Fibroblast growth factor-2 prevents synaptic pathology in minimal hepatic encephalopathy via NRG1/ErbB4 signaling

Qichuan Zhuge[1], Weishan Zhuge[2], Jian Wang[1], Yiru Ye[1], Xiaoai Lu[1], Ruiming You[1], Leping Liu[1], He Yu[1], Xuebao Wang[3], and saidan ding[1]

[1]Wenzhou Medical University First Affiliated Hospital
[2]Wenzhou Medical College First Affiliated Hospital
[3]Wenzhou Medical University

May 5, 2020

Abstract

Background and Purpose: Minimal hepatic encephalopathy (MHE) is implicated in the impairment of memory function. Fibroblast growth factor-2 (FGF2) is involved in modulating synaptic and neuronal formation. Experimental Approach: The aim of this study is to examined the impacts of FGF2 on MHE pathology. Our study addressed whether FGF2 could trigger neuregulin 1 (NRG1) release to ameliorate synaptic impairment in MHE rats and in primary cultured neurons. Key Results: The results showed the decreased FGF2 expression in MHE brains. After treatment with FGF2, secreted neuregulin 1 (NRG1) and ErbB4 were increased, and the interaction of the 2 proteins was enhanced. Additionally, treatment with FGF2 or NRG1 induced synaptic formation, with increase in the activity of synapse and the density of dendritic spine, through Sirt1. NRG1 signaling was prevented by administration of FGF2, which acts through the FGFR1 in MHE rats. Finally, intracerebroventricular injection with FGF2 or NRG1 mitigated the impairment of synaptogenesis. Conclusions and Implications: The data suggest that FGF2 may be a promising latent therapeutic reagent for MHE pathogenesis.

Hosted file

`BJP\begin{CJK}{UTF8}{gbsn} \end{CJK}\selectlanguage{english}(1).doc` available at https://authorea.com/users/298561/articles/427864-fibroblast-growth-factor-2-prevents-synaptic-pathology-in-minimal-hepatic-encephalopathy-via-nrg1-erbb4-signaling