The role of ceruloplasmin on the Alzheimer's disease

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Abstract: Objective: Ceruloplasmin (CP), with ferrous oxidase activity, plays an important role in regulating iron metabolism and redox reaction. Previous studies have confirmed that the lack of CP gene (CP⁻/⁻), which could contribute to the pro-oxidant iron accumulation in the substantia nigra (SN) of Parkinson disease (PD). However, it’s not very clear that whether CP⁻/⁻ has influence on the occurrence and progression of Alzheimer's disease (AD). Methods: We collected the brain slices of AD patients, and detected the GPI-CP in hippocampus. At the same time, we set up two kinds of AD animal models with CP⁻/⁻: lateral ventricle injection of Aβ₂₅-₃₅ and APP transgenic mice (APP-CP⁻/⁻). Multivariable tests were used to examine the associations between CP⁻/⁻ and AD neuropathological damage in hippocampus. In addition, we constructed CP plasmids, which was specifically expressed in astrocyte, and pre-treated exogenous CP plasmid into the ventricle of Aβ-induced AD model. Results: We found that the level of CP was decreased in the hippocampus of AD patients and AD models. Results from APP-CP⁻/⁻ mice found that the absence of CP aggravated the memory impairment. The lack of CP furtherly induced the iron accumulation, which caused elevated oxidative free radicals and led to apoptosis through Bcl-2/Bax and ErK/P38 signaling pathway. The exogenous CP plasmid could alleviate the Aβ-induced nerve damage in hippocampus. Interpretation: These datas indicated that the deficiency of CP gene could aggravate the AD and exogenous CP could attenuate the Aβ-induced damage.
Keywords: Alzheimer’s disease, Amyloid-β, Ceruloplasmin, Oxidative stress, Iron