into such lineages. On the whole, this novel approach could improve current treatments for neurodegenerative diseases, by restoring the neural connectivity and activity.

Declaration of Interest Statement: None

https://doi.org/10.1016/j.ibneur.2023.08.311

P0307 / #3276

Topic: AS03 Stem Cells, Organoids, Neural Injury Neurotoxicity and Repair

NEURODEVELOPMENTAL EFFECTS OF CYPERMETHRIN IN HUMAN NEURAL STEM CELLS

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The lack of adequate models for the study of developmental neurotoxicity has made difficult to correctly assess the risk and effects of toxic exposure. Despite the large body of results on animals, these studies are costly, time consuming and the results are not always reliable to assess the impact of chemical compounds on the developing human brain because animal models do not perfectly reflect human physiology. *In vitro* systems are becoming a promising tool to assess the toxicological effects of chemical compounds on developmental neurotoxicity with promising results. Currently, stem cells are becoming a useful model to study this type of toxicity. Stem cells are undifferentiated cells with the potential to differentiate into more specialized cell types. They are present during brain development and into adult life, making them a more appropriate model for mimicking key events that take place during embryonic brain development. Cypermethrin (CYP) is one of the most widely used and highly effective synthetic pyrethroids. CYP can enter the body mainly through skin contact but also through inhalation or ingestion of food or water. The main mechanism of action of pyrethroids is the interaction with Na channels and the induction of prolonged depolarization in neurons. In this study, the human neural stem cell line hNS1 was used to evaluate the effects of CYP on early developmental stages. hNS1 cells were exposed to different concentrations of the pesticide and cell death, proliferation and cell fate specification were analyzed under differentiation conditions by immunocytochemistry and RT-qPCR. The results showed that this compound induces apoptotic cell death at the highest doses tested and a decrease in cells in the cell cycle. Besides, CYP causes a decrease in both neurogenesis and gliogenesis in hNS1 cells. In conclusion, CYP has toxic effects on hNS1 cells and should be further studied.

Declaration of Interest Statement: None

https://doi.org/10.1016/j.ibneur.2023.08.312

P0308 / #2398

Topic: AS03 Stem Cells, Organoids, Neural Injury Neurotoxicity and Repair

THE SHORT-TERM THERAPEUTIC POTENTIAL OF HUMAN HAIR FOLLICLE-DERIVED STEM CELLS AND THEIR CONDITIONED MEDIUM IN A RAT MODEL OF STROKE

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The short-term therapeutic impacts of stem cells and their derivatives were frequently reported in preclinical investigations of ischemic stroke (IS); however, several drawbacks including accessibility, abundancy, and ethical concerns limited their clinical application. We describe here for the first time the therapeutic potential of human hair follicle-derived stem cells (hHFSCs) and their conditioned medium (CM) in a rat model of IS. Furthermore, we hypothesized that a combination of cell therapy with repeated CM administration might enhance the restorative efficiency of this approach compared to each treatment alone. Middle cerebral artery occlusion was performed for 30 minutes to induce IS. Immediately after reperfusion, hHFSCs were transplanted through the intra-arterial route and/or hHFSC-CM administered intra-nasally. The neurological outcomes, short-term spatial working memory and infarct size were evaluated. Furthermore, relative expression of seven target genes in three categories of neuronal markers, synaptic markers and angiogenic markers were assessed. The hHFSCs and hHFSC-CM treatments improved neurological impairments and reduced infarct size in the IS rats. Moreover, molecular data elucidated that IS was accompanied by attenuation in the expression of neuronal and synaptic markers in the evaluated brain regions and the interventions rescued these expression changes. Although there was no considerable difference between hHFSCs and hHFSC-CM treatments in the improvement of neurological function and decrement of infarct size, combination therapy was more effective to reduce infarction and elevation of target genes expression especially in the hippocampus. These findings highlight the curative potential of hHFSCs and their CM in a rat model of IS.

Declaration of Interest Statement: None

https://doi.org/10.1016/j.ibneur.2023.08.313