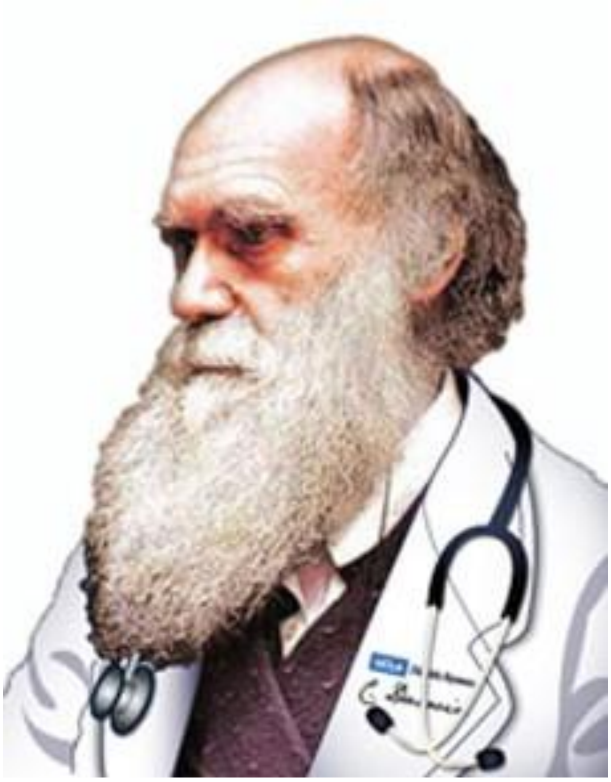
An Evolutionary Explanation of Burnout



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Introduction

1.1 'Disease' of the modern era

Although medical research has exterminated diseases such as the black plague and typhus, our modern environment exposed us to new epidemics like diabetes, multiple sclerosis, and Crohn's disease. One of those non-deadly but harmful threats to modern human beings is the risk of burnout. Burnout is a state of physical, emotional and mental exhaustion caused by excessive and prolonged stress[1]. The term 'burnout' was coined in the 1970s by Herbert Freudenberger, an American psychologist who used it to describe severe stress in the medical professions[2]. In 1984, another psychologist called Christina Maslach came with the *Maslach Burnout Inventory (MBI)*, which is nowadays the most common questionnaire for diagnosis[3]. In her concept, burnout is measured by three dimensions: Emotional exhaustion, depersonalization and personal accomplishment[3]. However, burnout can have a wide range of symptoms, and could for example be confused with depression. This makes it difficult to come to a general agreement about which of those symptoms are part of burnout and which are not. Consequently, there is still no clear definition of what burnout really is, and this makes clinical diagnosis inaccurate. Accordingly, because a universally accepted definition of burnout is lacking and not every case is reported, accurate prevalence estimates of the whole population are difficult to make. A survey from the Dutch government estimated that 17% of all employees self-reported burnout symptoms in 2018, but which fraction actually developed clinical burnout is unknown[4]. General practitioners (GPs) in the Netherlands reported around 265.500 burnout cases in 2018, which is a much smaller percentage (±1,5%)[5]. To summarize, we do not know what burnout exactly is, and how big the problem is or is going to be. What we do know is the rising media attention, especially since last May when the World Health Organisation (WHO) recognized the problem. Although it is not defined as a disease, the WHO officially recognized 'occupational burnout' as a syndrome in the 11th Revision of the International Classification of Diseases (ICD-11)[6]. In this ICD-11, it is characterized as three dimensions: (i) feelings of energy depletion or exhaustion; (ii) increased mental distance from one's job, or feelings of negativism or cynicism related to one's job; and (iii) reduced professional efficacy[6]. And even though the WHO explicitly states that burnout refers to the occupational context, scientists found that it can be experienced by groups such as students, athletes or by parents of chronically ill children as well[7,8,9]. This suggests that over-exertion in general, and not only work-related stress could lead to a burnout.

But what exactly is causing individuals to feel emotionally and physically exhausted and cognitively worn out? And by this I do not mean the workload or the continuous pressure, because we all know that the problem is non-existing when lying on the beach. Instead, I want to report here what the underlying physiological mechanisms are of this exhausted state. A few good nights of sleep do not heal a burnout; recovery periods can last up to 3 years, involving inability to read, remember and plan[10].

Researchers tried to elucidate which processes in the body are disbalanced, and almost all obvious physiological measures have been performed to find a hint of change in burned out patients. To give a few examples; fMRI studies looked at empathy-related brain activity[11], serum cortisol was measured to find changes in the HPA-axis[12], PET scans to find alterations in the limbic brain structures[13] and thyroid-stimulating hormone (TSH) was measured in plasma[14]. Some of these studies came up with significant findings, but overall there seems to be no consistency in burnout research. A recent meta-analysis by Jonsdottir et al.[15] reviews the current position of burnout research, stating that *"existing research cannot confirm any homogenous reliable endocrinological or immunological changes related to burnout".* One of the reasons seems to be the heterogeneous definition of this syndrome, making it difficult to compare existing studies. Next to discrepancies in methodology, there are large natural individual differences in stress reactions. The physiological reaction consists of multiple systems like the activation pathway of the adrenal and thyroid gland, the immune system and the release of catabolic and anabolic hormones[16]. Furthermore, the stress system also involves cognitive, emotional and behavioral responses. Altogether, one cannot expect every individual response to stress and burnout to have similar outcome, making the search for a biomarker a difficult endeavor.

In conclusions, there is still no unambiguous mechanism found that could underlie burnout. Modern medicines' inability to fit this syndrome in a conceptual framework restrains the chance of finding a solution. Besides, medical research is focused on understanding 'how' the syndrome develops, while there are no strong hypotheses yet on 'why' it even exists. Therefore, it would be valuable to look at alternative research strategies. A scientific approach that is getting increasing attention lately, and which keeps individual differences in focus, is the field of Evolutionary Medicine.

1.2 An evolutionary approach in medicine

Evolutionary medicine is a combination of evolutionary biology and medicine that changes the way researchers look at diseases (Fig.1). In the words of Randolph Nesse, one of the founders of this field*: "It uses the basic science of evolutionary biology to find ways to prevent and treat disease, and it uses studies of disease to advance basic evolutionary biology"*[17]. The aim of this field is not to directly focus on the molecular and physiological mechanisms of how people get sick, but it rather asks the question of why people become sick. The foundation of evolutionary medicine is based on questions that are not directed at the disease itself, but at its symptoms. That is because a disease is not useful, but the symptoms of this disease could actually be adaptations to the causes of the disease. *"There is nothing useful about pneumonia, schizophrenia, epilepsy, or cancer. However, many symptoms of disease, such as pain, vomiting, cough, and fatigue, are adaptations. The systems that regulate such defenses are, for good evolutionary reasons, prone to failures that cause chronic pain, anxiety disorders, and many other diseases."*[18] Evolutionary medicine includes all aspects of evolutionary biology, like natural selection, adaptation, genetic drift and mutation, applied to medicine and public health[19]. An example would be that a doctor with more understanding of the functionality of certain traits and symptoms will know that fever is an adaptation of the body to kill or slow down the growth of pathogens. Therefore, inhibiting this protective response with medication is not in all cases the best option. Other than direct knowledge in the clinic, evolutionary medicine provides basic understanding of processes like antibiotic resistance, which will eventually lead to the development of new treatments adapted to biological realities[20].

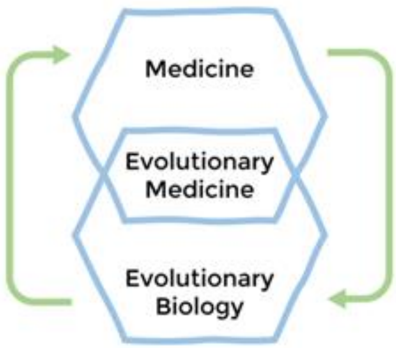

Fig. 1 - A multidisciplinary field. (Source: Author)

The most well studied topics by Evolutionary Medicine are addressing the biggest challenges in medicine like cancer, autoimmune diseases and cardiovascular disease. However, one should be able to apply this approach to every human disease or syndrome. This might yield alternative hypotheses about a functional trait and shine new light on why the disease persists among humans. Therefore, in this essay I will attempt to find an evolutionary explanation for burnout.

2 - Research question

→ Can evolutionary medicine be used to develop new hypotheses about the mechanistic origin of burnout?

3 - Methods

3.1 Guidelines for evolutionary studies

Where to begin when answering such a question? There are a few challenges in evolutionary studies, and scientists developed guidelines for those who want to give it a try[21]. These guidelines consist of a few questions to avoid pitfalls and confusion. As mentioned before, I am looking for an explanation of a trait that makes us susceptible to developing burnout; I will not directly try to explain the disease itself but rather the underlying trait. I will begin with finding the right trait. So at first, I will examine if the object of explanation is a uniform trait in the species, or if it varies among groups or individuals. The next question asks if the object of explanation has been influenced by evolution. This question emphasizes that our proposed trait should indeed be shaped by selection. For instance, we obviously did not evolve to upright walking creatures so that we can better sit in our office chairs. We also need to consider: what kind of trait is the object of explanation? Is it a fixed human trait, like our wisdom teeth? Or is the trait caused by genes that monitor environmental variation and adjust our phenotype accordingly, called a facultative trait? For example, sun tanning of our skin by melanin is an adjustment to the amount of UV-rays. These are the questions I will follow while investigating the trait underlying burnout.

3.2 Multiple answers could be true

The next methodological step for answering an evolutionary medicine question is to consider all viable hypotheses about the evolutionary reasons for a trait. In mechanistic science, the most educated guess is turned into one hypothesis, which is tested to be true or untrue. However, in the case of evolutionary questions multiple explanations could be correct, and they do not have to be mutually exclusive. That is why all categories of explanation should be considered objectively. In western societies, most chronic diseases arise when our bodies have difficulties staying healthy in our modern environment (e.g. virtually unlimited amount of food leading to obesity and cardiovascular diseases). This mismatch theory applies to the incompatibility between contemporary human lifestyle and the archaic conditions under which we originally evolved. Additional evolutionary reasons to explain why we get sick include trade-offs, when there is a cost-benefit consideration of a trait or if there is a compromise when different adaptations conflict.

3.3 Methods for testing the hypotheses

After I reason which hypotheses could explain the evolution of the trait underlying burnout, I will test under which criteria these hypotheses could be true. It is not always possible to perform evolutionary medicine experiments in the lab because simulating evolution is impossible in a short time span. However, there are other methods of examining if a hypothesis is valid, based on recent literature. As a first step, I can test if the hypothesis is consistent with modern evolutionary theory. For example: Does the hypothesis conform to a plausible speed of selection? Another option is the comparative method[22]. One can compare and contrast traits within subgroups, such as trait dimorphism between men and women. Or, compare the trait between evolutionary related species, to see if trait analogues are due to the same selection forces or because of phylogenetic relationships. This method can elucidate the adaptive significance and function of the trait, by showing its increase in evolutionary fitness. Additionally, some hypotheses can be tested with experimental methods by disrupting or augmenting a certain trait and testing the fitness consequences. There might be case studies describing a disruption or augmentation of a trait caused by a tumor or some kind of syndrome. This could provide new insight into the functionality of a trait. With the methods all set, I will now proceed with the evolutionary investigation of the trait that makes humans vulnerable to burn out.

4 – The trait of interest

4.1 Which trait best fits the picture?

Which quantifiable measurement of an organism could be the trait making us susceptible to burnout? If one would ask a layperson what could cause burnout, this person would say: "Too much stress, of course!" Although this explanation is not the complete answer when looking at mechanistic and ultimate questions, this might be the right target to start our evolutionary questioning. Ursin et al.[23] described the stress response as a general, unspecific alarm response occurring whenever there is a discrepancy between what is expected or the 'normal' situation (set value) and what is happening in reality (actual value). So does the stress response fit the guidelines for evolutionary questions?

The first question of the proposed guidelines is whether the trait varies among individuals: that is definitely the case, and exactly the reason what is making burnout research so difficult, the differences in stress response. For example, Kudielka et al.[24] explains all factors that makes humans respond differently to stress, including experience, social factors, psychological interventions, personality, and genetics. The second question is, if the stress response is influenced by evolution. According to Ellis et al.[25] the variation in stress-response phenotypes has been shaped and maintained by natural selection, stating that it is indeed influenced by evolution. Later in this essay it will be tested if this is indeed the case. The third question asks what kind of trait the object of explanation is. The stress response is not a fixed but a facultative trait as the body adjusts phenotype according to the surrounding environment: If there is no stressful cue like a bear or a deadline coming up, there is no stress response. In conclusion, the stress response fits with the first three criteria of the guidelines for evolutionary studies to burnout.

4.2 Evolutionary history of stress

Even the most primitive life forms have two states: activity and rest. In higher organisms such as humans, the activity state became more complex. It is not simply a state of arousal, but a complex interplay between several physiological responses. Natural selection likely selected for different arousal subtypes, such as alertness for danger, anxiety, rage, and sexual activity, creating adapted responses to diverse situations[26].

The human stress response was first described by Walter Cannon in 1915. He characterized how the human body is activated in response to threats or dangers: The fight-flight response[27]. This specific state of arousal starts in the brain, where the amygdala signals potential danger to the hypothalamus, our primary command center. This structure communicates to the rest of our body via the direct autonomic nervous system, via the adrenal medulla for adrenaline and noradrenaline production and via the pituitary and adrenal cortex for the secretion of cortisol. This last pathway, called the HPA-axis, results in a glucose boost and suppression of the natural- and upregulation of the specific immune system[28]. Altogether, this fight-flight response redistributes energy to the body parts vital for action, and reduces energy expenditure on systems like the digestion of food. By tactically shifting the bodies' homeostasis, it increases its coping ability in certain situations.

4.3 Overactivity of the stress response

As described above, the acute stress response system sounds like a useful system especially for surviving dangerous situations, but this shifting of homeostasis is not for free. It is calorically expensive, it interferes with behavior like feeding and mating, and it can cause tissue damage. So after the acute response a period of recovery should occur. If the stressor persists or the time in between stressors is not enough for recovery of homeostasis, we talk about chronic stress. As mentioned before the exact state of damage or depletion in the body is not known, and can differ largely based on the causal factors. However, several studies indicate the detrimental effects of prolonged activation of the sympathetic system, and constantly high levels of circulating stress hormones. Chronic stress impairs learning and memory in rodent studies[29]. MRI studies on subjects with chronic stress found cortical thinning in the frontal cortex, and increased amygdala volumes[30]. Also, it increases risk of hypertension[31] and coronary artery disease[32]. Furthermore, prolonged activation of the stress system suppresses both cellular and humoral immunity[28], and impairs wound healing[33].

In conclusion, overexpression of stress causes exhaustion and physiological changes to the body and the brain that may be the causal factor leading to burnout. The question is now, why evolution did not shape systems to protect against these damaging aspects of an originally beneficial response?

5 - The different evolutionary hypotheses

5.1 Mismatch theory

The work load is too high, there is too much pressure from society, life is always busy, traffic jams, economic or political crisis and an overload on information from social media. These things are often mentioned as the causes of stress, and therefore the leading idea in the explanation of burnout vulnerability seems to be the mismatch between our bodies and environments. *Homo sapiens* evolved approximately 200.000 years ago[34]. Since then, our genotype has not changed that much, but our environment has[35]. We were hunter-gatherers most of our evolutionary history, and many of our behaviors and traits that were beneficial then, have reduced or absent adaptive purpose today[36]. Hunter-gatherers are exposed to stressors that are more physical, whereas they are mainly social and mental in our sedentary and civilized societies. The term “Evolutionary mismatch” is applied to the negative consequences of the incompatibilities between human lifestyles today and the conditions under which we originally evolved[37]. If there is evidence that stress and burnout are more common in modern environments, and that environmental characteristics predicts its variation, then the mismatch theory explains why contemporary activation of the stress response often yields net costs.

Although the mismatch theory seems to be the most commonly used explanation, there are more possible hypotheses underlying our vulnerability to burnout which we should consider objectively.

5.2 Trade-off

Success accompanied by a considerable amount of stress is not only found in the human working populations: it also appears in the model nematode *Caenorhabditis elegans.* A study from Casanueva et al.[38] discovered that worms with a greater stress response are better at coping with deleterious mutations than their totally relaxed counterparts. However, this came with a cost: these healthier and stress-responding worms are less good at reproducing, revealing an important evolutionary trade-off between health and fertility. Could the stress response that reduces fitness when it is chronically activated, be accompanied by a trait that increases fitness? Does success eventually yield more net benefits than the costs of a stressful job, or is there a different advantage attached to stress? It could be possible that stress is shaped by the trade-off between immediate benefits and long-term costs, occurring in a different stage of life[39]. Evaluating variations in the trait, and the costs and benefits from certain deviations could provide evidence for the trade-off hypothesis.

5.3 Defense for certain situations

Another explanation of stress, is that selection shaped it as a defense to offer protection in certain situations, but can cause harm and suffering otherwise. A clear example of such a defense is pain: it is always undesirable, but without our ability of feeling pain we would be covered in burns and cuts. So the trait pain is a defense against certain situations where we get wounded, infected and possibly die. If there are articles that demonstrate that a (chronic) stress response is somehow protective, and that the mechanisms that regulate the expression responds appropriately to cues indicating the presence of the relevant danger, then it advocates for the stress response as a defense[21].

6 - Testing the different hypotheses

6.1 Consistency with evolutionary theory

The first approach of testing our proposed evolutionary hypotheses is to investigate if they are consistent with modern evolutionary theory. The mismatch theory could involve some arguments that fit the rules of evolution to a lesser extent. To recap, the mismatch theory states that the incompatibilities between human lifestyles today and the conditions under which we originally evolved causes our vulnerability for chronic stress and burnout. But is that really the reason what is causing our stress system to derail?

Although the methods section stated otherwise, it is interesting to look at the heritability of burnout ('the disease') instead of investigating the functionality of the stress response ('underlying trait'). A Swedish twin study found that genetic factors explained 33% of the individual differences in burnout symptoms. However, they state that environmental factors explained a substantial part of the variation as well. In a previous study they also showed that burnout clustered in families, but that this effect was mainly due to a shared environment by family members, rather than by genetic factors[40].

The review of Brenner et al.[36] lists these possible environmental factors that create an evolutionary mismatch, causing chronic psychological stress. In modern, industrialized populations, the number of daily choices increased largely compared to that of our ancestors. Choices of vocational and family roles are presented in an overwhelming manner, which may be incompatible with the number of factors that our brains has evolved to consider simultaneously (41). Additionally, the rise of bureaucracies and middle management created jobs that fail to provide personal satisfaction, whereas the work in preindustrial societies directly provided food, shelter and other vital goals[42]. Our social roles also changed, and urbanization led to an increased amount of interactions with strangers: a study showed that in a train to Stockholm adrenaline levels of the passengers increased with train crowdedness[43]. Another study published in Nature[44] showed with brain scans that people who grew up in cities have altered negative emotions processing such as stress, compared to people from the countryside.

The facts mentioned above could explain an increased amount of (mainly) psychosocial stress. Nevertheless, in my opinion this summation of changed environmental factors does not directly prove that the mismatch theory explains the modern human's vulnerability to burnout. Considering the environmental conditions of our ancestors, one could say that we did create a stable environment with healthcare, police, no predation and unlimited food. It is true that the type of stressor changed, but are we not able to adapt in a different way, as highly evolved species? Apparently, in stress research the term 'mismatch' is also used regarding individual adaptation and parental programming, which covers only one or a few generations instead of more than 100.000 years. Nederhof et al.[45] uses a definition of the mismatch hypothesis occurring within the individual. Here they argue that aversive experiences early in life trigger adaptive processes, thereby

Fig 2 – Two options for creating a mismatch between early life stress and adult stress. (Source: Nederhof et al., 2012) rendering an individual to be better adapted to aversive challenges later in life. According to this variant of the mismatch hypothesis, individuals are more vulnerable for disease if a mismatch occurs between the early programming environment and the adult environment (see figure 2).

Next to the effects within the individual, the maternofoetal interaction also influences the stress response. In a review of Meaney et al.[46] it is argued that the HPA axis is responsible for this, such that (i) the effect of maternal adversity on foetal growth is mediated by adrenal glucocorticoids and (ii) environmental adversity alters maternal physiology and behaviour, which then programs HPA activity in the offspring. This is confirmed in other rodent studies, where foetal prenatal stress decreases hippocampal glucocorticoid receptor expression and increases basal glucocorticoid levels as well as both ACTH and glucocorticoid responses to stress[47,48]. This so called 'programming', explains why the environmental experience of the parent is translated through an epigenetic mechanism of inheritance into phenotypic variation in the offspring[49]. Programming is an adaptive response that may increase fitness of the offspring when the environment stays the same, but can be maladaptive if the environment shifts, causing deficient responses to stressors later in life[50].

To summarize, it is not likely that a significant proportion of our genotype changed since the beginning of *Homo sapiens,* but our environment has. This is hypothesized to create a mismatch, making us vulnerable for stress and burnout. However, one should not underestimate the capabilities of epigenetics, a phenomenon that does not need to evolve for thousands of years to adapt a species to its environment. The studies mentioned show that the stress response seems to be influenced by the maternal environment and epigenetics to a large extent. The question is which of these systems creating a mismatch, genetics or epigenetics, has the biggest influence. Anyhow, epigenetic programming hints more towards the stress response being a defensive mechanism, being expressed to an optimal point where the costs equal the benefits.

6.2 Comparative methods

What has been a major dilemma of evolutionary biology is the persistence of genetic variation in traits of adaptive significance. Why would selective forces not have filtered out the most optimal trait? In this section the comparative method is used on a few examples, in order to find hints of adaptive significance of the stress response.

Modern humans vs. prehistoric humans

The term stress and burnout are not even a century old, but the stress response system has been a vital mechanism for the *homo sapiens* since the beginning. Other than being a useful response for fighting or flighting the mountain lion, it would be interesting to evaluate if chronic stress and burnout were present among the hunter-gatherers. One study done by Stephen Webb[51] looked at pre-historic stress in Australian Aborigines by using both skeletal stress markers (cribra orbitalia, Harris lines and dental hypoplasia) and other markers of disease. The results showed that, although large temporal and spatial differences in stress were observed, there has been a hunter gatherer population in southeastern Australia with high amounts of chronic stress. Another study found that the transition from hunter-gatherers to early agriculture in the Nile valley was also a transition period with high stress and poor health. The skeletal remains scored for dental hypoplasia indicated high physiological stress and growth interruption[52]. Palaeopathological studies in Peru found cortisol levels in archaeological hair suggesting that high stress levels were a regular part of life in the pre-modern period[53]. These studies question if high amounts of stress is an entirely modern phenomenon. If periods of chronic stress and decreased health were indeed a part of the pre-historic humans as well, than this is in opposition with the mismatch theory.

Personalities

Burnout seems to be more prevalent in individuals with high empathy levels, and this is confirmed by the fact that medical professionals and other 'caring' professions are at higher risk for burnout[11,54]. Tei and colleagues found with an fMRI-study that severity of burnout in medical professionals is explained by 'reduced' empathy-related brain activity, which is also correlated with stronger emotional dissonance and empathic disposition. This seems to match with a study[30] mentioned in the introduction. Thus, at least in healthcare, excessive empathy and frequent exposure to emotionally-demanding tasks can exhaust the brain structure that is responsible for this behavior. Although there are other types of burnout that are not specifically empathy related, this variation in the trait could make one think that it has a protective function in these cases. Could it be protection for the individual, in the sense that too much empathy for others means less self-care, which decreases evolutionary fitness? This could also be correlated to the different coping styles between the sexes, which is investigated below.

Men vs. women

Men and women have different psychological and biological responses to stress[55]. One existing hypothesis states that the difference in the stress response exhibited by man is more characterized by the 'fight-or-flight' reaction, while women respond more with a 'tend-and-befriend' reaction. This alternative response is described by Taylor et al.[56]: *Tending involves nurturant activities designed to protect the self and offspring that promote safety and reduce distress; befriending is the creation and maintenance of social networks that may aid in this process. Neuroendocrine evidence from animal and human studies suggests that oxytocin, in conjunction with female reproductive hormones and endogenous opioid peptide mechanisms, may be at its core.* This hypothesis is supported by fMRI findings, showing that limbic activation in women is more consistent with a 'tend-and-befriend' rather than a 'fight-or-flight' response to stressful situations. At the biochemical level, men tend to have a higher secretion of ACTH, but the total basal cortisol levels are comparable to women. This reflects that women have an increased sensitivity of the adrenal cortex compared to men[57]. Kajantie et al.[58] comes up with a more evolutionary reason for the sex differences in the stress response. *Between puberty and menopause, adult women usually show lower HPAA and autonomic responses than men of same age, which is likely the result of estrogen exposure. A universal evolutionary requirement, is to promote optimal growth and development of the foetus, including buffering the effects of excess maternal stress and, perhaps, to facilitate optimal transfer of information about the prevailing environment.* Considering this important function, it could be that the stress response for woman is shaped to optimize the development of the offspring, while in men evolution shaped the response more suitable for whatever male tasks they carried out.

Altogether, there are several differences found in the stress response between men and women. More important is the proposed function of these differences: Women are shaped to have different social and familial roles, and have to optimize the conditions for the foetus. Men are likely shaped to have a stress response that suits the male competitive role better. However, if these gender differences in stress response also result in a distinct risk of burnout, is not widely accepted among researchers. This is probably dependent on the type of stressor that can eventually result in a burnout. One study showed for example, that in 50 healthy volunteers, men showed significantly greater cortisol responses to the achievement challenges, while the female group showed higher response to the social rejection challenges[59]. This could in some sense be considered as a trade-off, since these different roles and personalities all have a beneficial function for the population.

Humans vs. Animals

The most renown example of a comparison between stress in humans and animals comes from Stanford Professor Dr. Robert Sapolsky, who wrote the book: 'Why zebra's don't get ulcers' (60). He explains that zebra's do not think about the lion, when the lion is not there. Humans on the other hand, can worry about the lion or any other imagined threat whenever they want to. This ability is all thanks to our highly developed prefrontal cortex, which has been around for thousands of years. This advocates for the trade-off hypothesis: The benefits of having this superior alternative trait, a brain area for higher cognitive function comes with the costs of increased psychosocial stress and risk of burnout. Imagining how far the human species is from extinction nowadays, hints that the benefits have been well worth the costs in evolution. Sapolsky also points out, that only in the last hundreds of years, mankind lives long enough to die of degenerative disease and stress-related diseases. This hints to a trade-off hypothesis: The stress response is shaped by the trade-off between immediate benefits and long-term costs, occurring in a different stage of life. If it was unlikely to reach the age where the long-term costs became harmful, which might still be the case in most animal species, than it makes more sense why evolution shaped this stress-response to be damaging.

In contrast, when looking at studies about the impact of chronic social stress on rodents, this can impact their normal functioning with analogy to human burnout. Rygula et al.[61] found anhedonia and motivational deficits in rats that were subjected to 5 weeks of daily social defeat. Additionally, they found decreased body weight gain and increased weight of the adrenal glands, which are correlated with stress effects. This study indicates that chronic social stress in rats will cause changes in physiology and behavior, showing that this disbalance of the stress response is also possible outside the human species. This result seems to counteract the trade-off hypotheses of a highly evolved prefrontal cortex and burnout, because animals seem to 'burnout' as well, when you exhaust the stress response.

6.3 (Hypothetical) Experimental methods

Human stress knock-out

One hypothetical study that can be conducted to evaluate the function of the stress response is a genetic knock-out study. In humans, this would not be ethical. However, there is a disease that shuts down part of the stress response, called Addison's disease. This (mostly) auto-immune reaction attacks the adrenal cortex, and causes hypocortisolism. In response, the pituitary increases secretion of adrenocorticotropin (ACTH) in an effort to stimulate the adrenal glands. Primary adrenal insufficiency results in orthostatic hypotension, agitation, confusion, circulatory collapse, abdominal pain, and fever[62]. These features are caused by acute infection, metastasis or hemorrhage and can lead to death if not treated. This disease, which resembles a disruption in normal HPA-axis functioning and stress response, provides evidence for how important our stress response is for survival. Stress seems often to be accused as something negative and damaging, while this disease shows us that it is more a protective defense for way more severe diseases or symptoms. This result advocates for the stress system as being a defense.

7 - Discussion

In this essay, an attempt was made to find an evolutionary explanation for burnout. Although it is impossible to prove a final proof in an essay, it was a good way to investigate if evolutionary medicine could be used to develop new hypotheses about the mechanistic origin of burnout. We still do not know what burnout is exactly, and from the literature it has become clear that the involvement of physiological systems like the nervous, endocrine and immune system is different for every individual, as is the threshold. Based on exploring the functionality of the stress response, evolutionary reasons for burnout vulnerability have been postulated.

Three different hypotheses were under investigation: The mismatch hypothesis, the trade-off hypothesis and the stress response being a defense. These hypothesis are considered objectively, but are not necessarily mutually exclusive. It appears that the trade-off and defense theory explain the functionality of stress as a vital trait. The mismatch theory on the other hand, explains why the system gets overloaded, and homeostasis cannot be maintained. Although it has not been proven that burnout is more common in modern societies, other forms of mismatch, like maternal programming may be important in burnout development. Additionally, city life and crowdedness are modern stressors, but cannot account for the reason why people get burnout.

To answer the question if evolutionary medicine can be used to develop new hypotheses about why humans are shaped to be vulnerable for burnout, the answer is yes. Although the stress response is not really a demarcated phenomenon with all its different physiological systems involved, the change of perspective to functionality was still useful. For example, the finding that the stress response is shaped differently in men and women, to increase fitness of the offspring is interesting to keep in mind for burnout research. This could implicate that the pathways leading to burnout has sex differences, meaning that prevention should also have a gender specific approach.

Another eye opener was the influence of epigenetics in stress responses. Adapting the trait to the environment where the offspring is possibly going to grow up in, can increase fitness if a mismatch does not occur between expectations and outcome. The ability to modulate this trait by turning certain genes on or off, contrasts the belief that our genes are programmed to live in an environment with bears and without social media. Although the collected evidence in this essay is far from complete, it does prove the usefulness of the evolutionary approach to medicine.

The finding that every stress response is different per individual due to gender, maternal effects, early environment, personality and so on, highlights the need for personalized prevention and treatment approaches to diminish the costs of an overactive stress response. In my opinion, these individual differences also indicate that researchers should not aim too hard for finding a biomarker, but rather focus their research on how things like behavioral therapy can change a person’s response to stressful stimuli. Besides, the term stress should lose its reputation of something damaging, and become something that is protective as long as you do not push its limits. I would advise to start teaching about stress functionality and coping styles in primary and secondary school, to make kids aware of the symptoms indicating exhaustion of this protective trait.

Conclusion

Evolutionary medicine can be used to develop new hypotheses about the mechanistic origin of burnout. This topic should be addressed more elaborately in future studies. By including all environmental and genetic factors, new rehabilitation and prevention strategies can be designed to combat burnout.

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