SOCIAL SUPPORT AND RESILIENCE TO STRESS:

From Neurobiology to Clinical Practice

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ABSTRACT

Numerous studies indicate social support is essential for maintaining physical and psychological health. The harmful consequences of poor social support and the protective effects of good social support in mental illness have been well documented. Social support may moderate genetic and environmental vulnerabilities and confer resilience to stress, possibly via its effects on the hypothalamic-pituitary-adrenocortical (HPA) system, the noradrenergic system, and central oxytocin pathways. There is a substantial need for additional research and development of specific interventions aiming to increase social support for psychiatrically ill and at-risk populations.

INTRODUCTION

Social support is exceptionally important for maintaining good physical and mental health. Overall, it appears that positive social support of high quality can enhance resilience to stress, help protect against developing trauma-related psychopathology, decrease the functional consequences of trauma-induced disorders, such as

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posttraumatic stress disorder (PTSD), and reduce medical morbidity and mortality.[1] However, despite strong evidence demonstrating the beneficial effects of social support on medical and psychological wellbeing, the field of psychiatry has contributed relatively little to developing, testing, and implementing effective evidence-based interventions aimed at increasing social support for patients and at-risk populations. In this review article, we aim to summarize key studies on social support in the context of resilience to stress and explore possible brain mechanisms mediating social support's positive influence on mental health outcomes. We will begin with a brief overview of the neurochemistry of the stress response and resilience to stress. Within this framework, we will then review the emerging literature on the neurobiology and the behavioral mediators of social support. Next, we will review studies that have investigated the effects of social support on medical illness, and finally, conclude with a discussion on social support's clinical significance for psychiatry.

RESILIENCE TO STRESS: PUTATIVE MECHANISMS

Psychological resilience represents a process of adapting well in the face of adversity. The psychosocial and neurobiologic characteristics of resilience to stress are extremely complex, and their discussion is beyond the scope of this article (for a thorough review see Southwick, et al.[1]). However, the literature suggests the sympathetic nervous system and hypothalamic-pituitary-adrenocortical (HPA) system are extensively involved in stress response and resilience.[2]

The sympathetic nervous system (SNS) responds to stress by increasing heart rate, constricting blood vessels, increasing blood pressure, and slowing digestion. Numerous lines of evidence from psychophysiology and neuroendocrine studies indicate that the noradrenergic system is often dysregulated in PTSD. For example, chronic PTSD is associated with high baseline cerebrospinal fluid NE concentrations.[3] McFall, et al., demonstrated that subjects with combat-related PTSD had greater increases in plasma epinephrine, pulse, and blood pressure in response to viewing a combat movie.[4] Notably, the heightened autonomic activity of PTSD patients peaked during the resting period after the combat film, and the authors argued that an impairment of the mechanisms involved in terminating the noradrenergic response to stressors was implicated in the pathophysiology of PTSD. When the SNS is strongly activated, neuropeptide Y (NPY) and galanin are released with norepinephrine to maintain SNS activity within an optimal activation range (reviewed by Southwick, et al.[5]). Indeed, highly resilient special operations soldiers tend to have high levels of NPY[6,7] in contrast to combat veterans diagnosed with PTSD who have reduced levels.[8] The overall net effects of NE hyperactivity thus may depend on the balance between NE, NPY, and galanin. This supports the notion that resilience to stress is associated with the regulation of noradrenergic activity within an optimal window.

In response to acute and chronic stress, the hypothalamus secretes corticotropin-releasing factor (CRF), which in turn induces the release of adrenocorticotropin hormone (ACTH). ACTH stimulates the synthesis and release of cortisol and dehydroepiandrosterone (DHEA) from the adrenal gland. In the short run, cortisol mobilizes and replenishes energy stores and contributes to increased arousal.[9] However, if stress remains chronic, prolonged elevations of glucococorticoids may cause serious adverse effects, such as immunosuppression, hypertension, dyslipidemia, and osteoporesis.[10] In contrast to cortisol, DHEA exerts antiglucocorticoid and antiglutamatergic activity in the brain and may confer neuroprotection (reviewed by Charney[2]). For example, a negative correlation has been demonstrated between DHEA levels and PTSD symptom severity in women.[11] Morgan, et al., found a positive correlation between DHEA/cortisol ratio and performance among special forces soldiers during high stress training.[12] Similarly, allopregnalolone, another neuroactive steroid, dampens the HPA activity. Rasmusson, et al., has reported lower cerebrospinal fluid levels of allopregnanolone in those diagnosed with PTSD compared to controls.[13] In conclusion, DHEA and allopregnalolone may confer resilience to stress by helping to terminate HPA-activation and preventing harmful effects of prolonged exposure to glucocorticoids.

In summary, stress resilience seems to be associated with an ability to keep the HPA-axis and noradrenergic activity within an optimal range during stress exposure and terminate the stress response once the stressor is no longer present. Based on these findings, we may postulate that for social support

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to increase stress resilience, it should enhance the ability to optimize the neurochemical stress response summarized above.

WHAT IS SOCIAL SUPPORT?

Social support has been described as "support accessible to an individual through social ties to other individuals, groups, and the larger community."[14] The National Cancer Institute's Dictionary of Cancer Terms defines social support as "a network of family, friends, neighbors, and community members that is available in times of need to give psychological, physical, and financial help" (www.cancer.gov). Theoretical models of social support specify the following two important dimensions: (1) a structural dimension, which includes network size and frequency of social interactions, and (2) a functional dimension with emotional (such as receiving love and empathy) and instrumental (practical help such as gifts of money or assistance with child care) components.[2] Most research has found that quality of relationships (functional dimension) is a better predictor of good health than quantity of relationships (structural dimension), although both are important.[1]

It should be noted that the optimal source of social support may depend on the developmental stage of the person who is receiving the support. For example, parental support seems to be more valuable in early adolescence than it is in late adolescence.[15] It has been shown that the perception of social support is associated with the degree of social interaction in the elderly and with instrumental support in younger adults.[16] Moreover, the type of social support seems to be important in conferring resilience to stress. In a sample of childhood sexual abuse survivors, a combination of self-esteem support (the individual perceives that he or she is valued by others) and appraisal support (the individual perceives that he or she is capable of getting advice when coping with difficulties) was most useful in preventing the development of PTSD.[17]

THE PSYCHOBIOLOGICAL MEDIATORS OF SOCIAL SUPPORT

Investigators have explored the ways in which social support may enhance mental and physical health. It has been argued that rich social networks may reduce the rate at which individuals engage in risky behaviors,[18] prevent negative appraisals,[19] and increase treatment adherence. In general, resilient or hardy individuals are thought to use active coping mechanisms when dealing with stressful life situations.[20] Using a time lag model for the prediction of depression, Holohan, et al.,[21] found that high social support predicted less subsequent depression in patients with acute and chronic cardiac illness and that this relationship was partly mediated by the use of an active coping style. Importantly, in this cohort, social support preceded and facilitated the use of active coping mechanisms.

There is an emerging literature on social support and the neurobiological pathways through which it acts to foster resilience and reduce the risk for developing mental illness. In preclinical studies, social isolation has been associated with increased heart rate and blood pressure, hypercortisolemia, and atherosclerosis. For example, among cynomolgus monkeys, resting heart rate increases during separation and isolation but returns to normal when monkeys are reunited with their social group;[21] cortisol rises in squirrel monkeys[22] and wild baboons[23] during isolation; at postmortem examination, atherosclerosis has been significantly greater in swine[24] and in female monkeys[21] living alone vs those living in social groups. Further, evidence suggests chronic stress and lack of social support increases cardiac risk (e.g., endothelial injury, increases platelet accumulation), in part, through prolonged sympathetic activation.[25]

In human studies, low social support has been associated with physiological and neuroendocrine indices of heightened stress reactivity, including elevated heart rate,[26] increased blood pressure,[27] and exaggerated cardiovascular and neuroendocrine responses to laboratory stressors. For example, in laboratory studies mental arithmetic[28] and public speaking tasks[29,30] cause significantly smaller rises in heart rate, blood pressure, and cortisol among subjects supported by another person compared to subjects who are alone. These findings are consistent with the results of a study conducted by Steptoe, et al., who reported an overall increased noradrenergic and HPA reactivity in lonely individuals.[31]

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The brain mechanisms, including the neural circuits and neurotransmitter systems, that underlie the acquisition and processing of social information are extremely complex and far from being completely understood. However, animal studies indicate that the regulation of social attachment and promotion of positive social interactions may be heavily dependent on two neuropeptides known as

oxytocin and vasopressin.[32] Oxytocin is critical for learning social cues and has been shown to enhance maternal care in rats.[33] Differential oxytocin and vasopressin receptor expression patterns in specific areas of the brain (ventral pallidum and medial amygdala) have been shown to influence the type and duration of social attachments formed by voles. For example, montane voles typically avoid social contact except while mating; they have lower levels of oxytocin receptors in the nucleus accumbens compared to prairie voles, which are highly social and typically monogamous.[34] Oxytocin also exerts anxiolytic effects that are associated with attenuated secretion of corticosterone in lactating rodents.[35]

The role of oxytocin in human social behavior has been investigated as well. The Trier Social Stress Test is a laboratory stressor that involves simulation of an aversive job interview and public speaking with negative feedback, resulting in a robust increase in anxiety and salivary cortisol. Both oxytocin and social support reduced anxiety in healthy men undergoing this procedure.[36] Interestingly, the same study showed that subjects who received the combination of oxytocin and social support had the least amount of anxiety and lowest cortisol responses to stress. Taken together, these results suggest that oxytocin promotes social behavior and may inhibit the HPA axis reactivity to stress.

THE IMPACT OF SOCIAL SUPPORT ON HEALTH OUTCOMES

Social isolation and low levels of social support have been shown to be associated with increased morbidity and mortality in a host of medical illnesses. For example, in the well-known Alameda County Studies, men and women without ties to others were 1.9 to 3 times more likely to die from ischemic heart disease, cerebral vascular disease, cancer, or a host of other diseases within a nine-year period compared to individuals with many more social contacts.[37] The effect of social support on life expectancy appears to be as strong as the effects of obesity, cigarette smoking, hypertension, or level of physical activity.[25]

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Numerous epidemiological studies have reported that poor social support is associated with the onset and relapse of depression,[38] negative treatment response to dysthymia,[39] seasonality of mood disorder,[40] and the presence of depression comorbid in several medical illnesses, such as multiple sclerosis,[41] cancer,[42] and rheumatoid arthritis.[43]

The Vietnam War may serve as an important example of failed social support during times of high stress and trauma. Johnson and colleagues found that many Vietnam veterans experienced homecoming as a highly stressful experience.[44] These veterans reported "being insulted, feeling angry, resentful, and alone." In this cohort of treatment-seeking, outpatient veterans with PTSD, homecoming stress was the strongest predictor of the frequency and intensity of their PTSD symptoms. The authors concluded that the lack of social support confirmed the veterans' perception of rejection and lead to feelings of detachment.[44]

In contrast to low social support, high levels appear to buffer or protect against the full impact of mental and physical illness. The relationship between good social support and superior mental and physical health has been observed in diverse populations, including college students, unemployed workers, new mothers, widows, and parents of children with serious medical illnesses.[45]

Strong social support has been shown to be an important factor in decreasing functional impairment in patients with depression[46] and in increasing the likelihood of recovery.[47] Further, the risk of developing PTSD upon exposure to combat trauma is inversely correlated with social support. For example, Boscarino, et al.,[48] after controlling for trauma exposure, found that Vietnam veterans with high levels of social support were 180-percent less likely to develop PTSD as compared to those with low levels of social support.

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CONCLUSION

The literature reviewed above clearly demonstrates the harmful consequences of poor social support and the protective effects of having access to rich and functional social networks on maintaining physical and psychological health. The exact biopsychosocial mechanisms underlying the positive influence of social support on resilience to stress

are unknown. There is undoubtedly a complex interplay of various environmental and genetic factors that mediate the effects of social support on health outcomes. Evidence for such a gene-environment interaction involving social support comes from a pioneering study by Kaufman and her colleagues who have shown that social support may confer resilience to stress by moderating genetic risks for depression in maltreated children.[49] In this study, the combination of the met allele of the brain-derived neurotrophic factor (BDNF) gene and the two short alleles of the serotonin transporter (5-HTT) gene predicted the highest depression scores in maltreated children; and this vulnerability was moderated by the presence of social support.[49] This important finding demonstrates that an individual's environment may be modified to attenuate his or her genetic risk for developing mental illness even in the presence of environmental stressors, possibly by modifying gene expression. In fact, animal studies suggest maternal care can alter the expression of the glucocorticoid receptor gene via affecting DNA methylation and chromatin structure.[50]

Dampening HPA activity may be another major mechanism through which social support enhances resilience to stress. In fact, findings from animal and translational studies reviewed above show that social support reduces stress-induced cortisol release. It is possible that stress-induced oxytocin release augments social affiliation, which in turn reduces negative appraisals and arousal. It is open to speculation whether social support affects DHEA and/or NPY levels, which may then help to regulate HPA and noradrenergic systems, respectively.

In summary, social support seems to moderate genetic and environmental vulnerabilities for mental illness, possibly by effects through other psychosocial factors, such as fostering effective coping strategies, and through effects on multiple neurobiological factors. It will be important for psychiatric researchers to conceptualize, test, and apply effective interventions specifically aimed at increasing social support for psychiatrically ill or at-risk populations. This represents an important challenge for our field.

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