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# Self-confidence as an immune-modifying psychotherapeutic intervention for COVID-19 patients and understanding of its connection to CNS-endocrine-immune axis

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Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) not only costs millions of human lives across the globe but also causes uncountable damage to mental health. As the incidence of COVID-19 continues to rise, so does the psychological burden. COVID-19 patients often encounter a variety of psychological stresses, including occupational damage, uncertain future of the family, and even fear of death which cause anxiety and distress, compromising the immune system, and influencing the severity of the disease. Beyond this, stressed individuals are more likely to practice unhealthy habits such as indifference to sleep and food that put them at greater risk.

The CNS (central nervous system)-endocrine-immune axis is known to be crucially implicated in the stress-mediated dysregulation of the immune response [1]. Following CNS stimulation, stressors provoke the release of several hormones, including catecholamines (epinephrine and norepinephrine), adrenocorticotropin (ACTH), cortisol, growth hormone, and prolactin. Excess secretion of these stress hormones results in overactivation of immune cells and dysregulation of an immune response. Moreover, this interaction between the CNS and the immune system is bidirectional [1]. For example, cytokines (such as IL-1) produced by immune cells stimulate the hypothalamus to release corticotrophin-releasing hormones which further trigger secretion of stress hormones, resulting in immune malfunction.

However, interventions that can alleviate psychological stress may control an acute immune response. Self-confidence, a function of mental strength and positive attitude of an individual, is such an intervention that may hold a potential capacity to control stress-mediated immune dysfunction. Several factors, including psychological counseling, social supports, spiritual connections, food habit, health supports, control on emotions, positive thoughts, and reasons for living may help develop self-confidence. Substantial evidence suggests an association between psychological well-being and immune response [2]. It has been observed that psychological intervention was associated with an increase in immune responses by natural killer cells and T cells [3]. Zhao *et al.*, (2016) found that

enhancing immune response as indicated by levels of CD4+, CD8+, CD4+ / CD8+ ratio, and free cortisol in serum were involved with the psychological intervention [4]. The level of phagocytes was increased following the psychological intervention [5]. An increase in natural killer (NK) cells after psychological treatments indicates an increase in immune responses [3].

Like psychological intervention, spiritual connections and social supports also boost up the immunity. For instance, an increase in immune cells ( $CD4^+$) was observed in patients with IBD [6] and AIDS [7] in response to religious coping and social support. An increase in cortisol response and cortisol awakening response is known to increase immune response in healthy adolescents [8]. Fancourt *et al.*, (2016) showed that music could have a better therapeutic effect on immune responses as was evident by increased levels of cortisol, noradrenaline, beta-endorphin, oxytocin, chemokines and cytokines in cancer patients [9]. Love to the universe, a reason to live may improve the immune system against HIV/AIDS [10]. Religious rituals such as intermittent fasting are recognized to have various health benefits, including boosting up immunity, resistance to stress, and suppressing the aging process [11, 12]. In our recent reviews, we proposed fasting and pharmacological intervention by *Nigella sativa* seed as prospective options against COVID-19 [13, 14]. Besides, regular exercise and healthy diets rich in functional ingredients and essential micronutrients will help boost immunity and the anti-stress process.

Although self-confidence is a proven quality to succeed in many aspects of our daily life including education, business environments, and politics, it is plausible that confidence could be a vital aspect in combating both communicable (such as COVID-19) and non-communicable diseases/states (such as neurodegenerative diseases and depression). These conditions are often further complicated by patients thinking negatively of their capacities. Using brain imaging studies, it has been revealed that if one thinks positively, "the value areas" of the brain regions including the prefrontal cortex and striatum become activated, leading to the person feeling confident [15]. This process engages brain circuits that are involved in rewards and pleasures so that a person feels better. Taken together, self-confidence may enhance the threshold of vulnerability and prevent further deterioration in COVID-19 infection.

Since there is no specific treatment for COVID-19 yet, the only means to survive from this disease is to consolidate the immune system. In addition, as the immune system is closely linked to the neuroendocrine system, any kind of psychological stresses that overwhelm this association causes immune dysfunction. In this context, self-confidence that can mitigate psychological stresses posed by COVID-19 can play an important role in consolidating immune response against this disease (Figure 1). An in-depth understanding of how psychological stresses overactivate the neuroendocrine-immune axis, weakening the immune system, and how self-confidence interferes with the overwhelmed immune response may offer a prospective strategy for the prevention as well as effective management of COVID-19.

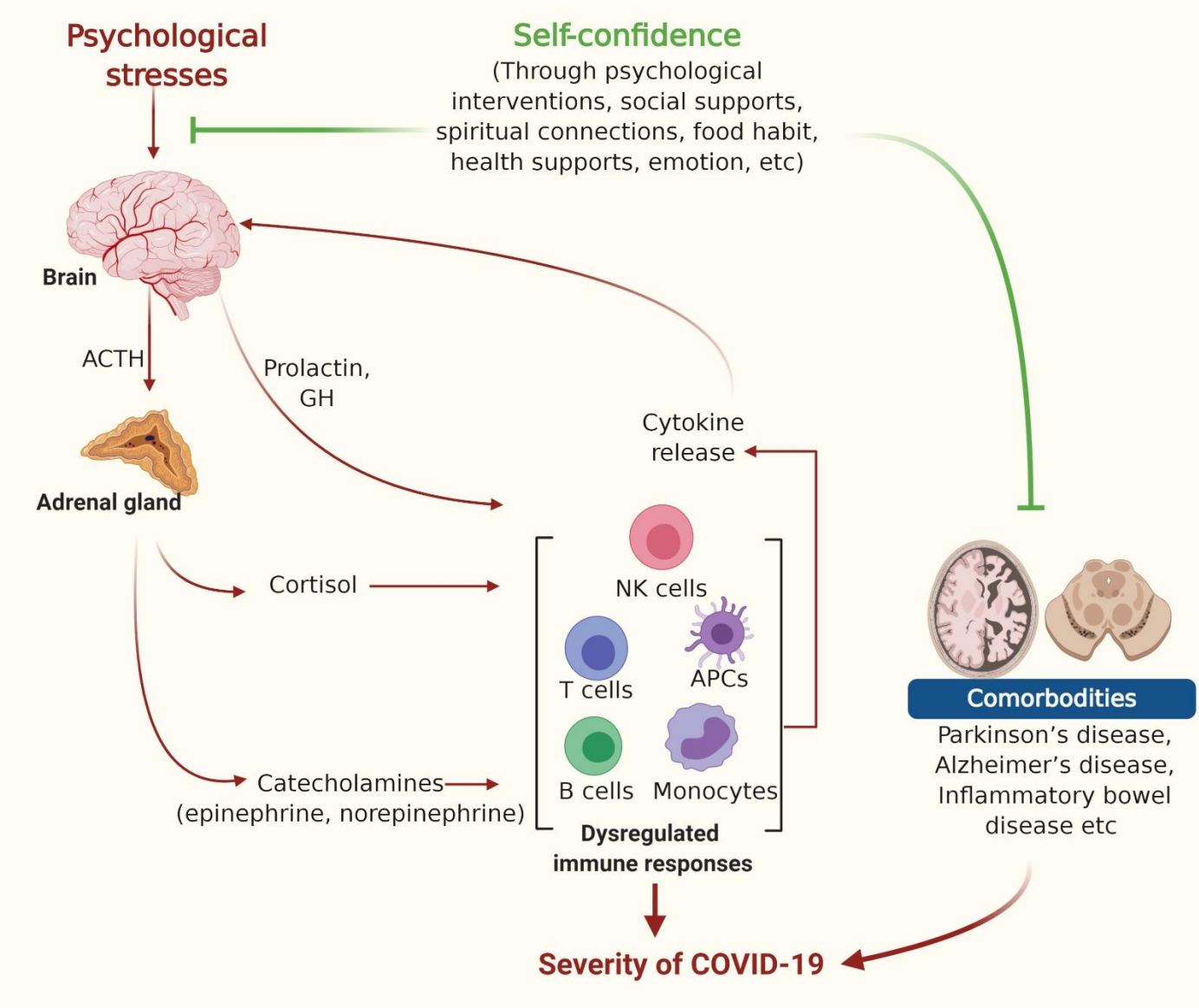


**Figure 1.** Possible mechanisms involved in the impact of self-confidence on COVID-19. Developing self-confidence through psychological interventions, social supports, spiritual connections, food habits, health supports, and positive thinking can potentially reduce psychological stress, thereby consolidating immune functions [1]. Besides, self-confidence can help improve non-communicable diseases such as neurodegenerative as well as inflammatory bowel diseases. As a consequence, self-confidence enables an individual to overcome COVID-19 and reduces the risk of contracting the disease. ACTH, adrenocorticotrophic hormone; GH, growth hormone; NK, natural killer, and APCs, antigen presenting cells.


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## AUTHOR CONTRIBUTIONS

This work was a collaboration among all the authors. MJU designed outlines and drafted the manuscript. MAH, MNI, and MJU wrote the initial draft of the manuscript. MJU, MAH, and MNI reviewed the scientific contents described in the manuscript. All authors read and approved the final submitted version of the manuscript.

## CONFLICT OF INTEREST

The authors do not declare any conflict of interest.

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