J Neurol Neurophysiol 2015, 6:3
http://dx.doi.org/10.4172/2155-9562.S1.026

OMICS International
conferenceseries.com

4th International Conference and Exhibition on
Neurology & Therapeutics
July 27-29, 2015 Rome, Italy

Administration of either nicotinamide mononucleotide or over expression of SIRT1 prevents and treats peripheral neuropathy in type 1 and type 2 diabetic mouse models

Avinashrao Sagi
University of Maryland, United States

Objective: Silent Information Regulator Proteins (SIRTs) are a family of Nicotinamide Adenine Dinucleotide (NAD+) dependent deacetylases that play critical role in regulating energy metabolism. We tested in mouse models of STZ-induced (T1D) and High Fat Diet (HFD)-induced (T2D)diabetic neuropathy if the over expression of SIRT1 protein or administration of NMN, a precursor to NAD^+, would prevent peripheral neuropathy. We elucidated the effect of NMN onSIRT1 levels and mitochondrial respiration in diabetic neurons.

Research Design and Methods: An Adult C57BL6 mouse was used. T1Dwas induced by STZ and T2D was induced by using HFD.NMN was administered subcutaneously 100 mg/kg every other day for 2 months.A doxycycline-inducible neuron-specific SIRT1 over expression (SIRT1OE) C57BL6mice was used to test the protection against STZ &HFD-induced neuropathy. Neuropathy was measured by sensory nerve functions,Nerve Conduction Velocity (NCV) and Intra Epidermal Fiber Density (IEFD). Dorsal Root Ganglion (DRG) neurons were exposed to high levels of glucose and its effect on the levels of NAD+, SIRT1 activity and mitochondrial respiration were investigated.

Results: Administration of NMN to STZ-induced diabetic mice had no effect on blood glucose and insulin levels, but it improved sensory function of peripheral neurons: measured Measured by Von Frey monofilament testing for the sensory withdrawal and byHargreaves paw withdrawal thermal latency; normalized sciatic and tail motor nerve conduction velocities, and prevented loss of IEFD in skin samples from hind-paw. In DRG neurons, exposure to high glucose (25 mM) compared to 5 mM glucose, caused a decrease in NAD+ levels, SIRT1 activity, increased oxidative stress, increased PGC-1α acetylation and decreased mitochondrial respiration.The Aaddition of NMN (50 μM) prevented the above mentioned high glucose changes to DRG neurons.SIRT1OE mice had no effect on blood glucose and insulin levels in STZ-induced diabetes but it improved sensory function of peripheral neurons. On the other hand, SIRT1OE had effect on blood glucose and insulin levels in HFD-mice and it improved peripheral neuron sensory function.

Conclusions: Either intraperitonealadministration of NMN or SIRT1OE reversed STZ-induced and HFD-induced peripheral neuropathy changes. The mechanism of NMN to prevent and treat neuropathy &SIRT1OEresistance to high glucose is related to preservation of NAD+, promotion of SIRT1 activity and increased mitochondrial respiratory function.

ASagi@som.umaryland.edu