speaking tasks were most consistently effective in inducing myocardial ischemia in patients with coronary heart disease (Strike & Steptoe, 2003). It is possible that this is due to the more naturalistic nature of the task than, for example, mental arithmetic or Stroop task. However, care should be taken when interpreting the effectiveness of a certain task to induce physiological changes between studies, as it is hard to compare the stressfulness of tasks between studies. Ambulatory recording techniques are available for the assessment of physiological measurements in real-life setting. Even though these field studies cannot be standardized between participants, it is worth noting that there is evidence that the laboratory cardiovascular responses to mental stress were predictive of ambulatory physiological assessments (Strike & Steptoe, 2003).

Cross-References

- ▶ Cardiovascular Recovery
- ▶ Immune Responses to Stress
- ▶ Mental Stress
- ▶ Psychological Stress
- ▶ Psychophysiologic Reactivity
- ▶ Stressor
- ▶ Trier Social Stress Test

References and Readings

Carroll, D., Lovallo, W. R., & Phillips, A. C. (2009). Are large physiological reactions to acute psychological stress always bad for health? *Social and Personality Psychology Compass, 3*, 725–743.

Kirschbaum, C., & Hellhammer, D. H. (1993). The 'Trier Social Stress Test' – A tool for investigating psychobiological stress responses in a laboratory setting. *Neuropsychobiology, 28*, 76–81.

Larsen, B. A., & Cristenfeld, N. J. (2011). Cognitive distancing, cognitive restructuring, and cardiovascular recovery from stress. *Biological Psychology, 86*, 143–148.

Lovallo, W. R. (1997). *Stress & health, biological and psychological interactions*. Thousand Oaks: Sage.

Obrist, P. A. (1981). *Cardiovascular psychophysiology: A perspective*. New York: Plenum Press.

Steptoe, A., Hamer, M., & Chida, Y. (2007). The effects of acute psychological stress on circulating inflammatory factors in humans: A review and meta-analysis. *Brain, Behavior, and Immunity, 21*, 901–912.

Strike, P. C., & Steptoe, A. (2003). Systematic review of mental stress-induced myocardial ischaemia. *European Heart Journal, 24*, 690–703.

Stroop, J. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology, 18*, 643–662.

Turner, J. R. (1994). *Cardiovascular reactivity and stress*. New York: Plenum Press.

Van Eck, M. M., Nicolson, N. A., Berkhof, H., & Sulon, J. (1996). Individual differences in cortisol responses to a laboratory speech task and their relationship to responses to stressful daily events. *Biological Psychology, 43*, 69–84.

Veldhuijzen van Zanten, J. J. C. S., Ring, C., Burns, V. E., Edwards, K. M., Drayson, M., & Carroll, D. (2004). Mental stress-induced hemoconcentration: Sex differences and mechanisms. *Psychophysiology, 41*, 541–551.

Stress Testing

- ▶ Exercise Testing

Stress Vulnerability Models

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Synonyms

Stress diathesis models

Definition

Vulnerability models are used to identify factors that are causally related to symptom development. Stress vulnerability models describe the relation between stress and the development of (psycho-)pathology. They propose an association

between (1) latent endogenous *vulnerability factors* that interact with stress to increase the adverse impact of stressful conditions, (2) *environmental factors* that influence the onset and course of (psycho-)pathology, and (3) *protective factors* that buffer against or mitigate the effects of stress on pathological responses.

Description

The prevalence of stress-related mental disorders encompassing mood and anxiety disorders in Europe is above 20%. This morbidity is associated with high health care costs, disability, and potential mortality. It is widely acknowledged that there are individual differences in how stressful people judge a particular event to be as well as in their ability to cope with adverse stressful life events. While historically stress was said to play an initiating role in the development of pathology, only a minority of people who experience adverse stressful life events go on to develop pathology. To distinguish people who develop pathology from people who do not (i.e., are resilient), vulnerability processes are suggested that predispose individuals to psychopathology when confronted with severe stressors. In the late 1970s, Zubin and Spring were the first to introduce this idea in the field of behavioral medicine by postulating a vulnerability model for schizophrenia. Specifically, they suggested that humans inherit a genetic predisposition to mental illness. However, an interaction between the genetic vulnerability and biological or psychosocial stressors is necessary to develop the disorder. The relationship between predispositional factors (or diathesis) and development of pathology has been described in four basic stress vulnerability models.

Stress Vulnerability Models

The first and most simple stress vulnerability model, the *dichotomous interactive* model, suggests that when predispositional factors are absent, even severe stress will not result in pathology. Instead, it is only when predispositional factors are present that stress may, depending on the severity of the stress, lead to the expression of pathology. Alternatively, the *quasi-continuous* model suggests varying degrees of predisposition with a continuous effect of predispositional factors on pathology once a threshold has been exceeded. The third, more extensive *threshold* model incorporates an individually specific threshold that is determined by the degree of vulnerability and the level of experienced stress. Finally, perhaps the most comprehensive model is the *risk-resilience continuum* model in which vulnerability is viewed as a continuum ranging from vulnerability to resilience, integrating different levels of severity of pathology into the model. Here, resilient characteristics that can make people more resistant to the impact of stress are also emphasized. Note that according to this latter model, even highly resilient individuals might still be at risk for developing pathology when experiencing extreme stress, but their individual threshold will be higher and the symptomatology likely less severe. Collectively, these four models are used to describe the relation between predispositional factors and the development of various pathologies.

Vulnerability Factors

In general, stress vulnerability models postulate that a genetic vulnerability interacts with adverse life events or stressors to produce pathology. This gene-environment interaction with regard to stress and the development of pathology has been most extensively investigated in mood disorders such as depression. Gene-environment interaction studies use monozygotic twin, adoption, and family studies as tools to identify predispositional factors in shared and non-shared environments in order to differentiate genetic from environmental influences. In twin studies, a higher prevalence of pathology in monozygotic twins reared in different environments is used to confirm a genetic predisposition, whereas in adoption studies the effect of the environment

(adoptive parents) can be offset against the effect of genes (biological parents). Using these methods the heritability of major depression, has been estimated at around 40%.

At the neurochemical level, the serotonin (5-HT) system has been implicated in depression. 5-HT regulates among others mood, activity, sleep, and appetite. Accumulating evidence indicates that individuals with a serotonergic vulnerability, manifested in a more sensitive brain serotonergic system, have an increased likelihood of developing mood-related disorders. Specifically, polymorphisms in the 5HT transporter system (5-HTT) have been associated with stressful life events, a heightened risk for depression, and reactivity to negative emotional stimuli. Individuals carrying two copies of the short variant of the 5-HTT allele (i.e., 5-HTTLPR), a less active gene resulting in fewer 5-HTT transporters, display an increased sensitivity to the impact of mild stressful life events, an excessive amygdala activity to fearful faces and produce elevated and prolonged levels of cortisol in response to a laboratory stressor compared to individuals with the long variant of the 5-HTT allele. The heritability of the stress hormone response has also been investigated with family studies in relatives of patients with depression using neuroendocrine functioning tests. For example, studies with the dexamethasone suppression test, a drug test used to measure the effectiveness of the negative feedback mechanism of the hypothalamic-pituitary-adrenal (HPA) axis at the level of the pituitary, have found an amplified set point of the HPA axis in relatives of depressed patients compared to healthy controls.

Moreover, 5-HT is also involved in the modulation of the HPA axis and its associated regulatory actions in the secretion of cortisol, the major human glucocorticoid stress hormone. Cortisol binds to two corticosteroid receptors in the brain, namely, the mineralocorticoid receptor (MR) and the glucocorticoid receptor (GR). Two mechanisms of cortisol binding are known. First, cortisol can bind to the hormone response element on DNA to influence gene expression (intracellular MR and GR binding properties). Secondly, cortisol can bind to membrane versions of the corticosteroid receptors to influence glutamate transmission and gene expression in the brain. The MR controls the basal HPA activity through inhibition of the HPA axis, facilitating the selection of adaptive behavioral responses and preventing minor adverse stressful life events to disturb homeostasis. In contrast, the GR promotes recovery after stress as well as the storage of information for future events. The balance between the MR and GR receptors determines the threshold and termination of the HPA axis response to stress. Studies have demonstrated that individuals with polymorphisms in the GR gene display higher cortisol responses and inefficient recovery of the HPA axis following standardized laboratory stress tests, thus revealing predisposition factors for stress-related pathology.

Genes can have a direct effect on the development of various brain systems. To illustrate this point, altered gene expression can reduce plasticity in brain circuits regulating mood, anxiety, and aggression and thereby decrease one's ability to cope with stressful life events. Moreover, genes can bias brain circuits to inefficient information processing which can result in the expression of pathology (e.g., intrusive memories in patients suffering from posttraumatic stress disorder). Genetic polymorphisms are then viewed as vulnerability factors given that they produce an increased sensitivity to the impact of stressful life events. However, it should be kept in mind that replication studies of candidate gene associations in pathology are relatively sparse and that most disorders are polygenetic. Additionally, the net outcome of a stressor is at least in part determined by the individual's personality traits that may be formed by genes, potentially indirectly influencing the selection of environments and thus the risk of exposure to adverse effects.

Lifespan models have examined the relation between early life stressful events, later stressful life events and pathology development. Undifferentiated neuronal systems are dependent on early experience during development. It is suggested that early life stress results in inefficient information processing and sensitization of brain circuits involved in regulating stress reactivity, which

may ultimately render people more vulnerable. Different brain structures have specific developmental trajectories resulting in a variety of pathological response after stress across the lifespan. For example, prenatal stress originating from maternal stress or postnatal environmental stress such as the quality of parental care influences the regulation of the HPA axis. However, exposure to a manageable stressor during childhood can also desensitize the stress circuits, producing experience-based resilience in which brain systems tend to become less reactive to future stress. Early life stress can hence be protective in that it can negate or diminish the negative outcomes or alternatively promote adaptive functioning in the context of adverse stressful life events. Additionally, other psychosocial factors during development like social support, parental care, and affective style have been identified as potentially protective factors that can enhance adaptive coping during or after stress. In a similar vein, brain frontal alpha asymmetry has been suggested to bias individuals' affective style and emotion regulation capacities. Specifically, left frontal activation has been linked to approach behavior and suggested to be an indicator of decreased vulnerability to depression whereas right frontal activation is viewed as a predispositional factor, lowering the threshold for adverse impact of stressful conditions.

In sum, stress vulnerability models underscore that the nature and intensity of the stressor in combination with genetic vulnerability factors, phenotypic vulnerability factors (personality, neuroendocrine reactivity), and both genetic and phenotypic protective (resilience) factors determine the impact and sequela of adverse stressful life events.

Cross-References

- ▶ Corticosteroids
- ▶ Cortisol
- ▶ Family Studies (genetics)
- ▶ Family Stress
- ▶ Gene-Environment Interaction
- ▶ Glucocorticoids
- ▶ Hypothalamic-Pituitary-Adrenal Axis
- ▶ Individual Differences
- ▶ Resilience
- ▶ Stress
- ▶ Stress Reactivity
- ▶ Stress Responses
- ▶ Stress Test
- ▶ Stress: Appraisal and Coping
- ▶ Stress, Caregiver
- ▶ Stressor
- ▶ Twin Studies

References and Readings

Coan, J. A., & Allen, J. J. B. (2003). The state and trait nature of frontal EEG asymmetry in emotion. In K. Hugdahl & R. J. Davidson (Eds.), *The asymmetrical brain* (pp. 565–616). Cambridge, MA\London: MIT Press.

Curtis, W. J., & Cicchetti, D. (2003). Moving research on resilience into the 21st century: Theoretical and methodological considerations in examining the biological contributors to resilience. *Development and Psychopathology, 15*, 773–810.

DeRijk, R. H., & de Kloet, E. R. (2008). Corticosteroid receptor polymorphisms: Determinants of vulnerability and resilience. *European Journal of Pharmacology, 583*, 303–311.

Gotlib, I. H., Joormann, J., Minor, K. L., & Hallmayer, J. (2008). HPA axis reactivity: A mechanism underlying the associations among 5-HTTLPR, stress, and depression. *Biological Psychiatry, 63*, 847–851.

Ingram, R. E., & Luxton, D. D. (2005). Vulnerability-stress models. In B. L. Hankin & J. R. Z. Abela (Eds.), *Development of psychopathology: A vulnerability-stress perspective* (pp. 32–46). Thousand Oaks, CA: Sage.

Lupien, S. J., McEwen, B. S., Gunnar, M. R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature Reviews Neuroscience, 10*(6), 434–445.

Oitzl, M. S., Champagne, D. L., van der Veen, R., & de Kloet, E. R. (2010). Brain development under stress: Hypotheses of glucocorticoid actions revisited. *Neuroscience and Biobehavioral Reviews, 34*, 853–866.

Stahl, S. M. (2008). *Stahl's essential psychopharmacology: Neuroscientific basis and practical applications* (3rd ed.). New York: Cambridge University Press.

Van Praag, H. M., de Kloet, E. R., & van Os, J. (2004). *Stress, the brain and depression*. New York: Cambridge University Press.

Zubin, J., & Spring, B. (1977). Vulnerability-a new view of schizophrenia. *Journal of Abnormal Psychology, 86*, 103–126.