

## 13

## Psychological Stressors: Overview

S.M. Monroe<sup>1</sup>, G.M. Slavich<sup>2</sup><sup>1</sup>University of Notre Dame, Notre Dame, IN, USA <sup>2</sup>University of California, Los Angeles, CA, USA

## O U T L I N E

<b>Historical and General Considerations</b>	<b>109</b>	<b>Human Life Stress Research</b>	<b>112</b>
<i>Historical Matters</i>	109	<b>Methodological Considerations and Recent Developments</b>	<b>113</b>
<i>Early Ideas and Research</i>	110	<i>Animal Laboratory Research</i>	113
<b>Conceptual Developments</b>	<b>111</b>	<i>Human Studies of Stressful Life Events</i>	113
<i>Stressor Characteristics</i>	111	<i>Human Studies Employing Other Measures of Psychological Stressors</i>	114
Animal Laboratory Research	111	<b>References</b>	<b>114</b>
Human Experimental and Field Studies	111		
<i>Individual Differences</i>	112		
Animal Laboratory Research	112		

## Abstract

Psychological stressors are social and physical environmental circumstances that challenge the adaptive capabilities and resources of an organism. These circumstances represent an extremely wide and varied array of different situations that possess both common and specific psychological and physical attributes. The challenge for theory, research, and practice is to abstract and understand the specific qualities and characteristics of environmental exposures that most strongly elicit noxious psychological and biological responses, which in turn can lead to serious mental and physical health problems over the life course. In the present article, historical perspectives and conceptual considerations are addressed first, which provides the context for the subsequent discussion of key issues for defining and assessing psychological stressors. Susceptibility to psychological stressors is subject to individual differences, which can alter the impact and adverse consequences of such environmental exposures, necessitating a discussion of these moderating influences as well.

HISTORICAL AND GENERAL  
CONSIDERATIONS

## Historical Matters

The term “stress” has become very popular in contemporary society, and is commonly invoked to explain a

wide variety of psychological and medical problems. Along with this fashionable trend, it is commonly assumed that psychological stressors represent a concern of particularly present-day origins, or at least that they have become much more prominent and pervasive with advances in modern technologies and the apparent quickening pace of life. As a consequence of these perceived pressures, it is also commonly believed that with this accelerating progress of civilization, more people are succumbing to mental and physical disorders than ever before.

Historical accounts, however, caution against such limited perspectives and suggest that similar ideas about stressors, civilization, and disease have been common for quite some time. Sir Clifford Allbutt<sup>1</sup> expressed such sentiments quite clearly well over 100 years ago, writing:

To turn now...to nervous disability, to hysteria...to the frightfulness, the melancholy, the unrest due to living at a high pressure, the world of the railway, the pelt-ing of telegrams, the strife of business...surely, at any rate, these maladies or the causes of these maladies are more rife than they were in the days of our fathers?

### KEY POINTS

- The terms “stress” and “psychological stressors” have a long and varied semantic history.
- Contemporary usage of these terms often reflects these varied, and often, vague meanings.
- More precise definitions and scientifically useful measures of psychological stressors have come from animal laboratory research as well as human experimental and field studies.
- Important themes for better understanding psychological stressors include the specificity of effects associated with particular types of psychological stressors and individual differences in response to psychological stressors.

The tendency to view life as being challenging or stressful may be even more basic to human cognition than is readily apparent. The Greek myth of Sisyphus is enlightening in this regard. The perpetual work of pushing a boulder up a mountain—only to have gravity bring it back down after each and every effort—captures some of the qualities and characteristics linked to modern views of psychological stressors and the challenges of everyday life. Perhaps there is something fundamental about the human condition and psyche that fosters a perception of the world as a place rife with unrelenting demands that can never be fully met, resulting in common subjective states of fatigue and distress that can lead to ill health. Each era may bring its unique colorations to such perceptions, and its own attributions regarding their origins.

It is against this perhaps universal psychological backdrop of belief and bias in thinking that modern work on psychological stressors must be critically examined. Psychological stressors and related concepts have been popular explanatory devices throughout recent, and not-so-recent, history. As a result of their phenomenological allure and tempting explanatory power, these ideas have often been loosely formulated and accepted at “face value.” Owing to conceptual fuzziness and ambiguity, not only has progress in science been slowed, but non-scientific issues and ideas are permitted to masquerade as scientific truths.

The concept of psychological stressors is rich with possibilities for shedding light on important matters in adaptation, dysfunction, and disease. The concept is paralleled, though, by the potential pitfalls that may accompany its intuitive, yet potentially misleading, appeal. The challenge is to translate the fertile ideas about psychological stressors into more precise concepts,

definitions, and operational procedures. With more sound definitional and methodological procedures in place, the utility of stress concepts for understanding adaptation and maladaptation in relation to mental and physical disorders will be better understood.

### Early Ideas and Research

A broad template for understanding the organism's reactions to challenging environmental circumstances was laid down by Claude Bernard and Charles Darwin during the nineteenth century. Each of these influential individuals in his own way touched on the tension resulting from the ongoing adaptation of the organism to changing and challenging environmental circumstances.<sup>2</sup> Yet it was not until the early-to-mid twentieth century that such generality and complexity was translated into more specific terminology and technologies. These efforts can be traced to at least three different lines of thought and research.

The early work of Walter Cannon dealt with ideas about common emotions and their physiological consequences, particularly with respect to the body's maintenance of homeostasis.<sup>2</sup> This line of study was complemented shortly thereafter by the animal laboratory studies of Hans Selye, wherein acute and severe stressors were systematically investigated. It was in Selye's work that the concept of stress most forcefully emerged. Stress was defined in terms of “the nonspecific response of the body to any demand” (Ref. 3, p. 74). Stressors, in turn, were defined as “that which produces stress” (Ref. 3, p. 78). Yet from another vantage point, Adolph Meyer popularized the “life chart” methodology. This approach emphasized the importance of the dynamic interplay between biological, psychological, and social factors, such that important life events became focal points for studying health and disease. Collectively, these activities, and the multiple lines of research they generated, served to initiate specific awareness of, and interest in, psychological stressors.<sup>4</sup>

Other developments arising outside of science also contributed to the emerging idea that psychological stressors could lead to both mental and physical disorders. Prior to World War II, psychopathology was predominantly attributed to genetic factors or to acquired biological propensities; so-called “normal” people without such taints were thought to be largely invulnerable to serious mental illness. However, World War II dramatically altered thinking in medical and psychiatric circles to incorporate the idea that severe stress could precipitate breakdowns in previously healthy individuals.<sup>2,4</sup> Once this conceptual shift began, it underscored the multiplicity of health consequences associated with severe stressors. It also opened the door for enlarging conceptual perspectives on

psychological stressors for considering how less severe, yet still aversive, aspects of the social and physical environment might also promote pathology.

## CONCEPTUAL DEVELOPMENTS

Upon the foundations of stress research and theory laid down by Selye, Cannon, and Meyer, along with the influences of experiences of World War II, contemporary inquiry into the effects of psychological stressors became a topic of increasing interest and, eventually, of extensive empirical inquiry. Two general themes can be discerned that underpinned advances in theory: first, characteristics of psychological stressors, and second, individual differences in response to psychological stressors.

### Stressor Characteristics

Despite general agreement about the importance of psychological stressors for health and well-being, determining exactly what it “is” about stressful circumstances that is deleterious has proven challenging. An initial question of considerable theoretical importance involved the basic nature of psychological stressors: Are they better viewed in a unitary manner as “nonspecific demands” on the organism (as Selye postulated) or as a class of conditions that harbor specific bodily demands? Investigators from two traditions—animal and human research—addressed this issue, with parallel and sometimes intersecting developments. Although considerable progress was made, stressor characteristics remain one of central topics of importance in current thinking on psychological stressors.<sup>4-6</sup>

### Animal Laboratory Research

A great deal of work in the 1960s and 1970s addressed whether specific psychological characteristics of stressors possess qualitatively distinct implications for the organism. Initially this work revealed how particular features associated with environmental stressors might be important for adverse outcomes (as opposed to the more psychologically neutral general, or nonspecific, adaptive demands). Such research went on to probe different types of psychological stressors and their effects. It became of central interest to understand in a more differentiated way the effects of diverse psychological stressors.

Animal laboratory studies adopted ingenious ways to differentiate psychological components associated with environmental stressors. The findings from these studies demonstrated that distinctive psychological characteristics were responsible for many immediate behavioral or physiological responses. For example, specific psychological characteristics of stressors, such as undesirability or

controllability, were important for the development of various disorders.<sup>7</sup> It became clear, too, that other characteristics of stressors were pertinent. For example, different parameters of shock administration (acute, intermittent, or chronic) produced distinctive physiological effects in animals. Further, such differences could increase, decrease, or not influence the development of particular diseases.<sup>2</sup> Lastly, psychological stressors could not only influence immediate psychobiologic functioning, but also have long-term effects by permanently altering the psychobiological characteristics of the organism.<sup>2</sup>

As the importance of specificity of stressor or “stimulus” characteristics became apparent, questions about the specificity of stress responses also arose. What were the implications of specific stressor characteristics for different facets of psychological and physiological functioning? Such theoretical developments greatly extended the framework for inquiry, requiring attention to multiple characteristics of stressors in relation to multiple psychological and biological processes and outcomes. Relatively simple, singular response indices (e.g., corticosteroids, catecholamines) were replaced by more complex patterns of behavioral and biological effects, or profiles of neuroendocrine responses. Other intriguing levels of conceptualization have been proposed. For example, psychological stressors may promote fundamental disruptions in oscillatory regulation of basic biological functions, or reversions to earlier modes of functioning.<sup>2</sup>

Overall, research on psychological stressors from animal research has moved beyond unidimensional and linear concepts of stressors and their effects. More recent thinking has adopted a larger framework for understanding the diverse characteristics of stressors that influence particular response systems of the organism. The systems of interest have expanded from single systems to patterns or profiles of response across multiple indices.

### Human Experimental and Field Studies

Investigators of psychological stressors in humans also conducted innovative laboratory and field studies.<sup>8</sup> The early work focused on the aversive subjective attributes, particularly perception or appraisal, of psychological stressors as evaluated in an experimental setting.<sup>8</sup> Research on stressful life events also began around this time, and it is in this area that research on psychological stressors perhaps reached its pinnacle in terms of both productivity and popular interest.

Extrapolating from animal laboratory studies on the one hand, and integrating with Meyer's life chart procedures on the other, Thomas Holmes and Richard Rahe first formulated the idea that distinctive changes in one's life circumstances—specific and documentable life events—could be defined and assessed in an objective manner. The work was initially based on case histories of some 5000 tuberculosis patients, from which they

derived a list of 43 life events “empirically observed to occur just prior to the time of onset of disease, including, for example, marriage, trouble with the boss, jail term, death of spouse, change in sleeping habits, retirement, death in the family, and vacation” (Ref. 9, p. 46). The Schedule of Recent Experiences (SRE) was developed and published,<sup>10</sup> and by 1978 alone, over 1000 publications had utilized this convenient method for probing questions pertaining to stress and illness.<sup>9</sup>

The common feature associated with these disparate life changes—the stressor characteristic of primary concern—was thought to be the degree of social readjustment caused by the event: “The relative importance of each item is determined not by the item’s desirability, by the emotions associated with the item, nor by the meaning of the item for the individual; it is the amount of change that we are studying and the relationship of the amount of change to the onset of illness” (Ref. 9, p. 47). This viewpoint is consistent with Selye’s ideas about stressors and stress (i.e., stress as the nonspecific response of the body to any demand). Hence, the psychologically neutral notion of the “readjustment” required of life changes was conceptualized as the characteristic responsible for vulnerability to a wide variety of psychological and physical maladies.

Much as the emphasis in animal laboratory studies shifted from psychological neutral concepts of “any demand,” the emphasis in the stressful life events literature shifted from the neutral concept of “readjustment” to concepts involving the undesirable social-psychological characteristics of events. Human studies of life events consequently began to focus on the particular characteristics of psychological stressors and their potentially unique effects. The principle of specificity also was extended from the characteristics of stressors to the specific consequences of such experiences, elaborating theory about the importance of specific psychological stressors for specific responses and eventually for specific types of disorder or disease.<sup>5</sup> A vast literature on this topic exists, with diverse conceptualizations of psychological stressors and myriad methods to measure them.<sup>6,11</sup>

Most recently, researchers have focused on interpersonal loss and social rejection as psychological characteristics that may make some experiences particularly deleterious for health and well-being.<sup>12</sup> Life events with these qualities, called “targeted rejection” events, are among the strongest precipitants of depression.<sup>13</sup> Additionally, there is some evidence that targeted rejection events uniquely trigger biological responses that promote disease.

Research on the desirability of events, along with the more general issue involving stressor characteristics, brought into focus another important topic in the study of psychological stressors and their impact on health and well-being: individual differences. What one person

might experience as being undesirable, another person could experience as being desirable. As discussed next, a variety of considerations come into play for explaining variability in the effects of psychological stressors on health.

## Individual Differences

There is considerable variability in response to psychological stressors across individuals. Even under extremely stressful conditions, not all animals or individuals breakdown. Additional factors are useful to effectively model the variability in effects attributable to psychological stressors. Progress in understanding this matter has again come from both the basic laboratory and human studies of psychological stressors.

### Animal Laboratory Research

Although there were characteristic features of physiologic responses to the stressors employed in the early paradigm adopted by Selye, not all animals responded to stress in an identical manner. Further, individual differences in response were even more pronounced when the less severe types of stressors were used.

Factors such as prior experience, availability of “coping” responses, and attributes of the social and experimental context (e.g., social ties) were found to moderate the influence of psychological stressors. For example, when rats are exposed to electric shock, animals that cannot predict shock occurrence (via warning tones) develop a six-fold increase in gastric ulceration compared to their yoked counterparts (who receive the warning tones).<sup>2,7</sup> Additional research demonstrated the delicate and often subtle interplay between stressor, social context, and resources available to the organism in moderating response outcomes. These lines of study, too, suggested that individual differences in susceptibility also could be viewed within a dynamic and developmental framework over time. For instance, laboratory animals repeatedly exposed to severe psychological stressors can become neurobiologically sensitized to the stressors, such that progressively less severe degrees of stress acquire the capability of triggering the pathogenic responses.<sup>14,15</sup> Moreover, considerable animal research has now demonstrated that exposure to stressors early in life can have long-lasting effects on stress reactivity over the life course.<sup>16</sup>

### Human Life Stress Research

The importance of individual differences is perhaps most apparent in studies of human life stress and its consequences. A consistent criticism of life events research was the relatively weak association between psychological stressors and disorder. It was assumed that many considerations moderated stress effects, and the elucidation of such factors would increase the predictive strength



of the association between psychological stressors and disorder. Again, a number of factors were believed to influence the impact of psychological stressors, ranging from environmental factors, such as the availability of social support, to more individual factors, such as prior experience and coping abilities. Developmental considerations also are important in recent theorizing about individual differences in reaction to psychological stressors, with the idea that prior exposure to severe psychological stressors renders individuals more sensitive and thereby susceptible to increasingly lower levels of psychological stress.<sup>14</sup>

A major arena for understanding individual differences in response to psychological stressors has been the topic of perception. The early and elegant laboratory studies of human stress indicated the importance of such individual differences in perception, or appraisal, of stressors, and such thinking was readily incorporated into theory and method.<sup>8</sup> Studies of life events, for example, would use subjective weights of events experienced by the study participants. Once this avenue of inquiry was opened, it also brought to the forefront a variety of influences on perception, along with other factors that might influence stress responsivity. Thus, research not only began to focus on appraisal of stressors, but also on coping, social support, personality, and other considerations that in theory could moderate the effects of psychological stressors.

Most recently, research has examined genetic factors that may shape health risk following psychological stressors. Some candidate polymorphisms have been identified, but empirical support for these factors has been mixed, likely due in part to poor stress measurement and the fact that polymorphisms exert effects only when genes are “turned on” by certain environmental influences.<sup>17</sup> As a result, a new field of research on “human social genomics” has emerged that examines how different psychological stressors activate genes that are relevant for health.<sup>18</sup>

As research progressed, it became clear that making some distinctions was easier in theory than in practice. Although it made good sense to consider an individual's subjective perception of psychological stressors, for example, employing such information in scientifically sound manner was difficult. When it came to measurement, serious problems became apparent. For example, owing to depression-based perceptual biases, a depressed person might have a skewed perception of events and rate them as particularly negative (irrespective of the objectively stressful qualities per se). Such concerns raised a paradox for investigations. Namely, while a large part of what one wants to know about pertains to the individual's personal appraisal of psychological stressors, methodological concerns caution against direct use of such information. Consequently, alternative

approaches were developed to avoid the pitfalls of using subjective reports and associated problems with these methods.

## METHODOLOGICAL CONSIDERATIONS AND RECENT DEVELOPMENTS

While concepts and methods intertwine and, united, nurture progress, at times one or the other component may unduly influence development (for good or for bad). This comment is applicable to research on psychological stressors, where the methods adopted in animal laboratory research have constrained theory, and where methods adopted in human life stress research have misled theory on psychological stressors.

### Animal Laboratory Research

The original work of Selye typically employed situations that were overpowering or unavoidable for animals. Such conditions did not permit an evaluation of behavioral responses or of other moderating influences that could influence an animal's adaptation to stressors. Further, it was realized that this paradigm did not provide information about responses to stressors of high ecological and evolutionary relevance, such as those found in the animal's natural environment and evolutionary history. Thus, such an approach masked the implications of less severe but more normative psychological stressors on physiology and behavior, which in turn might represent a more fertile area of inquiry into stressor effects.<sup>2</sup> Finally, the nature of the stressor employed in the early animal laboratory studies, too, contributed to the aforementioned difficulty in differentiating physical from psychological effects, which inhibited progress in the arena of conceptual development.

Overall, the range of psychological stressors was constrained by the methods adopted. Theory, in turn, was constrained to account for the consequences of stressors under such restricted and relatively unnatural environmental conditions. More recent research has benefited from methods involving the assessment of a more diverse array of psychological stressors that incorporate the assessment of a wider variety of behavioral and biological response possibilities. Current perspectives based on these broader methodological approaches suggest that the organism's responses are often “exquisitely specific” nuances of stressors encountered.<sup>2</sup>

### Human Studies of Stressful Life Events

The bulk of empirical work on human life stress has been based on self-report checklist methods. The

prototype of this approach is the SRE, the instrument that catalyzed research on the topic. The popularity of the SRE was due to the combination of the intuitive appeal of the stress concept, the ease and apparent objectivity of the method, and the overall impression of scientific legitimacy.

The methodological paradigm launched by the SRE, however, embodied several problems. It became clear that subjects did not report life events in a reliable manner over time, and that investigators did not adequately control for the directionality of effects in research designs (e.g., being depressed could bring about life events such as “trouble at work,” “difficulties with spouse,” and so on). Indeed, many of the initial items on the SRE were direct indicators of disorder or illness. For example, some of the key criteria for defining clinical depression were represented in the original SRE (“Major change in eating habits,” “Major change in sleeping habits”). If measures of life events were directly confounded with the presence of disorder, or contaminated by the effects of pre- or coexisting disorder, then clearly general theory about psychological stressors, as well as theory about the characteristics of psychological stressors, rested on flawed information.<sup>5</sup>

In response to these methodological concerns, investigators designed semistructured interview protocols and developed explicit guidelines, decision rules, and operational criteria for defining and rating life events.<sup>4,5</sup> These developments further highlighted serious problems with self-report checklist methods. For example, there is too much subjective leeway permitted in defining what constitutes an “event” with self-report procedures, resulting in unacceptable variability of content within ostensibly uniform categories of events.<sup>4</sup> To have a more firm methodological foundation, more elaborate and extensive interview and rater-based procedures were employed, helping to standardize measurement across individuals.

In general, interview and rater-based approaches enhance the reliability of life event assessments and provide stronger predictions of particular kinds of disorders following the occurrence of psychological stressors.<sup>5,6,19,20</sup> Procedures such as these, too, provide a solid foundation upon which to build in terms of developing taxonomies of psychological stressors and their effects.<sup>4</sup> Although such approaches are more time-intensive and costly, they represent the current-day gold standard for assessing psychological stressors.

## Human Studies Employing Other Measures of Psychological Stressors

Other methods have been developed for assessing psychological stressors. None of these approaches has received the degree of attention devoted to the work on

life events, yet each may have useful properties for the study of psychological stressors. Two lines of investigation are noteworthy.

First, many investigations have targeted people who experience a specific life event and compared them to controls who have not experienced the event. For example, individuals who become unemployed are compared to individuals who do not experience this event in relation to a variety of psychological and physical processes and outcomes. Such work is useful for examining a potentially more homogenous process with more readily identifiable outcomes. On the other hand, these studies may oversimplify the psychological stressors associated with an event, and not specifically articulate the different components within the general event that are most pernicious for health. For example, the effects can be partitioned into a variety of stressful themes that, although often intercorrelated, may not have uniform effects. Thus, although people who become unemployed in general may experience as loss of self-esteem, loss of income, loss of daily schedule, and so on, each particular situation may pull more or less for heightened responses along these different dimensions. Research sensitive to variability in the component characteristics will be most useful for research on psychological stressors.

Finally, there also have been efforts to measure psychological stressors through questionnaire or diary methods, inquiring about less major but common daily experiences, chronic conditions, appraisal processes, and other indicators or correlates of psychological stressors.<sup>11</sup> A promising recent avenue of research involves ecological momentary assessment, where subjects can be prompted throughout the day to respond to queries about their circumstances and psychological states. Such procedures help minimize problems with standard retrospective methods, although may still pose challenges for reliably assessing major types of life events.<sup>21</sup>

In closing, it is appropriate to return to the concerns and caveat with which the discussion began. The specter of biases in the measurement of psychological stressors consistently must be borne in mind, and methods employed must be rigorously attentive to such concerns, to provide a solid empirical foundation upon which theory and research can build for this important area of investigation.

## References

1. Allbutt C. Nervous diseases and modern life. *Contemp Rev.* 1895;67:217.
2. Weiner H. *Perturbing the Organism: The Biology of Stressful Experience.* Chicago, IL: The University of Chicago Press; 1992.
3. Selye H. *The Stress of Life.* 2nd ed. New York, NY: McGraw-Hill; 1976.
4. Dohrenwend BP, ed. *Adversity, Stress, and Psychopathology.* New York, NY: Oxford University Press; 1998.

5. Brown GW, Harris TO, eds. *Life Events and Illness*. London: Guilford Press; 1989.
6. Monroe SM. Modern approaches to conceptualizing and measuring life stress. *Annu Rev Clin Psychol*. 2008;4:33–52.
7. Weiss JM. Psychological factors in stress and disease. *Sci Am*. 1972;226:104–113.
8. Lazarus RS. *Psychological Stress and the Coping Process*. New York, NY: McGraw-Hill; 1966.
9. Holmes TH. Development and application of a quantitative measure of life change magnitude. In: Barrett JE, ed. *Stress and Mental Disorder*. New York, NY: Raven Press; 1979:37–53.
10. Holmes TH, Rahe RH. The social readjustment rating scale. *J Psychosom Res*. 1967;11:213–218.
11. Cohen S, Kessler RC, Gordon LU, eds. *Measuring Stress: A Guide for Health and Social Scientists*. New York, NY: Oxford University Press; 1995.
12. Slavich GM, Irwin MR. From stress to inflammation and major depressive disorder: a social signal transduction theory of depression. *Psychol Bull*. 2014;140:774–815.
13. Monroe SM, Slavich GM, Georgiades K. The social environment and depression: the importance of life stress. In: Gotlib IH, Hammen CL, eds. *Handbook of Depression*. 3rd ed. New York, NY: Guilford Press; 2014:296–314.
14. Monroe SM, Harkness KL. Life stress, the ‘kindling’ hypothesis, and the recurrence of depression: considerations from a life stress perspective. *Psychol Rev*. 2005;112:417–445.
15. Post RM. Transduction of psychosocial stress into the neurobiology of recurrent affective disorder. *Am J Psychiatr*. 1992;149:999–1010.
16. Zhang T-Y, Meaney MJ. Epigenetics and the environmental regulation of the genome and its function. *Annu Rev Psychol*. 2010;61:439–466.
17. Monroe SM, Reid MW. Gene-environment interactions in depression: genetic polymorphisms and life stress polyprocedures. *Psychol Sci*. 2008;19:947–956.
18. Slavich GM, Cole SW. The emerging field of human social genomics. *Clin Psychol Sci*. 2013;1:331–348.
19. Dohrenwend BP. Inventorying stressful life events as risk factors for psychopathology: toward resolution of the problem of intracategory variability. *Psychol Bull*. 2006;132:477–495.
20. Hammen C. Stress and depression. *Annu Rev Clin Psychol*. 2005;1:293–319.
21. Shiffman S, Stone AA, Hufford MR. Ecological momentary assessment. *Annu Rev Clin Psychol*. 2008;2005(4):1–32.