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Proinflammatory Cytokines and Oxidative Stress Decrease the Transport of Dopamine Precursor Tyrosine in Human Fibroblasts

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Abstract

Background: Proinflammatory cytokines and oxidative stress responses have been extensively implicated in the pathophysiology of neuropsychiatric disorders over the past 2 decades. Moreover, disturbed transport of the dopamine precursor (i.e., the amino acid tyrosine) has been demonstrated, in different studies, across fibroblast cell membranes obtained from neuropsychiatric patients. However, the role and influences of proinflammatory cytokines and oxidative stress, and the reasons for disturbed tyrosine transport in neuropsychiatric disorders, are still not evaluated.

Aims: The present study aimed to assess the role of proinflammatory cytokines and oxidative stress, indicated in many neuropsychiatric disorders, in tyrosine transportation, by using human skin-derived fibroblasts.

Methods: Fibroblasts obtained from a healthy control were used in this study. Fibroblasts were treated with proinflammatory cytokines (IL-1β, IFN-γ, IL-6, TNF-α), their combinations, and oxidative stress, optimized for concentrations and incubation time, to analyze the uptake of 14C-tyrosine compared to untreated controls.

Results and conclusion: This study demonstrates that proinflammatory cytokines and oxidative stress decrease the transport of tyrosine (47% and 33%, respectively), which can alter dopamine synthesis. The functionality of the tyrosine transporter could be a new potential biomarker to target for discovering new drugs to counteract the effects of proinflammatory cytokines and oxidative stress in the pathophysiology of neuropsychiatric disorders.

Keywords: Dopamine precursor; Human fibroblasts; Neuropsychiatric disorders; Oxidative stress; Proinflammatory cytokines; Tyrosine transport.

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