Interest in the interplay between mind and body is deep-rooted. Written accounts in Western society are found as far back as the second century, when the physician Galen remarked that cancer seemed to occur more frequently in melancholic (depressed) than sanguine (happy, spirited) women [1]. In traditional Eastern medicine, mind and body have been considered entwined for centuries, and this attitude continues to today (see [2] for an overview). Relative to these examples, it is only recently that scientific inquiry has taken an interest in the mind-body connection. The past three decades have witnessed an explosion of discoveries in this area, and we have seen psychological factors related to physical ailments from asthma to heart disease [3–9]. The present review focuses on just one aspect of mind-body interaction, but one with far-reaching effects. We review evidence for the relationship between psychological stress and immune function. Using a conceptual model, we review psychological, behavioral, and physiological responses to stressful events before entering into a more in-depth discussion of the potential role of subjective experiences of stress.

The Model

Stressors can produce profound health consequences. In one epidemiological study, for example, all-cause mortality increased in the month following a severe stressor – the death of a spouse [10]. Theorists propose that stressful events trigger cognitive and affective responses which, in turn, induce sympathetic nervous system and endocrine changes, and these ultimately impair immune function. [7,11–14]. Potential health consequences are broad, but include rates of infection [15,16], HIV progression [17,18], and cancer incidence and progression [10,19,20]. Figure 1 depicts the major steps in this hypothesized chain of events, along with their mediators and moderators. Each step in this model (i.e. stressor, psychological stress response, physiological stress response, immune changes, and disease processes) is hypothesized to be causal. Individual difference factors (e.g. personality) moderate the effect of stressors on psychological stress response.

This literature is rapidly developing. The purpose of this review is to highlight one aspect which promises to be of great interest in the coming years: the role of individual differences in the subjective experience of stress and their implications for immune function. As we will describe, subjective stress is often implicitly considered in this literature but rarely explicitly studied. In fact, data supporting the causal role of subjective stress in immune change are surprisingly weak.

Stressors and the Psychological Stress Response

Stressors and the stress response are distinct concepts. Stress is classically defined as a perturbation of the normal homeostasis of the body that results when environmental demands exceed a person’s perceived resources to meet those demands [21]. More recent theorists have introduced a broader view of stress involving allostasis, or “stability through change.” This view conceptualizes bodily systems as existing in a state of fluidity that is responsive to environmental demands. Repeated demands, however, tax the body’s ability to respond and return to normal, producing “wear and tear” or “allostatic load [22]. In both theories, an
environmental demand (the stressor) precedes one’s reaction to the demand (the stress response).

Theories suggest that the principal aspect of the psychological stress response is cognitive - the event must be perceived as stressful. Lazarus and Folkman’s [21] model of stress and coping proposes that, in response to a potentially stressful stimulus, an individual appraises the threat value of the stimulus (primary appraisal), as well as his or her capacity to respond to the stimulus (secondary appraisal) [21], and this appraisal process determines the type, direction, and intensity of the stress-related emotions (i.e. anxiety, anger, guilt, sadness, shame, envy, and disgust; [23]). Appraisals vary based on individual differences such as personality traits, past experience with the stimulus, and perceived self-efficacy [21,23,24]. Thus, stress responses can vary, even when the precipitating events are similar.

Although responses vary, most investigations examine stress by studying stressors, which are circularly defined as events which most people would find stressful. Indeed, data confirm that, on average, people undergoing divorce, bereavement, family caregiving, academic examinations, daily hassles, and financial hardship report greater distress than those not experiencing these stressors [25–32]. Consistent with theory, data also show that individuals vary in their subjective reactions to stress, and this variation is often based on individual differences in personality, coping, self efficacy, and social characteristics [21,23,24,33–42].

The Behavioral Stress Response

In addition to cognitive and emotional effects, stressors can promote behavioral change. Although there are some exceptions, people generally pursue less healthy behaviors when under stress, and these effects are seen whether “stress” is defined as the presence of stressful events or perceptions of stress. For example, people reporting greater perceived stress are likely to exercise for less time on fewer days, report lower self-efficacy for meeting exercise goals, and report feeling less satisfied with their exercise [43,44], and these effects are particularly strong among older adults [45]. Stress is also related to sleep difficulties. It is not only the leading cause of temporary insomnia, but lack of sleep may also be a source of stress [46]. Stressors such as job demands and lack of control at work correlate with insomnia, sleep deprivation, and daytime fatigue [47].

Stress is not only associated with diminished health-promoting behaviors, but also with increased health-damaging behaviors. Alcohol intake is likely to increase when individuals are under stress [48–51]. Among students, controlling for daily coping, affect, and weekly drinking trends, participants drink more alcohol on days when perceived stress is high [52]. People under stress also smoke more cigarettes [53–55] and report that smoking cessation is more difficult [56,57]. Finally, diet is also affected, as people typically eat more “fast food,” higher calorie foods, and more fat and sugar when under stress [58–61].

Like psychological responses to stress, behavioral responses are moderated by individual differences. For example, use of alcohol in response to stress is moderated by gender (men are more likely to use alcohol to cope than women; [62]), coping style (individuals who cope through avoidance are likely drink in response to stress; [58]), and social support (people with high social support reduce alcohol intake during stress, while those with low support increase alcohol intake; [44]). Dietary choices are also moderated by individual differences. While most people increase caloric intake during periods of high perceived stress, this effect is strongly pronounced in those who typically restrain their intake (e.g. dieters; [63]), and others reduce caloric intake during stressful periods [64]. These behavioral changes could combine with the cognitive and emotional effects of stressors to affect immune function.
The Physiological Stress Response

Cognitive and emotional events cannot influence immune function directly. Instead, stress is thought to affect immune function through central nervous system control of the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic-adrenal medullary (SAM) axis (for reviews, see [12,65–67]). These axes are illustrated in Figure 2. Briefly, the HPA axis is activated when stress-related sensory signals are processed in the paraventricular nucleus of the hypothalamus, triggering release of corticotropin-releasing hormone (CRH). This hormone stimulates the release of peptides from the pituitary, most notably adrenocorticotropin hormone (ACTH) and β-endorphin. ACTH, in turn, induces the release of glucocorticoids (cortisol in humans) from the adrenal cortex.

Activation of the SAM axis begins with the processing of stress-related sensory signals in the locus coeruleus of the pons. Release of CRH from the hypothalamus further contributes to activation of the SAM axis. Sympathetic nerve fibers trigger release of catecholamines (norepinephrine and epinephrine) into the bloodstream by the adrenal medulla, and peripheral sympathetic nerve fibers release additional norepinephrine. This axis produces the classic “fight or flight” response, characterized by increased heart rate and respiration and a redirection of blood flow from the digestive organs to the skeletal muscles.

Hormones released from the HPA and SAM axes can affect immune function. Glucocorticoids are believed to have strong effects on the immune system, but catecholamines, CRH, and opioids also play a role [68]. Although the specific modes of action are not fully understood, some immune cells, most notably lymphocytes and macrophages, express receptors that are responsive to high levels of circulating glucocorticoids [67]. Glucocorticoids can directly suppress the actions of T lymphocytes and macrophages and may affect cell trafficking and circulation [65,66]. Further, glucocorticoids affect the production and release of cytokines. When circulating glucocorticoids levels are elevated, T-cell production of pro-inflammatory cytokines, such as interleukin-2 and interferon-γ, is suppressed. These altered cytokines, in turn, exert influence on multiple aspects of immune function, including cell cytotoxicity, proliferation, and secretion of additional regulatory cytokines [65].

Lymphocytes and macrophages also express catecholamine receptors. Norepinephrine and epinephrine can affect the production of cytokines in vitro, suppressing interleukin-12 and enhancing interleukin-10. Such an imbalance could increase an individual’s risk for viral infection and tumor growth. Further, these alterations in cytokine secretions combine with CRH to impair the functioning of NK cells [69].

The Behavioral Stress Response and Immunity

In addition to CNS and endocrine effects, stress-related behavioral changes can have immune consequences. As noted above, stressed individuals have poorer sleep, exercise, and dietary habits, and they may increase drug and alcohol use. While relatively little is known about the immune effects of such behaviors, some evidence suggests that better health behaviors yield better immune functioning. First, exercise is thought to have protective effects on immune function, especially among older adults [70,71]. In fact, a recent randomized study shows exercise to improve healing times in experimentally-produced wounds [72]. Second, dissatisfaction with sleep correlates with lower numbers and poorer functioning of immune cells [73–75]. Third, although moderate amounts of alcohol intake appear to have beneficial effects on immune function, high alcohol intake has been shown to be detrimental to immune function [76]. Interestingly, health behaviors may even moderate the physiological consequences of stress. Exercise has been shown to buffer the effects of stress [45,77], while smoking intensifies them [78].
Stressors and Immunity

The model presented in Figure 1 depicts the psychological stress response (perceived stress, distress) as the mediator in the relationship between stressors and immunity. Although most researchers would characterize subjective stress as an important element, the majority of studies examining the physiological effects of stress have studied stressors rather than the stress response. That is, rather than assessing whether individuals perceive that their circumstances are stressful, researchers identify an event that most people would find stressful and assess immune function in relation to it. Research designs include repeated measures designs, which compare a group’s immune function during “stressed” and “nonstressed” time periods (e.g. during academic examinations vs. during summer break), and case-control designs, which compare groups experiencing a stressor (e.g. caregiving) to those not experiencing the stressor. Among studies comparing humans within “stress” and “non-stress” conditions, both laboratory and naturalistic stressors have been examined. The former permit greater experimental control, whereas the latter are associated with greater stimulus impact. Acute laboratory stressors (e.g. speech task, problem-solving task) are usually short (less than 30 minutes), and an experimental design is used. Naturalistic stressors include brief (e.g. academic examinations, natural disasters, space flight) and chronic stressors (e.g. bereavement, caregiving, job-related stress).

Immune outcomes are typically enumerative or functional analysis of immune cells (such as B and T cells) and immune substances (such as antibody and cytokines). Natural killer (NK) and T lymphocytes have received the most study, as these measures have been in use for decades and have clinical relevance. T lymphocytes are considered part of the specific (or acquired) immune system, because they demonstrate “memory,” showing an enhanced response upon second presentation of an antigen [79]. They are divided into three classes: (a) T-helper cells, which are identified by their expression of the CD4 marker, are involved in the initial recognition of a foreign protein (an antigen); (b) T-cytotoxic cells, which express the CD8 marker, have the ability to lyse cells to which they bind; and (c) T suppressor cells primarily inhibit the action of other T-cells. Natural Killer cells are a distinct class of lymphocytes that are considered part of the non-specific (or natural) immune system. They can lyse both allogenic (non-self) and autologous (self) cells without prior sensitization [80], producing a rapid response to initial infection. Additional immune outcomes are chosen for their clinical relevance. These outcomes include antibody response to in vivo vaccine, susceptibility to cold viruses, and wound healing [15,81,82].

Stressors produce reliable immune changes. Meta-analytic reviews have summarized results from the large number of studies using the "stress/non-stress" paradigm [83–85], revealing consistent immune changes in the presence of psychological stressors. In the most recent review, Segerstrom and Miller [85] analyzed different types of stressors separately and found that the immunological effect of stressors depends on their duration (as has been noted by others, see [83,88]). Distinct data patterns were found with acute (<30 minutes), brief naturalistic (days or weeks), and chronic stressors (years).

First, Segerstrom and Miller [85] identified 85 studies which employed acute, laboratory stressors (e.g. public speaking). These stressors appear to elicit redistribution of immune cells [89]. The most prominent effect observed is an increase in numbers of natural killer cells in peripheral blood with accompanying increases in NK cell cytotoxicity assays (although per cell NK cytotoxicity is not seen to increase). Coincident increases were also seen in numbers of T-cytotoxic cells, neutrophils, and large granular lymphocytes in peripheral blood. As the time frame in these studies is too short for production of new immune cells, increases of circulating cells are likely due to their movement from other areas. In addition to cell redistribution, impaired cellular immunity was observed. T cell function (proliferative response to mitogens) was diminished with acute stressors. Researchers have speculated that changes
in response to acute stress are an aspect of the adaptive “fight or flight” response, and thus generally beneficial [88]. These changes have been interpreted as a shift away from specific immunity (e.g. T cell function) toward natural immunity (e.g. NK cells, neutrophils; [85]), and this shift toward the faster-acting natural immunity mechanisms might yield improved response to physical injury.

The second pattern, seen in response to brief naturalistic stressors (e.g. academic examinations), contrasts with acute stressors [85]. Specifically, meta-analysis of 63 studies of brief stressors showed no reliable changes in numbers of circulating white blood cells. Instead, consistent reductions in T cell proliferation and NK cell cytotoxicity were seen. Additionally, the cytokine profile changed, with increases in interleukin-6, interleukin-10, and decreases in interferon-γ. These effects are consistent with a shift away from cellular (Th1) immunity toward humoral (Th2) immunity [85,90]. The third pattern, seen in chronic stressors (e.g. caregiving), implies broad immune impairment. Meta-analysis of 23 studies suggested that both natural and specific immunity are impaired. Reductions are seen in NK cell cytotoxicity, T cell proliferation, and antibody response to influenza vaccination.

Despite differences in the immune results with acute, brief, and chronic stressors, the mechanisms by which stressors affect immune function are believed to be similar. Specifically, perception of stress triggers the activation of the HPA and SAM axes, initiating hormonal influence on immune systems. The detrimental effects of chronic stress have been explained as the overuse of systems whose function is to address short term threats (c.f., “allostatic load”; [88]). It has been observed that chronic stress reduces the flexibility of the immune system to adjust to new challenges (see [91], for a discussion). For example, animals that have been chronically stressed showed decreased HPA responsiveness to novel stressors [92]. This inflexibility could potentially lead to poorer immune response to challenge across a variety of situations (e.g. T cell proliferation, response to immunization).

Interpretation of the literature comparing “stress” to “non-stress” conditions involves the implicit consideration of subjective stress. As noted above, events are chosen for study based on the researcher’s judgment that most people would find them stressful. Indeed, some studies have measured perceived stress or distress and confirmed that, on average, participants report greater subjective stress when in the “stress” condition (e.g., [93,94]). This literature is therefore naturally interpreted to show that subjective stress (a feature which all the events have in common) produces immune change.

Although all the events under study share the property of being stress-producing, all the participants do not necessarily share the property of experiencing stress. There may be some participants included in the studies who would not consider the event stressful (and for them the event would not be a “stressor”). Despite this possibility, the data show that, on average, people do consider the events stressful and, on average, they show immune change. What these studies do not tell us, however, is whether perception that an event is stressful is necessary for immune change.

**Psychological Moderators of the Stress Response**

Additional studies that implicitly consider subjective stress are those investigating individual differences (e.g. personality, coping) and the stress response. As described above, ample research shows that individual differences moderate people’s psychological reactions to stressors. In addition, some evidence shows that individual differences moderate people’s physiological reactions to stressors, including their immune responses.

Personality factors can moderate immune response to stress. For example, men who are high in hostility show greater change in blood pressure, cortisol, and NK cell cytotoxicity when
discussing a marital problem with their wives as compared to nonhostile men [95]. In an investigation of naturally-occurring acute and chronic stressors, optimistic women showed little immune change (NK cell cytotoxicity) after acute stressors, while showing large immune changes after chronic stressors [96]. Additional personality traits have shown cross-sectional correlations with immunity (i.e. repression, defensiveness, introversion, pessimistic attributional style, and trait anxiety; [97–102].

Coping can also moderate the immune response to stress. For example Stowell and colleagues [103] showed that active coping was associated with better T cell function when stress was high, while avoidance coping appeared beneficial when stress was low. Other studies confirm the relationship between coping efforts and immune outcomes [41,104–106].

Researchers speculate that personality and coping moderate immune function by affecting subjective stress (as depicted in Figure 1). For example, hostile individuals may perceive more threat (i.e., primary appraisal [21]) and experience greater anger in response to conflict than non-hostile people. Coping could also affect the appraisal process. Effective copers might have high expectations of their ability to respond to the event (i.e. secondary appraisal), and this might reduce anxiety. One study explicitly tested the hypothesis that personality could affect immunity via subjective stress. In a study in which all participants were undergoing a stressor (entering law school), Segerstrom and colleagues [107] measured optimism, perceived stress, mood, and immune outcomes on two occasions. Optimism was, indeed, related to immunity (T-helper cell counts and NK cell cytotoxicity). Further, the hypothesized pathway was supported. Mood partially accounted for the relationship between optimism and T-helper cell counts, while perceived stress partially accounted for the relationship between optimism and NK cell cytotoxicity. Thus, as depicted in Figure 1, it is plausible that personal characteristics ultimately affect the physiological stress response through their effects on subjective stress.

The Psychological Stress Response and Immunity

Examination of the psychological stress response, per se, can be accomplished through participants’ self-reports. Questionnaires of subjective stress (perceived stress, emotional distress) can be correlated with immune measures, and this can be done in samples in which all participants are undergoing a stressor or in the general population. Subjective stress is also incorporated into “checklist” methods of assessing stress. Participants are asked to recall stressful events they have experienced. Typically, they are presented with a list of events and asked to identify which events they have experienced within the past year and how upsetting they found them to be. In contrast to studies in which the researcher identifies the stressor, this design has the advantage that the events under study are identified as stressors by the participants. Experimental methods of investigating subjective stress are less common, but have been employed. Perceptions of stress may be manipulated through stress protocols or through clinical interventions designed to alleviate stress.

The model outlined in Figure 1 implies that subjective stress (perceived stress and distress) will be more closely related to immune outcomes than are the events themselves. However, the observed relationships between subjective stress and immunity are surprisingly weak. Experimental manipulations of perceived stress, self-reports of subjective stress, participant-identified stressors, and clinical interventions have all yielded mixed results in determining the role of subjective stress in affecting immunity.

No experimental study has attempted to manipulate perceptions of stress (independent of the presence of a stressor) to affect immune response; however, one experimental study showed that manipulation of perceptions can affect cardiovascular response to stress. Tomaka and colleagues presented participants with one of two sets of instructions for a mental arithmetic stress task. One instructional set was intended to emphasize threat, while the other portrayed

Cellscience. Author manuscript; available in PMC 2008 July 16.
the task as a challenge [108]. As predicted, stronger cardiovascular reactions (heart rate, cardiac output, pre-ejection period, and total peripheral resistance) were seen in the threat condition. Because cardiovascular and immunologic responses to acute stress tend to coincide [109, 110], these results may be relevant for immune function. Other studies of acute laboratory stressors measured participants’ perceptions of the stressor, and these support the findings of Tomaka and colleagues. Although they did not manipulate stress perceptions, researchers observed larger physiological responses among participants who appraised the task as more overwhelming and less controllable [111,112].

Correlational studies have investigated subjective stress and immunity in naturalistic stressors. Many significant relationships between perceptions of stress and immune outcomes have been reported, yet overall, these results are not robust. Perceived stress correlates with reduced neutrophil activity [113], impaired response to vaccines [114–116], increased susceptibility to the common cold [15], and lower pro-inflammatory cytokine production in wounds [117], [118]. Emotional distress has also been correlated with immune function. With greater distress, NK and T cell function are lower [119–121], and interleukin-6 (a predictor of future disability among older adults) is higher among spousal caregivers of Alzheimer’s patients [122]. The clinical relevance of distress is implied by the work of Jabbaiaj and colleagues [123], who showed that distress predicted response to a hepatitis vaccine.

Despite the promising results of correlational studies such as these, the true relationships between subjective stress and immune function are yet unknown. Metaanalysis of 21 studies in which global perceived stress was correlated with immunity in the general population showed no significant relationships [85]. Meta-analysis of 9 studies in which participants were experiencing a common traumatic stressor (e.g. cancer diagnosis [124]) showed only NK cell cytotoxicity to relate to subjective stress, and the effect was modest (r = −.15, p = .02). The reviewers cited limited numbers of studies and methodological issues as potential explanations for the null results.

The “checklist” method is a more common way to assess stress in relation to immunity. Like subjective reports of stress, checklist methods should theoretically show stronger relationships with immunity than do researcher-identified stressors, because the events are identified as stressful by the participants. However, like correlational studies of subjective stress, results are surprisingly weak. In fact, meta-analysis of 53 studies using this approach found no consistent relationship between life event checklists and immunity [85].

Finally, psychological interventions have sought to improve immune function by reducing subjective experiences of stress [125]. In fact, some psychological interventions have successfully improved both subjective stress and immune function in stressed populations [126–130]. Predictably, other interventions have not affected immune function [131–135], and overall, only relaxation interventions appear to have reliable effect on immune function [125]. Most importantly, psychological improvements may not coincide with immune improvements. While some interventions showed immunological benefits to correspond to psychological benefits (e.g. [136]), others have not (e.g. [127]). Further, some psychological interventions have demonstrated psychological improvements without affecting immunity (e.g. [137]), or immune improvement without affecting subjective stress (e.g. [138]).

The Ambivalent Role of Subjective Stress

How can we explain the fact that stressors are consistently related to immunity, but the hypothesized causal factor, perceived stress, is not? How do we explain the capacity of individual differences such as personality to modulate the physiological stress response, if the subjective experience of stress is irrelevant? Circumstantial evidence implies that subjective
stress is an important factor in determining the physiological stress response, but studies that directly test the relationship do not confirm this.

While it may be true that there simply have not been enough studies examining this question [85], it is nevertheless surprising that results are not stronger among published studies. One consideration is the nature of self-reported data. These data can be influenced by individual differences in the ways people interpret and report their subjective experience. For example, some individuals may be prone to chronically under-report their subjective stress, others to over-report it. In addition, there may be persistent individual differences in tonic levels of immune measures [139]. Such individual differences could obscure the true relationships between subjective stress and immunity.

A longitudinal study offers the possibility of evaluating these confounding factors while also testing the effects of a stressor. Because each subject serves as his or her own control, differences between subjects can be differentiated from change within subjects over time. Three studies offer examination of subjective stress and immunity in a longitudinal design. Their results highlight the importance of change in subjective stress relative to absolute levels of stress. In the first study, Maes and colleagues measured students’ perceived stress and immune function at two time points, mid-semester and during the examination period [89]. They found that the difference in perceived stress across the two time-points correlated with the difference in immune cell counts and in the T-helper/suppressor ratio. Students whose perceived stress increased the most also showed the greatest change in immunity. The second study, by Stone and colleagues, employed multiple measurement time-points and found that students showed lower antibody titers to a harmless protein on days when their negative mood was high relative to days with low negative mood [140]. In the third, a Japanese investigation of the immune effects of confinement, change in mood over the confinement period predicted immune change, although overall level of mood did not. Two groups of 5 subjects each were confined for 10 days, and participants rated their mood daily. Participants were classified as “sensitive” or “non-sensitive” based on their mood change. Sensitive participants showed greater change in mood over the confinement period as well as greater immune change across all measures (percentages of granulocytes, natural killer cells, and CD69 positive cells) as compared with non-sensitive participants [141].

A second consideration with self-report data is its dependence on the participants’ ability to accurately rate their psychological state. Theorists have suggested that the cognitive processing required to produce a physiological stress response need not be conscious [14]. Participants might subconsciously appraise an event as threatening, yet be unable to report this appraisal. In particular, participants who use denial and repression to cope may be less aware of their subjective state. In fact, people who use denial or repressive coping report little psychological distress, yet their physiological response is consistent with participants reporting high stress [14,142].

**Conclusions**

Conclusive evidence demonstrates that stressful events are related to immune change. For acute stressors, this relationship is causal, and it is reasonable to interpret causality from chronic stressors as well. The present review explores an aspect of the stress response with significant theoretical and clinical implications: subjective experiences of stress. Perceptions of stress and emotional distress are proposed to be the mechanisms by which events elicit immune change. In addition, subjective stress has been used to explain between-subject variability in the immunological stress response, and clinical researchers seek to mitigate the immunological consequences of stress by improving subjective stress. These interpretations persist despite modest support for an association between subjective stress and immune function.
Two potential solutions to this dilemma are explored. First, longitudinal data may better illuminate the role of subjective stress in immune function than do cross-sectional studies. A few data suggest that change in subjective stress is more relevant for immune function than are absolute levels [89,140,141], but more research is needed to establish this. Second, it is possible that the appraisal of events as stressful is not always accessible to the conscious mind [14]. Participants using repression or denial may not be aware of feelings of stress, yet may show stress-related physiological reactions. Consistent evaluation of such traits is needed to evaluate this possibility.

Clarification of the role of subjective stress in immune change has both theoretical and clinical implications. It will further our understanding of how stressful events modulate immune activity as well as identifying targets for psychological intervention. With these tools in hand, we become better equipped to improve the health and quality of life for those enduring chronic stress.

References


Figure 1. Hypothesized pathway by which stress affects immune function and, ultimately, disease processes. NB: CNS = central nervous system; HPA = hypothalamic-pituitary-adrenal; SAM = sympathetic-adrenal-medullary.
Figure 2.
Main components of the hypothalamic-pituitary-adrenal (HPA) and sympathetic-adrenal-medullary (SAM) axes. NB: CRH=corticotropin releasing hormone; ACTH=adrenocorticotropin hormone.