Psychosocial Stress and Cardiovascular Disease Risk: The Role of Physical Activity

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Chronic stress and depression are associated with increased risk of cardiovascular disease and poorer prognosis, and physical (in)activity may be a key underlying biobehavioral mechanism. Physical activity has antidepressant effects, and physically fitter, more active individuals seem to be more biologically resilient to psychosocial stressors. This article will present data from a series of population cohort studies and laboratory-based psychophysiological studies to explore the role of physical activity as a protective factor against the effects of psychosocial stress on cardiovascular disease. These mechanisms may improve the treatment and prevention of stress-related illnesses and, thus, has important implications for public health and clinical care of high-risk patients. Key words: cardiovascular disease, depression, epidemiology, physical activity, psychophysiology, stress.

CVD = cardiovascular disease; IL = interleukin; TNF-α = tumor necrosis factor α; CRP = C-reactive protein; BDNF = brain-derived neurotrophic factor; HPA = hypothalamic-pituitary-adrenal.

INTRODUCTION

Psychosocial risk factors involve a wide range of different variables including mental stress, depression, anxiety, hostility, loneliness, and social circumstances and networks. Evidence from prospective cohort studies in humans that has emerged over the last several decades consistently demonstrates an association between various psychosocial risk factors and future risk of cardiovascular disease (CVD) in both initially healthy samples and patients with cardiac disease (1–4), with effect sizes that are comparable with conventional risk factors such as hypertension, obesity, and smoking (5).

The issue of how to tackle factors such as chronic stress and depression for disease prevention has been an area of considerable interest and intense debate in clinical and research work. For treatment to be successful, it is essential to understand the pathways that might explain the associations between psychosocial stress and disease. Our understanding of the mechanisms is evolving (see Fig. 1), and this knowledge base continues to develop. The reasons that the underlying pathways linking stress and CVD are incompletely understood can be partly attributed to methodological limitations and lack of controlled trial data. At present, the evidence base is largely limited to findings from observational population studies and psychophysiological experiments. Population studies enable large numbers of participants to be observed over time for hard clinical endpoints, although causal inferences cannot be established. Testing of acute psychophysiological stress involves the assessment of individual differences in biologic responses to standardized stressors that can be related to psychosocial stressors, thus, is a useful technique to investigate underlying mechanisms (6,7).

Physical activity is a potentially important mediator of the link between stress and CVD. The last 50 years of epidemiological research in physical activity has provided strong evidence for the beneficial effects of physical activity on both cardiovascular (8,9) and mental health outcomes (10,11), although the causality of the former cardiovascular effects is much better established than that on mental health outcomes (12,13). The aim of this article is to provide a selective review of the evidence for physical activity as a key intermediate pathway in the association between psychosocial factors and CVD.

EPIDEMIOLOGICAL EVIDENCE

In recent years, epidemiological approaches to modeling the relationship between stress and CVD have been refined; traditionally, researchers have aimed to test if the association between exposure (stress) and outcome (CVD) is maintained after adjustments for numerous covariates. However, more contemporary studies have started to treat covariates such as physical activity as mediators, thus examining the extent to which effect estimates are changed when a potential mediator is added to the model. Such an approach is grounded in theory and must conform to the main criteria for mediation; that is, the exposure should be associated with the potential mediator(s), the potential mediator should predict the outcome, the exposure variable should be associated with the outcome, and this association should be significantly attenuated after adjustment for the mediator. Evidence from contemporary studies (14–18) has clearly demonstrated that participants categorized as stressed/depressed report lower physical activity levels, which can explain up to 30% of the association between stress/depression and CVD (see Table 1). For example, among 6576 healthy community-dwelling participants, those reporting psychological distress at baseline were at 50% increased risk for a CVD event during a 7-year follow-up (14). Subsequent adjustment for physical inactivity in the models was associated with a 22% reduction in the strength of association between distress and CVD events, despite accounting for other covariates such as, age, sex, socioeconomic status, smoking status, and other conventional CVD risk factors. Similar findings were observed among 1017 outpatients with stable coronary disease from the Heart and Soul study (15). In a small cohort of 909 healthy, older European men, physical inactivity explained a negligible amount of the association between depression and CVD mortality during a 10-year follow-up (18), although depression and inactivity combined to produce an additive risk increase of 33%. In one of the largest behavioral intervention trials to date, consisting of 2481 patients with myocardial infarction experiencing depression and low perceived social support, treatment with cognitive behavior therapy had no effect on event-free survival...
Figure 1. A conceptual framework for the possible mechanisms that explain the association between psychosocial risk factors and cardiovascular disease. HPA = hypothalamic-pituitary-adrenal; SNS = sympathetic nervous system.

after a 29-month follow-up, despite significant improvement in depression and perceived social support (19). However, in a secondary analysis of the cohort in the Enhancing Recovery in Coronary Heart Disease Patients study, self-reported exercise in the 6 months after myocardial infarction was associated with more than a 50% reduction in the risk of subsequent death (20). Physical inactivity not only carries cardiovascular health risks but also is important in predicting the onset of physical decline in older adults (21) and partly explains the link between depression and disability (22). Thus, physical decline, together with perceived barriers toward physical activity, such as fear and negative experiences, low self-efficacy, and lack of knowledge, may partly explain the increased risk of physical inactivity among participants with depressive symptoms. In addition, cognitive factors such as impaired executive function, with reduced ability to handle, process, and retain new information, may also partly explain why depressed patients are less likely to adhere to treatments and lifestyle modification.

A clear limitation of the existing work in this area is that most studies are unable to provide a robust test of mediation because the potential mediating variables are usually measured at the same point in time as the markers of stress exposure, thus making it difficult to determine the temporal nature of the association. Indeed, the association of stress with intermediate risk factors for CVD might be bidirectional in that stress not only causes disturbances in behavior and pathophysiological markers but also vice versa. For example, physical activity seems to be protective against the development of depression and stress-related illness, although individuals with mental illness are less likely to undertake any activity (23). These types of issues might be resolved in the future by the use of contemporary statistical approaches that reveal individual heterogeneity in the direction of the effect (24). Another weakness of this area is the reliance on self-reported physical activity. One of the most significant developments in field over the last decade has been the introduction of small solid-state accelerometer devices that now permits physical activity to be assessed objectively over several days at low cost, thus making it feasible to incorporate such measures in large-scale population studies such as the National Health and Nutrition Examination Survey. Physical activity epidemiologists have traditionally used self-report measures, which have the possibility of introducing reporting biases and making it more difficult to precisely define the dose-response association between physical activity and health. Objective measures are able to not only assess intensity and duration of activity more effectively but also better delineate the duration of continuous bouts of activity and periods of prolonged inactivity (sitting) (Fig. 2). Very few studies have examined associations between objectively assessed physical activity and mental health, and those that have reveal inconsistent findings (25–29). Some of these limitations inherent to epidemiological studies can be reduced by investigations that use experimental manipulations of physical activity levels and those using stress reactivity paradigms.

**EXERCISE AND CARDIOVASCULAR STRESS REACTIVITY**

Psychophysiological stress testing can be used to establish the mechanisms and time trajectories underlying the association between stress and CVD. Although acute psychophysiological responses are not clinically meaningful in themselves, they represent the way in which individuals respond to daily stressors in their normal lives and if elicited regularly might have clinical relevance. A body of work has examined the association between psychophysiological stress reactivity and cardiovascular risk (6), which, on balance, suggests that the effect sizes are modest but consistent after accounting for established

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Exposure and Outcome</th>
<th>% Explained by Physical Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamer et al. (14)</td>
<td>Healthy general UK population (n = 6576)</td>
<td>GHQ-12; CVD events, 7.2-y follow-up</td>
<td>22%</td>
</tr>
<tr>
<td>Whoo et al. (15)</td>
<td>Patients with cardiac disease (n = 1017)</td>
<td>PHQ-9; recurrent CVD, 4.8-y follow-up</td>
<td>31%</td>
</tr>
<tr>
<td>Hamer et al. (16)</td>
<td>UK elderly population (n = 1007)</td>
<td>GDS-15; CVD death, 9.2-y follow-up</td>
<td>25% (12.5% activity; 12.5% function)</td>
</tr>
<tr>
<td>Win et al. (17)</td>
<td>Healthy general US population (n = 5888)</td>
<td>CES-D; CVD death, 10.3-y follow-up</td>
<td>26%</td>
</tr>
<tr>
<td>Kamphuis et al. (18)</td>
<td>Healthy European elderly men (n = 909)</td>
<td>Zung Self-Rating Depression Scale; CVD death, 10-y follow-up</td>
<td>9%</td>
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CVD = cardiovascular disease; GHQ-12 = General Health Questionnaire; PHQ-9, Patient Health Questionnaire; GDS-15, Geriatric Depression Scale; CES-D, Centre for Epidemiological Studies Depression scale.
risk factors. Paradoxically, both exercise and mental stress elicit substantial cardiovascular reactivity, although these responses are considered healthy in the context of exercise, whereas the same reactivity measures are purportedly “bad” when examined in the context of mental stress. In fact, similarities between central and peripheral responses to exercise and mental stressors have led to the theory of “cross-stressor adaptation” (30), where adaptations resulting from regular exercise lead not only to improved physiological control during exercise but also in response to psychological stressors. Because exaggerated responses to mental stress can have detrimental effects on health, the potential stress-buffering effects of exercise are of importance. Much of the existing psychophysiological work relating to physical activity has focused on cardiovascular responses. Several experiments have tested the impact of single bouts of exercise, the aim of which is to examine whether stress reactivity or rate of recovery is modified after physical activity; others have made comparisons of stress responses in physically fit and unfit individuals; and training studies in which psychophysiological stress responses are compared before and after exercise training.

Studies examining the effects of acute exercise have resulted in relatively consistent evidence, such that a single bout of exercise is associated with buffering of blood pressure and cardiac responses to standardized behavioral challenges in the laboratory (31). Studies that have examined psychophysiological responses in relation to physical fitness (an indicator of training status) and exercise training have produced more mixed results. In an early meta-analytic review of 34 studies, aerobic fitness was associated with nearly half a standard deviation reduction in blood pressure stress reactivity (32), but more recent updated reviews suggested both positive and inverse associations between fitness and heart rate reactivity (33,34). Dishman and Jackson (33) reported that fitness was related to greater heart rate reactivity but better recovery from mental challenge in 73 studies, although these effects were diminished when only randomized controlled exercise training studies were included and when fitness was measured as peak oxygen uptake. In contrast, Forcier and colleagues (34) demonstrated an inverse association between fitness and heart rate reactivity in an analysis containing only studies with evidence of an exercise training effect. A common problem in this area is limited sample size that can often lead to studies with insufficient statistical power. This issue was, however, addressed in a recent controlled trial consisting of 149 healthy, young sedentary participants who were randomized to a 12-week exercise program, followed by a further 4 weeks of sedentary deconditioning (35). Participants performed various stressors before and after the intervention, including a public speaking task, mental arithmetic, and the Stroop Color-Word task, although there was no indication of any stress-buffering effects after exercise training. In addition, a recent trial that examined the effects of 8-week exercise training on muscle sympathetic nervous activity measured directly from the peroneal nerve found no evidence of sympathoinhibition (36). Another study examined exercise training in the context of weight loss in obese children and found that weight loss through 4 months of exercise training and diet, but not diet alone, improved vasodilatation responses to the Stroop mental challenge (37). This suggests that exercise in combination with weight loss might be important in attenuating cardiovascular reactivity in response to mental challenges.

One of the difficulties in interpreting data from short-term (often 8–12 weeks) exercise trials is that individual changes in fitness are usually modest, which suggests that a short period of exercise training may not be sufficient to induce the type of chronic adaptations required to observe stress-buffering effects. Here, a comparison of persons with a longer history of low and high levels of habitual physical activity may be helpful. Much of the research in this field has relied on self-report measures of physical activity, and the problems with these are well known. We therefore conducted a study to examine the association between objectively measured habitual physical activity levels and psychophysiological responses in women (29). Participants

Figure 2. Data from an accelerometry device that was worn by a healthy male participant during a 24-hour period. The data emphasize the complex patterns of activity that can be captured by an objective measure. To view image in color, please visit: www.psychosomaticmedicine.org.
wore an accelerometer device during waking hours for 1 week and, in addition, recorded their daily moods and took part in psychophysiological testing. We observed robust associations between objectively assessed physical activity and daily mood (Fig. 3), although no associations were found with cardiovascular reactivity to behavioral stressors administered in the laboratory. Further work is required to examine if habitual physical activity is more closely linked with physiological reactivity to naturalistic stressors. In addition, sedentary behavior may play an important role (38), although no work has examined if sedentary behavior (prolonged sitting) is related to psychophysiological responses independently of physical activity. Taken together, inconsistencies in this area may be due, in part, to small sample sizes, insufficient exercise training effects, inconsistencies in methodology (i.e., design, types of stressors, and types of stress response measures), failure to account for the aftereffects of a recent bout of acute exercise, and other confounding factors. Furthermore, based on the law of initial values, it is likely that exercise will have the greatest effects in those individuals with heightened responses from the outset or some degree of underlying disease pathology. For example, exercise has been strongly associated with stress-buffering effects in participants with parental history of hypertension (39) and chronically stressed individuals such as caregivers (40) compared with healthy low-risk individuals. It should also be noted that previous studies have generally tended to measure blood pressure intermittently with conventional arm cuffs, which may not capture the full contour of the response that can be obtained using beat-to-beat devices.

The potential stress-buffering benefits of regular exercise may be largely accounted for by the fact that exercisers are more often in the postexercise window when they encounter daily stressors. The attenuation in blood pressure reactivity immediately after a single bout of acute exercise is thought to be best explained by a reduction in regional vascular resistance mediated by sympathetic nervous inhibition (41). Indeed, studies have shown that reduced noradrenaline response to a behavioral stress task was the best single predictor of the attenuation in postexercise blood pressure stress responses (42). Furthermore, significant increases in postexercise β1- and β2-receptor responsiveness were observed, indicating that the blood pressure response was primarily blunted by enhancing β2-mediated vasodilatation (42). Taken together, improvements in hemodynamic function during mental stress may be an important mechanism contributing to the stress-buffering effects of acute exercise in relation to CVD risk.

PHYSICAL ACTIVITY, STRESS, AND INFLAMMATION

The immune system may play an important role in psychobiologic processes that link psychosocial stress with CVD and other health outcomes (43). Acute mental stress has been shown to induce increases in circulating inflammatory markers such as interleukin (IL)-6 and tumor necrosis factor α (TNF-α) (44), and these responses are more pronounced in participants with enduring chronic stress and depressive symptoms (45,46), although less pronounced in physically fit participants (47). Numerous studies have also demonstrated elevated concentrations of various inflammatory markers at rest in differing populations reporting depressive symptoms (48). A large amount of interest has focused on the potential anti-inflammatory effects of exercise. It has been argued that the increases in circulating IL-6 that are observed after an acute bout of exercise promote an anti-inflammatory environment by increasing IL-1 receptor antagonist and IL-10 synthesis while inhibiting proinflammatory markers such as TNF-α (49). The cytokines released during exercise are thought to originate from exercising skeletal muscle, which work in a hormone-like fashion exerting specific endocrine effects on various organs and signaling pathways. Unlike IL-6 release during acute mental stress, which seems to be dependent on activation of the nuclear factor kB signaling pathway (50), intramuscular IL-6 expression is regulated by a network of signaling cascades that are likely to involve the CA2+/NFAT and glycogen/p38 MAPK pathways. This might partly explain why exercise-induced IL-6 release is not acting as a strong proinflammatory agent. This hypothesis is also consistent with data from numerous observational studies demonstrating an inverse association between regular physical activity and various proinflammatory markers (51). Results from controlled exercise trials have not always consistently found reductions in inflammatory markers after intervention, although given that most health benefits from exercise are established through chronic training adaptations, it is difficult to draw firm conclusions from short-term exercise trials often only lasting for

![Figure 3](image-url) A. The association between physical activity and daily positive mood. B. Depressive mood measured from the Centre Epidemiological Studies Depression scale. Physical activity groups reflect the tertile of average daily minutes actively recorded by accelerometry (≤213.88, 213.89–262.33, and ≥262.34 minutes/d).
STRESS, CVD, AND PHYSICAL ACTIVITY

3 months. In the Whitehall II cohort, we recently demonstrated that maintenance of habitual physical activity for 10 years was associated with lower levels of C-reactive protein (CRP) and IL-6 at follow-up and that the differences in inflammatory markers between active and inactive remained stable over time (52).

Given the described link between both psychological stress and exercise with inflammatory pathways, it can be hypothesized that better mental well-being experienced by regular exercisers might be partly explained by an underlying inflammatory mechanism. We conducted a study in a sample of 3609 older adults from the English Longitudinal Study of Ageing, to examine if the association between persistent depressive symptoms and inflammatory markers during a 2-year follow-up could be partly explained by physical activity behavior. Participants with recurrent elevated depressive symptoms at both time points displayed significantly elevated levels of CRP and fibrinogen at follow-up compared with nondepressed participants, and this relationship was partly explained through lower levels of physical activity in participants with depressive symptoms (53). The anti-inflammatory effects of exercise might also be relevant at a neurobiological level because alterations in neurotransmitter function involving serotonin, norepinephrine, and dopamine are known to induce depression and are targets for currently available psychopharmacological treatments. Exercise is thought to alter serotonin metabolism, release endogenous opioids, and increase central noradrenergic neurotransmission, which may all contribute to antidepressant and anxiolytic effects. The dopaminergic system is thought to play a key role in depression, and polymorphisms of the dopamine D2 receptor gene have also been implicated in physical activity behavior (54). Further research has focused on the hippocampus, where exercise-induced neurogenesis and growth factor expression has been proposed as potential mediators (55). An emerging theory is that exercise enhances several growth factors such as brain-derived neurotrophic factor (BDNF) and insulin-like growth factor, which mediate the protective and therapeutic effects of exercise on depression. It has been shown that an acute bout of exercise increases peripheral levels of serum BDNF in an exercise intensity-dependent fashion, but resting levels of BDNF do not seem to be affected by long-term exercise training (56), suggesting that other compensatory mechanisms might be at play. In connection to the effects of exercise on neurotrophins, the endocannabinoid system might represent an important mediating signaling pathway (57).

Another important aspect may be the interaction of the immune system with the hypothalamic-pituitary-adrenal (HPA) axis and autonomic nervous system. After mental stress, the sensitivity of the immune system to dexamethasone inhibition (a synthetic version of the hormone cortisol that has potent anti-inflammatory properties) is reduced, as manifest by a reduction in this hormone’s capacity to suppress the production of inflammatory cytokines (58). In endurance-trained individuals, however, an acute bout of exercise has been shown to increase tissue sensitivity to glucocorticoids (59). HPA axis dysregulation and cortisol hypersecretion have been implicated in adverse mental health and cardiovascular outcomes. For example, in a healthy subsample of participants from the Whitehall II cohort, we showed that exaggerated cortisol responses to two behavioral stress tasks were predictive of coronary artery calcium progression during a 3-year follow-up and incident hypertension (60,61). Exercise may have beneficial effects on HPA functioning because some studies have shown lower stress-induced cortisol responses in physically trained compared with untrained individuals (62,63). However, we failed to replicate previous findings in our work that examined associations between objectively assessed physical activity levels and cortisol responses to acute mental stress (29). In addition, recent data demonstrated higher levels of cortisol in the hair of trained athletes compared with controls, suggesting greater chronic exposure to cortisol in trained individuals (64). Some of these inconsistencies might be attributed to differences in measures because cortisol from hair is a reflection of chronic exposure but does not necessarily provide information about glucocorticoid sensitivity or acute variations, which are better assessed through psychophysiological studies and diurnal sampling. Thus, teasing apart chronic effects from acute variations in daily diurnal patterns will be an interesting avenue of future research.

In summary, the link between physical activity and stress could be explained through several biologic processes including the inflammatory, dopaminergic, and neuroendocrine systems, which might have relevance to CVD pathology and other diseases in which inflammatory processes play a contributing role. However, there is a lack of experimental and longitudinal evidence to show the long-term health consequences of physical activity on these biologic pathways.

THE EXERCISE WITHDRAWAL PARADIGM

Exercise training trials are costly and require a large amount of manpower in administering supervised exercise sessions. In addition, one of the difficulties in interpreting data from short-term (often 8–12 weeks) exercise trials is that individual changes in fitness are usually modest and some participants are nonadherent, which suggests that a short period of exercise training may not be sufficient to induce the type of chronic adaptations required to observe stress-buffering effects. The exercise withdrawal paradigm therefore represents a useful, more practical alternative because mood disturbances can be elicited in habitual exercisers after a 1- to 2-week withdrawal from their regular training activities, which provides a model to investigate the links between exercise, stress, and the underlying biology. We and others have hypothesized that mood disturbances caused by withdrawal from regular exercise might act as a mild inflammatory stimulus. However, recent studies have been unable to confirm this hypothesis. Several studies, including one of our own that have successfully induced an increased negative mood after several weeks of exercise withdrawal, did not find any robust changes in a range of inflammatory markers such as IL-6, CRP, TNF-α, fibrinogen, and soluble intracellular...
adhesion molecule-1 (65,66). Similarly, 1-week withdrawal from exercise in highly active men did not elicit any substantial changes in CRP, IL-6, TNF-α, and circulating leukocyte concentration (67). In the same study, no changes in inflammatory markers were observed among sedentary participants who undertook 30 minutes of brisk walking each day for 1 week. Healthy men who reduced their daily step count by 85% for 2 weeks developed impaired glucose tolerance, attenuation of postprandial lipid metabolism, and a 7% increase in intra-abdominal fat mass, although plasma cytokines and muscular expression of TNF were not altered (68). However, another study reported that reduced parasympathetic nervous activity as measured by heart rate variability was predictive of negative mood after exercise withdrawal (69). These findings are consistent with emerging data on underlying molecular mechanisms. For example, the expression of exercise-regulated muscle genes such as the transcriptional coactivator PGC1α, which is thought to promote anti-inflammatory effects (70), is known to be rapidly induced after a single bout of acute exercise, although it quickly reverts back to basal levels. In contrast to the transient changes after acute exercise, greater levels of PGC1α are present in chronically trained exercised muscle than in untrained muscle. Thus, there is a clear difference between short-term and long-term adaptations, which might explain why a short 2-week exercise withdrawal period in trained participants is insufficient to see changes. Furthermore, adherence to exercise withdrawal in regular, fit exercisers may be problematic because habitually active individuals are less likely to agree to stop their training regimen and perhaps compensate in other ways to maintain a physically active lifestyle (e.g., taking up active commuting for the period of exercise withdrawal). This creates other inherent limitations because removing self-chosen leisure time behaviors may in itself induce psychological distress regardless of exercise cessation.

In a further study, we investigated the impact of exercise withdrawal on psychophysiological responses to mental stress because this method can sometimes detect differences that might not otherwise be seen under resting conditions. Although the effects of cytokines are often thought to be transient, they may provoke a time-dependent sensitization so that the response to a later cytokine or stressor stimulus is enhanced, resulting in an increased vulnerability to depressed mood (71). We experimentally manipulated physical activity levels by asking a group of habitual exercisers to withdraw from their regular training for 2 weeks (72). The adherence to exercise withdrawal was mixed, as indicated by objective accelerometry physical activity records, but in participants with greater mood disturbances (assessed using the 28-item General Health Questionnaire) after a 2-week withdrawal, we observed significantly higher inflammatory responses to mental stress compared with those with low or no mood disturbance. In the same study, cortisol responses to mental stress were higher in the exercise withdrawal phase compared with the control period, with a significant difference emerging at 20 minutes poststress. These results, although preliminary, suggest that inflammatory and neuroendocrine factors may, in part, mediate the protective or buffering effect of physical activity on stress-related physiological activation.

To summarize, the exercise withdrawal paradigm offers a promising way in which to elucidate some of the mechanistic pathways linking physical activity to stress and CVD risk. Future work is needed to better understand the temporal relationship between exercise-induced mood disturbances and changes in inflammatory and neuroendocrine factors.

**CONCLUSIONS AND FURTHER WORK**

Numerous intermediate mechanisms might explain the link between psychosocial factors and CVD and other diseases, including behavioral and biologic processes. Increasing our knowledge about these mechanisms will contribute to more effective prevention and treatment strategies and help establish priorities for the allocation of health care and research resources. Taken together, the currently available data from epidemiological studies suggest that physical activity plays an important role in explaining the association between psychosocial factors and CVD. Interventions that reduce the magnitude of psychophysiological responses are also of interest because exaggerated responses to mental stress can have detrimental effects on health. Regular exercise is known to be an effective lifestyle intervention in the primary prevention of CVD, and this could be partly mediated through the buffering of hemodynamic, neuroendocrine, inflammatory, and hemostatic responses to daily mental stressors. There is reasonably strong evidence to suggest that a single bout of acute exercise can blunt cardiovascular stress responses, and because these effects last for 2 to 4 hours, a person that exercises 3 times a week may be in a stress-buffered state up to 12 hours a week. Data from chronic training intervention studies on the effects beyond the aftereffects of a recent bout of acute exercise are less consistent. Inconsistencies in this area may be due, in part, to small sample sizes, insufficient exercise training effects, inconsistencies in methodology (i.e., design, types of stressors, and types of stress response measures), and other confounding factors. At present, there is evidence suggesting that exercise might also modify biologic stress responses (cortisol, inflammatory markers), although further experimental work is needed to extend the current findings.

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STRESS, CVD, AND PHYSICAL ACTIVITY


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