Published in final edited form as:

Acad Psychiatry. 2013 January 1; 37(1): 6–10. doi:10.1176/appi.ap.11100187.

Physiological and neurobiological aspects of stress and their relevance for residency training

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Introduction

Research investigating the undesirable outcomes of residency training mostly focuses on the effects of stress and long work hours on patient outcomes [1] as well as physician satisfaction [2], mental health [3–5], and recruitment and retention [6,7]. There is little research, however, examining the physiological and physical health implications of the stress of such training on physicians themselves. While current research falls short of fully understanding the health effects of medical training, there are some data, mostly from other populations, that our own “health practices” are ruining our health. With the newer and more restrictive set of ACGME residency requirements recently implemented in July 2011, it is an especially salient time to consider further research into the health effects of residency training that might knowledgeably inform policy organizations. While there may be historical reasons and advantages for the current residency paradigm, such as health care demand and training experience, it is nevertheless important that we understand the physiological and neurobiological, or psychoneuroimmunological (PNI), implications of this training on our young doctors.

The stresses on today’s residents seem perhaps greater than several decades ago [8], though there are no direct comparison studies. Indeed, many residents report experiencing much stress and anxiety with undesirable repercussions extending beyond their work life, though such feelings are rarely discussed [9,10]. In this paper, we will first discuss the importance of resident well-being before reviewing potential PNI and health effects associated with the stress of medical training. We will consider “stress” to include sleep deprivation, perceived psychological stress, mood alterations, and social isolation. Finally, we consider possible long-term sequelae of such training as well as outcomes of work hour reform.

The Importance of Resident Well-Being

The Institute Of Medicine issued a report in 2008 setting guidelines for resident duty hours to enhance sleep, supervision, and safety [11], spurred in large part by the findings that adverse events, including death, were the result of sleep-deprived and over-extended interns and residents [12]. These recommended changes are undeniably important to curtail such events, however, they fail to recognize the mental and physical health-related effects of such

conditions on its trainees. While forty-five percent of outpatients visiting primary care physicians report being excessively bothered by stress in the last month [13], we physicians seem to do little to practice what we preach to our patients. By comparison, residents report a greater number of health complaints than the average worker [14]. It is imperative to the integrity of the functioning of our health care system that we as physicians care for each other and ourselves as we would our patients. Further knowledge regarding the health effects of residency training could greatly inform health care policy creation.

The stress-promoting/health-depleting effects of the practice of medicine as an attending are also of great importance. Due to its unique conditions, however, residency exemplifies the definition of effort-reward imbalance, i.e. high-cost/low-gain conditions, which have been associated with adverse health outcomes [15]. Further discussion of stress effects on attendings is beyond the scope of this article.

While there may be historical reasons and advantages for the current residency training experience, such as health care demand and training experience, the scope of the current article

Physiological implications of conditions associated with medical training

Sleep deprivation

Sleep loss or deprivation is a stress-provoking experience for most residents in both the physical and psychological sense. Sleep research is admittedly complex and variable depending upon the population examined and definition of sleep deprivation used; however, there is evidence that acute sleep loss results in disrupted affect regulation and an increase in somatic complaints, anxiety, depression, and paranoia in healthy adults [16]. The stress of sleep deprivation is associated with temporary changes in cerebral metabolism, cognition, emotion, and behavior consistent with mild prefrontal lobe dysfunction [17] as well as decreased reaction time and vigilance [18].

Though a smaller body of literature, there is some research investigating the effects of sleep deprivation specifically in medical residents, which demonstrates that young doctors are as susceptible to its effects as non-residents. They exhibit significant slowing in cognitive processing and decline in reaction times on vigilance testing post-call [19,20]; another study demonstrated 84% scoring within the range on the sleepiness scale for which clinical intervention is indicated [21]. These deficits translate into functional and job impairments as well [22–25].

Sleep deprivation itself is associated with altered immune function, including impaired host-defense mechanisms, increased susceptibility to viral- and bacterial pathogens, decreased natural killer (NK) cell numbers and activity, and modified cytokine profiles favoring the proinflammatory state [26–29]. Indeed, sleep deprivation is a risk factor for human disease; however, objective and subjective measures of the effects of resident sleep deprivation differ, making mere resident questioning insufficient for evaluation of sleep [18].

Perceived stress and mood alterations

Sleep, stress, and mood are inextricably linked, with residents repeatedly reporting sleep loss and fatigue as having a major adverse impact on their mood, relationships, and quality of life [21,30]. Furthermore, interns report higher levels of burnout and depression and lower levels of empathy at the end of their intern year as compared to the beginning [30]. Indeed, there is a conglomeration of detrimental psychological responses that seem to result from medical training which have their own physiological consequences.

The adverse physiological and health effects of stress and negative mood are well established [31–37], with a few of these physiological responses being elevated white blood cell count, decreased NK cell activity, and altered cortisol secretion [38,39]. Likewise, stress is associated with elevated hormone levels, including glucocorticoids, catecholamines, prolactin, growth hormone, and nerve growth factor [40] which result in reactivation of viruses as well as decreased NK cell activity, lymphocyte proliferation and overall numbers, and antibody production. This cascade of neurohormonal changes ultimately significantly impacts health by delayed wound healing, impaired responses to infection and vaccines, and cancer development and progression, among other processes. While little research has been done explicitly on medical residents in terms of altered physiological functioning, data from other studies clearly demonstrate that conditions associated with residency training promote poor immune function.

Most studies examining resident stress physiology center around being on-call, which inherently confounds increased on-call stress with sleep deprivation. Nevertheless, significantly elevated or altered levels of adrenocorticotrophic hormone (ACTH), cortisol, testosterone, and luteinizing hormone have been observed post-call and are associated with increased levels of stress, anxiety, and depressive symptoms [41,42]. While on-call, surgical residents achieve stress levels of tachycardia and exhibit a significant increase in their level of circulating white blood cells [43]. Recently, Brant *et al.* [44] found that while residents did not report a change in stress levels over the course of a rotation, they exhibited evidence of neuro-endocrine changes consistent with hypothalamic-pituitary-adrenal (HPA) axis dysregulation. This suggests that residents may be under-reporting physiologically meaningful psychological stressors. *It is important to consider that residents vary in their perceptions of stress as well as their applied coping strategies, and therefore demonstrate significantly varied neurohormonal responses* [45].

Social isolation

Residents report suffering from shrinking social networks and reduced marital satisfaction during their time of training [46]. The psychophysiological implications of social isolation and stress are well established among the general population [47]. Social isolation predicts morbidity and mortality from multiple disease processes possibly via excessive stress reactivity and impaired physiological repair or maintenance processes, as well as health behaviors [48]. Collegial social support and job control are important factors contributing to the stress-related health of residents [14]. Research is needed focusing on the physiological and health effects, both short and long term, of social isolation or support in residents.

Most of the existing studies examining the physiological and neurobiological consequences of medical training suffer from methodological limitations including small sample sizes, confounding variables (e.g. sleep, timing of physiologic sampling, residency type, etc), and lack of adequate controls. Furthermore, interpretation of findings in this area is variable, with some literature interpreting a normalization of physiologic parameters equating to better coping strategies [43]. Clearly, more research is needed to investigate the physiological effects and their associated clinically relevant health outcomes of medical training, as other relevant studies provide evidence that resident conditions promote poor health via multiple mechanisms and pathways.

Long-term sequelae of medical training

To my knowledge, there are no studies evaluating long-term health sequelae of residency or health care practice-related stress. There is indication from other literature, however, that there are indeed long-term effects. A meta-analysis of 15 studies showed that short sleep duration of less than 5–6 hours per night is associated with a 48% greater risk of developing or dying from coronary heart disease and a 15% greater chance of developing or dying from a stroke [49]. Short sleep duration is associated with multiple physiologic mechanisms that may implicate it as a cause of cardiovascular disease (CVD). Changes in circulating levels of leptin and ghrelin are associated with short sleep duration [50] and facilitate the development of obesity [51] and insulin resistance [52]. Other candidate mechanisms relating decreased sleep and undesired health outcomes include increased cortisol secretion and altered growth hormone [53]. Short sleep duration activates an inflammatory response with implications not only for CVD, but for other chronic diseases including cancer [54]. Sleep deprivation also impairs immunity by causing a decreased response to vaccination [55].

Other residency-associated stressors are also associated with mechanisms implicated in adverse longer-term health outcomes. Burnout, which includes emotional exhaustion, physical fatigue, and cognitive weariness, is associated with elevated cortisol and development of cardiovascular disease in other populations [56], and there is an enormous literature on psychological stress and its short and long-term impact on cardiovascular disease [57]. Psychologically adverse work environments in general may accelerate immunosenescence [58]. Conversely, we see that the presence of positive psychological states, such as well-being, may afford protection against illness and disease via mechanisms involving neuroendocrine, immune, cardiovascular, and sleep pathways [59].

Outcomes of work hour reform

Resident duty hours were first regulated by the ACGME in 2003 and the newer, more restrictive set of program requirements were implemented in July 2011. Do they go far enough to successfully ameliorate the effects of resident stress? Perhaps these new requirements will be the necessary impetus to thoroughly investigate whether these restrictions are enough to mitigate the psychophysiological effects of residency-associated work, sleep, and stress conditions. This will be important to determine, as even with night float systems in place, objective sleepiness among residents can still be an issue [60]. Some

purport that perhaps the increased on-call workload and intensity actually undermines resident well-being [61], while yet others demonstrate a quality-of-life improvement after the 2003 reform [62]. The efficacy of work hour restriction on sleep and performance seems to be dependent not only on the number of sleeping hours, but also involves the pattern of sleep loss and whether residents are actually sleeping more or differently [60,63]. Even modest sleep loss is associated with altered T and NK cell function [64] as well as significant sleepiness, psychomotor impairment, and increased secretion of proinflammatory cytokines [65]. Vgontzas concludes that “given the potential association of these behavioral and physical alterations with health, well-being, and public safety, the idea that sleep or parts of it are optional should be regarded with caution”[65].

Conclusion

Given the emphasis on preventive care to better control the leading causes of morbidity and mortality in our increasingly aged population [47,66] as well as the newly revised duty hour restrictions, it is an especially salient time to consider that while our youngest physicians train to become the next cohort of health care providers, they routinely endure potentially health-depleting conditions. Data from the PNI literature provides us with much insight into some of the physiological and neurobiological outcomes that residency training may incite, as little has been done to investigate this population in particular. Residency is a unique and somewhat extreme situation in which trainees have little control over their environment, however, research investigating potential pathophysiological outcomes in this population may also be extrapolated to practicing physicians and improve the health of our healthcare providers overall.

Acknowledgements

This work was supported in part by funding from the National Institutes of Health (NIH) (Grants T32 073452 and UL1RR031973). The author would like to thank Jan A. Moynihan, PhD and Jeffrey M. Lyness, MD of the University of Rochester Department of Psychiatry for their input and editorial comments during manuscript preparation.

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