Fatty-acid-binding protein 3 is critical for α-Synuclein uptake and MPP^+-induced mitochondrial dysfunction in dopaminergic neurons

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α-Synuclein is an abundant neuronal protein that accumulates in insoluble inclusions in Parkinson's disease and other synucleinopathies. Fatty acids partially regulate α-Synuclein accumulation, and mesencephalic dopaminergic neurons highly express fatty acid-binding protein 3 (FABP3). We previously demonstrated that FABP3 knockout mice show decreased α-Synuclein oligomerization and neuronal degeneration of tyrosine hydroxylase (TH)-positive neurons *in vivo*. In this study, we newly investigated the importance of FABP3 in α-Synuclein uptake, 1-methyl-4-phenylpyridinium (MPP^+)-induced axodendritic retraction, and mitochondrial dysfunction. To disclose the issues, we employed cultured mesencephalic neurons derived from wild type or $FABP3^{-/-}$ C57BL6 mice and performed immunocytochemical analysis. We demonstrated that TH^+ neurons from $FABP3^{+/+}$ mice take up α-Synuclein monomers while $FABP3^{-/-}$ TH^+ neurons do not. The formation of filamentous α-Synuclein inclusions following treatment with MPP^+ was observed only in $FABP3^{+/+}$, and not in $FABP3^{-/-}$ neurons. Notably, detailed morphological analysis revealed that $FABP^{-/-}$ neurons did not exhibit MPP^+-induced axodendritic retraction. Moreover, FABP3 was also critical for MPP^+-induced reduction of mitochondrial activity and the production of reactive oxygen species. These data indicate that FABP3 is critical for α-Synuclein uptake and mitochondrial functions in dopaminergic neurons, thereby preventing synucleinopathies, including Parkinson's disease.