Highlighting inflammatory markers in anxiety disorders

Anxiety disorders, often originating early in life, are very common and effect 28.3% of the population. With this high prevalence comes an associated cost to the economy, mostly related to the extensive overuse of primary care services and the associated use of inappropriate medical testing, misdiagnosis and the often less than ideal treatment choices. It is therefore essential to conduct research in the field of anxiety disorders to further understand the causes of these disorders, as well as to potentially identify specific markers that could lead to early and accurate detection.

Anxiety disorders are often comorbid with other medical conditions including diabetes, rheumatoid arthritis, and cardiovascular disease; all which involve the inflammatory system. As such, recent interest has been placed on the role of the neuroinflammatory system in psychiatric disorders and specifically whether the hypothalamic pituitary adrenal (HPA) axis and the inflammatory biomarkers can provide more information in order to facilitate further understanding of the causes of the anxiety disorders and development of better treatment approaches.

When an individual is under a stressful event, the HPA axis is activated due to the release of corticotropin releasing hormone (CRH) and arginine vasopressin (AVP), which stimulates the release of adrenocorticotropic hormone (ACTH). ACTH released into the blood stream will stimulate the release of glucocorticoids, such as cortisol from the adrenal cortex, directly or indirectly resulting in a release of a variety of cytokines (immune modulating chemicals), which play a variety of roles in the central nervous system, including allergic response, repair following injury, and endocrine regulation via the HPA axis, mediate information between the central nervous system and the immune system.

T-helper cells are divided into Th1 and Th2 cells, which primarily function to activate cell-mediated immunity (cells designed to directly attack what is considered foreign or untoward) and humoral immunity (immune cells which release chemicals to generally facilitate the immune response), respectively. Th1 cells secrete the cytokines interleukin (IL)-2, tumor necrosis factor-alpha (TNF-?), and interferon-? (IFN-?), and Th2 cells secrete cytokines IL-4, 5, 6, 10, and 13. In anxiety, posttraumatic stress, and obsessive compulsive disorders, the balance between Th1 and Th2 cells is often shifted to Th2 dominance, such that IL-6 and TNF-? are increased.

We reviewed the scientific literature between 2004 to 2014 in anxiety, posttraumatic stress, and obsessive compulsive disorders in regard to the role of neuroinflammation and biomarkers in these disorders. Dysfunction of the HPA axis, as well as dysfunction in the release of pro- and anti-inflammatory cytokines has repeatedly been shown to be related to the presentation of anxiety disorders. That is, those suffering from anxiety disorders, including social anxiety disorder (SAD), generalized anxiety disorder (GAD), and panic disorder (PD), as well as posttraumatic stress disorder (PTSD) and obsessive compulsive disorder (OCD) are under a substantial amount of both psychological and somatic stress, including anomalous activity of the immune system.

In particular, HPA hyperactivity has been recognized in those with a diagnosed anxiety disorder and this has been further demonstrated in studies which have shown decreases in HPA activity following successful anxiety treatment through pharmacological (particularly selective serotonin reuptake inhibitors) and cognitive therapy. Increases in TNF-? and IL-6 have been shown to play a central role in PTSD and OCD research, such that increases in these cytokines are often associated with worsening of these disorders, supporting the role of neuroinflammation in these disorders.

Although there is a wealth of scientific information in this field, contradictory findings remain. This is is often the result of less than ideal methodology further necessitating the need for continued research. Nonetheless, current findings provide support for the role of biomarkers serving as potential diagnostic tools for assessing those at risk of anxiety, posttraumatic stress, and obsessive compulsive disorders. For example, previous research has shown that cortisol levels are predictive of a PTSD diagnosis in soldiers following deployment, as well as in newborns born to mothers with OCD.

In summary, the role of the neuroinflammatory system continues to be seen within a variety of medical disorders but excitingly in association with a variety of psychiatric disorders. Continued research into diagnostic biomarkers may be a pathway to future enhanced detection and treatment and ultimately suffering associated with these disorders.

Publication

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