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Nonsuicidal self-injury in children and adolescents: Pathogenesis

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INTRODUCTION

Nonsuicidal self-injury is the deliberate destruction of body tissue in the absence of any intent to die and occurs for purposes that are not socially sanctioned [1-3]. The behavior most commonly takes the form of skin-cutting, burning, and severe scratching [4,5]. Nonsuicidal self-injury occurs at high rates in adolescents and is associated with adverse clinical outcomes such as suicide attempts [6,7].

We conceptualize nonsuicidal self-injury as a distinct entity that differs qualitatively from suicidal behavior [2]. However, others argue that self-injury with and without suicidal intent represent different versions of the same behavior [8].

This topic discusses the pathogenesis of nonsuicidal self-injury, and focuses primarily upon adolescents because the behavior occurs far more often in this age group than in children [9]. In addition, the material is restricted to youth who do not have intellectual disabilities.

Separate topics discuss the epidemiology, clinical features, assessment, and treatment of nonsuicidal self-injury, as well as the epidemiology, evaluation, and management of suicidal ideation and behavior in children and adolescents:

• (See "Nonsuicidal self-injury in children and adolescents: Epidemiology and risk factors".)

- (See "Nonsuicidal self-injury in children and adolescents: Clinical features and proposed diagnostic criteria".)
- (See "Nonsuicidal self-injury in children and adolescents: Assessment".)
- (See "Nonsuicidal self-injury in children and adolescents: General principles of treatment".)
- (See "Nonsuicidal self-injury in children and adolescents: Prevention and choosing treatment".)
- (See "Suicidal behavior in children and adolescents: Epidemiology and risk factors".)
- (See "Suicidal ideation and behavior in children and adolescents: Evaluation and management".)

TERMINOLOGY

Nonsuicidal self-injury is a behavior characterized by the deliberate destruction of body tissue in the absence of any intent to die and occurs for purposes that are not socially sanctioned [1-3]. By definition, nonsuicidal self-injury is distinguished from suicidal behavior; socially accepted practices such as tattoos, piercings, and religious rituals; accidental self-harm; and indirect self-injury through behaviors such as disordered eating or substance use disorders. Self-injurious behavior that is accompanied by **any** intent to die is classified as a suicide attempt, which is consistent with the practice of most clinicians and researchers [2,10,11]. This approach deliberately errs on the side of safety by categorizing ambivalent behaviors, which include any intention to die, as suicidal [2].

Additional information about the terminology of nonsuicidal self-injury is discussed separately. (See "Nonsuicidal self-injury in children and adolescents: Clinical features and proposed diagnostic criteria", section on 'Terminology'.)

PATHOGENESIS

Although the pathogenesis of nonsuicidal self-injury remains largely unknown, our understanding continues to advance. The etiology likely involves psychological, social, and biological factors (see figure 1 in article) [2]. In addition, several risk factors have been identified. (See "Nonsuicidal self-injury in children and adolescents: Epidemiology and risk factors", section on 'Risk factors'.)

One model suggests that nonsuicidal self-injury results from the interplay of distal and proximal risk factors [2]. Specifically, individuals have a predisposition or accumulation of distal risk (eg, childhood maltreatment), which leads to intrapersonal (eg, high negative emotions and

cognitions) and interpersonal (eg, poor communication skills) vulnerability factors. These vulnerability factors make it difficult for individuals to respond adaptively to stressors; this difficulty managing stress, combined with other vulnerability factors specific to nonsuicidal self-injury (eg, social learning and self-punishment), increase the likelihood that self-injury will occur.

Although studies have not directly tested this full model, research does support the role of multiple behavioral and other psychological factors, social and interpersonal factors, and biological factors that map onto this model of nonsuicidal self-injury [2,12]. However, studies of the pathogenesis typically use cross-sectional designs, making it unclear whether abnormalities in these factors represent etiologic causes, sequelae, neither, or both. In addition, most prior studies of etiologic factors (eg, neuroimaging studies) were relatively small.

Behavioral and psychological factors — The most widely studied psychological factors related to nonsuicidal self-injury are the functions, or motivations, that maintain and may also cause the behavior.

Function of the behavior — Nonsuicidal self-injury may begin and persist because the behavior serves one or more main functions for patients. Functions (motives) can be understood by examining the factors and events that immediately precede nonsuicidal self-injury (antecedents) and the factors and events that follow the behavior (consequences) [2,13].

One empirically supported model hypothesizes that the primary functions of nonsuicidal self-injury exist within two dichotomous categories [3,4,13-16]:

- **Reinforcement** Reinforcement of nonsuicidal self-injury can be positive or negative.
 - Positive reinforcement is the delivery or addition of a desirable stimulus Nonsuicidal self-injury may be sustained because the behavior induces a pleasant state, generates attention from others, or is experienced as a deserved punishment.
 - Negative reinforcement is the removal of an undesirable or aversive stimulus –
 Nonsuicidal self-injury may be sustained because the behavior alleviates negative
 emotions such as anxiety, depression, or anger; reduces distressing thoughts such as
 self-criticism or suicidal ideation; or removes unwanted social demands or
 circumstances (eg, parents stop fighting).
- Consequences Consequences of the behavior arise from either intrapersonal or social processes.
 - Intrapersonal consequences for nonsuicidal self-injury behavior are internal (sometimes referred to as automatic) and are generated within the individual.

• Social consequences arise from interpersonal interactions.

Based upon this model, nonsuicidal self-injury behavior is caused and maintained by at least one of the following four primary functions (figure 1) [2,4,13,14,17-20]:

- Intrapersonal (or automatic) negative reinforcement The behavior reduces (regulates) negative and aversive thoughts and emotions such as anger, sadness, and anxiety.
- **Intrapersonal (automatic) positive reinforcement** The behavior generates desired feelings and thoughts (eg, feeling something other than numbness, "even if it's pain"; or experiencing satisfaction from having punished oneself).
- **Social negative reinforcement** The behavior facilitates an escape from undesired social demands and unbearable social situations (eg, a child is permitted to stay home from school).
- **Social positive reinforcement** The behavior elicits a positive response from others, such as attention or support from family or friends.

Patients most often report that nonsuicidal self-injury serves to regulate or manage negative emotions (intrapersonal negative reinforcement) [4,14,21-25]. On average, nonsuicidal self-injury serves more than one of the four functions [26].

A standard part of evaluating patients for nonsuicidal self-injury is an individualized functional assessment to identify the behavior's antecedents and consequences and determine how the behavior is maintained. Understanding the functions of nonsuicidal self-injury can inform treatment planning [27]. (See "Nonsuicidal self-injury in children and adolescents: Assessment", section on 'Psychological assessment'.)

Attributional style and hopelessness — Youth may be more vulnerable to nonsuicidal self-injury if they respond to negative life events with attributions that are internal (rather than external), stable (rather than transient), and global (rather than specific) [28]. As an example, following a breakup with a significant other, adolescents are at increased risk for nonsuicidal self-injury if they attribute the breakup exclusively to their own shortcomings (internal) that they perceive as trait-like deficits (stable) that may prevent them from ever having a healthy relationship (global). Related to this pessimistic attributional style, hopelessness about the future and the likelihood of their situation improving is one of the most robust risk factors for nonsuicidal self-injury [21].

Self-criticism — Multiple studies link self-criticism to engagement in nonsuicidal self-injury; other terms used for self-criticism include negative self-image, negative self-evaluation, self-disgust, and self-hatred (an extreme form of self-criticism) [2,12,29-31]. Self-criticism may predict future engagement among those with a prior history of nonsuicidal self-injury [29]. In particular, youth who report hating themselves may be most at risk for nonsuicidal self-injury [31]. In addition, self-criticism may mediate the association between negative interpersonal experiences (negative parental experiences and peer victimization) and nonsuicidal self-injury [30].

Additional support for this pathway to nonsuicidal self-injury comes from research on the self-punishment function of nonsuicidal self-injury (see 'Function of the behavior' above), which is commonly reported among adolescents [4,13]. In a sample of college students with a history of nonsuicidal self-injury (n = 183), the most commonly reported motivation for initial onset of the behavior was "angry at myself," which was reported by 40 percent of the sample [32].

Implicit identification — The implicit identification or self-identification hypothesis suggests that over time, individuals who engage in nonsuicidal develop a strong association between nonsuicidal self-injury and themselves; this self-identification with nonsuicidal self-injury leads individuals to select this behavior in times of distress over more adaptive coping strategies [33]. To test this hypothesis, researchers developed a brief, computer-based test that uses reaction times (instead of explicit self-reports) to examine the strength of association between self-injury images and the self [33]. Multiple studies using the test indicate that adolescents engaging in nonsuicidal self-injury exhibit stronger implicit self-identification with nonsuicidal self-injury than youth not engaging in the behavior [33-35]. In addition, a one-year, prospective community study of adolescents (n = 662) found that implicit identification with nonsuicidal self-injury predicted continued engagement in the behavior, even when controlling for past history of the behavior [34].

Social factors — Social factors that may be involved in the pathogenesis of nonsuicidal self-injury include childhood maltreatment and various peer influences ranging from bullying and peer victimization to social contagion.

Childhood maltreatment — Multiple studies indicate that childhood maltreatment (neglect or abuse) is associated with nonsuicidal self-injury. However, many youth who were neglected or abused do not self-injure, and many youth who self-injure were not neglected or abused.

Studies that have found an association between childhood maltreatment and nonsuicidal self-injury include the following [21]:

- A review of 26 studies (n >85,000 children, adolescents, and adults) concluded that childhood maltreatment, especially sexual abuse, was associated with nonsuicidal self-injury [36].
- A meta-analysis of six studies examined the association between childhood maltreatment and nonsuicidal self-injury in adolescents (sample size not reported); maltreatment consisted of sexual abuse, physical abuse, emotional abuse, physical neglect, and/or emotional neglect. The likelihood of engaging in nonsuicidal self-injury was greater in adolescents who were maltreated than those who were not (odds ratio 4.4, 95% CI 4.1-4.8). [37].
- A subsequent study assessed 2038 child and adolescent patients and identified a lifetime history of nonsuicidal self-injury in 592 [38]. After controlling for potential confounding factors (eg, age, psychopathology, and social support), sexual abuse (odds ratio 1.6) and physical abuse (odds ratio 1.5) were associated with nonsuicidal self-injury.

One review hypothesized that trauma symptoms, rather than traumatic events per se, explain (mediate) the relationship between childhood maltreatment and nonsuicidal self-injury [39]. Another study suggested that psychiatric disorders (eg, depressive and anxiety disorders) may explain the association between childhood maltreatment and nonsuicidal self-injury [40].

Indirect forms of childhood maltreatment, such as witnessing domestic violence, are also associated with nonsuicidal self-injury in youth [41].

Peer influences — The pathogenesis of nonsuicidal self-injury behavior may include peer influences [15,42]. The research suggests that peer influences may occur through socialization and selection effects:

- One hypothesis is that socialization, or in some cases social contagion, may occur, such that the behavior in one individual is subsequently emulated by friends or acquaintances. Evidence for social contagion of nonsuicidal self-injury has been found in both clinical and community samples of youth [43].
 - Social contagion may also occur indirectly through exposure to media such as music, movies, the internet, and social media (eg, Instagram) [44,45]. Youth may also learn other new methods or techniques for nonsuicidal self-injury through these sources.
- A second hypothesis states that nonsuicidal self-injury among peers may occur due to selection effects; that is, youth befriend peers with the same interests and behaviors, such as nonsuicidal self-injury [42].

Social learning may be more important for the onset of nonsuicidal self-injury, whereas other reinforcement factors may be more important for the maintenance of nonsuicidal self-injury [1,43]. (See 'Function of the behavior' above.)

Other — Relationships and interpersonal stressors are associated with both the onset and maintenance of nonsuicidal self-injury. These interpersonal factors include:

- Peer victimization (including bullying and cyberbullying) [46-48]
- Loneliness and social isolation [46]
- Interpersonal loss [49]
- Perceived and actual parental criticism [50,51]
- Difficulty communicating with family members [52]

In addition, nonsuicidal self-injury can be socially reinforced because the behavior helps adolescents obtain something they want in their environment, such as support (positive social reinforcement), or because the behavior removes something negative from their environment, such as interpersonal demands (negative social reinforcement). (See 'Function of the behavior' above.)

Other social factors that are associated with onset and maintenance of nonsuicidal self-injury are discussed separately. (See "Nonsuicidal self-injury in children and adolescents: Epidemiology and risk factors", section on 'Risk factors'.)

Biological factors — Relatively little research has examined biological models of nonsuicidal self-injury in adolescents. Nevertheless, it appears that several neurobiologic systems may be involved in the pathogenesis of nonsuicidal self-injury. As an example, nonsuicidal self-injury may be caused by disruptions in neurobiological systems related to the regulation of emotions [53]. This is consistent with evidence that patients engage in nonsuicidal self-injury to regulate negative affect. (See 'Function of the behavior' above.)

Genetics — Genetic factors (vulnerabilities) may be involved in nonsuicidal self-injury:

- A study of adult patients with unipolar major depression (n = 195) found that after controlling for borderline personality disorder and childhood sexual abuse, the T allele of the G protein beta-3 was associated with a lifetime history of nonsuicidal self-injury (odds ratio 4, 95% CI 2-11) [54].
- A national registry study of adult monozygotic and dizygotic twins (n >10,000) found that the relative contribution of genetic factors (heritability) to nonsuicidal self-injury was 37 percent for men and 59 percent for women, and the remaining contribution was

attributable to nonshared (unique) environmental factors [55]. This study also suggested that there may be overlapping genetic influences on the transmission of nonsuicidal self-injury and suicide ideation. However, other evidence suggests that the familial transmission of suicide attempts and nonsuicidal self-injury is distinct [56,57].

Neurotransmitters — The pathogenesis of repeated nonsuicidal self-injury may perhaps involve endogenous opioids, but evidence of serotonergic and dopaminergic dysfunction is less consistent.

Endogenous opioids — Repeated nonsuicidal self-injury, which is characterized by decreased pain sensitivity, may involve endogenous opioids. The opioid self-administration hypothesis proposes that individuals engage in nonsuicidal self-injury to release endogenous opioids, perhaps due to chronically low opioid levels. Chronically low levels of endogenous opioids may make opioid receptors hypersensitive and in turn make the analgesic effects of endogenous opioids more potent [58]. Support for the opioid self-administration hypothesis includes one study (n = 29), which found that patients with repeated nonsuicidal self-injury had lower baseline cerebrospinal fluid levels of endogenous opioids (beta-endorphin and metenkephalin) than controls [59].

In addition, the endogenous opioid system may mediate the emotion regulation function of nonsuicidal self-injury. Specifically, a literature review suggests that individuals with nonsuicidal self-injury have lower baseline levels of endogenous opioids, that engagement in nonsuicidal self-injury is associated with the release of opioids, and that opioids released during nonsuicidal self-injury may help to regulate negative affect [17].

Decreased pain sensitivity in patients with nonsuicidal self-injury and the use of nonsuicidal self-injury to regulate negative emotions are discussed separately. (See "Nonsuicidal self-injury in children and adolescents: Clinical features and proposed diagnostic criteria", section on 'Physical pain' and 'Function of the behavior' above.)

Others

- Serotonin Studies of the serotonergic system and nonsuicidal self-injury have yielded inconsistent results [59-61], with some studies suggesting that decreased serotonergic function is associated with nonsuicidal self-injury, whereas other studies suggest that serotonergic function is not related to the behavior [59].
- Dopamine Evidence linking dopaminergic function to nonsuicidal self-injury is also mixed and largely inconsistent [59,62,63].

Hypothalamic-pituitary-adrenal axis — Altered functioning of the hypothalamic-pituitary-adrenal axis, which is central to the body's stress-response system, may be associated with nonsuicidal self-injury:

- Adolescents engaging in nonsuicidal self-injury may exhibit a blunted response to acutely stressful situations [1]. As an example, during a standardized laboratory test intended to induce psychosocial stress, cortisol ("stress hormone") responses were attenuated in female adolescent patients with past-year nonsuicidal self-injury (n = 14), compared with female healthy controls (n = 14) [64].
- In addition, research suggests that adolescents engaging in nonsuicidal self-injury may have higher morning cortisol levels, potentially in anticipation of strain to be experienced over the course of the day. Specifically, greater salivary cortisol upon awakening was found in adolescent psychiatric patients with at least five episodes of nonsuicidal self-injury in the past six months (n = 26), compared with age- and sex-matched healthy controls (n = 26) [65].

Neuroimaging — Some evidence suggests that altered neural circuitry may underlie nonsuicidal self-injury [58]. Functional magnetic resonance imaging studies comparing individuals with and without nonsuicidal self-injury have found differences in the activity of multiple brain areas and in the functional connectivity between regions [66,67]. Some of the differences involve the manner in which adolescents engaging in nonsuicidal self-injury process social rejection and other emotional information. As an example:

- Compared with non-self-injurious youth, adolescents engaging in nonsuicidal self-injury may exhibit distinct neural responses to social rejection, and may be more sensitive to and have greater difficulty regulating responses following social rejection:
 - One study found that adolescents exhibited enhanced activation in the putamen (part of the region central to the brain's salience network) during a social exclusion task compared with conditions of social inclusion or passive watching [68]. This pattern was unique to the nonsuicidal self-injury group (n = 14), compared with age-matched healthy controls (n = 15) and adults with borderline personality disorder (n = 15).
 - Another study using the same social exclusion paradigm found that, although subjective ratings of feeling excluded were comparable, there were differences in neural processing during this task. Depressed adolescents engaging in nonsuicidal self-injury (n = 14) exhibited greater activation in the prefrontal cortex, compared with both adolescent patients with depression who did not engage in nonsuicidal self-injury (n = 14) and adolescent healthy controls (n = 15) [69].

- Adolescents engaging in nonsuicidal self-injury also may have altered neural patterns when viewing emotional imagery and material related to nonsuicidal self-injury. In a study that compared female adolescents with and without nonsuicidal self-injury (total n = 18) and that controlled for depression, the nonsuicidal self-injury group responded to standardized emotional images and images related to nonsuicidal self-injury with greater activation in limbic and frontal regions, suggesting greater emotional hyperarousal and attempts to compensate with emotion dysregulation [70].
- Other research suggests that adolescents engaging in nonsuicidal self-injury may exhibit aberrant amygdala-cortical connectivity [71]. In one study comparing female adolescents engaging in nonsuicidal self-injury (n = 25) with female adolescent healthy controls (n = 20), the nonsuicidal self-injury group exhibited atypical amygdala-frontal connectivity during resting state and during an emotional face-matching task. In addition, the nonsuicidal self-injury group was also distinguished by atypical connectivity between the amygdala and supplementary motor areas. Taken together, these findings may suggest one potential mechanism linking negative affect to habitual engagement in nonsuicidal self-injury.
- One study examined how patients engaging in nonsuicidal self-injury may exhibit distinct neural processing of pain and "relief" from pain (suggesting reward) [72]. Compared with non-self-injurious youth (n = 15), youth engaging in nonsuicidal self-injury (n = 13) exhibited greater activation in several reward/pain-processing regions and a greater positive association between the degree of subjective relief induced by the painful stimulus and the activity of multiple brain regions (eg, precuneus, supramarginal gyrus, posterior cingulate gyrus, and occipital gyrus).

INFORMATION FOR PATIENTS AND FAMILIES

Multiple resources are available for patients with nonsuicidal self-injury and their families. (See "Nonsuicidal self-injury in children and adolescents: General principles of treatment", section on 'Information for patients and families'.)

SUMMARY

 Nonsuicidal self-injury is a behavior characterized by the deliberate destruction of body tissue in the absence of any intent to die and occurs for purposes that are not socially sanctioned. (See 'Introduction' above and 'Terminology' above.) • The pathogenesis of nonsuicidal self-injury is largely unknown. However, research suggests that multiple factors may be involved, including behavioral and other psychological factors, social or interpersonal factors, and biological factors. (See 'Pathogenesis' above.)

Nonsuicidal self-injury may start and persist because the behavior serves one or more functions that help patients feel better. These functions arise from events that immediately precede and follow nonsuicidal self-injury. One model hypothesizes that the four primary functions of nonsuicidal self-injury differ depending upon whether reinforcement of the behavior is positive or negative, and whether the consequences of the behavior arise from intrapersonal (internal) or social processes:

- Intrapersonal negative reinforcement The behavior reduces negative and aversive emotions and thoughts.
- Intrapersonal positive reinforcement The behavior generates desired feelings and thoughts.
- Social negative reinforcement The behavior facilitates an escape from undesired social demands and unbearable social situations.
- Social positive reinforcement The behavior elicits desired social outcomes, such as attention or support, from others.

Patients most often report that nonsuicidal self-injury serves to regulate or manage negative emotions (intrapersonal negative reinforcement). (See 'Function of the behavior' above.)

- Social factors that may be involved in the pathogenesis of nonsuicidal self-injury include childhood maltreatment and peer influences such as social contagion. (See 'Social factors' above.)
- Several neurobiological systems may be involved in nonsuicidal self-injury, including genetic factors, endogenous opioids, and altered functioning of the hypothalamic-pituitary-adrenal axis. In addition, altered neural circuitry (eg, related to social rejection and emotional processing) may underlie the behavior. (See 'Biological factors' above.)

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