Abstract

Tau is a microtubule-associated protein that stabilizes neuronal microtubules under normal physiological conditions. Tau is a phosphoprotein, and the degree of phosphorylation is important for the normal functions of tau. We use a transgenic mouse model that expresses pathological human tau (PH-Tau). Animals expressing PH-Tau show cognitive decline, neuronal death and synaptic dysfunction.

In our lab, we currently work on two projects: the effect of Direct Current Stimulation on clearance of PH-Tau in vitro and in vivo, and on understanding of the link between Alzheimer’s disease and Diabetes.

Methods

Due to the COVID-19 pandemic, students were not allowed in the lab, so I performed statistical analysis of the data obtained by Professor Viktoriya Morozova on immunocytochemistry data and analyzed glucose levels data obtained by Dr. Alejandra Alonso and Dr. Abdeslem Elidrissi and had the opportunity to participate in the scientific discussions as well. Statistical analysis of the data was performed using Excel. Descriptive statistics are presented as mean and standard deviation (SD). Significance of differences between PH-Tau expressing animals and animals not expressing PH-Tau was evaluated by a paired t test. P<0.05 was regarded as statistically significant.

Results

Figure 1: Effect of tcDCs on PH-Tau levels on mice brain in vivo: PH-Tau transgenic mice were treated with tcDCs. The stimulations were given with 48 hours intervals between each stimulation. 7 days following the stimulation mice were sacrificed, the brains were removed, and the levels of human tau were analyzed using immunohistochemical analysis (brain sections were stained with an anti-human tau antibody (green) and the nuclei were stained with DAPI (blue)) and compared to unstimulated mice. The immunohistochemical analysis demonstrated that PH-Tau levels decreased to a 39% in Hippocampus of stimulated PH-Tau expressing mice.

Figure 2: Short stimulation induced accumulation of PH-Tau nerve protected cells. This is a primary neuronal culture. Tau was added to neuronal cultures 3 hours prior or 3 hours after electrical stimulation. Neurons were cultured in 24 well plates and half of the culture media was removed and replaced with fresh media 2 days after cultures were stimulated. Stimulation was performed with 1000 Hz, 15 milliseconds, 4 Hz for 10 min with 1 min intervals between each session. After 60 minutes neurons were fixed, processed for ICC and double labeled with tau (2B10), human tau (green) and tubulin (red). Stimulated cultures have significantly less accumulation of PH-Tau and processes stained by tubulin staining (red) is increase in fasted compared to unstimulated cultures.

Figure 3: Glucose levels were analyzed using a glucose reading meter.

Discussion/Conclusion

Transcranial direct current stimulation increases expression of heat shock protein 70 (Hsp70) and slows progression of Alzheimer’s disease (AD) pathogenesis.

Using transcranial direct current stimulation showed to decrease the levels of PH-Tau significantly. Suggested that the use of electrical stimulation might be a great therapeutic tool and beneficial for patients with Alzheimer’s disease. Overall, our results demonstrate that tcDCS is a good technique to elevate Hsp70 levels in both, in vivo and in vitro systems. The presence of PH-Tau is enough to a show significant increase in level of glucose in the fasting serum. In the animals that express PH-Tau, might be the link that we are seeing between diabetes and Alzheimer’s disease.

References


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