

Joint Event on
9th International Conference on
PARKINSONS & MOVEMENT DISORDERS

&
10th International Conference on
NEURODEGENERATIVE DISORDERS & STROKE

February 10, 2022 | Webinar

The association of insulin resistance in CNS and Parkinson's disease

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Type 2 diabetes is a risk factor for many neurodegenerative diseases. Insulin receptor distributes widely in brain including hypothalamus, hippocampus cerebellum, amygdala and cerebral cortex. Insulin signal contributes to many neuronal functions such as neuronal proliferation or synapse activation. Especially, Alzheimer's disease has been proposed as "Type 3 diabetes". Study found increased insulin resistance in Alzheimer's disease patient's brain as elevated phosphorylated serine 616 of insulin receptor substrate -1 (p-IRS-1 S616) in hippocampus neuron. Diabetes also increases the risk of Parkinson's disease (PD). The role of insulin signal in PD disease development is largely unclear. Clinical study found that PD patients with dementia (Parkinson's disease dementia, PDD) are two times more likely to have insulin resistance than the patients with PD without dementia. Insulin therapy through intranasal delivery also protects dopaminergic neuronal death in rat substantia nigra and alleviates motor deficits in a 6-OHDA induced PD rat model. In order to reveal the insulin signaling in neurons, neuron-derived extracellular vesicles (NDEVs) in blood provides a close information of insulin signal status in patients' neuron. We found that PD patients exerted significantly higher level of p-IRS-1 S312 in blood NDEVs than controls patients and patients with DM only. In addition, the levels of p-IRS-1 S312 in NDEVs was positively associated with the severity of tremor in PD patients after adjusting of age, sex, hemoglobin A1c, and body mass index (BMI). These findings suggested the association between dysfunctional insulin signaling pathway with PD. The role of altered p-IRS-1S312 in blood NDEVs as a segregating biomarker of PD required further cohort study to assess the association with the progression of PD.

Biography

Szu-Yi Chou is an associate professor, the PhD program for neural regenerative medicine. She started her career in Chang Gung University department of medical biotechnology and laboratory science, Taiwan in 1991. She got master in National Defense Medical Center, department and graduate Institute of Biology and Anatomy, Taiwan in 1998. She completed her PhD in the field of Neurodegenerative disease in National Defense Medical Center and post doctorate in Institute of Biomedical Science (IBMS), Taipei, Taiwan. Her research interests are Neuronal cell biology, Neurodegenerative disease animal model, Cell biology and molecular biology, Neuroendocrinology and Physiology – system physiology, circulation, and cardiovascular disease.

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