

The Hormesis Model for Building Resilience Through Adversity: Attention to Mechanism in Developmental Context

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Abstract

In developmental science, resilience refers to children and youths' ability to recover and pursue positive development in the face of stress related to adversity. Extant research has documented protective factors and ecological contexts that mitigate the impact of adversity and thereby promote resilience. One intriguing aspect of resilience is that individuals also develop strength in response to early adversity. However, very little theoretical guidance exists on the developmental mechanisms and contexts through which early adversity may lead to strengthening effects that confer the process of resilience. The strengthening mechanism in the context of specific circumscribed environmental stress is a process known in the field of toxicology as *hormesis*. It is proposed here that the study of resilience in developmental and psychological sciences can benefit from shifting more attention to the hormesis model. The hormesis model is reviewed and discussed as a promising perspective on mechanisms, developmental timing, and context through which adversity strengthens or impedes resilience.

Keywords

resilience, hormesis, stress and adversity, curvilinear, steeling, toughening, inoculation

The quest to understand how individuals sustain and overcome adversity draws an enormous interest in psychological science. Over the past two decades, research has advanced from employing reductionist approaches that sought to identify single traits within resilient individuals to investigating resilience as a systemic and dynamic process—one that emerges through interactions between neurobiological and multiple ecological contexts (Bonanno et al., 2015; Denckla et al., 2020; Masten & Cicchetti, 2016; Rutter, 2012; Secombe, 2002; Ungar, 2018; Yates & Masten, 2004). However, it is still unclear why some individuals are strengthened and show resilience in *response to* (and not *despite*) adverse experiences within their ecological contexts. Scarce research tests how adversity in and of itself can promote strengthening effects that confer resilience to future stress (Dienstbier, 2015; R. T. Liu, 2015; Seery et al., 2013). Other disciplines suggest that the strengthening effect of low-to-moderate levels of adversity is bound by a well-defined process called *hormesis* (E. J. Calabrese & Baldwin, 2002; Mattson, 2008). Hormesis is defined as a biphasic dose-response relation in which a low-to-moderate severity of environmentally mediated stress (adversity) induces positive adaptation up to a threshold of stress level. Once this threshold has been reached, stress loses its salutary effect and eventually becomes deleterious (E. J. Calabrese & Baldwin,

2002; Mattson, 2008). Effectively applied to examine molecular inoculation processes in toxicology and, more recently, in biomedical disciplines (E. M. Calabrese, Mattson, 2017), hormesis gets limited attention in psychological research on resilience. This paper considers the scientific utility of adapting the hormesis model to study the strengthening effects in response to stress that underlies part of the psychological resilience process during child development.

Studies on the resilience process show increasing interest in the strengthening effects of exposure to stress-related psychosocial adversity (Arbel et al., 2020; Davies et al., 2007; Davies et al., 2021; R. T. Liu, 2015; Repetti & Robles, 2016). Over the past 10 years, hundreds of articles have investigated resilience; yet studies that examine the beneficial effects of limited stress and adversity remain rare (see Table 1 for review). The shortage of research in the area may stem from multiple reasons, such as a lack of awareness

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of this effect as a fundamental component of resilience and limited theoretical guidance on how to advance the underlying mechanisms of strengthening effect in response to adversity in resilience science. The lack of attention in developmental science to strengthening effects of stress have noted by Sir Rutter, a pioneer, and leader of child psychiatry and resilience research in psychological science: “The human evidence on this point is much weaker, largely because there have been so few attempts to investigate the matter” (Rutter, 2012).

In contrast, research on hormesis has existed for more than a century in biomedical fields, with booming literature on mechanisms that underlie the hormetic effect (E. J. Calabrese, 2013). This paper briefly provides a historical account and empirical evidence supporting the hormetic dose-response effect across biomedical disciplines and behavioral research with animals (D. M. Lyons & K. J. Parker, 2007). Next, evidence is reviewed of hormesis as a framework that can expand upon existing strengthening metaphors by referencing mechanisms and developmental contexts in which adversity may support or impede resilience. The aim here is to discuss a theoretically bound model of the mechanism and process through which low-to-moderate adversity can promote resilience and demonstrate its relevance to developmental science.

The Origins of Hormesis: A Brief Historical Tale

Hugo Schulz, a pharmacology professor at the University of Greifswald in Germany, first identified hormesis while studying the effect of various disinfectants on yeast metabolism (Schulz, 1887). Shultz showed that at low levels, certain toxins acted as stimulants. However, high doses of the same toxins produced an inhibitory effect (for additional historical review, see (Calabrese, 2008). These findings were revolutionary because until that time, exposure to toxins was exclusively thought to be associated with a fatal risk to the organism. Schulz’s discovery that low doses of a toxic agent can induce positive effects on biological systems provided the foundation for hormesis (Southam, 1943).

Although curvilinear dose-response associations have been tested in psychological science, the hormetic response process’s definition goes beyond a curvilinear association. In the hormetic process, toxins are gradually introduced and continuously stimulate positive adaptation, developing into a strengthening mechanism, but only up to a certain stress level threshold or “turning point” (E. M. Calabrese, Mattson, 2017). At this critical threshold, the stressor ceases to operate beneficially and begins to operate destructively, undermining the organism’s adaptation. Thus, the hormetic response function requires a strengthening process that precedes a pivot point at which maladaptation to toxicity follows (E. M. Calabrese, Mattson, 2017).

Gaining strength from exposure to toxins is not a new scientific idea. It first became evident in the study of *inoculation* within the field of immunology. Inoculation refers to a method in which an antigenic substance is introduced into the body to trigger an immune response against a specific disease. As early as 1798, Edward Jenner, an English physician, observed that milkmaids previously infected with cowpox (a bovine analog of smallpox) developed an immunity to smallpox. This observation led to the discovery of inoculation processes in medicine. To investigate inoculation processes in the biomedical fields, researchers now consider how blood proteins produce antibodies in various animals’ reactions to different kinds and levels of antigens. Other behavioral disciplines have adopted the idea of developing immune-type responses, including studying resilience in psychological science (Rutter, 2012; Stealing effect, see Figure 1). Despite theoretical interest in inoculation concepts, research has yet to test the hormetic process’s contribution to the human development of resilience. To facilitate the application of hormesis in the study of resilience in psychological science, I present a conceptual model of psychological hormesis, followed by a discussion about the distinction of the hormesis model from other metaphors.

Psychosocial Stressors, Stress, and the Hormesis Model

In behavioral sciences, stress is defined as a psychobiological state in which the individual’s homeostasis is threatened by an environmental input (i.e., stressor), triggering a cascade of biological stress processes that mediate a cognitive-behavioral adaptive response (Chrousos, 2009; Levine, 2005). Among humans, psychosocial stress is often subjective such that it refers to human perception of being under threat and/or duress (Chrousos, 1998; Ursin & Eriksen, 2004). The acute and situational stress reaction is a healthy and adaptive response to environmental threats or challenges (Ursin & Eriksen, 2004). In contrast, when psychosocial stressors are not transitory, elicit prolonged stress, and are beyond one’s control, the neurobiological impacts can become toxic, resulting in neurobiological damage and attendant cognitive/behavioral maladaptation (Bruce S McEwen et al., 2015). Despite the documented adverse linear effects of prolonged and cumulative stress, individuals vary significantly in the way they experience and can sustain resistance to a range of psychosocial stressors (Gorka et al., 2016; Ong et al., 2006; Oshri et al., 2017; Repetti & Robles, 2016). These individual differences stem in part from how severe stressors are perceived to be, which is partly determined by individual and environmental contexts.

The hormesis model of psychosocial stress draws attention to biphasic dose-response relations between stress severity

Table 1. Human subject studies that test nonlinear psychological effects of stress and adversity.

Title	Authors/Year	Stressor Dev. Age	Participant Age	Stressor	Effects metaphor Used	Adjustment Outcome	Developmental Timing or Environmental Context	Key Findings
Childhood (Birth–12)								
Interparental conflict as a quadratic predictor of children's reactivity to interparental conflict and school adjustment: Stealing effects or risk saturation?	(Davies et al., 2022)	4–6 y.o.	Mage = 4.6 y.o.	Interparental conflict	Curvilinear, stealing, j-shape	Emotional reactivity and behavioral dysregulation	Preschool (environment)	Curvilinear associations are observed between interparental conflict and child emotional reactivity. Moderate conflict predicts lower emotional reactivity.
Family context in association with the development of child sensory processing sensitivity	(Li et al., 2021)	2–4 y.o.	Mage = 2.97	Environmental harshness in the family context	Curvilinear, quadratic, U-shaped	Sensory processing sensitivity	Supportive/adverse environment	A curvilinear association exists between environmental harshness and sensory processing sensitivity (SPS). Moderate amounts of adversity show reductions in SPS.
Unique effects of socioeconomic and emotional parental challenges on children's executive functions	(Finch & Obradović, 2017)	Lifetime	Mage = 5.61 y.o.	Parent-related emotional challenges	Quadratic, U-shape, stealing effect	Working memory, inhibitory control, and rated executive function skills	N/A	Socioeconomic challenges were linearly related to child executive function (EF), while parent-related emotional challenges (EC) were quadratically related to child EF.
Adolescence (12–18)								
The curvilinear effect of mothers' parenting stress and attunement on Children's internalizing symptoms: A six wave study of mother–youth dyads across the transition to adolescence	(Arbel et al., 2020)	8–12 y.o.	Mage: 10.1	Maternal parenting stress	Curvilinear; U-shaped effect	Youth internalizing symptomatology	Moderator: Maternal attunement	Curvilinear pattern observed for maternal parenting stress on youth self-reported internalizing symptomatology. Moderate maternal stress revealed the least youth internalizing, whereas low and high maternal parenting stress produced elevated internalizing.
Parent–child attunement moderates the prospective link between parental overcontrol and adolescent adjustment	(K. F. Miller et al., 2018)	12–18 y.o.	Mage = 12.69	Parental overcontrol (OC)	Curvilinear	Youth risky behavior	Perceived attunement (moderator)	Maternal and paternal overcontrol was curvilinearly related to adolescent risky behaviors; this relationship was moderated by the youth's perception of their parent–child attunement.
Social experience calibrates neural sensitivity to social feedback during adolescence: A functional connectivity approach	(Rudolph et al., 2021)	Lifetime adversity	Mage = 16.3	Exposure to family adversity and exposure to peer adversity	Curvilinear, quadratic	Functional connectivity: Seed regions: 1.) ventral striatum and 2.) amygdala	Social reorientation in adolescence (context)	Findings detail several curvilinear associations between family/peer adversity exposure and functional connectivity in regions related to salience detection, social cognition and emotional memory.
Cumulative social-environmental adversity exposure as predictor of psychological distress and risk behavior in urban youth	(Day et al., 2016)	Lifetime	10–13 y.o.	Lack of protective resources within the family and neighborhood (LPR)	Curvilinear	Violence and drug use	Neighborhood, school and peer group risk level (contextual moderator)	Lack of protective resources (LPR) index had a curvilinear relationship with violence and drug use. This relationship was further quadratically moderated by neighborhood, school and peer group risk level. Moderate LPR level was associated with lower violence and drug use.
Young adulthood (18–30)								
Childhood interparental conflict and HPA axis activity in young adulthood: Examining nonlinear relations	(Hagan et al., 2014)	Prior to 16 y.o.	Mage = 18.7	Childhood interparental conflict	Quadratic, curvilinear, stress inoculation, buffering effect	Cortisol output and reactivity in late adolescence/young adulthood	None	Moderate frequency of interparental conflict (IPC), IPC exposure may be associated with lower cortisol activity at a later developmental stage.
An upside to adversity? Moderate cumulative lifetime adversity is associated with resilient responses in the face of controlled stressors	(Seery et al., 2013)	Lifetime	Undergraduates	Cumulative lifetime adversity	Quadratic, U-shaped effect/relationship	Study 1: Catastrophizing, pain intensity, pain unpleasantness, immersion time, and negative affect Study 2: Cardiovascular reactivity to challenge	None	Study 1: Cumulative lifetime adversity produced a U-shaped relationship with catastrophizing, pain intensity and unpleasantness, and post exposure negative affect. Adversity. Study 2: Results showed a significant inverted U-shaped quadratic relationship at mean adversity.

(continued)

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Young adulthood (18–30)								
Adverse life events, cardiovascular responses, and sports performance under pressure	(Moore et al., 2018)	Lifetime	Mage = 21.94	Cumulative adverse life events	Curvilinear, quadratic, “silver-lining” of adversity	Cardiovascular response to stress/challenge	None	Participants reporting a moderate/moderate-high amount of adverse life events experienced beneficial effects to their cardiovascular response to challenge/stress.
Is perceived stress linked to enhanced cognitive functioning and reduced risk for psychopathology? Testing the hormesis								
Hypothesis	(Oishi, Cui, Carvalho, et al., 2022)	Emerging adulthood	Mage = 28.84	Perceived stress	Hormesis, curvilinear, inoculation, toughening, steeling	Internalizing and externalizing symptoms	None	Cognitive functioning was seen as a potential mediating mechanism underlying the curvilinear associations between perceived stress and externalizing, but not internalizing, behaviors.
The role of perceived negative childhood experiences in the context of recent stress: Testing competing theoretical models	(Lazić et al., 2021)	Childhood	19–30 y.o.	Perceived negative life experiences	Curvilinear, quadratic, stress immunization	Life Satisfaction and ability to bounce back	None	Low and high levels of perceived negative life experiences were associated with low life satisfaction, and reduced ability to bounce back, but the highest levels of negative life experiences reported the lowest life satisfaction and ability to bounce back. Mild negative life experiences are related to the highest life satisfaction and ability to bounce back.
Late adulthood (30 and older)								
The curvilinear relationship of early-life adversity and successful aging: The mediating role of mental health	(Holtge et al., 2019)	Early life	Mage = 66.82	Early-life adversity (ELA)	U-shape, curvilinear, steeling	Quality of life	Mental health (mediator)	An inverse U-shaped association was found between early-life adversity (ELA) and quality of life and mental health. However, it was not observed between ELA and physical health.
Strength through adversity: Moderate lifetime stress exposure is associated with psychological resilience in breast cancer survivors	(Dooley et al., 2017)	Lifetime	Mage = 58.8	Acute and chronic lifetime stress exposure	Quadratic, curvilinear	Positive affect, negative affect and intrusive thoughts	None	The count of acute stress was quadratically related to positive affect, negative affect, and intrusive thoughts. However, chronic stress exposure did not have a quadratic relationship.

Note. A limited literature search of hormetic publications over the last 10 years. Databases included are APA PsycInfo, Family and Society Studies Worldwide, Psychology and Behavioral Sciences Collection, Child Development & Adolescent Studies, APA PsycArticles, Family Studies Abstracts, and Google Scholar. The following search terms were used: Stress, stressor, resilience, adaptation, early-life adversity, early-life stress, poverty, deprivation, threat, trauma, household dysfunction, maltreatment, emotion regulation, stressors, risk AND steeling, j-shape, curvilinear, quadratic, dynamic, convex, saturation, inoculation, and immunization theory. The initial results were filtered by publication year (2012–2022), subject (human, adult, children, psychological stress, resilience, psychological & physical disorders, developmental psychology, psychological & physical disorders), and type (academic journals), leaving 2556 results. Resultant publications were reviewed for their applicability to hormetic principles and ultimately reduced to 14 studies.

and outcomes rather than modeling either the linear beneficial or adverse effect of stress on psychological functioning (Kendig et al., 2010; Mattson, 2008). Figure 1 presents a generic model for psychosocial hormesis that demonstrates the relation between stress severity and psychological adjustment. The present paper focuses on the conceptual aspects of the hormesis model and its generalization to psychological sciences (for mathematical algorithms of the hormesis model, see (E. J. Calabrese & Baldwin, 1997)). Accordingly, the hormetic effect is bound to a model that encompasses the mechanisms that underlie the nonlinear dose-response effect of environmental stressors on organismic adaptation (E. J. Calabrese & Mattson, 2017). The mechanism of the psychosocial hormetic effect can be divided into two areas: *strengthening* and *protection*, which are divided under the curve by an inflection point that is referred to as the stress level threshold. The “strengthening effect” (shaded in blue on the left side of the threshold in Figure 1), referred to as an “overcompensation” response in the hormesis literature (E. J. Calabrese, 2015), is characterized by a process in which an adaptive response system ushers in a neurobiological mechanism that prepares or conditions the individual for future threats. The “buffering effect” (shaded in red on the right side of the threshold in Figure 1) commences when stress severity reaches an inflection point (threshold of stress). The inflection point is defined by the maximum level of stress in which strengthening occurs (as measured by improvement in adjustment outcomes) and the beginning of decreased adjustment benefits from higher stress levels. This area is named buffering because individuals are shielded by their previous strengthened abilities, suggesting that micro-stress-induced defense mechanisms provide protection and promote resilience. The toxic stress zone is outside of the hormetic effect and has been discussed in various models of stress on development (Shonkoff et al., 2012). At the toxic point, as the stress is beyond the level that the individual can derive benefit from it, the effect of stress is deleterious as it causes physical and psychological harm to the individual.

In psychological science, a specific dosage value of psychosocial stress that would correspond to the stress threshold cannot universally be determined due to multiple reasons related to measurement issues (Slavich, 2016) and moderating influence of contexts (Repetti & Robles, 2016; Ungar, 2013). First, psychosocial stress can emanate from different environmental stressors (e.g., cultural, neighborhood, family, interpersonal) and often refers to various constructs (e.g., socioeconomic stress, family stress, perceived stress). In addition, what is considered stressful is often subjective, and therefore, its perceived severity varies across individuals (Lazarus & Folkman, 1984; Thornton & Andersen, 2006). Even when referring to the same stressor (e.g., harsh parenting), any given construct can often be measured by multiple instruments using distinct metrics. Thus, determining a universal threshold for a psychosocial hormetic effect is challenging. Nonetheless, among a sample

of individuals, the threshold can be specified per the individual’s own context and relative to other individuals’ locations on the curve.

Existing Inoculation Metaphors

Strengthening through stress conceptualizations related to hormesis are widespread in psychological research (DiCorcia et al., 2013; Dienstbier & PytlikZillig, 2021; Rutter, 2012; Seery, 2011; Seery et al., 2010). These strength-building processes are referred to by a wide range of metaphors such as “inoculation,” “steeling,” “reparation,” or “toughening,” and more (Dienstbier, 1989; 2015; Dienstbier & PytlikZillig, 2021; David M Lyons & Karen J Parker, 2007; Obradović, 2012; Rousseau et al., 2003). Metaphors have been used to explain strengthening stress effects on a range of psychological functioning domains. For example, during childhood, the attachment benefit from parent–child separation stress was termed the *everyday stress resilience hypothesis* (DiCorcia et al., 2013). This hypothesis suggests how repeated exposures to separations (e.g., leaving home for preschool) eventually facilitate prolonged and adaptive separation from the parent (Bretherton, 1992). Accordingly, infant resilience separation stress is hypothesized to emerge through regulating daily life stressors related to separations from their mothers (i.e., main attachment figure). Analogous processes are evident in clinical research on posttraumatic growth (PTG), a complex process that emerges over time as individuals find meaning through their trauma. These processes are distinct from hormesis in that psychological strengthening is not necessarily a product of a dose-response or biphasic curve in relation to stress; albeit various PTG studies do show curvilinear effects (Coroiu et al., 2016; Dar & Iqbal, 2020; Kleim & Ehlers, 2009; Shakespeare-Finch & Lurie-Beck, 2014). However, the discussion on the PTG literature is deliberately limited here because this paper seeks to introduce the hormesis model to explain resilience processes in non-clinical populations.

Some resilience scholars (Rutter, 2012) referred to a *steeling effect* to describe their observations that adverse experiences can lead to an inoculation-like effect and attendant strengthening (Rutter, 2006). From an applied and basic science perspective on human development, steeling is a critical concept for assisting children in adapting and becoming more prepared for future challenges. However, beyond a statistical test with a curvilinear function, a delineated model of what steeling is and how to test it is lacking. In addition, empirical evidence of steeling is limited (Arbel et al., 2020), or rare (Davies et al., 2021; Oshri et al., 2022), and the underlying mechanisms are seldom specified. Accordingly, a restricted search of the non-clinical literature of studies published over the last 10 years (2012–2022) that used curvilinear tests concerning stress and resilience yields 14 out of 2566 studies (see Table 1).

Interestingly, no studies are found that used the term hormesis. Table 1 also shows that various metaphors describe

the nonlinear strengthening effect of low-to-moderate stress on psychological adjustment. Most studies report small effect sizes and provide alternative interpretations of strengthening effects. Moreover, to examine this effect, studies use different testing standards. The hormesis model may help consolidate this literature as it bears the potential to provide a cohesive and established model-based theoretical framework on how stress can lead to adjustment benefits and thereby facilitate more research in the areas of developmental science and resilience.

Hormetic Mechanism

The hormesis model includes a mechanism that underlies the strengthening effect through adaptations referred to as *preconditioning* (Calabrese, 2016). Preconditioning is the underlying process (See Figure 1b) that includes biological and chemical reorganizations in response to environmental exposure to low-to-moderate stress levels. In the hormesis model, preconditioning ensues via a process initiated by earlier and lower levels of environmental pathogen exposure, which unfolds over time and results in a cascade of bio-behavioral changes toward preparation for future stress exposures. Accordingly, the strengthening or inoculation phase of a preconditioning process is often triggered at a separate time and space, gaining the name precondition¹ as the organism is preconditioned (reorganized or strengthened) to be better prepared for future risky encounters (E. J. Calabrese, 2016a). This adaptive biological reorganization in response to extracellular environmental agents is critical for evolutionary processes promoting organismic resilience (Bhattacharya & Rattan, 2019; Mattson, 2010). The idea that limited stress exposure prepares live systems for later stress is shown across disciplines (Agathokleous & Calabrese, 2022). Preconditioning has been shown to be triggered by multiple types of stressors, including psychological, emotional, and physical (Arumugam et al., 2006; E. J. Calabrese, 2016a, 2016b). Indeed, in psychological science, there is an increase in research on the biological embedding of psychosocial stress—how the experience of psychosocial stressors leads to alterations in human biology. Psychological adaptation to trauma, for example, is evident neurobiologically in neuroplastic processes such as a change in synaptic connections, neurogenesis, and selective pruning.

The attention to preconditioning as a process changed in 1986 through a publication by (Murry et al., 1986) on the benefits of preconditioning to short episodes of ischemia (obstruction of blood supply to tissues) in a dog's heart. In a series of studies, Murry's laboratory has demonstrated that preconditioning in the form of repeated brief episodes of ischemia bears no harmful consequences but rather a salutary effect. Therefore, they showed that multiple momentary ischemic episodes protect the myocardium from a subsequent sustained ischemic insult. These findings were revolutionary because they suggested that limited early exposure to

ischemia, among the most lethal risk factors for cardiac mortality, can be used to protect the heart from ischemic injury and potential death. Given extant support for the hormesis model and its effects across disciplines, its application in psychological sciences remains to be further seen. Drawing from models of cellular hormetic mechanisms (receptor and cell signaling-mediated hormetic mechanisms) and work from the psychological science literature, a developmental perspective on hormesis is advanced next.

Developmental Timing and Contexts for Hormesis

Hormesis in Context

Informed by ecological perspectives, resilience is increasingly viewed as a dynamic process that emerges from interactions between risk and protective factors (Masten, 2014; Ungar, 2004). Although still hypothetical due to a lack of empirical evidence, this paper suggests that the hormetic effect may vary across individuals. Interindividual differences in the timing and strength of hormesis are expected due to variability in biological or environmental vulnerabilities and resources (brackets shown in Figure 1 denote potential interindividual variability). Indeed, contexts from multiple levels of analysis (e.g., community, family, school, individual) moderate the effect of psychosocial stress on risk and resilience (Masten & Narayan, 2012; Oshri et al., 2017; Ungar, 2013; Ungar & Liebenberg, 2013; Yule et al., 2019), suggesting that individuals may respond differently to even equal types and magnitude of stress. Depending on their social context, some youth may be more equipped to cope with and strengthen from a given stressor. Such contexts can buffer the effects of the stressor from becoming severe and toxic. For example, low-to-moderate levels of perceived stress can potentiate benefits in working memory performance via curvilinear neural activation effects among young adults with access to increased psychological and social resources (Oshri et al., 2022).

Developmental Timing

Developmental timing is a critical aspect of developmental science and the study of resilience (Cicchetti & Blender, 2006). Extant research on resilience suggests that vulnerability to environmental stress changes during different times in development (Frankenhuis & Walasek, 2020). Across development, there are limited times when an individual is exceptionally responsive and neurobiologically flexible or malleable to environmental input (Fox, Levitt, & Nelson III, 2010). These time points are often classified either as "critical" or "sensitive" periods. Critical periods include the presence or absence of environmental experience that could lead to irreversible change (Fox et al., 2010; Hensch, 2005;

Trachtenberg & Stryker, 2001). In contrast, sensitive periods include developmental time in which the individual is more amenable to neural changes, for better or worse (Knudsen, 2004; Thomas & Johnson, 2008). Such time-dependent plasticity underscores the potential for learning and adaptation throughout the lifespan (White et al., 2013). Studies applying the concept of neuroplasticity to resilience research provide evidence for peak periods of sensitivity to positive environmental influences (Bruce. McEwen, 2016). However, the preponderance of early stress and adversity research on sensitive periods and developmental plasticity produced empirical documentation of either positive/stimulating or negative/adverse environmental effects. Most developmental studies show that earlier age exposure to chronic stress confers a significantly more harmful impact on children and youth (Gee & Casey, 2015; Lupien et al., 2018; Maggi et al., 2010; G. E. Miller et al., 2011; Oshri et al., 2019).

Experience-Expectant and Experience-Dependent Learning

Stress to brain-related changes is manifested in experience-expectant and experience-dependent neuroplasticity models (Gabard-Durnam & McLaughlin, 2019). Experience-expectant neural changes (e.g., learning) refer to the time-bound biological preparedness for change in response to environmental stimuli. Sensitive periods are vital to this model because, during specific times, neurobiological changes in response to environmental stimuli are more malleable than at other times (Zeanah et al., 2011). Language acquisition is an example of a learning type explained chiefly through the experience-expectant model of change in a developmental context. During sensitive periods, active formation of new synaptic connections is triggered in response to environmental input. Experience-dependent neural changes are exclusively activated by environmental events/stimuli and ultimately facilitate learning. Because the effectiveness of neuroplasticity varies during development, experience-dependent learning processes are more salient in specific developmental timing (Galván, 2010). For example, learning to ride a bicycle is an experience-dependent process that is more efficiently acquired at an earlier age. Other learning processes are less dependent on developmental timing. For example, expanding general knowledge on world history can be obtained across development and are less reliant on “sensitive periods.”

The underlying neurobiological and psychological hormetic effects are primarily part of experience-dependent mechanisms. The prediction of hormesis may be empirically informed when considering the impact of adversity in the context of sensitive periods of neurobiological change. It is, therefore, plausible to expect that specific timing of psychosocial stress may lead to an adaptive strengthening of coping capacities (Repetti & Robles, 2016; Seery et al.,

2010). Thus, it is essential to inquire in which developmental stages salutary effects of adversity emerge and the potential for a hormetic effect to occur. Emerging research provides some primary evidence with children. In a study on cognitive performance, Nweze et al. (2020) compared children exposed to stress associated with rearing deprivation presented in institutional homes to non-deprived control children. Using a multifaceted neurocognitive test battery that included assessment of inhibition, set-shifting, and working memory, the study reported that parentally deprived children performed significantly better than the non-deprived group in the working memory task. The results are consistent with developmental evolutionary models suggesting that enhanced working memory abilities among the deprived group may stem from positive adaptation to a stressful environment (Ellis et al., 2022). This research joins emerging evidence in developmental science on the circumscribed, but potential beneficial effects stress has on cognitive development. Yet, studies continue to fall short in documenting the dosage, timing, and underlying mechanism of stress exposure.

Given that existing literature shows that stress-related developmental plasticity peaks in childhood and again in adolescence (Sicorello et al., 2020), it is plausible to propose that the process of hormesis would be influenced by developmental *timing and context*. Accordingly, the pre-conditioning process, and its neurobiological underpinnings, are likely to be more effective for hormesis when presented during sensitive periods. Early-life exposure to moderate levels of toxins may potentiate neural adaptations catalyzed by conditioned responses that empower youth to tolerate new stressors later on in life. This hormetic mechanistic process may undergird inoculation substrate for adverse environments (Figure 2). Overall, the benefits of hormesis in elucidating the process of resilience are likely to be anchored to the developmental timing when hormesis may be more effective. It is desirable and even vital to examine whether there are empirically identifiable critical periods for hormesis, which would assist in pinpointing opportunities for resilience interventions.

According to this developmentally informed process, the *preconditioning* mechanism that underlies the hormetic effect will vary by developmental timing. In the presence of low-to-moderate stress, a learning process is initiated. This process involves neural changes in structure and function triggered to cope with adverse environmental stressors (e.g., perceived stress, punishment, aversive learning). Yet, as suggested by experience-dependent learning research, the capacity for change declines systematically across development (See Figure 2), with an expected temporary incline in adolescence. Specifically, hormetic neural changes in response to adverse environmental stimuli are expected to decrease with time (age is reflected in the X-axis) as manifested in a linear reduction in neuroplasticity (illustrated by the fading blue area across development). This decline is expected to momentarily halt during adolescence, which is an additional window of

opportunity that is characterized by an increase in neuroplasticity (shown by red spots in Figure 2) (Dahl et al., 2017; Fuhrmann et al., 2015). The strengthening phase includes an experience-dependent learning progression in response to low-to-moderate levels of adversity. The phase involves hormetic-induced changes in the strength of neural connections, synaptogenesis (formation of new synaptic connections), and pruning of existing connections.

The hormetic neural changes switch at a threshold in which more severe adversity is toxic. At this level, adversity impedes learning and growth and is replaced with toxicity (with increased intensity and duration) that causes a reduction in neural adaptations to cope with a stressor. Per Figure 2, adverse experiences can elicit greater neuroplasticity earlier rather than later in development (illustrated with fading red). Developmentally, triggered preconditioning and attendant hormetic inoculation effect will vary by age (shown by a steeper curve). Further, from a developmental ecological perspective, the hormetic process will depend on moderating effects of ecological contexts. Interindividual differences in neural adaptation are expected to vary as a function of more proximal (e.g., biological, personality) and more distal factors (i.e., family, social environment, and developmental resources; as shown by the different yellow lines). This individual variability may fluctuate as a function of neurobiological differences in stress reactivity and personality (Oshri et al., 2018; Oshri et al., 2013), psychological resources (Cui et al., 2020; S. Liu et al., 2020), or family protective resources (Vanderbilt-Adriance & Shaw, 2008).

The Perils and Challenges of Applying Hormesis in Psychological Science

Although testing for hormesis continuously expands the knowledge base on resilience processes at cellular and molecular levels, it has yet to be applied in psychological science. It can be challenging to draw parallels between “toxic” psychological environments and chemical toxins. Applying the concept of hormesis to psychological and developmental sciences comes with ethical considerations. There is a need to clarify the specific environmental conditions that define stress before the hormesis model can be appropriate for studying human developmental resilience. When testing the hormesis hypothesis in psychological science, theoretical articulation of a toxin’s strengthening effect is critical because not every toxin will elicit a hormetic effect. For example, mercury (methylmercury) is a causative agent of a wide range of disorders in mammals and humans (dos Santos et al., 2016; Hussain et al., 1999). Even at low levels of exposure, with sensitive measurement tools (Castoldi et al., 2008), mercury is a toxin that does *not* initiate any molecular or cellular benefits to humans (Zahir et al., 2005) and mammals (da Silva Santana et al., 2019).

Parallel to a pathogenic chemical toxin with no hormetic effect, humans’ adverse child-rearing environments can also be considered toxic. However, the determination of “toxicity level” in terms of human stress level can be nuanced. Although parenting or familial environments are a shaping force behind children’s socioemotional development, the literature shows that sexual abuse is unequivocally harmful. No level of sexual abuse could be considered developmentally beneficial for a child. Similarly, other types of adversity have been considered unequivocally harmful. For example, Dienstbier and colleagues suggested that an early loss of a parent was a traumatic experience that is unlikely to be a toughening experience (Dienstbier, 2015).

In contrast, such determination can be contested because some traumatic experiences lead to psychological growth (Bonanno & Kaltman, 1999; Tedeschi & Calhoun, 2004; Westphal & Bonanno, 2007). In addition, other areas of harsh parenting have been shown to result in psychological growth. For example, lower levels of interparental conflict, a less severe psychosocial stressor than sexual abuse, is curvilinearly linked to emotional reactivity and behavioral dysregulation in children (Davies et al., 2021). Attributing harsh parenting as hormetic versus non-hormetic toxic environmental stressor underscores the need for an accurate conceptualization and definition of “psychosocial toxins.” The definitional challenge is partially addressed by Shonkoff and colleagues’ (Shonkoff & Levitt, 2010) proposal to classify stress as positive, tolerable, and toxic. Shonkoff’s taxonomy may assist in determining which environmental experiences may induce a hormetic response, as well as those that are toxic and therefore not expected to yield any benefits.

Lastly, in psychology, stress can come in various forms of psychosocial stressors (e.g., family or community violence). The expected response in psychological or cognitive adaptation to these stressors may vary by context. Children adapt to adverse conditions by developing specialized competencies that promote a resilient response, but such developmental adaptations only occur within a narrower specific context (Ellis et al., 2017; Frankenhuis & de Weerth, 2013). Adaptive responses to stress are accounted in part by theories on biological sensitivity to context, such as cognition (Frankenhuis & de Weerth, 2013) through stress reactivity (Ellis & Del Giudice, 2019) and coping strategies (Clarke, 2006; Seery et al., 2013). In a meta-analytic study, Clarke (2006) reported that specific psychosocial stressors were associated with active coping, a crucial aspect of youth resilience. Hence, because psychosocial stress is a complex construct that varies by individual and environmental contexts, it is challenging to derive an objective quantification of stress severity that will yield a hormetic effect.

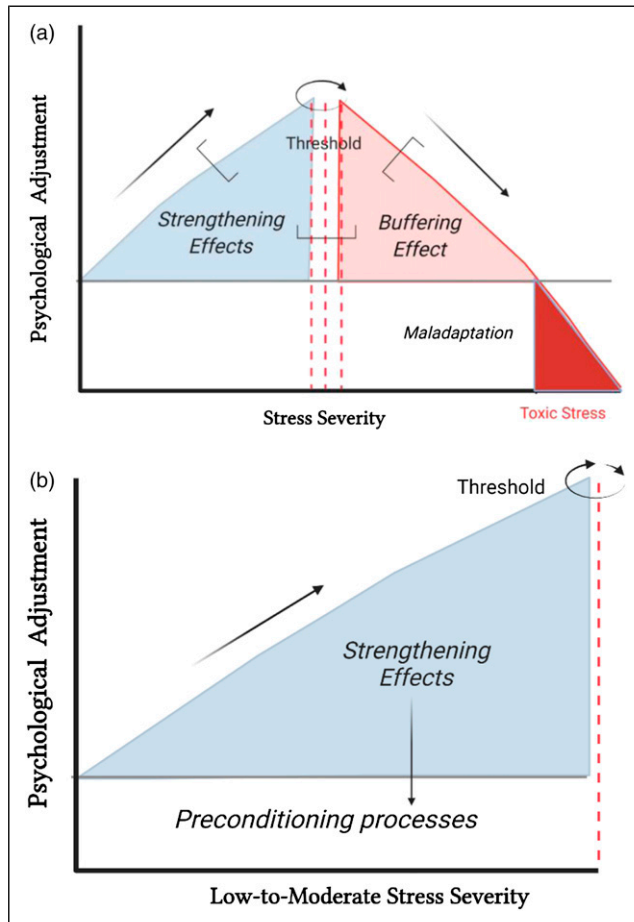


Figure 1. (a) Generic Psychosocial Stress Hormetic Process. (b) Preconditioning in the Hormetic Model.

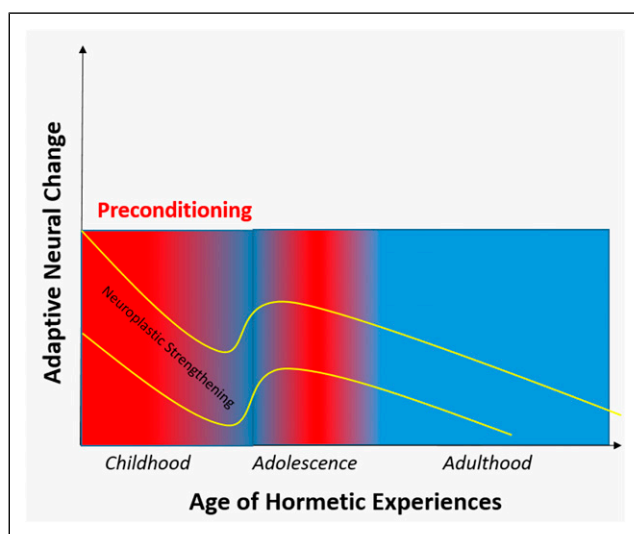


Figure 2. Individual Differences in Hormetic Strengthening Process Across Development.

How Can Hormesis be Tested With Human Subjects?

While it is evident that some stress levels can have strengthening effects that may inoculate or precondition humans from future encounters with stressors, it is less clear how to study hormetic effects among human subjects. The answer would differ for applied versus basic research. In applied and clinical setting, cognitive behavior therapy techniques have been employing gradual exposure to limited controlled to build tolerance to a wide range of anxiety disorders (Craske et al., 2008; Foa, 2011; Foa et al., 1995). The idea share similarities with the concept of preconditioning in the hormesis model; Specifically, in exposure therapy gradual exposure to stress along with cognitive behaviors strategies allow patients to engage in corrective learning and attendant fear extinction (Craske et al., 2008). These clinical strategies aim in building tolerance to environmental stressors that have been otherwise eliciting severe anxiety symptoms for children with anxiety disorders. Given that clinical science application is beyond the scope of this paper, thoughts about basic research will be the focus of the discussion. Hormetic effects of acute stress have been elegantly experimentally shown in laboratory conditions (e.g., inducing stress by immersing hands in ice-cold pressor task; Seery et al., 2013). However, when studying human resilience, laboratory conditions are less germane to understanding resilience to prolonged experiences of psychosocial stressors. Examining hormetic effects and their benefit to human resilience requires modeling exposure to psychosocial stressors that are not acute but more prolonged stressful ecologies (e.g., socioeconomic hardship, food insecurity, harsh parenting). Thus, researchers interested in data on environmental stressors will have to resort to adverse events that occur “naturally” and use correlational designs.

Because adverse childhood experiences (ACEs) are unfortunately very prevalent, working with “naturally” occurring data is a feasible idea. Estimates suggest that 57.8% of adults have experienced at least one ACE, and 21.5% report having experienced more than three ACEs (Giano et al., 2020). Indeed, growing correlational studies form hypotheses on the salutogenic effects of low-to-moderate stress (Höltge et al., 2018). For example, data on inner-city youths show the development of coping skills as an adaptation to exposure to moderate levels of community violence (Ng-Mak et al., 2004; Voisin et al., 2011). Similarly, in a study with an ethnically diverse sample of 102 kindergarteners (M age = 5.61 years), emotional challenges were associated with executive functions in a curvilinear (inverted U-shaped) way (Finch & Obradović, 2017). Specifically, mild-to-moderate parental emotional challenges were related to more optimal performance in executive functions. Albeit limited in size, this literature shows that when researchers in psychological science hypothesize and test for nonlinear outcomes from varying levels of environmental stress, results are consistent with the concept of hormesis and can help us further

understand the mechanisms in which stress can induce strengthening effects.

Conclusions

The development of human resilience continues to spark avid interest and curiosity, spurring investigations across the psychological sciences. This interest stems partly from the high prevalence of adversity and the omnipresence of resilience across the lifespan. Most research in psychological sciences focuses on protective factors that buffer the effect of stress and adversity and promote resilience. Despite its intuitive conceptual appeal, models that test the strengthening effects of stress (e.g., stress inoculation or the steeling hypotheses) are seldom tested or shown in developmental resilience research. The present paper sought to homogenize this body of research by introducing a psychosocial hormesis model in psychological sciences in general and in developmental science in particular.

The lack of empirical evidence on the strengthening effect of stress among children and youth hinders progress in child development research interested in generating knowledge on the inoculation mechanisms and potential applications of the resilience processes. Why strengthening through adversity effects are rarely investigated in developmental science is hard to determine, yet a couple of plausible hypotheses emanate from the present paper. Perhaps the existence of multiple metaphors to describe strengthening via adversity (e.g., steeling or toughening), and the fact that this effect is vaguely defined, impedes empirical research from effectively operationalizing and testing strengthening processes statistically. Another possibility may lie in the challenge of investigating and experimentally implementing the strengthening effect in basic and prevention science, respectively. How can investigators induce stress or “toxic experiences” to model potential benefits against future stress? Similarly, how can prevention programming dictate adversity to instill strengths when such an implementation can be ethically problematic and experimentally challenging? These questions render it essential to discuss the specifics of applying the hormesis model to the study of resilience in developmental science.

With the question of understanding the prevalence of resilience, more recent research has been seeking to examine the latent evolutionary benefits of exposure to psychosocial adversity (Ellis et al., 2017). Hormesis is particularly relevant for the accumulating body of research that views resilience as an *ontological* (within an organism’s lifespan) adaptation process to challenging input from specific environments (Forbes, 2000). The focus on the preconditioning mechanisms and the inoculation process are critical in the hormesis model as these concepts are theoretically based on evolutionary adaptive responses (Mattson, 2010). Thus, the hormesis model is particularly applicable to studying resilience across the lifespan and in multiple developmental contexts. However, rarely do stress adaptation models use

hormesis to elucidate resilience processes. Further analysis is needed on hormetic effects and their association with resilience in humans. It is proposed here that the hormesis model has the potential to augment testable hypotheses in the process of human resilience.

Transferring the hormetic concept from the biological disciplines to psychological science requires further conceptual refinement to avoid misuse of the idea. Each domain of resilience in developmental science (e.g., family, cognitive, stress biology) should formulate a mechanism for how a specific kind of low-grade adversity may lead to an inoculation process in the individual. The hormesis model may shed light on the limited but meaningful effect of low-to-moderate adversity and related stress, thereby serving as a guiding principle for examining human resilience. Consequently, the concept of hormesis bears a promising potential for generating novel resilience and developmental science hypotheses by inviting studies to seek new conditions that induce stress inoculation processes.

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Note

1. Historically, the documentation of preconditioning was referred to as radio-praxis by the French embryologist Paul Ancel, who published multiple experiments with x-rays and plants. Ancel showed that pre-exposing lentil plants to X-rays boosted their growth and shielded them from future structural damage. In contrast, exposure to excessive X-ray doses would rapidly destroy non-“preconditioned” plants (See Calabrese 2013 for detailed review).

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