Analysis of cadmium effect on neural cells energetic metabolism using Seahorse technology

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Abstract: The heavy metal cadmium (Cd) is a widespread toxic pollutant, mainly released by anthropogenic activities, responsible for adverse effects on organisms. Human exposure can occur through different sources and once absorbed it accumulates throughout a lifetime (biological half-life of 20-30 years). Several organs are target of Cd toxicity, such as brain; indeed, Cd exposure has been related to impaired functions of the nervous system and to neurodegenerative diseases. Cd may enter the brain by increasing blood brain barrier permeability or through the olfactory nerves, exerting its toxicity in several ways, such as interfering with essential metal ions homeostasis, depleting cell's antioxidant defence systems or damaging mitochondrial with a consequent alteration of energetic metabolism.

Using Seahorse technology, we have evaluated energetic metabolism of SH-SY5Y neural cells treated with $CdCl_2$ (10-20 µM) for 24h. Cd treatment caused an increase in extracellular acidification rate, index of enhanced glycolysis, compared to control. The evaluation of glycolytic parameters confirmed this shift to anaerobic metabolism, such as the greater ATP production from glycolysis than oxidative phosphorylation in Cd-treated cells. Moreover, evaluation function through Mito stress test showed a less functionality of mitochondria if Cd is given to the cells. Finally, the evaluation of fuel oxidation demonstrated an equal dependency on glucose among the groups, while we observed a dose-dependent decrease in fatty acid oxidation together with an increase in glutamine dependency in the presence of Cd. Taken together these results showed a Cd effect on bioenergetic metabolism, with a shift to anaerobiosis due to mitochondrial damage.