A Developmentally Informed Perspective on the Relation Between Stress and Psychopathology: When the Problem With Stress Is That There Is Not Enough

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A common tenet of several prominent theories of stress and psychopathology (e.g., stress exposure) is that experiencing high rates of life stressors is associated with greater risk for negative mental health outcomes. Although there has been substantial empirical support for this position, another possibility that has received considerably less attention to date is that early life stressors may share a curvilinear rather than monotonic relation with psychological well-being. In what has been termed the "steeling effect," "stress inoculation," and "antifragility," exposure to moderate stressors early in life may confer resilience to potential detrimental effects of later stressors. An interesting implication of this model is that *low* levels of early life stressors, relative to normatively moderate rates, may be associated with greater sensitivity to future stressors. The present article reviews preliminary evidence consistent with this possibility, drawing on behavioral and neurobiological studies in animal models, and the more modest literature on neurocognitive, psychological, and psychophysiological functioning in humans. Limitations of the clinical literature and possible directions for future research are discussed, including naturalistic longitudinal studies with clinical outcomes, and for research examining moderators and mechanisms, across multiple levels of analysis (e.g., cognitive, immunological, and neurobiological).

Keywords: life events, psychopathology, resilience, steeling effect, stress

The notion that stressful life events often precede and confer heightened risk for negative mental health outcomes has long been the subject of considerable theoretical and empirical interest.[1] Indeed, this basic stress exposure model of psychopathology, and particularly a subsequent elaboration, the diathesis-stress model (i.e., the notion that stressors interact with preexisting diatheses to increase risk for mental illness), feature prominently in several theoretical conceptualizations of psychopathology (e.g., Beck, 1987; Nock, 2010; Nolen-Hoeksema, 1991; Walker, Mittal, & Tessner, 2008). Consistent with these models, life stressors have been implicated in the etiology of several forms of mental illness (Beards et al., 2013; Klauke, Deckert, Reif, Pauli, & Domschke, 2010; Liu & Miller, 2014), particularly depression (Hammen, 2005; Kessler, 1997).

A basic assumption underlying stress exposure models of mental illness is that the risk for disorder associated with stressful life events operates in a linear fashion. This assumption also holds true across different conceptualizations of diathesis-stress interactions. In particular, one common characterization of diathesis-stress in-

teractions is that both life stress and the diathesis of interest are dimensional constructs and interact in an additive manner (e.g., Abramson, Metalsky, & Alloy, 1989). That is, in what is essentially a titration model, a high loading on the diathesis requires only a modest amount of stress for risk for the negative outcome in question, whereas a low diathetic loading requires a greater amount of stress for comparable risk for the same outcome. Regardless of diathetic loading, however, increases in life stressors are assumed to be associated with corresponding increases in pathogenic risk. Although other diathesis-stress models differ in their characterization of the diathesis (i.e., as purely dichotomous, or taxonic with dimensional variation within the taxon), they are nonetheless consistent in positing that a monotonic relation exists between life stressors and risk for mental illness once the diathetic threshold has been reached (for a more detailed discussion of these different characterizations of diathesis-stress interactions, see Monroe & Simons, 1991).

Drawing on a developmental perspective, the current article discusses and elaborates on an interesting additional possibility that has garnered considerably less empirical attention to date, but which has potential to refine our understanding of the relation between life stressors and psychopathology. That is, life stressors,

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[1] The current review follows Brown and Harris's (1978) approach to defining stressor severity based on the objective impact an event would have on a typical individual under identical circumstances. This approach separates out individual differences in subjective stress response to the event, which is instead viewed within this conceptual framework as a product of objectively occurring stressors and an individual's pre-existing vulnerabilities (i.e., a diathesis-stress interaction; for detailed discussions of this issue, see Hammen, 2005; Liu, 2013; Monroe & Harkness, 2005).

particularly during childhood, may have a curvilinear rather than linear relation with risk for psychopathology later in life. More specifically, in what has been termed the "steeling effect" (Garmezy, 1986; Rutter, 2012), "stress inoculation" (Dienstbier, 1989; Gunnar, Frenn, Wewerka, & Van Ryzin, 2009), and "antifragility" (Taleb, 2012), exposure to moderate stressors early in life may confer resilience to potential detrimental influences of later stressors.[2] Within the context of the steeling effect, moderate stressors (or "positive" stressors according to a recent lexicon; Shonkoff et al., 2012) are not overwhelming, yet are sufficiently challenging to present an opportunity for the development of endogenous resources better to manage future stressors. In contrast, severe stressors typically overwhelm the individual's current ability to manage them, and minimal stressors are not sufficiently arousing significantly to stimulate the development of relevant resources.[3]

It then follows that *low* levels of early life stressors, relative to moderate ones, may be associated with greater sensitivity to future stressors. This position is consistent with the view that resilience emerges from normative rather than rare or exceptional developmental experiences and processes (i.e., overcoming common and moderate rather than extreme adversity, such as a reduced contact with a close older sibling moving away to college in contrast to losing the sibling to a tragic accident; DiCorcia & Tronick, 2011; Masten, 2001).

The current review begins with an overview of preliminary evidence supporting the existence of steeling in animal models, before turning to the even more modest literature on the steeling effect in humans. Apart from one notable exception indicated below, only research intended to assess the steeling effect is discussed. Next, this article will discuss several limitations that characterize the existing literature, and provide recommendations for future methodological advancement. Finally, it will conclude by articulating potential mediating mechanisms, across multiple levels of analysis that may underlie the steeling effect as it relates to mental illness, with the view of informing future research in this area. Although the steeling effect may be to some degree involved in the etiology of several forms of psychopathology, a transdiagnostic discussion of steeling is beyond the scope of the current article. Instead, the primary focus will be on its potential relevance to depression, this being perhaps the one disorder that has received the most theoretical and empirical consideration to date in relation to life stressors.

Empirical Findings

Animal Studies

Evidence from existing studies comes primarily from the animal literature, particularly research conducted with rodents and nonhuman primates. It should first be noted that interpretation of the following findings as supportive of the steeling effect must be tempered by the observation that these studies generally examined their outcomes of interest in relation to a very limited range of early stressors, with stressors at two levels of intensity (e.g., absence vs. presence of stress) being most common. Therefore, these studies offer only a partial test of the steeling effect, and must be regarded as preliminary until validated by research demonstrating a *curvilinear* relation between a full range of stressors and these same outcomes.

Early studies in this area found that, when compared with counterparts in a nonstressor (i.e., nonhandled) condition, neonatal rats in a moderate stressor condition, operationalized as postnatal handling, which included brief, repeated maternal separations (e.g., for 3–15 min), displayed improved learning, a greater tendency to explore their environment, a reduced behavioral fear response and an attenuated hypothalamic-pituitary-adrenal (HPA) axis response to stressors experienced in adulthood (Denenberg, 1964; Levine, 1957; Lyons, Parker, & Schatzberg, 2010; Meaney, 2001). In one interesting study that attempted to approximate the effects of moderate stressors (operationalized as brief handling) on negative symptoms of schizophrenia, pups in the moderate stressor condition, when compared with those in the nonhandled condition, were less affected by phencyclidine (i.e., a compound known to produce and worsen schizophrenia symptoms in humans) and exhibited lower levels of the HPA-axis mediated stress hormone ACTH in response to a subsequent stressor (Tejedor-Real, Sahagún, Biguet, & Mallet, 2007).

A very similar pattern of findings has been documented in a series of studies with squirrel monkeys. In particular, when compared with nonstressed counterparts, infant squirrel monkeys in the moderate stressors condition, operationalized as temporary separation from their natal group, exhibited an eventual reduction in basal levels of several stress hormones (i.e., ACTH and cortisol) when placed in a novel environment. Although monkeys in both conditions experienced initial increases in both ACTH and cortisol levels in response to being placed in the novel environment, these increases were less pronounced in those in the moderate stress condition. Moreover, monkeys in the moderate stress condition displayed reduced anxious behavior, as well as greater exploratory behavior and food consumption in the novel environment (Parker, Buckmaster, Schatzberg, & Lyons, 2004). A comparable set of findings comes from another study (Parker et al., 2007) also operationalizing moderate stressors as temporary separation from the natal group during infancy. When compared with the no-stressors condition, the moderate stressors condition was associated with greater curiosity and novelty-seeking behaviors in adolescence (i.e., exploration of a novel environment, object exploration, and preference for interaction with novel rather than familiar objects).

Evidence consistent with the steeling effect has been found not only for behavioral and psychophysiological outcomes, but neurocognitive ones as well. Operationalizing early moderate stressors

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[2] For ease of discussion, the term "steeling effect" will be used in reference to this phenomenon throughout the rest of this article.

[3] It is worth briefly mentioning that although the steeling effect may initially seem to contradict other models of life stressors, particularly stress sensitization, the two are in fact complementary processes. Stress sensitization is the view that after experiencing of life stressors or depression, individuals become sensitized to the depressogenic effect of future stressors such that the level of stressors required to trigger recurrent depression is lower than that needed to precipitate first onset (Monroe & Harkness, 2005; Post, 1992). Both the steeling effect and stress sensitization may be similar in being the product of early stress experiences, but differ in the nature of the stressors involved. Just as the steeling effect is the potential product of *moderate* stressors, so may stress sensitization result from *severe* stressors. Indeed, severe childhood adversity, particular child abuse, has been previously implicated in depressogenic stress sensitization (Hammen, Henry, & Daley, 2000; Harkness, Bruce, & Lumley, 2006; Kendler, Kuhn, & Prescott, 2004).

as involving temporary removal from the natal group, one study (Parker, Buckmaster, Justus, Schatzberg, & Lyons, 2005) found evidence of better performance in this condition than in the non-stressed condition on a later cognitive control task. Consistent with this finding, moderate stressors experimentally induced using this paradigm are associated with greater prefrontal myelination and larger ventromedial prefrontal cortices (Katz et al., 2009), areas of the brain that have been associated with poorer decision-making and reduced activation in suicidal individuals (Bridge et al., 2012; Currier & Mann, 2008; van Heeringen, Bijttebier, & Godfrin, 2011).

Although the studies discussed thus far have focused on steeling arising from stressors experienced in early life, there is some evidence consistent with the possibility that moderate stressors in adulthood may also produce a steeling effect. A moderate social stressor condition, operationalized as temporary separation from a companion, when compared with a nonstressor control condition, was related in one study (Lyons, Buckmaster et al., 2010) to subsequently greater hippocampal neurogenesis in male squirrel monkeys and corresponding improvements on a spatial learning task.

Finally, it should be noted that an early controversy regarding maternal separation paradigms (e.g., handling in the case of rodent pups, and separation from the natal group in the case of monkeys) stemmed from the initial view that, rather than a reflection of steeling, the better outcomes observed with the maternal separation conditions were maternally mediated (Smotherman & Bell, 1980). That is, maternal separations elicited greater maternal stimulation when handled rats were returned to their nests (e.g., nursing, licking, and grooming behavior), and, in some cases, this increased maternal care was sustained across development (Lee & Williams, 1974; Lyons, Parker et al., 2010). It has been argued that this greater maternal care, rather than the moderate stress of separation, was what conferred later-life resilience.

Subsequent studies have addressed this controversy by removing the confound of increased maternal care in examining moderate stressors. One such study (Parker et al., 2006) compared monkeys in three conditions: a moderate stressor condition operationalized as temporary removal from the natal group and the mother; another moderate stressor condition operationalized as temporary removal with the mother, from the natal group; and a nonstressed condition involving no separation from the natal group. There were no differences between the two moderate stressor conditions in terms of long-term changes in maternal attention. In fact, monkeys in the moderate stressor condition that did not involve separate from their mothers experienced a short-term reduction in maternal care when returned to the natal group. Both moderate stressors conditions, when compared with the non-stressed condition, were associated with milder HPA-axis activation in response to stressors in adulthood.

Collectively, these studies are suggestive of the potential positive effect of moderate stressors across different levels of analysis, by behavioral responses later in childhood and adulthood to stressful stimuli (e.g., a novel environment), performance on cognitive tasks, neurotransmission, neuroendocrine functioning, and neurodevelopment, particularly in brain regions known to be particularly sensitive to stress (i.e., prefrontal cortex, hippocampus, and amygdala; McEwen, 2007) and structural and functional differences in certain forms of psychopathology (e.g., depression; Clark,

Chamberlain, & Sahakian, 2009). One clear and unique advantage of these analogue studies of steeling in animal models is that the experimental control in stress induction protocols allows for greater confidence regarding the causal nature of any observed relation, and that it is not simply due to confounding variables. Nonetheless, what is notably less clear is the translational validity of these findings to clinical phenomena in humans. More specifically, it is uncertain to what degree these findings accurately model the pathogenesis of negative mental health outcomes in humans.

Human Studies

Although the animal literature described above is notably limited, the research evaluating the steeling effect in humans is more modest still, particularly within the context of predicting mental health outcomes. Indeed, no study to date has directly assessed its relevance to clinically significant outcomes and related impairment (e.g., whether early life stressors share a curvilinear relation with risk for depression, when confronted with stressors later in life, as well as severity of symptoms, course, and related functional impairment). Presented below is a discussion of research on the steeling effect and cognitive and neurobehavioral functioning in humans, followed by a review of studies of this phenomenon in relation to mental illness.

Support for the steeling effect comes from a study by Gunnar, Frenn, Wewerka, and Van Ryzin (2009), which found a complex relation between early life stressors, operationalized in terms of duration of institutional care history, and neuroendocrine reactivity. In this study, three levels of stressor severity were compared: a nonstressor condition operationalized as having no history of adoption, a moderate stressor condition consisting of early adoption/foster care, and a severe stressor condition as operationalized as later adoption/foster care placement. Children in the moderate early stress condition exhibited reduced cortisol activity in response to the Trier Social Stress Test in comparison with children with minimal and severe stress conditions. Interpretation of these findings within the context of the steeling effect is qualified, however, insofar as institutional care and foster care involve non-normative and often severe early stressors, and thus differ from the moderate stressors hypothesized to be most relevant to the steeling effect (DiCorcia & Tronick, 2011; Masten, 2001). In a series of studies, Seery and colleagues found cumulative lifetime adversity, as measured as a dimensional construct with a life event checklist across several event categories (e.g., personal health, relationships, environmental disasters), to be curvilinearly related to impairment and health care utilization in a sample of predominantly middle-age adults with chronic back pain (Seery, Leo, Holman, & Silver, 2010), as well as to cardiovascular reactivity to an ostensible intellectual assessment test, and to pain tolerance in response to a cold pressor task in college students (Seery, Leo, Lupien, Kondrak, & Almonte, 2013).

As for studies of clinically relevant outcomes, one of the first in this area longitudinally followed children living during the Great Depression (Elder, 1974). Although not originally designed to test the steeling effect, this study found that older children, compared with younger ones, tended to exhibit better emotional and psychological functioning in the long run. The reasoning was that older children were more directly exposed to the stress of the socioeco-

nomic hardships of the time, having to assume adult responsibil-
ities to help the family. The skills and experiences thereby ac-
quired placed them well for managing future stressors. A confound
exists, however, which complicates interpretation of this study as
supportive of the steeling effect. That is, fathers who experienced
significant financial loss tended to become more irritable, punitive,
and inconsistent in disciplining their children, and boys old enough
to find employment outside the home were exposed to less of this
chronic stress than were younger counterparts (Elder, 1974). An-
other study observed a curvilinear relation between a continuous
measure of early family related stressors and an implicit, but not
explicit, measure of anxiety in a female adult sample (Edge et al.,
2009). Early family related stressors were measured continuously
using a self-report checklist of an array of parenting experiences
between early childhood and mid-adolescence (e.g., arguments
between parents). An acknowledged limitation of this study is its
selection of adults free of current psychopathology, which signif-
icantly constrains its generalizability to clinically significant anx-
iety.

Perhaps the most methodologically rigorous test of the steeling
effect with clinical phenomena to date comes from a study of
cumulative lifetime adversity, measured continuously with a life
events checklist across multiple domains, in a nationally represen-
tative adult sample in relation to posttraumatic stress disorder
(PTSD) symptoms, general psychological distress, and functional
impairment (Seery, Holman, & Silver, 2010). For all outcomes,
low and high lifetime adversity, relative to moderate lifetime
adversity, were associated with poorer response to recent stressors
(i.e., over past 6 months), assessed as a continuous variable using
the same measure for lifetime adversity. Although perhaps offering
the strongest support thus far for the steeling effect in the context
of mental health outcomes, a limitation of this study was that its
measure of functional impairment was based on interference due to
either physical or emotional health, and thus it was impossible to
ascertain the effect for this outcome that related uniquely to
psychological impairment.

Future Directions: Definitional Considerations, Methodologies, and Mediators

Definitional Considerations

An issue in need of clarification is the precise nature of stressors
involved in the steeling effect. Even if defined as moderate and
normative stressors that are sufficiently challenging to allow for an
opportunity to develop skills to cope with future stressors, other
important considerations remain. In particular, one definitional
challenge is that individual differences may exist in what consti-
tutes a moderate stressor. It is likely that the level of stressors that
may be termed "moderate" and conducive to the development of
resilience mechanisms underlying the steeling effect is not the
same across all individuals. Rather than a single specific and
uniform set-point, it seems likely to be dependent upon, or mod-
erated by, individual differences in preexisting resilience and vul-
nerability factors (see Figure 1). For example, a specific stressor
may be moderate for an individual who has already developed a
degree of resilience from prior steeling experiences, but relatively
more severe for another individual without this same level of
preexisting resilience.

In terms of preexisting vulnerability factors that may moderate
the level of stressor required for resilience factors emerge, endur-
ing personality variables appear to be promising candidates. Al-
though several personality traits may serve to facilitate or hinder
the steeling effect, one trait that may be of particular importance
here is neuroticism, defined as the tendency to experience distress
and negative affect (Eysenck, 1967; John, Robins, & Pervin,
2008). This trait has been associated with a host of mental disor-
ders, especially depression. Indeed, neuroticism is not only asso-
ciated with depression, but also with a worse prognosis for this
disorder (Goldstein & Klein, 2014). This trait has also be associ-
ated with greater stress sensitivity (Espejo et al., 2011), and has
been found to interact with life stressors to predict depression
severity and a worse course for this disorder (Brown & Rosellini,
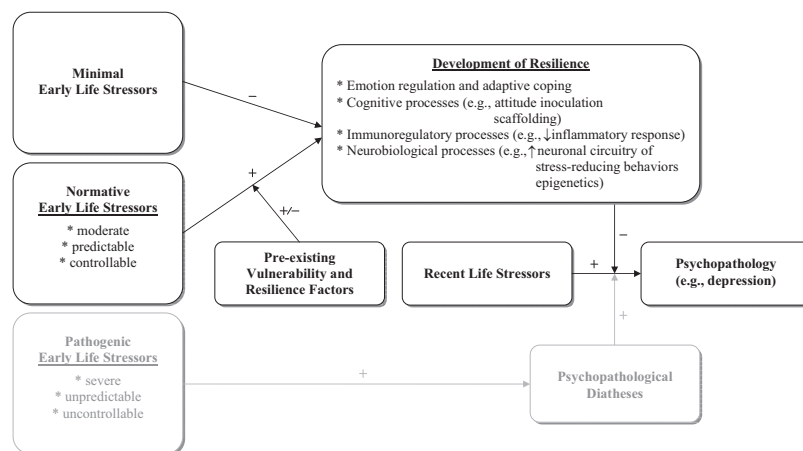

Figure 1. A model of potential mediational and moderational processes underlying the steeling effect. Note:
For context, the pathway through which severe early life stressors confer heightened risk for negative mental
health outcomes is included in gray font. + indicates a positive relation; − indicates a negative relation.

2011). Given the stress sensitivity associated with neuroticism, it is conceivable that the level of stressor required for a steeling effect may be lower in individuals high in this trait relative to those with low neuroticism.

A personality trait related to the broader construct of neuroticism and implicated in depression (Beck, 1987) is a hopeless or pessimistic cognitive style. Pessimism may interact with moderate stressors to shape the development of resilience. In particular, it would not be unreasonable to expect that pessimists who hold negative expectations of success in overcoming moderate stressors may be less likely to persist when they encounter one, and are thus unlikely to develop the skills to master future ones. In contrasts to more optimistic counterparts, pessimists have a tendency to adopt avoidant coping strategies, particularly when confronted with an immediate stressor (Carver, Scheier, & Segerstrom, 2010; Nes & Segerstrom, 2006).

The degree to which such dispositional factors moderate the emergence of resilience factors following moderate stressors remains unknown. Empirical consideration of such factors is important insofar as it may yield a more comprehensive understanding of the steeling effect. If these traits do indeed exert a moderational effect on the processes involved in the steeling effect, their exclusion may potentially obscure the presence of this phenomenon. It may be, for example, that moderate stressors lead to the development of resilience skills associated with the steeling effect, but only among individuals low in pessimism. Alternatively, it may be that the stressor severity threshold for the steeling effect to occur is lower among those high in pessimism than low pessimism counterparts. Clarification of the exact nature of this relation awaits future research.

Age differences may also exist with the steeling effect. More specifically, although there appears to be preliminary evidence that resilience related to this phenomenon may result from moderate stressors occurring at different stages across the life span, from the infancy into adulthood (e.g., Lyons, Buckmaster et al., 2010), childhood may be a particularly important time for the development of the steeling effect. In fact, childhood stressors appear to have more lasting effects than do those occurring in adulthood (Zannas & West, 2014). Just as childhood may be a period of particular sensitivity to the long-term effects of severe stressors in relation to stress-related psychopathology (e.g., depression; Cyranowski, Frank, Young, & Shear, 2000; Weber et al., 2008, and suicidal behavior; Pompili et al., 2011), so too may this be the case for the potential beneficial effect of moderate stressors. That the majority of studies to date have focused on stressors in childhood and adolescence is consistent with this view.

If childhood is indeed a sensitive period to the development of resilience through the steeling effect, an important next step would be to delineate the developmental processes underlying this period of sensitivity. For example, the transition to adolescence is marked by an increase in the rates of life stressors (Compas, Davis, & Forsythe, 1985), particularly interpersonal ones in girls (Rudolph & Hammen, 1999). This may be in some measure due to the greater autonomy and importance of peer relationships often observed at this age (Bhavnagri & Parke, 1991; Rudolph & Hammen, 1999). Therefore, it may be that this period of development affords individuals with increased exposure to moderate stressors, and thus opportunities to develop the resilience associated with the steeling effect. Whether, and why, certain periods of development are in

fact especially sensitive to the development of the steeling effect, however, has yet to be empirically assessed. Future studies directly comparing moderate stressors experienced in different age groups are necessary to resolve this question adequately.

Individual differences in moderators of the stressor severity level required for steeling to occur may be determined in examinations of mediating mechanisms of the steeling effect. To the degree that individual differences do indeed moderate the stressor severity threshold for resilience mechanisms associated with steeling, tests of moderated mediation are especially applicable. It may be, for example, that variation in genetic correlates of neuroticism (e.g., the 5-HTT gene; Canli & Lesch, 2007) interact with early stressors in predicting subsequent development of neurobiological mechanisms that confer resilience to future stressors. Potential mediators of the steeling effect are discussed in more detail below.

Several other notable properties of moderate stressors are hypothesized within the context of the steeling effect to be associated with subsequent resilience. For example, whereas stressors that are unpredictable (e.g., sudden death of a healthy relative due to violent circumstances) and uncontrollable (e.g., moving away because of changes in parents' employment situation) are associated with greater stressor severity, stressors that are predictable (e.g., death of a relative after a period of declining health) and controllable (e.g., moving away for college) are generally viewed as less severe.

Such stressor properties are accounted for in state-of-the-art contextual threat life stress interviews (e.g., Bifulco et al., 1989; Hammen & Brennan, 2001). Event characteristics such as suddenness or unexpectedness of the event, as well as its frequency and having a past history of similar events, are incorporated in determinations of each event's stress severity. These interviews are also designed to separate out subjective stress appraisals influenced by preexisting vulnerability factors from objectively determined stress ratings (for a discussion of the importance of this issue, see Hammen, 2005; Monroe & Harkness, 2005).

Although such interview-based approaches may reliably differentiate individual events in terms of their relative level of severity (Daley, Hammen, & Rao, 2000), it would be important to conduct a comprehensive assessment of early stressors, rather than to focus on individual stressors in isolation; the potential beneficial effect of a moderate stressor may be offset by a substantially more severe one. The challenge then is in determining what constitutes moderate stressors relevant to the steeling effect, not at the level of individual stressors, but at the cumulative level. That is, what range of cumulative stressors is associated with steeling? As noted above, this challenge is compounded by individual variability in what may be termed moderate stressors. Furthermore, the marked paucity of research in this area leaves the answer to this question decidedly unclear.

One potential means of empirically moving toward greater conceptual clarity regarding the parameters of cumulative minimal, moderate, and severe stressors may be initially to assess different levels of stress in purely relative terms. For example, this could involve comparing the average stressor level with high and low stressor levels in relation to depression in a given study. Another basic approach to determining what constitutes moderate stressors could be to observe the stressor level corresponding to the peak in the curvilinear relation between a continuous measure of cumulative stressors and depression. Although such approaches

are admittedly crude, they may serve as a useful starting point to build more sophisticated models of the steeling effect, incorporating, for example, considerations of individual differences in the likelihood of experiencing steeling when exposed to moderate stressors as determined in the initial investigations (i.e., intrapersonal moderators). Additionally, one approach that may provide a relatively more nuanced understanding of the steeling effect may be to examine potential preexisting intrapersonal factors positively and negatively associated with depression across a range of stressor severity.

Another unresolved issue is whether specific types of stressors are most relevant to the steeling effect. Do interpersonal stressors (e.g., conflict with a friend), for example, differ from noninterpersonal ones (e.g., parent becoming unemployed) in their potential to lead to the development of resilience associated with steeling? The answer, in large measure, depends on what forms of psychopathology are influenced by the steeling effect. If moderate but not severe stressors confer a steeling effect, and a curvilinear relation is predicted, it stands to reason that depression and other stress-related disorders (i.e., those precipitated by severe stressors) may be promising candidates. A well-documented relationship exists between life stressors and depression (Hammen, 2005). Inasmuch as interpersonal stressors, in particular, have been implicated in the etiology of this disorder (Hammen, Marks, Mayol, & DeMayo, 1985; Kendler, Gardner, & Prescott, 2002), future research assessing for curvilinearity in this relation is warranted.

A similarly intriguing possibility is that a degree of specificity may exist between the types of moderate early stressors an individual experiences and the types of future stressors in which this individual may later experience steeling. For example, it is conceivable that moderate early interpersonal stressors may be more associated with steeling in the context of future interpersonal stressors than in the context of other types of stressors (e.g., financial stressors). Such a possibility, in some measure, mirrors diathesis-stress congruency models of depression, according to which risk for this disorder is greatest when there is a match between an individual's vulnerability and the type of stressor the individual experiences (for a discussion of the literature in this area, see Hammen, 2005). The possibility of similar congruency between early stressors and resilience to subsequent ones would be important to consider empirically, and would require assessment of stressors across a broad range of contexts.

Methodological Considerations

Collectively, the current studies provide preliminary support for the relevance of the steeling effect in humans. Although studies directly relating to psychiatric outcomes are notably lacking, the existing findings validate the need for additional research. Several important methodological considerations merit discussion to guide future studies in this area.

First, the steeling effect essentially involves an interaction between early and recent life stressors in predicting depression. That is, the strength of the relation between the proximal stressors and risk for depression is dependent upon the severity of distal stressors, with individuals who experienced moderate early stressors being least vulnerable to recent ones. This model would predict the differences between low, moderate, and high early-life stressors in relation to depression to be relatively small in the absence of more

recent stressors. In contrast, these differences would be magnified significantly when recent stressors are moderate to severe, with individuals who experienced moderate early-life stress being less vulnerable to recent ones than are those who experienced minimal and severe early stress (see Figure 2). Thus far, only one study has explicitly evaluated the interaction component of the steeling effect (Seery, Holman et al., 2010), with the rest assessing main effects for early-life stressors in relation to outcomes of interest.

A second methodological consideration is the need for fully prospective assessments, particularly in the case of early-life stressors. All human studies of this phenomenon utilized evaluations of the cumulative occurrence of earlier stressors recalled over lengthy retrospective periods in adulthood (for discussions of limits of recall for life events, see Brown & Harris, 1982; Monroe, 1982; Paykel, 1997).

Third, all previously mentioned human studies of episodic stressors featured life stress checklists, with a summary of endorsed event items serving as an indicator of the stressor severity. This approach, however, is generally insensitive to fine-grained distinctions between life stressors of differing levels of severity. In cases where sensitivity in measurement of stressor severity is paramount, the previously mentioned contextual threat interviews (e.g., Bifulco et al., 1989; Hammen & Brennan, 2001) offer substantial advantages over self-report life events inventories (for detailed discussions of this methodological issue, see Hammen, 2005; Monroe, 2008).

Furthermore, to establish the clinical relevance of the steeling effect, or more specifically, the implication of low levels of early-life stressors, future research in this area should incorporate interview-based assessments of symptoms, syndromes, and related functional impairment. In addition to ensuring that the steeling effect is evaluated in relation to clinically meaningful outcomes, this approach facilitates precise dating of the onset of discrete outcomes (e.g., the onset of depression). When used in conjunction with life events interviews for etiologically relevant recent stressors, this approach allows for greater certainty in determinations of proximal stressors temporally preceding clinical outcomes of interest.

Research on the steeling effect is clinically informative to the extent that it yields potential targets for prevention and treatment efforts. Therefore, in addition to establishing that exposure to moderate early-life stressors confers resilience to psychopathology later in life, it would be important to elucidate the mediating
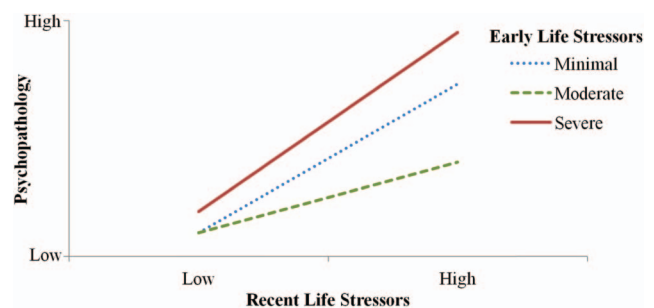

Figure 2. Risk for psychopathology as a function of the interaction between early and recent life stressors. See the online article for the color version of this figure.

mechanisms and moderators underlying this relation. How does exposure to moderate early-life stressors lead to the development of resistance to later stressors? To date, few human studies (for an exception, see Gunnar et al., 2009) have examined constructs closely related to psychopathology, and which may be potential candidates for mediators. Furthermore, none have evaluated potential personality traits that may exert a moderational influence on the steeling effect.

In summary, an ideal design for studying the steeling effect would feature a contextual threat life stress interview administered in early childhood to a sizable sample, so as to allow for substantial range in early-life stressor severity. Additionally, it would involve repeated measures of potential mediators and interview-based assessments of both life stressors and psychopathology continued prospectively into adulthood. To provide a full test of the steeling effect, several analyses could then be conducted. Specifically, if the steeling effect does indeed involve a moderational relation between early and recent life stressors with respect to subsequent psychopathology, several predictions would hold true in the presence, but not absence, of recent life stressors, and could be statistically tested: (a) a quadratic function would exist between early-life stressors and the psychopathological outcome variable of interest; (b) a similarly curvilinear relation would be observed between early-life stressors and the putative mediator; (c) the mediator would, in like manner, share a curvilinear relation with the mental health outcome variable; and (d) the mediator would account for the relation between early-life stressors and psychopathology. To the degree that these relations hold in the presence, but not absence of, of recent stressors, the steeling effect can be essentially described as a moderated mediation model.

Longitudinal studies of sufficient duration may in some ways prove challenging, especially given the time lag between early-life stressors and subsequent clinical outcomes. A fully prospective design is generally required, given that nonsevere stressors are retained in memory over fairly brief periods (Brown & Harris, 1982; Monroe, 1982). One promising option for employing preliminary tests of the steeling effect is to adopt a relatively short-term naturalistic longitudinal design, focusing on intermediate outcomes (i.e., potential mediating mechanisms of the steeling effect) rather than distal ones. What follows below is a discussion of several potential mediating mechanisms and moderators with suggestions for evaluating them.

Mediating Mechanisms

Within the context of the steeling effect, the long-term resilience associated with moderate early-life stressors is hypothesized to be the product of endogenous processes involved in navigating these same stressors (Rutter, 2012). Additionally, overcoming the psychophysiological arousal elicited by these moderate stressors may lead to lasting physiological adaptations that increase the individual's ability to manage more stressful events in the future (Chorpita & Barlow, 1998). Inasmuch as these processes are important to steeling, minimal early-life stressors may result in heightened risk for some of the same clinical outcomes as is the case for severe early stressors, but through markedly different processes (i.e., equifinality). That is, according to several etiological conceptualizations of psychopathology (e.g., Cole, 1990, 1991; Rose & Abramson, 1992), experiencing severe stressors in early childhood

may lead to the development of psychopathological diatheses. In contrast to being characterized by the *presence* of elevated diathetic loading, non-normatively minimal early-life stressors may result in greater sensitivity to future stressors, according to the steeling effect, because of a relative *absence* of resilience factors.[4]

In the same manner that the study of diatheses may yield promising targets of risk for clinical intervention, more clearly articulating the specific mediating mechanisms underlying the steeling effect is important insofar as they may point to potential targets for, and means of, strengthening resilience within the context of clinical treatment efforts. Drawing on the developmental and social psychological literatures, as well as neurobiological and immunological findings, several promising possibilities are elaborated below. A model of the steeling effect incorporating these potential mediators is summarized in Figure 1.

Emotion Regulation and Adaptive Coping

Several intrapersonal processes are likely to be involved in the steeling effect. Adaptive coping and emotion regulation may be especially relevant examples of such processes. Indeed, in some ways moderate stressors may function as an ideal context in which to develop and practice these skills. Specifically, they may present ecologically valid opportunities to acquire and exercise coping and emotion regulation skills, which may equip them well for managing more challenging stressors in the future. Again, the moderate stressors involved in the development of these skills should be elevated enough to induce a temporary negative affective state, but not so severe as to be overwhelming. This possibility is entirely consistent with a functional perspective on emotions in that moderate negative emotions are not viewed as wholly detrimental, but can be beneficial if effectively regulated and facilitate learning. For example, in an observational study involving an experimental frustration induction task, feelings of anger were associated with later increases in adaptive behavior in a healthy community sample of children (Dennis, Cole, Wiggins, Cohen, & Zalewski, 2009). This perspective regarding the potential beneficial effects of moderate stressors on adaptive coping is also notably consistent with principles underlying exposure-based treatments for anxiety disorders (e.g., exposure to stimuli eliciting distress of sufficient intensity to lead to the development of skills for coping with increasingly stressful stimuli in a fear hierarchy; Abramowitz, Deacon, & Whiteside, 2012). The potential relevance of adaptive coping and emotion regulation to steeling may be tested more directly, however, through assessing whether change in emotion regulation skills, between the start and end of a 6-month naturalistic follow-up period, possesses a curvilinear relation to the intervening life stressors. The degree of change in emotion regulation skills may, in turn, be subsequently assessed within a diathesis-stress framework in relation to later life stressors and depression.

Cognitive Mechanisms

Attitude inoculation, or inoculation theory (Aronson, Wilson, & Akert, 2007; McGuire, 1961, 1964), may offer an interesting

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[4] Also note that resilience and risk factors are relatively distinct constructs rather than simply opposite ends of the same continuum (Johnson, Wood, Gooding, Taylor, & Tarrier, 2011).

account from the social psychological literature for the development of resilience through the steeling effect. According to this theory, exposure to weak arguments against an individual's views should "inoculate" the individual to future arguments that pose stronger threats to these same beliefs. The initial argument should be sufficiently weak to pose no genuine challenge to the individual's views, but must still be strong enough to motivate the individual to counter it with arguments in support of their own beliefs. These newly formed counterarguments provide resistance to stronger future threats to the individual's views. This theory has received considerable empirical support (Banas & Rains, 2010).

This phenomenon may be similarly applicable to cognitive aspects of resilience relevant to the steeling effect. In particular, young children tend to possess positive self-views (Harter, 1988, 1990) and a tendency to maintain them (Rose & Abramson, 1992). In their developmental extension of the hopelessness theory of depression (Abramson et al., 1989), Rose and Abramson (1992) posited that elevated and repeated threats to self-esteem, especially verbal victimization, may lead to the replacement of benign or positive self-inferences with more negative inferential tendencies, resulting in cognitive vulnerability to depression when confronted with later stressors. Within the framework of inoculation theory, an intriguing sociocognitive account of the steeling effect may be that more moderate verbal threats early in life elicit the generation or reinforcement of positive self-inferences to counter these early threats (e.g., "I really am a good person; that person does not know what they are talking about"), with the consequence being that the individual becomes more cognitively resistant to stronger future interpersonal stressors threatening their self-esteem.

Finally, another potential cognitive explanation for how resilience is acquired with the steeling effect may be found in Vygotsky's (1978) concept of the zone of proximal development (ZPD). Vygotsky (1978) defined the ZPD as "the distance between the actual developmental level as determined by independent problem solving and the level of potential development as determined through problem solving under adult guidance or in collaboration with more capable peers" (p. 86). Interpreted within the context of the steeling effect, it may be that minimal stressors provide limited opportunities for potential instrumental, problem-solving, or adaptive skill development, the child consistently operating within their development level. Contrastingly, moderate stressors may function as a context within which the level of potential development may be achieved. Finally, severe stressors may present situations exceeding the child's level of potential development, and thus are experienced as overwhelming. Consistent presentation of such stressors may eventually lead to a feeling of lacking control, and eventually helplessness (Seligman, 1972), with subsequently encountered moderate stressors possibly yielding little potential for advancing toward the level of potential development. It should also be noted that Vygotsky (1967) suggested that the learning that occurs within the ZPD may at times be aversive (i.e., stressful), especially during experiences of short-term failure.

Importantly, when viewed within the framework of the ZPD, the steeling effect does not occur solely through intrapersonal processes. Rather, others facilitate the child's resilience skill development when confronted with a stressor (i.e., scaffolding).

The child may learn from observing their parents' appraisals and behaviors in response to the child's moderate stressor (i.e., parental modeling; Kliewer, Sandler, & Wolchik, 1994). Additionally, positive expressivity (i.e., the tendency to express positive emotions) in parents has been associated with better emotion regulation skills in toddlers and greater persistence when confronted with a stressor (Brophy-Herb, Stansbury, Bocknek, & Horodynski, 2012). It may be that this positive caregiver response provides the child with an optimal situation for practicing skill development.

Immunological Mechanisms

Given that the potential protective effect of moderate stressors has been described in terms of "inoculation" (e.g., Dienstbier, 1989; Gunnar et al., 2009) and "immunization" (e.g., Garmezy, 1986), it is perhaps not surprising that it has also been often viewed as analogous to immunization within the context of physical health. Of relevance to the current discussion, the hygiene hypothesis (Strachan, 1989) posits that the lack of early-life exposure to common pathogens (e.g., as a result of improved sanitation) leads to a reduction in childhood infections but also a corresponding increased likelihood of an underdeveloped immune system. As a consequence of this absence of immune training, moderate exposure to pathogens later in life results in an immunological hypersensitive reaction as manifested, for example, in asthma, allergies, and other autoimmune diseases. This hypothesis has received empirical support for several physical health outcomes (i.e., respiratory problems, Ball et al., 2000; Côté et al., 2010; colds, Ball, Holberg, Aldous, Martinez, & Wright, 2002; and ear infections, Côté et al., 2010).

An intriguing novel development is the extension of the hygiene hypothesis to account for one manifestation of psychopathology, depression (Raison, Lowry, & Rook, 2010; Rook, 2009), based in part on accumulating evidence linking proinflammatory cytokines and C-reactive protein to the pathophysiology of this disorder (Mills, Scott, Wray, Cohen-Woods, & Baune, 2013; Wium-Andersen, Ørsted, Nielsen, & Nordestgaard, 2013). According to this view, reduced exposure to microorganisms that stimulate immune responding early in life may result in the development of sustained elevations of depressogenic cytokines and lead to an exaggerated inflammatory response to future psychosocial stressors, thereby heightening risk for depression. Drawing on this immunoregulatory account of moderate early-life biological stressors and depression, one may find a certain parallel in accounting for the manner through which moderate early psychosocial stressors lead to the steeling effect. If this hypothesis holds true, and psychosocial stressors do indeed elicit an immunological response, moderate early-life psychosocial stressors, like normative early exposure to microorganisms, may induce immediate immune responding that leads to attenuated immune responses to subsequent psychosocial stressors.

Neurobiological Mechanisms

How may the steeling effect develop on a neurobiological level? Controllable and uncontrollable stressors may have differential effects on adaptive early-life neuronal functioning (Huether, 1996,

1998; Lehmann, Brachman, Martinowich, Schloesser, & Herkenham, 2013), the former potentially resulting in noradrenergic stimulation, which facilitates neuronal activation associated with behavioral responses to the stressor. Over time, the experience-dependent plasticity associated with intermittent exposure to these stressors strengthens the neuronal pathways relevant to enhanced behavioral responding. That is, the behaviors associated with the successful management of experienced stressors (e.g., instrumental, problem-solving, and coping strategies) and their underlying neuronal circuitry become reinforced (Zannas & West, 2014). In contrast, uncontrollable stressors also activate the release of corticotrophin releasing hormone (CRH) and vasopressin, which in turn activate the HPA-axis, and thereby glucocorticoid activity. A by-product of this stress response is the hippocampal atrophy previously described in animal models and characterized in depression (MacQueen & Frodl, 2011).

Indirect evidence suggestive of the possibility that the HPA-axis may function as a mediator of the steeling effect comes from a study that found neonatal exposure to moderate doses of glucocorticoids (operationalized as 33 mg/L) to be associated with enhanced performance on a cognitive flexibility task in adulthood relative to no-dose and high-dose (operationalized as 100 mg/L) conditions (Macrì et al., 2009). However, the potential effects of different stressor types at the neurobiological level, and by extension, the relevance of this distinction to the steeling effect, await direct empirical investigation (Franklin, Saab, & Mansuy, 2012; Saaltink & Vreugdenhil, 2014).

Finally, an intriguing possibility yet to be empirically assessed is that the steeling effect may involve mechanistic changes at the epigenetic level. There is recent evidence implicating severe early-life stressors in pathogenic epigenetic changes (e.g., via DNA methylation) linked to depression (Weder et al., 2014). An interesting possibility worth considering is that moderate stressors may also lead to epigenetic changes, but of a more adaptive nature. If an approximate analogy may be permitted, it could be noted that a moderate physical stressor in the form of voluntary exercise, when measured dichotomously, has recently been found be associated with hypomethylation at the BDNF (brain-derived neurotrophic factor) IV region and increase in BDNF expression (Gomez-Pinilla, Zhuang, Feng, Ying, & Fan, 2011). To evaluate the steeling effect, changes in degree of DNA methylation over a 6-month period may be assessed relative to stressors naturally occurring over the same intervening period. If a steeling effect does exist, a curvilinear relation should be observed.

Endogenous responses to parental experiences may also be an important factor in the potential epigenetic changes associated with the steeling effect. Indeed, there is an accumulating body of evidence that parent–child interactions can influence DNA methylation (Curley, Mashoodh, & Champagne, 2011), with a similar pattern of findings emerging in the animal literature (Champagne, 2013). For example, in one human study, parental support appeared to moderate the relation between low socioeconomic status and epigenetically modified proinflammatory signaling (Chen, Miller, Kobor, & Cole, 2011). Although the exact nature of this interaction remains to be elucidated, it may be that the positive influences of parental support are internalized by the offspring which manifest as changes at the epigenetic level, and these neurobiological changes, in turn, may

confer resilience to later stressors in a manner consistent with the steeling effect. To address this possibility, research on epigenetic changes associated with moderate stressors is needed to match the currently predominant focus and burgeoning literature on severe stressors.

Conclusion

Although several researchers have forwarded the view that early-life stressors may share a curvilinear relation with risk for negative outcomes in response to future stressors (e.g., Dienstbier, 1989; Garmezy, 1986; Gunnar et al., 2009; Rutter, 2012), empirical evaluations of the steeling effect in humans have been notably wanting, and remain largely absent from the clinical literature. Several significant methodological limitations are prevalent across the existing research, not least of which are the lack of fully prospective evaluations of this phenomenon and contextual threat life stress interviews necessary for accurate and sensitive measurements of stressor severity. Fully evaluating the steeling effect is admittedly challenging, not least because of the considerable follow-up time interval required between early-life stress assessment and the onset of the primary clinical outcomes of interest. Several methodological approaches (e.g., a naturalistic longitudinal design), as well as a focus on uncovering potential moderators and mechanisms as intermediate outcomes, may be promising means of advancing research in this area.

Despite the relative empirical neglect of the steeling effect in relation to psychopathology, its potential clinical implications are not insignificant. In particular, if moderate early-life stressors mitigate the pathogenic effects of later-life stressors through the development of resilience factors, it then follows that the experience of minimal early-life stressors prevents the child the opportunity to develop resilience, and consequently leaves him or her sensitive to subsequent stressors. Thus, in contrast to the well-known risk for psychopathology associated with severe early childhood experiences, individuals with minimal early-life stressors may be a relatively unrecognized and understudied at-risk subset of the population. Future research elucidating the processes through which resilience occurs with the steeling effect may have the potential to inform clinical intervention efforts with at-risk individuals at both ends of the early-life stress continuum. That is, inasmuch as the absence of resilience factors, rather than the presence of diatheses, best characterizes individuals with minimal early childhood stressors, the most relevant clinical intervention strategies are likely notably different than is usually the case with individuals with significant early stress experiences. Rather than assessing for and addressing potential diatheses, focusing on developing resilience factors, particularly in the form of adaptive coping, emotion regulation skills, and cognitive inoculation, may yield greater clinical gains.

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