Abstract
For a cognitive conceptualization, stress arises when environmental demands are perceived as taxing or potentially exceeding one's own capacity or resources to manage them, and there is threat to well-being if coping responses do not satisfy such demands. A cognitive vulnerability factor enhancing stress is trait anxiety, through hypervigilant processing styles involving selective orienting to threat cues, biased negative interpretation of ambiguous stimuli, and focusing attention on unfavorable thoughts. Short-term episodes of mild-intensity stress can facilitate cognitive functions, mainly encoding and memory consolidation of task-relevant stimuli, and in implicit memory or simple declarative tasks. However, exposure to high-intensity stress impairs the formation and retrieval of explicit memories and cognitive processes requiring complex or flexible reasoning. Long-term stress, particularly during childhood and adolescence, consistently undermines cognitive mechanisms. This can be due to chronic elevations of glucocorticoids inhibiting neurogenesis, which damages important functions in the hippocampus and, possibly, the prefrontal cortex.

ENVIRONMENTAL, BIOLOGICAL, AND COGNITIVE COMPONENTS OF STRESS

The major adaptive goal of evolved organisms is to survive and also to thrive. Such adaptive functions, nevertheless, have to be achieved in a complex and hostile environment. Complex, because there are multiple stimuli to attend to and multiple demands that must be met. Hostile, because many of those stimuli and demands involve physical dangers (e.g., harms to health or well-being) or psychological threats (e.g., social rejection or loss), if responses are not satisfactory. Individuals thus need to be able, first, to detect demands and also to prioritize them depending on their relative adaptive importance; and, second, coping resources must be used to respond to the demands in a way that harm is minimized and benefit is maximized. In such conditions, stress develops with a general adaptive purpose, by potentiating an alerting mechanism in cognitive and neural systems, and by recruiting and mobilizing resources in behavioral and physiological systems.

But, what is stress, and how can it be at the core of crucial adaptive functions for organisms? There are three major components in stress. First, the environmental, objective stimulus conditions that constitute the demands on the individual, which are called stressors. By restricting our consideration of them to human environments, multiple classifications can be made such as physical (e.g., accidents, natural disasters, noise, extreme temperatures, crowding, etc.), biogenic (e.g., illness, injury, pain, hunger, etc.) stressors, and psychosocial stressors (e.g., divorce, aggression, loss of job, exams, failures, etc.). A common characteristic of all stressors is that they alter a current biological or psychological homeostatic state or a desired goal, and thus threaten well-being.

Second, stress is characterized by a biological response to the environmental demands. Essentially, the brain initiates a course of action that releases neurotransmitters, peptides, and hormones throughout the
body. Particularly, two systems are mobilized: the fast acting sympathetic nervous system (SNS) and the slower hypothalamus-pituitary-adrenal (HPA) axis. SNS responses include the release of the catecholamines adrenaline and noradrenaline from the adrenal medulla, which cause, for example, increases in heart rate and enhanced blood flow to skeletal muscles, and thus prepare the organism for a “fight-or-flight” behavioral response. Activation of the HPA-axis leads to the release of glucocorticoids (cortisol, in humans) from the adrenal cortex, causing, for example, an increase in the availability of energy substrates in different parts of the body, to support response resistance to environmental demands.

A third major component is the interpretation assigned by the individual to the objective stressor. The same objective stimulus, situation, or event may be more or less stressful, or not stressful, for different individuals, and even for the same individual in different contexts. In addition, the same physiological “stress response” can also be produced by nonstressful events. For example, components of the neuroendocrine response to appetitive, rewarding stimuli (e.g., sexual), events (e.g., social success), or physical activity (e.g., exercise) can be as large as when reacting to (aversive) stressful stimuli. This implies that stress cannot be defined only in terms of objective stimulus and response properties. Rather, it is commonly accepted that stress occurs when environmental demands tax or exceed the natural regulatory capacity of an organism, particularly when there is perceived uncertainty about the occurrence and the personal control of potentially threatening outcomes.

This introduction serves as a context for two cognitive approaches to stress: the cognitive origins and the cognitive consequences of the stress process. First, although some events (e.g., major life events or disasters) are objectively stressful for most individuals, the way they are (subjectively) perceived makes them more or less stressful. Also, for most daily hassles of mild intensity, the way they are perceived may determine their real impact, as to become stressful or not. The cognitive mechanisms—both the immediate triggers and the predisposing vulnerability factors—leading to perceive an event as stressful will be considered in section “Cognition and Stress: Cognitive Origins of Stress.”

COGNITION AND STRESS: COGNITIVE ORIGINS OF STRESS

Cognitive Appraisal

From a psychological perspective,1,2 stress was defined by Lazarus and Folkman3 as a kind of relationship between the person and the environment, in which the environmental demands are appraised as taxing the personal capacities and endangering well-being. Stress would occur when people confront circumstances that are perceived to exceed one’s own ability to manage them. In this conceptualization, a central construct is appraisal, as a cognitive process that evaluates an event in terms of its significance for the person’s well-being. Thus, the origin of stress would be cognitive, in that an environmental demand becomes stressful and activates the biological stress response to the extent that it is perceived and interpreted as threatening. This explains why the same objective situation or event (e.g., talking in front of a group of people) can be very stressful for one person or it may be less stressful, neutral, or even appetitive for others who could see it as an opportunity for benefits rather than potential harm. Nevertheless, while this view can generally be applied to most psychological stressors, the contribution of objective properties is probably greater for physical and biogenic stressors (e.g., noise, illness, etc.).

There are two classes of appraisal: primary and secondary.1,2 Primary appraisal is an evaluation of what is at stake in the encounter, that is, what the environmental demands are and their implications. Three major outcomes of primary appraisal have been described. First, circumstances can be appraised as “irrelevant” to the personal well-being, if the situation does not concern the person’s needs or goals,
in which case no stress develops. Second, the situation can be appraised as positive or benign, if it is appraised as preserving or enhancing the personal well-being, with no stressful effects, either. Third, the circumstances can be appraised as stressful if the personal needs or goals are implicated in the situation. It is in this third case that secondary appraisal intervenes, as an evaluation of the personal resources or capacity and the available options to deal with the demands. Depending on the outcome of secondary appraisal, four major types of stress can develop: threat, harm, loss, and challenge. Threat appraisal means that the person perceives an impending event that may have negative consequences. Harm appraisal is the perception that something bad has already happened. Loss appraisal constitutes a specific kind of harm appraisal in which something that is positively valued becomes inaccessible. All these three kinds of appraisal lead to distress, which is the typical form of stress. In contrast, challenge appraisal leads to a different form of stress that has been termed as eustress. Challenge appraisal still involves seeing the situation as demanding and taxing and potentially exceeding capacity, and therefore stressful, but also as an opportunity for obtaining benefits, which positively motivates effort and approach behavior.

The previous conceptualization of appraisal is formulated in a way that seems to entail strategic cognitive activity, as conscious, thoughtful, and voluntary analysis of environmental demands and personal resources. However, Lazarus himself—as the proponent of the appraisal conceptualization—admits that appraisal can also be performed through automatic cognitive processes. In any case, within either view, perception of unpredictability and uncontrollability are critical ingredients of appraisal in current cognitive views of stress. Unpredictability varies as a function of the degree of uncertainty about whether, when, where, how, or with what intensity a potential, threat, harm, or loss can occur. Uncontrollability varies as a function of the degree of uncertainty about whether and to what extent a person feels able to cope with the demands and minimize or avoid threat, harm, or loss. Unpredictability and uncontrollability will thus make environmental demands stressful. Furthermore, while uncertainty of control leads to an appraisal of threat, and perception of uncontrollability leads to appraisals of harm or loss, predictability of control leads to an appraisal of challenge.

**Cognitive Vulnerability**

As indicated above, the probability and intensity of the stress response significantly varies for different individuals, even for the same objective stressor. In addition, for a cognitive conceptualization of the stress process, the response is initiated and maintained depending greatly on the person’s appraisal of the stressor. This implies that there must be a vulnerability factor involving relatively stable personality characteristics, and that such factor must be related to cognitive styles in the processing of environmental demands. Three such cognitive vulnerability mechanisms may enhance perception of threatening demands. First, a hypervigilant style that leads observers to selectively attend to threat-related cues in the environment, among other multiple stimuli, with low-thresholds for detection of threat cues of minimal intensity. Second, a tendency to preferentially interpret in a threatening way ambiguous stimuli that can, otherwise, also have nonthreat meanings (e.g., a neutral facial expression, or even a smile, which can be interpreted as anger or even as contempt). And, third, once a situation has been appraised as stressful, the proneness to focus on worrisome thoughts, with anticipation of dangers and negative evaluations of one’s own coping capacity to face the demands. Understandably, selective attentional orienting toward threat cues, as well as biased negative interpretations of ambiguous stimuli, will enhance the probability of perceiving stressful demands. Relatedly, maintained rumination of internal representations of threat, harm, or loss, will increase the intensity and duration of the stress response.

Is there any type of personality characterized by such cognitive vulnerability processing styles? Research on trait anxiety and anxiety disorders (generalized anxiety disorder, obsessive-compulsive disorder, panic and post-traumatic stress disorder, social phobia, and simple phobia) has provided abundant evidence that people high in anxiety typically use all three types of processing mechanisms (for integrative reviews and meta-analytic studies, see Refs. 6–11). Hypervigilance and selective attention to threat cues in trait anxious people and anxious patients have been demonstrated with various tasks and measures, including gaze direction, attentional capture of covert attention, and lowered perceptual thresholds for threat stimuli. Similarly, interpretive bias or the preferential negative interpretation of ambiguous stimuli (words, sentences, and facial expressions) has proved to characterize trait anxious individuals and anxious patients, who also exhibit an enhanced risk estimation and predictive inferences of aversive consequences of ambiguous events. Relatedly, trait anxious individuals and anxious patients typically show a bias in the allocation of processing resources to threat-related internal representations, as evidenced by difficulties in inhibiting attention to such thoughts once threat has been detected. Given that a major biological function of anxiety is to facilitate the anticipation of threat detection, it is understandable that highly anxious people are especially prone to perceive stressful demands and to react with stress accordingly. What makes anxious people more able to detect and prioritize demands that may affect well-being, on one hand, also makes them more vulnerable to stress, on the other.
There is a neural substrate underlying the cognitive vulnerability styles of anxious individuals. A critical brain mechanism that has been proposed to account for all three cognitive biases in anxiety entails an amygdala hyperresponsivity to threat signals along with PFC hyporesponsivity. The amygdala, a subcortical neural structure, is typically engaged with emotional processing and is particularly sensitive to threat. The prefrontal cortices, particularly the lateral PFC, are associated with conscious emotion regulation and executive processes. Neuroimaging studies have shown enhanced amygdala activity and reduced PFC activity in high-anxiety individuals. Enhanced amygdala activation would lead to hypervigilance for threat and a bias toward negative interpretations of stimuli. Reduced recruitment of PFC mechanisms would impoverish control of negative thoughts and anticipation of aversive consequences, thus delaying disengagement from worrisome internal representations. In the absence of such inhibitory mechanisms, which would allow for the persistence of the biased attention and interpretation, stress perception and reactivity would increase.

**STRESS AND COGNITION: COGNITIVE CONSEQUENCES OF STRESS**

**Cognitive Effects of Acute Stress**

Acute stress refers to episodes of limited duration (generally occurring within minutes or hours; e.g., a speech in public or an exam), as compared to long-term stress (lasting for weeks or months; e.g., looking after an ill person or undergoing academic promotion). The duration of stress is a relevant factor affecting cognitive mechanisms and activities. In general, while acute stress can have both a beneficial and a detrimental cognitive influence, prolonged stress generally undermines cognition. Acute stress impinges upon cognition in many ways, with either facilitating or impairing effects, depending on a number of factors. Among cognitive factors, the specific cognitive operation (e.g., implicit vs. explicit memory, long-term vs. working memory, and goal-directed vs. habit learning) and information processing phase (e.g., encoding, consolidation, and retrieval) are particularly important (see reviews in Refs. 15–18).

More specifically, in humans, psychosocial stress occurring just before learning may have no effects on encoding, or it can either impair or improve learning. Memory for emotional information is generally enhanced by prior stress exposure, whereas memory for neutral information is less likely to be affected or it is even reduced by prior stress. The facilitating effect of stress on memory for emotional words has been observed particularly for negative rather than positive words. In addition, administration of cortisol before learning facilitates memory for emotionally arousing pictures. Stress or glucocorticoid administration just after learning generally has shown beneficial effects on memory consolidation processes. These effects appear to be particularly strong for emotionally arousing stimuli. In contrast, the exposure to stress or the administration of glucocorticoids shortly before memory testing of previously acquired information reduces retrieval performance. Again, these effects are most pronounced for emotionally arousing material.

Models have been proposed to explain the time-dependent effects of stress on memory. As indicated above, there are two main stress hormones, namely, glucocorticoids (cortisol) and catecholamines (epinephrine and norepinephrine). The glucocorticoids directly access the brain where they bind to receptors in three brain areas involved in learning and memory, such as the hippocampus, amygdala, and frontal lobes. Also, epinephrine can act on the brain via vagal afferents, noradrenergic cells in the nucleus of the solitary tract and the locus ceruleus, which in turn, stimulate the basolateral amygdala. This way, if an individual is stressed shortly before, during, or shortly after learning, rapidly acting catecholamine and glucocorticoid effects facilitate attentional and other encoding processes. In addition, delayed glucocorticoid actions suppress competing information processing immediately after learning and hence promote memory consolidation of the recently encoded information. If, however, an individual is exposed to stress a considerable time before learning, and glucocorticoid action is already active during learning, stress can impede new learning and memory processes. Such a stress-induced retrieval impairment would be due to the stressful episode competing with, or directly suppressing, the concurrent cognitive activities required for the retrieval of previously learned information.

In addition to the influence of acute stress on the learning and memory functions associated with the amygdala and hippocampus, higher-order cognitive functions supported by the PFC are affected. In general, under high stress, the more flexible higher-order “cognitive” functions tend to be replaced by more rigid “habit” memory functions in the control of learning and response. Nevertheless, the effects of stress are varied, with both impairment and improvement of working memory function, cognitive flexibility, and decision-making. Differences across studies in stress intensity, cognitive load, and timing can probably account for the discrepant findings. In support of this view, first, mild increases in monoamines, such as dopamines associated to moderate stress exposure, enhance functional connectivity within PFC networks. Second, in contrast, under highly stressful situations, an excessive release of neurotransmitters, such as norepinephrine, undermines PFC function and
associated behaviors. Third, a moderate increase in catecholamines boosts decision-making (leads to less risky decisions) while elevated cortisol impairs it (more risky decisions). Fourth, delayed—but not immediate—effects of glucocorticoid administration in humans improve working memory performance and increase neuronal activity during performance in the dorsolateral PFC depending on task load. This suggests that glucocorticoid receptors (GRs) in the PFC regulate stress-evoked dopamine efflux and the associated working memory impairment.

Cognitive Effects of Prolonged Stress

Unlike acute stress, which, at least when it is of mild intensity, can yield some favorable effects on various cognitive processes (mainly encoding and memory consolidation), repeated or prolonged stress typically causes functional cognitive deterioration, in addition to structural damage of some brain structures, such as the hippocampus. Available evidence for the impact of chronic stress on memory in healthy humans is, nevertheless, scarce, mainly due to the ethical constraints inherent to intentionally exposing humans to repeated stress.

Indirect evidence of the effects of stress, however, has been obtained from various sources. Considerable available data come from studies focusing on stress-related neuropsychiatric disorders (see reviews in Refs. 16, 18, 32–34). This approach has provided information about a link between accumulated exposure to stress and impaired hippocampal memory function in humans. Mental disturbances mimicking mild dementia, such as performance decrements in simple and complex attentional tasks, verbal and visual memory, encoding, storage, and retrieval, have been described in depressed patients with hypercortisolism, and also in steroid psychosis following glucocorticoid treatment. There is also evidence that chronic exposure to stress and/or glucocorticoids worsens cognition and neuropathology in humans with Alzheimer’s disease. Cognitive deficits are also reported in patients suffering from Cushing’s disease, a medical condition in which endogenous levels of glucocorticoids are chronically elevated. Relatedly, during human aging, a significant proportion of elderly individuals present an endogenous increase of glucocorticoid levels, and this increase has been related to decreased memory performance.

Importantly, such cognitive deficits have been attributed to reduced hippocampal volume due to chronic elevations of glucocorticoids. Presumably, long-lasting elevated levels of glucocorticoids inhibit neurogenesis (i.e., the formation of new neurons or synapses), which damages important memory functions in the hippocampus. Studies have revealed the presence of smaller hippocampal volumes in various psychiatric disorders such as depression, post-traumatic stress disorder, and schizophrenia, all of which involve glucocorticoid level dysregulations. For example, in major depressive disorder, a clinical syndrome that is highly sensitive to stress, the greatest degree of cognitive impairment occurs for memory dependent on hippocampal function, and it is the case that major depressive disorder patients have reduced hippocampal volume. Hippocampal atrophy associated with chronic exposure to high levels of glucocorticoids is also reported in Cushing’s patients and in elderly individuals. Hippocampal volume, however, increases and restores in part in such patients after treatment that diminishes cortisol levels to normal concentrations. After cortisol levels decline, structural volumetric increase in hippocampal volume is also accompanied by functional improvement in memory performance. This is a significant finding since it implies the possibility of functional reorganization of the hippocampus once the chronic stress has been taken away.

A special issue regarding the cognitive effects of long-term stress is concerned with early-life stress (ELS; for a review, see Ref. 33). ELS refers to prolonged stressful experiences during infancy (e.g., abuse or maltreatment, early institutionalization, neglect, etc.). Children undergoing such stressful experiences exhibit global cognitive deficits, including decreased intellectual performance, less academic success, as well as poorer language abilities, and deterioration of various aspects of executive functioning (e.g., attention, inhibitory control, planning), and such children require greater individualized education programs. These ELS cognitive deficits are also associated with smaller intracranial volume, reduced hemispheric integration and a smaller corpus callosum, and reduced hippocampus size. In addition, the PFC has a high density of GRs and dopaminergic projections that are stress-sensitive. This makes the PFC especially susceptible of being damaged by ELS, given that PFC networks undergo critical development during childhood and adolescence. Importantly, the fact that the PFC is critically involved in high-level executive cognitive processes implies that relevant cognitive functions are negatively affected. Altogether, these findings suggest that the cognitive-deficit correlates of ELS are due to the ELS detrimental influence on critical brain structures that are necessary for cognitive development. As a consequence, the early stress experiences, if prolonged, can be especially harmful on cognition.

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