Is there a Link Between NRF2 and Depression?

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Introduction: Depression is a common mental health disorder that affects millions of people worldwide. Recent studies have highlighted the role of oxidative stress and inflammation in the pathogenesis of depression. NRF2 is a transcription factor that plays a crucial role in cellular defense against oxidative stress by binding to antioxidant response elements (AREs) located in the promoter region of various phase II antioxidant enzymes and stress-responsive enzymes. Decreased Keap1-Nrf2 signaling has been implicated in the development of mood disorders, such as Major Depressive Disorder. Therefore, this review aims to evaluate the in vitro and in vivo evidence of the involvement of Nrf2 in depression.

Methods: A review was conducted on the PubMed database for articles published until March 8, 2022 Papers that evaluated NRF2 in animals and/or cell lines with depression and were published in English were included in the review. Studies that addressed other diseases/topics, systematic reviews, and those that did not address NRF2 were excluded. Quality assessment was performed according to Koch et al., 2022.

Results: Out of the 203 possibly relevant abstracts found through the PubMed search, 45 papers were included in the review. The results suggest that Nrf2 levels tend to decrease in animals exposed to oxidative stress or depressive behavior. When animals were treated with antidepressants or anti-inflammatory drugs, Nrf2 levels increased. Additionally, the study found that IL-10 and BDNF were key elements that were positively influenced by Nrf2 levels, protecting against oxidative stress through Keap1/Nrf2.

Discussion and conclusions: The findings suggest that Nrf2 activation may play a crucial role in controlling oxidative stress and inflammation during depression. Furthermore, it provides evidence of the involvement of Nrf2 in depression and highlights its potential as a therapeutic target. However, further studies on clinical samples are necessary to evaluate NRF2's putative effect in depression and antidepressant response.

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