social defeat and depression-like behavior in mice. Spearman correlation analysis revealed that the coefficients between the particular behaviors and plasma glucose levels were linearly correlated. In T1D mice, we observed a statistically significant decrease in the ACh levels of the brain regions studied. The AChE activity in both salt-soluble and detergent-soluble fractions was significantly increased in the same brain regions. In the Ins-treated T1D mice both ACh levels and AChE activity were efficiently reversed in a brain region-dependent manner. Additional biochemical and molecular mechanisms involved in cholinergic system adaptation in diabetes are currently under investigation.

Keywords: Behavior, Brain, Type 1 diabetes.

MON-079
Diabetes induces changes in motor proteins distribution in the rat retina: implications for axonal transport

F. I. Baptista[1,2], M. J. Pinto[3,4], F. Elvas[1,2], T. Martins[1,2], R. D. Almeida[3], A. F. Ambrósio[1,2,3,5]

[1]*Centre of Ophthalmology and Vision Sciences, IBILI,* [2]*Pharmacology and Experimental Therapeutics, IBILI,* [3]*CNC-Center for Neuroscience and Cell Biology,* [4]*PhD Programme in Experimental Biology and Biomedicine (PDBEB), Center for Neuroscience and Cell Biology, University of Coimbra,* [5]*AIBILI, Coimbra, Portugal*

Diabetic retinopathy is a leading cause of vision loss and blindness in working-age adults. It has been considered a microvascular disease, but increasing evidence has shown that the neural components are also affected, even before the detection of vascular changes. However, the mechanisms underlying neural dysfunction are not elucidated. Impairment of axonal transport is associated with several neurodegenerative diseases and might also play a role in diabetes-associated disorders affecting nervous system. In this study, we investigated the impact of type 1 diabetes (2 and 8 weeks duration) on KIF1A, KIF5B and dynein motor proteins in the retina. Additionally, since hyperglycemia is considered the main trigger of diabetic complications, we investigated whether prolonged exposure to elevated glucose could affect the content and distribution of motor proteins in retinal cultures.

The immunoreactivity of motor proteins was evaluated by immunohistochemistry in retinal sections and by immunoblotting in total retinal extracts from streptozotocin-induced diabetic and age-matched control animals. Primary retinal cultures were exposed to high glucose (30 mM) or mannitol (osmotic control; 24.5 mM plus 5.5 mM glucose), for seven days.

Diabetes decreased the content of KIF1A at 8 weeks of diabetes as well as KIF1A immunoreactivity in the majority of retinal layers, except for the photoreceptor and outer nuclear layer (ONL). Changes in KIF5B immunoreactivity were also detected by immunohistochemistry in the retina at 8 weeks of diabetes, being increased at the photoreceptor and ONL, and decreased in the ganglion cell layer (GCL). Regarding dynein immunoreactivity there was an increase in the GCL after 8 weeks of diabetes. No changes in the immunoreactivity of motor protein were found in retinal cultures.

The alterations in motor proteins detected in the retinas of diabetic animals suggest that axonal transport may be impaired under diabetes, which might contribute to early signs of neural dysfunction in the retina of diabetic patients and animal models.

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Keywords: diabetes mellitus, kinesin trafficking, Retrograde transport.

MON-080
Early cranial irradiation alters epigenetics parallel to reduced hippocampal neurogenesis in adult mice

T. Koç[1], E. B. Yılmaz[2], L. Şahin[3], T. Ergenoğlu[3], N. C. Öztürk[1], H. Öztürk[1]

[1]*Anatomy,* [2]*Radiation Oncology,* [3]*Physiology, Mersin University, Mersin, Turkey*

Radiotherapy is an effective tool in the treatment of pediatric malignancies but it is associated with adverse side effects, both short and long term. One of the cardinal late onset effects is cognitive deficits. Exposure of cranial irradiation to the early brain in rodents has been shown to potentially change the hippocampal neurogenesis levels in adulthood. Here, we demonstrated that epigenetics is also altered accompanying with the reduced hippocampal neurogenesis in the adult brain of C57BL6/J mice long after the early cranial irradiation.

For the experimental design, a single dose of 8 Gray (Gy) whole cranial irradiation at postnatal day 14 (P14) (Rad^{+} Group) or double doses (Rad^{++} Group) of 8 Gy both at P14 and P21 (total of 16 Gy) were administered to the pups. Additionally, a group of age and body weight matched mice were assigned as sham (anesthetic) or naive controls. Seven months after the cranial irradiation, three main groups of mice (Control, Sham and Rad) were first assigned for Open Field (OF) test to measure the locomotor activity, and afterwards for Morris Water Maze (MWM) paradigm to test the hippocampal dependent spatial learning and long term memory. No significant difference was observed between the groups in OF test. In the MWM paradigm, Rad^{+} and Rad^{++} groups displayed significantly weaker cognitive abilities as compared to the controls. Lastly, a significant dose-dependent difference of irradiation was also detected.

Following MWM experiments, we employed immunohistochemical stainings (im) with phenotypic neuronal and epigenetic markers to test the ongoing neurogenesis and epigenetic events in the P230 hippocampi. We found a significant decrease of Doublecortin-im (immature neuron marker) and Neuronal Nuclei-im (mature neuron marker) in the subgranular layer of the dentate gyrus of irradiated mice as compared to the controls. In the same hippocampal regions, there was also significant reduction of DNA methylation determinants (DNA methyl-transferase (DNMT) DNMT1-im, DNMT3a-im and Methyl-CpG Binding Protein 2-im positive cells). Our overall data suggests that exposure of cranial irradiation to the young brain alters not only the neurogenesis but also the epigenetic profile in adult hippocampus which may reflect the cellular base of the weakened cognitive abilities observed in the MWM experiments. All data was analyzed via parametric tests, using SPSS statistical software (V17).

Understanding the mechanism by which ionizing radiation affects epigenetic programming will provide insight into how to develop protection against the potentially harmful risks associated with radiation exposure.

Keywords: Adult Hippocampal Neurogenesis, Cranial Irradiation, DNA methylation.