Review

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Externalizing disorders and environmental risk: mechanisms of gene–environment interplay and strategies for intervention

Diana R Samek*,[1]
& Brian M Hicks[2]

[1]Human Development & Family Studies Department, Auburn University, Auburn, AL 36849, USA

[2]Department of Psychiatry, University of Michigan, Ann Arbor, MI 48109, USA

*Author for correspondence: di.samek@gmail.com

Although heritable, externalizing disorders have a number of robust associations with several environmental risk factors, including family, school and peer contexts. To account for these associations, we integrate a behavioral genetic perspective with principles of a developmental cascade theory of antisocial behavior. The major environmental contexts associated with child externalizing problems are reviewed, as are the processes of gene–environment interplay underlying these associations. Throughout, we discuss implications for prevention and intervention. Three major approaches designed to reduce child externalizing behavior are reviewed. Prevention and intervention programs appear to be most successful when they target individuals or communities most at risk for developing externalizing disorders, rather than applied universally. We end by commenting on areas in need of additional research concerning environmental influences on persistent externalizing behaviors.

Keywords: antisocial behavior • behavior genetics • developmental theory • environmental risk • externalizing disorders • gene–environment interplay

Externalizing disorders are characterized by problematic behavior related to poor impulse control, including rule breaking, aggression, impulsivity and inattention. Specific child and adolescent externalizing disorders include conduct disorder, oppositional defiant disorder and attention deficit hyperactivity disorder. Child and adolescent externalizing disorders are relatively common, with estimates ranging from 7 to 10% [1,2], and with higher prevalent rates in males relative to females [2,3]. Child externalizing disorders are highly predictive of impulse control disorders in adulthood including substance use disorders and antisocial personality disorder [4–7]. We provide a review some of the key theories and empirical findings on the developmental and behavioral processes that underlie the associations between externalizing and environmental risk factors. We also review three major prevention and intervention programs aimed at reducing adolescent externalizing behavior and applying basic research to public policy.

A developmental cascade model of antisocial behavior

Patterson and colleagues [8,9] have articulated an influential theory of antisocial behavior that is a model of the behavioral contingencies between parents and children in which each 'trains' the other to respond in ways that will increase and maintain a child's aggressive and oppositional behavior while simultaneously decreasing parents' control over such behaviors. Typically, such interactions are the result of children with a difficult or disinhibited temperament (difficult to soothe, high emotional reactivity, impulsive behavior and irregular in routines such as sleeping and eating) [10,11] and parents who employ ineffective parenting practices, such as inconsistent discipline that ultimately reinforces aggressive behaviors. A common pattern is that a child is noncompliant or aggressive, parents demand compliance, child protests and becomes more aggressive, parent makes threats or also becomes aggressive to coerce compliance, the child escalates

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his or her aggression and demands, parent fails to follow through on threats and ultimately gives in to the child's demands or fails to ensure the child terminates his or her disruptive behavior. Over time, a child learns to control other family members through these coercive cycles. To compound the problem, parents in such distressed families often ignore or respond inappropriately to children's prosocial behaviors contributing to additional deficits in prosocial skills.

Lacking a behavioral repertoire of cooperation, compliance and appropriate inhibition of negative emotions, children that instead rely on aggression and defiance in social interactions go on to experience substantial maladjustment in contexts such as daycare, school and among peers [12]. This often leads to even greater levels of aggressive, oppositional and defiant behavior that marginalizes these children in daycare and classroom settings [13]. Same aged peers similarly have negative reactions to such behaviors that then result in rejection by prosocial peers [14]. Such children also often have mild-to-moderate neuropsychological challenges such as lower than average IQ, deficits in working memory and executive function, learning disabilities and problems with attention [15,16]. When coupled with disruptive behavior problems, these neuropsychological deficits result in academic difficulties [17]. Teachers also tend to be less motivated to work with students who exhibit disruptive behavior [18].

For the aggressive child, this leads to frustration and embarrassment and disengagement from academic contexts. Failures to adapt to or find a 'place' in school and within a prosocial peer network often lead to depression, withdrawal and anger in early to middle childhood [19]. The accumulated losses resulting from these negative relationships and disengagement from the socializing agents of parents, school and prosocial peers then pushes these children to affiliate with deviant peers in later childhood and early adolescence [20]. Such deviant peer groups establish a culture that values and reinforces norm violations (a process known as deviance training) [21,22] and contributes to a dramatic escalation in antisocial behavior in adolescence including delinquency, early substance use and precocious sexual behavior, further weakening the bonds to the socializing influences and support networks of family, school and prosocial peers. The accumulating interplay of environmental and person-level risk then begins to limit the available contexts for antisocial youth; a dynamic process referred to as 'cascading constraints' [9]. In turn, these constraints then greatly increase the probability of poor outcomes such as school expulsion and educational disengagement, unemployment, criminal activity and arrest [23,24].

Heritability & gene–environment interplay in externalizing disorders

Before discussing the links and underlying mechanisms between environmental risk factors and externalizing, it is important to first note that the different externalizing disorders have a high rate of co-occurrence [2,25] and tend to run in families. Twin, adoption and family studies have shown that parent–child similarity on externalizing disorders is primarily accounted for by the genetic transmission of a general liability that increases risk to multiple disorders, rather than the transmission of disorder-specific liabilities [26–28]. The relative mix of genetic and shared environmental influences (i.e., environmental influences that contribute to similarity among relatives, in contrast to nonshared environmental influences that contribute to differences among relatives) that underlies the familial similarity on this general externalizing liability changes over the course of development. In childhood and early adolescence, there is a substantial contribution of shared environmental influences in addition to heritable influences [1,26], but by late adolescence and young adulthood, familial resemblance on the general externalizing liability is almost entirely due to genetic influences [29,30]. Given the large and persistent influence of genetic factors on the development of externalizing behaviors, it is important to understand the processes that account for exposure to high-risk environments, as well as how such environments may moderate inherited risk for externalizing.

Two mechanisms of gene–environment (GE) interplay are essential to understand the ways in which environmental influences correlate and interact with genetic risk in the development of externalizing: gene–environment correlation (rGE) and gene × environment (G × E) interaction. rGE refers to the fact that exposure to environmental risk is not random, but rather is partly a function of genetically influenced traits that help shape family contexts as well as the decisions and actions people take in selecting and shaping their environments [31,32]. Thus, while a large literature has demonstrated an association between parenting behaviors and child adjustment [33–37], a confounding factor in this theorized causal relationship is the extent to which parents and children share a genetic liability that contributes to both ineffective parenting practices and the child's disruptive behavior, a phenomenon known as passive rGE [38]. Evocative rGE can also occur, wherein, children evoke parental responses as a consequence of their own genetically influenced traits. Thus, a child with a genetically influenced disinhibited temperament style may evoke negative reactions from parents and other adults, such that harsh discipline and ineffective parenting may be as much a consequence as

cause of a child's externalizing behavior. Finally, active rGE refers to a situation in which heritable characteristics contribute to the selection of environments, typically environments that are consistent with and accentuate the selection traits. This might include affiliating with peers who have similar externalizing tendencies or a desire to go to parties where drugs and alcohol are available, providing additional contexts for further antisocial behavior and increasing conflict in the parent–child relationship.

Family influences: parents & siblings

Consistent with an rGE model, behavioral genetic research has shown that the association between negativity in the parent–child relationship and the child's antisocial behavior is largely accounted for by shared genetic influences [39–41]. A recent adoption study, however, ruled out passive rGE as a potential mechanism, as there was a moderate association between parent–child hostility and child externalizing in both adoptive and biological families [42]. Nonetheless, these results do not rule out the possibility of an evocative rGE. That is, rather than a causal environmental influence, parent–child hostility may to some degree be a reaction toward a child's genetically influenced externalizing behaviors. Consistent with this notion, Neiderhiser *et al.* [43] found distinct genetic influences on martial conflict about the child and parental monitoring that both overlapped with peer delinquency and later drug use, suggesting heritable child characteristics may contribute to parental behaviors that then increase risk for externalizing. These findings do not suggest that parenting interventions are futile; in fact, if shared genes are linking parenting behavior and child externalizing problems, it may be even more important to intervene on those that are the most susceptible to that genetic risk, rather than universally.

In addition to rGE processes linking parenting and child externalizing, several studies have also found evidence G × E interactions [44–46]. G × E interaction refers to the situation wherein the heritability or effect of genes on a trait (externalizing) is dependent on some condition of the environment (parenting). Multiple studies have now demonstrated that the genetic variance of externalizing increases in the context of greater parent–child conflict, negativity, punitive discipline and lower parental warmth [37,45,46]. In contrast, warm and supportive parenting practices seem to suppress genetic risk for externalizing [47]. These findings support proposals for the widespread use of parent training interventions to reduce externalizing disorders in childhood and adolescence [48]. Such interventions reduce the mean or absolute level of disruptive behaviors, and likely do so by altering the environment such that the context is no longer conducive to the expression of genetic risk factors. Teaching parents effective parenting skills may be particularly effective for a high-risk population, rather than universal parental training interventions. Indeed, community-based preventions have been shown to be more effective for high-risk versus low-risk children [49,50].

Besides the parent–child relationship, a large body of research has shown that aspects of the sibling relationship contribute to the development of externalizing disorders in childhood and adolescence [51–55]. Ineffective parenting and sibling conflict are highly correlated, and both independently predict subsequent peer difficulties and antisocial behavior [51]. Additionally, some have argued that sibling relationship difficulties and conflict in early and middle childhood may be an early indicator of problems likely to occur in social relationships outside the family [56–58].

There is also evidence that siblings often act as 'partners in crime' and engage in antisocial activity together [52,59], particularly when they are same sex, of similar age and report close relationships and mutual friends [54,60]. Indeed, twin, adoption and other genetically informative designs have shown that relationship factors (social closeness, contact and mutual friendships) account for a substantial proportion of sibling similarity in externalizing – particularly for substance use – via environmental mechanisms [61,62]. Thus, while parental transmission of externalizing disorders operates through a common genetic liability [26–28], sibling relationship influences on child and adolescent externalizing appear to be environmental in nature. To date, there has been limited research that has investigated sibling influences in prevention and intervention of externalizing in childhood or adolescence [56], although sibling facilitation of substance use (helping younger siblings get alcohol and drugs) appears to be a key source of sibling influence on adolescent substance use [63].

Academic difficulties & peer factors

In addition to the family environment, there is ample evidence that academic difficulties and rejection by prosocial peers are associated with child and adolescent externalizing problems [14,17,64–66]. Longitudinal studies have shown that externalizing problems in childhood predict subsequent academic difficulties in childhood [67] and adolescence [68], over and above prior academic competence. School environments also seem to have a moderating influence on genetic risk for externalizing similar to that of family contexts. Specifically, genetic influences on externalizing tend to be lower among children with better grades and among those who report greater academic engagement [69].

Though a number of selection factors (e.g., IQ and parental involvement) contribute to academic competence, if such contexts can be established and maintained, they can help to suppress existing genetic risk for externalizing problems. Involvement in extracurricular activities also seems to reduce risk for persistent externalizing problems [70,71], both by providing structure and an alternative to antisocial activities, and by fostering ties to school contexts.

Consistent with the sibling deviance literature, there is also overwhelming evidence that deviant peer affiliation is associated with antisocial behavior and substance use [72–75]. Moreover, deviant peer affiliation has been shown to amplify the association between harsh parental discipline and externalizing behaviors [76], indicating an interaction between peer and family influences on externalizing problems in adolescence. A logical target of intervention or prevention for externalizing then is peer groups of high-risk youth. Notably, Dishion *et al.* [77] have shown that such interventions often reinforce problematic externalizing behaviors, in part because many high-risk youth lack adequate social skills and involvement in more prosocial activities. As such, the conversations and social activities among friends who are both antisocial tend to be focused on the past and future commission of antisocial behaviors. However, a high degree of emotional and behavioral self-regulation may buffer against deviant peer influences [78], and cognitive emotional self-regulation is likely an important component to interventions for externalizing [79], particularly those that aim to offset risk imposed by deviant peer affiliation.

Genetic influences have also been demonstrated on deviant peer affiliation [80,81], which is interpreted as the consequence of active rGE processes [38]. That is, to some extent, people select friends based on their similarity on genetically influenced traits and interests, including attitudes toward norm violation. As a consequence, measures of deviant peer affiliation exhibit heritable variance, and the importance of genetic influences on peer selection increases from childhood into adulthood as people gain greater autonomy in selecting their social environments [80]. G × E interactions also underlie the association between peer deviance and externalizing problems, such that the genetic risk for externalizing problems increases in the context of more deviant peer groups [46,82,83]. While some children with externalizing problems may begin to affiliate with each other in childhood, the greater autonomy afforded adolescents results in a dramatic increase in the formation of deviant peer groups that then fuels a dramatic increase in antisocial behavior in mid-to-late adolescence [84]. Preventing or disrupting the influence of deviant peers is crucial to deflect the trajectory of persistent antisocial behavior, but accomplishing such a goal is exceedingly difficult in practice [77]. Thus, successful interventions might focus more on strengthening the parent–child or family bond, improving emotional self-regulation and fostering school bonding earlier in development, which should help to mitigate the influence of deviant peers in adolescence.

More broadly, a few studies have examined the influence of several environmental risk factors to identify more general principles of GE interplay in the development of externalizing. Hicks *et al.* [46] found that the genetic variance in externalizing increased in the context of greater environmental adversity as indexed by separate measures of parent relationship problems, deviant peer affiliation, academic disengagement and stressful life events. The aggregate finding is demonstrated in Figure 1. Beaver [85] also found that the genetic variance of serious and violent delinquency increased as the number of exposures to 13 different risk factors increased. Both findings suggest a general mechanism of GE interplay for externalizing such that genetic risk increases in the context of greater environmental adversity regardless of the specific risk exposure. Also, most environmental risk factors are correlated, such that people typically experience not just one but several exposures [46,86]. The nonindependence and heritable nature of externalizing and environmental risk then suggests that the most severe and persistent antisocial behavior is exhibited by a small group of people that carry an especially high loading of both genetic and environmental risk [84]. The likely mechanisms for this are rGE processes resulting in the greatest exposure to environmental risk among those that carry the greatest genetic vulnerability, resulting in G × E interactions that compound the deleterious effects of initial risk exposures.

A review of three major prevention & intervention programs

Given the high societal cost of adult externalizing behaviors, there is a societal imperative to intervene and ideally prevent such problem behaviors before their severity rises to the level of criminality, as such behaviors have potentially life-altering consequences for both perpetrators and victims. As 'cascading constraints' narrow an individual's potential developmental landscape [9,84], the earlier an intervention is implemented, the greater the likelihood for success in deflecting the trajectory toward persistent antisocial behavior.

Based on findings reviewed here and elsewhere, interventions for externalizing will be most successful if they selectively target those children at greatest risk. Key characteristics that distinguish such children include a disinhibited temperament, family history of

externalizing disorders and behavioral and academic problems in school. Key components of such interventions include parent training and support, fostering prosocial skills (e.g., practice emotional self-regulation, reduce sibling conflict and deviancy training, increase prosocial peer affiliation) and promoting school engagement and bonding (e.g., extracurricular involvement, additional instruction for those not succeeding academically). Here, we review three major programs designed to reduce externalizing problems that vary in the target population, level of intervention (e.g., individual, school) and intensity of intervention on these key contexts and processes (for additional program reviews and long-term follow-up results, see Henggeler & Sheidow [87], Fagan [88], Patterson *et al.* [89]). Effect sizes for these three prevention and intervention programs have been generally small to moderate [49,90,91].

Multisystemic therapy (MST) [92] is based on a social ecology framework [93], and aims to intervene across multiple systemic influences at the level of the individual, family and community, to reduce the likelihood of chronic and violent juvenile offenses. MST targets 12–17 year olds who have engaged in serious antisocial behavior (criminal felonies if prosecuted as an adult), and aims to foster a greater degree of parent–child and family bonding, mitigate the effects of deviant peers through parental supervision or involvement in prosocial peer activities, and increase engagement in school and extra-curricular activities. While the goal is to reduce risk factors and strengthen protective factors, it is done at the individual rather than universal level, as specific factors may be more relevant to some youth compared with others [94]. In general, MST has been shown to be quite effective in reducing serious juvenile offenses and substance use [90,95], even continuing into adulthood [96,97]). Notably, MST is a time- and labor-intensive intervention administered by a team of professionals that includes a therapist, social worker and other specialists. A therapist is on duty 24 h a day and 7 days a week to aid in crises, performs treatments in the adolescents' home at nights and on weekends and the treatment typically lasts 4 months. MST has been widely implemented, with MST programs operating throughout 30+ states in the USA, and some internationally [94].

Communities that Care (CTC) is a prevention program that has been shown to be successful at reducing substance use, delinquency and violent behavior [91,98]. However, CTC is implemented universally at schools and communities deemed at high risk (e.g., public schools in high-crime areas [98]), rather than toward individuals. CTC is less time-intensive compared with MST, and focuses on a broader population than those with serious juvenile offenses. Several

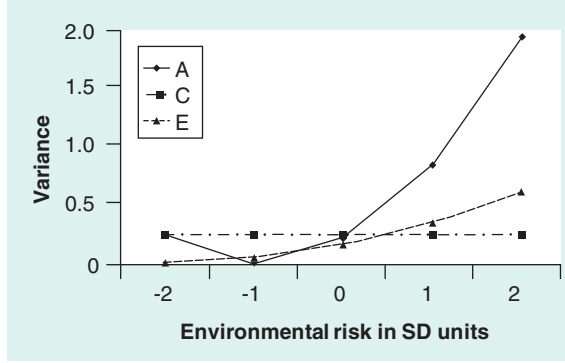

Figure 1. Gene–environment interaction: genetic variance in adolescent externalizing disorders varies as a function of environmental risk. This figure represents the overall pattern of findings described in Hicks *et al.* [46]. Environmental risk was evaluated in terms of mother– and father–child relationship problems, antisocial and prosocial peer affiliation, academic achievement and engagement and a composite of stressful life events (e.g., parental divorce). Across all environmental risk measures, genetic variance of adolescent externalizing disorders was greater in the context of greater environmental risk, and lower in the context of more protective environments. This figure shows findings in the aggregate across environmental risk measures.
A: Additive genetic influence; C: Shared environmental influences; E: Nonshared environmental influences.

program interventions are utilized, including teacher training (5 days), child social and emotional skill development (4 h via teachers), and parental training (7-week session). Trainings began with children in the first through third grade, and intervention effects have been demonstrated through age 18 [98], such that students in the intervention were less likely to report violent delinquent acts, heavy drinking, risky sexual behavior than those in the control condition.

A subsequent randomized trial of 24 small towns in seven states implemented CTC beginning in the fifth grade (again, targeting schools in high crime and low income areas), and has shown that delinquent behavior and alcohol and cigarette use were lower in CTC relative to control communities at the tenth grade [91]. By the 12th grade, CTC communities were more likely to abstain from substance use, but among people that had used substances, there were no differences in the intervention arm for past month or past year substance use, nor were there differences in past year delinquency or violence [99]. Results have also been partially replicated in Pennsylvania, where CTC had a significant effect on reduced delinquency and better academic performance, but had no significant effect on adolescent substance use through the 12th grade.

A final systemic prevention program we discuss is PROmoting School-community-university Partnerships to Enhance Resilience (PROSPER) [49,100–102].

The purpose of PROSPER is to link university-based prevention researchers to elementary and secondary school personnel (counselors, curriculum directors, principals) and community providers of youth services, to implement the most efficacious prevention strategy given the school's needs. In consultation with researchers, school personnel select from a menu of prevention programs that fit best with their overall goals and populations including school-based and parenting interventions. Thus, unlike CTC and MST, neither high-risk individuals nor whole schools are selected for interventions; rather, interventions are implemented based on the specific needs of the school or community. PROSPER, however, has been shown to be more effective for high-risk versus low-risk children [49]. Other studies have also found that similar family and school interventions are more effective at reducing alcohol use among high-risk adolescents [50].

Future perspective

While we have focused on research on the developmental cascade of antisocial behavior through adolescence, less research has evaluated the processes that contribute to the persistence versus desistence of antisocial behavior in adulthood. For example, there is an emerging literature demonstrating a causal influence of marriage on desistence from antisocial behavior, even after adjusting for genetic influences on selection into marriage [103–105]. It also remains unclear whether gene–environment processes observed in childhood and adolescence have long-lasting effects through young adulthood. It will be important for future research to address the long-term impact of family, peer and school or work environments on adult psychosocial outcomes.

Additionally, while there has been extensive work done to incorporate parent training into prevention and intervention programs aimed at reducing externalizing problems, there has been limited research that has incorporated siblings. Given the substantial sibling influences in child and adolescent externalizing behaviors, an important avenue of future research will be to address how sibling factors can be incorporated into prevention and intervention efforts [53,54]. A recent program titled 'Siblings are Special' (SAS) [56] has the long-term goal of reducing siblings' risk for maladjustment and substance use. SAS is implemented in a 12-week, after-school session, teaching children emotion regulation and problem-solving skills. It will be important to evaluate the efficacy of the program as data become available.

There has also been little research that has systematically evaluated the efficacy of the timing of interventions in childhood and adolescence. While earlier is generally better, how early is necessary versus optimal? Additionally, interventions may be most effective if they occur just prior to or at the beginning of crucial developmental transitions (e.g., pubertal onset, transitioning from elementary to middle to high school). It would be useful to compare the results of a specific program (MST, CTC and PROSPER) that intervened at various age groups (e.g., age 5, 10, 11, 12, 13 years and so on) and evaluate the adult outcomes of each program.

Finally, it will ultimately be necessary to understand the underlying mechanisms of behavioral change associated with interventions. For example, some have hypothesized that cognitive behavioral therapy attempts to improve cognitive abilities associated with antisocial behavior, and so should result in changes in brain activation in regions of the prefrontal cortex [106]. Also, given G × E interactions, there are also likely to be gene × intervention interactions such that different polymorphisms may moderate an individual's response to treatment [107].

Conclusion

Substantial evidence indicates that externalizing problems are embedded within a larger context of interacting individual and environmental influences. A largely inherited disposition toward behavioral disinhibition correlates and interacts with well-established environmental risk factors (parenting, peer and school contexts) to influence the developmental trajectory of externalizing problems. Prevention and intervention research aimed at reducing problematic antisocial behavior has been shown to be successful, particularly programs that target high-risk individuals early in development, and that focus on strengthening bonds to the socializing agents of family and school. To date, little research has incorporated siblings into prevention and intervention programs. Given the research demonstrating sibling similarity in adolescent substance use and externalizing problems, this area seems ripe for future prevention research to incorporate. Additionally, more research is needed that addresses the long-term impact of child and adolescent environmental contexts and interventions on adult outcomes, as well as to delineate the neurobiological mechanisms underlying change in externalizing behaviors.

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Practice points

- Externalizing behaviors (rule breaking, aggression) and disorders (conduct disorder, oppositional defiant disorder and attention deficit hyperactivity disorder) are relatively common, more prevalent in boys than girls, and are highly predictive of impulse control disorders in adulthood.
- A combination of a difficult child temperament and ineffective parenting practices helps to 'train' children to be aggressive and defiant as a means to control their environment. This aggressive interaction strategy generalizes to those within and outside of the family, leading to increased sibling conflict, rejection by prosocial peers and academic problems in early childhood. This developmental cascade continues by leading children to affiliate with deviant rather than prosocial peers, which reinforces antisocial attitudes and persistent antisocial behavior through adolescence.
- Externalizing disorders are substantially heritable, and gene–environment correlation and interaction processes result in greater exposure to environmental risk among those that carry that greatest genetic risk that results in a 'double whammy' effect of genetic and environment risk.
- Externalizing behaviors exhibit strong associations with family influences including parents and siblings, rejection by prosocial peers, academic difficulties and deviant peer affiliation. Each is influenced to some degree by heritable characteristics of the child, and greater environmental adversity of any kind is associated with a greater expression of genetic risk for externalizing.
- Three major programs are reviewed, including multisystemic therapy, Communities that Care (CTC), and Promoting-School-Community-University-Partnerships to Enhance Resilience (PROSPER). In general, these programs have small-to-moderate effect sizes on reducing externalizing problems and substance use in adolescence, and seem to be particularly effective when targeting children or communities most at risk for developing externalizing disorders.
- In the next 5–10 years, we expect to see more research that extends the developmental cascade hypothesis past adolescence, as well as longitudinal research focused on why externalizing behaviors persist or desist. Additionally, delineating the neurobiological mechanisms associated with treatment-related change in externalizing will help to inform both etiology and more effective intervention strategies.

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