

Monozygotic Twins Discordant for Being Bullied: A Step Closer to Understanding the Biology of Victimization

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Bullying is a pattern of aggressive and hostile behaviors perpetrated by a more powerful individual on those less powerful. Characteristics of bullies include those with more physical strength, assertive behavior, popularity, or some other socially valued characteristic.¹ Bullying behaviors may include verbal or physical harassments and attacks, social exposure of someone else's privacy, or social exclusion and isolation, among other acts that make the victim feel rejected and humiliated. It can be perpetrated face to face, by telephone calls, and more recently by e-mails, tweets, and other Internet resources. Through the use of "viral" technology, victims are potentially exposed to millions, thus intensifying the risk of humiliation and shame. Bullying occurs in diverse cultural, socioeconomic, and educational backgrounds and current estimates indicate that approximately 10% of young adolescents have been victims of bullying.¹

The widespread nature of bullying has likely led to the common perception that bullying is normative, that it is nothing more than an innocuous pattern of interaction between children or adolescents, for which no adult intervention is called for. However, during the past three decades, a consistent body of research has emerged documenting the major negative effects of bullying victimization on mental health. These include social isolation, depression, anxiety, aggressive behaviors (including perpetration of a vicious cycle through the bullying of others), psychotic symptoms, self-harm, and suicide ideation, attempts, and completion.¹

Randomized controlled trials have demonstrated the efficacy of universal and indicated school-based preventive strategies for bullying, several of them based on "zero tolerance" policies.^{2,3} Although it is clear that public health efforts

should focus on wiping out bullying altogether, such a global result is not likely to ensue anytime soon. In parallel, we must deepen our understanding of the developmental pathways and consequences of bullying. It is important to understand, among other issues, what characteristics make a child more susceptible to suffer from bullying, if there are specific pre-existing characteristics that increase the risk of its effects (especially the major ones, such as psychosis and suicide), and why some victims develop serious sequelae and others appear to endure with few scars.

Recently there have been a series of articles that addressed some of these questions^{4,5} and provided a window on the biological underpinnings associated with the negative outcomes of bullying. Studies such as these will allow us to begin to understand the biological effects of bullying victimization. We need to understand whether these effects can be better accounted by other factors, be they genetic, epigenetic, or pre-existing factors such as mental health symptoms, temperament characteristics, or environmental risks in schools, neighborhoods, and families. Prospective studies have identified internalizing symptoms, early aggressiveness, low self-regard, and decreased assertiveness, in addition to school size, neighborhood problems, maltreatment, and domestic violence as risk factors for subsequent bullying victimization.^{1,5} Testing and demonstrating biological effects of bullying victimization while controlling for possible pre-existing characteristics that may confound the association are complex tasks that cannot be achieved without sophisticated and rigorous methodologic approaches.

The elegant study by Ouellet-Morin and colleagues⁶ that appears in this issue of the *Journal* tested the causal effect of bullying in modifying the

hypothalamic-pituitary-adrenocortical (HPA) axis. The HPA axis is one of the main systems responsible for the physiological stress response and has been implicated in the pathophysiology of several mental disorders. The researchers have been following a large representative birth cohort of twins who were assessed for bullying at various times during childhood. Because monozygotic twins share 100% of their genome and (in this sample) are raised by the same family within the same environmental context, it is possible to assume that if differences between twin pairs are detected, these are the result of specific or individual experiences. To study if bullying per se resulted in disruption of HPA axis activity, the investigators used a multi-wave, cross-informant strategy and identified children who were definite victims of bullying and who were monozygotic twins of children who were definitely *not* victims of bullying.

Twin pairs were invited to a laboratory visit where they were exposed to a psychosocial stress test paradigm to assess the activity of their HPA axis using cortisol secretion. Although twin pairs presented equivalent pre-existing characteristics that could potentially influence the test results and experienced similar levels of distress during the paradigm, twins who were bullied did not display the expected cortisol increase after the stress test. The cortisol response was normal among twins who were not bullied. In addition, the investigators detected an inverse correlation trend between severity of bullying and cortisol secretion, further supporting their main findings.

Environmental stressors that occur at a young age have been shown to persistently affect HPA axis functioning in animal models and in humans.⁷ Subsequent stressors during childhood and adulthood, such as maltreatment and abuse, have also been shown to affect the HPA axis in developmentally specific ways.⁸ One plausible

explanation of how bullying leads to changes in the function of the HPA axis is through epigenetic mechanisms (such as methylation), which can “turn on” and “turn off” the functioning of genes.⁷ In this model, variation in environmental experience directly “turns off” key genes associated with stress reactivity, resulting in disrupted activity of the HPA axis.

Findings such as those published in this issue of the *Journal* add to what is already known about the biological basis of the adverse effects of environmental stressors, in this case bullying. Negative environments directly modify the genome of vulnerable individuals and thus compromise the ability of these individuals to deal with stress. The demonstrated causal effect of bullying victimization on HPA axis activity, which was detected because of the sophisticated discordant monozygotic twin design, indicates a possible mechanism through which bullying can lead to negative mental health outcomes. Taken together, these results continue to raise the call for more aggressive strategies focused on preventing bullying victimization in an effort to attenuate or interrupt psychopathological processes that can likely lead to mental disorders.⁹ &

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