms, diagnosable depression, and suicidality in relation to stressful life events than individuals homozygous for the long allele. This epidemiological study thus provides evidence of a gene-by-environment interaction, in which an individual's response to environmental insults is moderated by his or her genetic makeup.

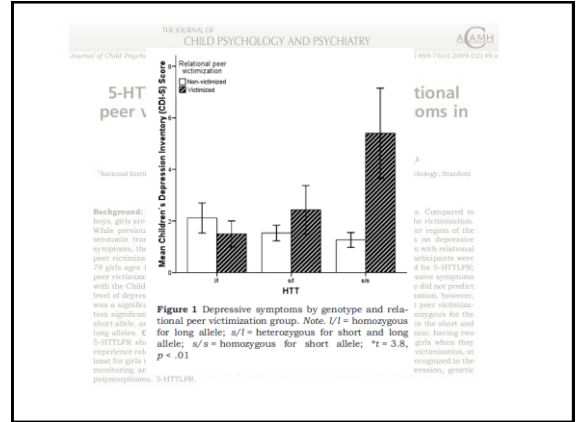


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5-HTTLPR moderates the effect of relational peer victimization on depressive symptoms in adolescent girls

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Background: Relational peer victimization is associated with internalizing symptoms. Compared to boys, girls are more likely to be both relationally victimized by peers and distressed by the victimization. While previous studies have reported that a functional polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) moderates the effect of stressful life events on depressive symptoms, the present study is the first to evaluate the interaction of this polymorphism with relational peer victimization to predict level of depressive symptoms in young girls. **Methods:** Participants were 78 girls ages 10 to 14 who had no current or past Axis I disorder. Girls were genotyped for 5-HTTLPR, peer victimization was assessed with the Social Experiences Questionnaire, and depressive symptoms with the Children's Depression Inventory. **Results:** The 5-HTTLPR polymorphism alone did not predict level of depressive symptoms; the interaction of 5-HTTLPR and relational peer victimization, however, was a significant predictor of depressive symptoms. Follow-up analyses indicated that peer victimization significantly predicted level of depressive symptoms only for girls who were homozygous for the short allele, and not for girls homozygous for the long allele or who were heterozygous for the short and long alleles. **Conclusions:** The findings support the diathesis-stress model of depression: having two 5-HTTLPR short alleles confers vulnerability to depressive symptoms in adolescent girls when they experience relational peer victimization. These findings also suggest that relational peer victimization, at least for girls with genetic vulnerability, is a significant source of stress and should be recognized in the monitoring and prevention of bullying. **Keywords:** Peer victimization, bullying, depression, genetic polymorphisms, 5-HTTLPR.



Beyond the vulnerability of genes...

- Peer victimization changes the function (and structure?) of the developing child's brain

Peer Victimization → Psychosocial Maladjustment

- Longitudinal studies have shown that peer victimization causes maladjustment which includes depression e.g., Arseneault et al, 2006; Kim et al., 2006; Kumplainen & Rasanen, 2006; Sourander et al., 2006

Stressful Event → Depression

- Causal link is consistent with literature on depression e.g., Duggal et al., 2000; Goodyer, et al., 1985; Kaufman, 1991; Williamson et al., 1998

Peer Victimization → HPA axis dysregulation → BLUNTED

- Relationship b/w victimization and dysregulation of the HPA axis estimated via the stress hormone cortisol e.g., Kliewer, 2006; Vaillancourt et al., 2008, Knack et al., in press; see also Knack & Vaillancourt, in press for review

AGGRESSIVE BEHAVIOR
Volume 34, pages 294-305 (2008)

Variation in Hypothalamic-Pituitary-Adrenal Axis Activity Among Bullied and Non-bullied Children

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Bullied girls ↓ cortisol

Bullied boys ↑ cortisol

We examined the relationship between self-reported bullying and cortisol levels in a sample of middle-class 12-year-old children. Using multilevel regression and applying orthogonal polynomial contrasts to model the observed circadian pattern in the data, we found that occasional and frequent verbal victimization was associated with hypersecretion of cortisol when controlling for sex, parental status, age, depression and anxiety. This relation, however, was moderated by sex. For boys, occasional exposure was associated with higher cortisol levels, whereas for girls exposure was associated with lower cortisol levels. The present study highlights the need to consider the plight of peer-victimised children seriously, as it is associated with alterations to the HPA axis that affect males and females differently, and likely diminishes a person's ability to cope with stress, possibly placing them at risk for psychopathology and ill health. *Aggr. Behav.* 34:294-305, 2008. © 2007 Wiley-Liss, Inc.

Keywords: bullying; HPA axis; cortisol; children; multilevel modeling; sex differences

A Discordant Monozygotic Twin Design Shows Blunted Cortisol Reactivity Among Bullied Children

Isabelle Choulet-Morin, M.D., Andrea Danese, M.D., Ph.D., Lucy Bowes, Ph.D., Santa Shakoor, M.Sc., Antony Ambler, M.Sc., Carmine M. Pariante, M.D., M.Sc.Frank, Ph.D., Andrew S. Papadopoulos, Ph.D., Avshalom Caspi, Ph.D., Terrie E. Moffitt, Ph.D., Louise Arseneault, Ph.D.

Objective: Childhood adverse experiences are known to engender persistent changes in stress-related systems and brain structures involved in mood, cognition, and behavior in animal models.

“Results from this natural experiment provide support for a causal effect of adverse childhood experiences on the neuroendocrine response to stress”.

Patterns of cortisol secretion after the DST. Specifically, bullied twins exhibited a blunted cortisol response compared with their nonbullied MZ co-twins, who showed the expected increase. This difference in cortisol response to stress could not be attributed to children's genetic makeup, their familial environments, pre-existing and concomitant individual factors, or the perception of stress and emotional response to the DST. Conclusion: Results from this natural experiment provide support for a causal effect of adverse childhood experiences on the neuroendocrine response to stress. *J. Am. Acad. Child Adolesc. Psychiatry*, 2011;50(5):574-582. Key words: early-life stress, cortisol, HPA axis, discordant MZ twin design, bullying

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VOLUME 50 NUMBER 5 JUNE 2011

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    graph LR
      A[Depression] --> B[HPA axis dysregulation]
    
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•Depression also linked to HPA dysregulation— ↑ cortisol e.g., Holsboer, 1995; Markopoulou et al., 2009; Stoke & Sikes, 1987; see McEwen 2003 for review).

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    graph LR
      A[Depression] --> B[Structural and functional changes of the brain]
    
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•Link b/w depression and stress-related structural and functional brain changes e.g., Horna et al., 1997; Leon-Carrion et al., 2009; Michopoulos et al., 2008

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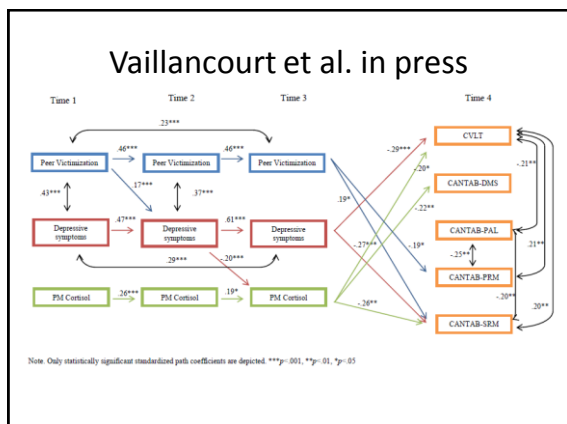
    graph LR
      A[High circulating glucocorticoids (GCs)] --> B[Structural and functional changes of the brain]
    
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•Animal studies clearly demonstrated that excessive exposure to GCs leads to structural changes in the brain which includes neural cell death

•Cortisol binds to GC receptors

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    graph LR
      A[Peer Victimization] --> B[Depression]
      B --> C[HPA dysregulation]
      C --> D[Disrupted Neurogenesis]
    
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- Vaillancourt et al. (2010a, 2010b) suggest, understanding biological underpinnings of peer relations helps legitimize the plight of peer-abused children and youth
- Encouraging policy makers and practitioners to prioritize the reduction of school bullying

