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Impact of sirtuin-3 in cognitive deficits of Parkinson's disease

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Parkinson's disease (PD) exhibits non-motor symptoms (NMS), including cognitive and neuropsychiatric deficits, and often appear a decade or more before the first signs of motor symptoms. Sirtuin-3 (SIRT3) is a member of the sirtuin family of mitochondria NAD(+)-dependent deacetylase that acts as a regulator of mitochondrial protein function. Emerging evidence demonstrates that activation of SIRT3 exhibits neuroprotection, while reduced SIRT3 exacerbates neuropathogenesis, suggesting SIRT3 is a critical target for neurodegenerative pathogenesis and therapeutics. Here, we evaluated the impact of SIRT3 in PD cognitive deficits including hippocampal synaptic and neural network impairments in PD mouse models. First, we compared hippocampal synaptic function between SIRT3 KO and WT mice, and found that 4-month-old SIRT3 KO mice showed deficits of hippocampal functions including impaired both hippocampal CA1 LTP maintenance and fEPSP amplitude after 40 Hz stimulation for 4 seconds. Second, we found that hippocampal theta oscillations (induced by 50 μM CCh) and gamma oscillations (induced by 100 Hz stimulation for 200 ms) were significantly impaired in SIRT3 KO mice compared to WET mice. Third, when mice were treated with low dose rotenone (RTN, 0.8 mg/k.g., i.p. for 7 days), WT mice did not show detectable change of synaptic function and network synchronizations, while SIRT3 KO mice showed impaired hippocampal CA1 region PPF, LTP and gamma oscillations. Finally, mitochondrial dysfunction in hippocampal slices can be restored by SIRT3 activator, ketone. Collectively, our data suggest an important role played by SIRT3 in hippocampal synaptic and neural network function, which may underlie the cognitive deficits in PD.

Biography

Jie Wu has completed his PhD from Sun-Yat Sen University of Medical Sciences, China in 1990 and Post-doctoral studies from Tohoku University, Japan and New Mexico University School of Medicine, USA between 2013 and 2017. Now, he is a Professor and the Director of Neurophysiological Laboratory at Barrow Neurological Institute, St. Joseph's Hospital. He has published more than 140 papers in reputed journals with total citation of 2,883, h-index 31 and i10 index 82. He has been serving as an Editor in Chief and Editorial Board Member of repute.

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