Toxic effects following acute exposure to methylmercury in cardiomyocytes

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Methylmercury is the most common and toxic form of organic mercury. In particular, fish products are the main source of methylmercury in the diet. For decades, the toxic effects of mercury were associated mainly with the central nervous system and also with cardiovascular system. In fact recent studies have suggested that methylmercury exposure predisposes to a greater risk of cardiovascular disease, increases vascular resistance and induces hypertension.
The mechanism by which this compound produces cardiotoxic effects is not fully elucidated, but probably involves an increase in oxidative stress by NADPH oxidase activation. It's important to understand the reason of cell damage and the molecular mechanisms induced by methylmercury to revert these effects.
In this study we investigated the toxic effects following acute exposure to methylmercury in cardiomyocytes. In particular the cell line H9c2 was treated with increasing concentrations of methylmercury (0,5, 1, 5, 10, 25, 50, 75 and 100 μM) for 24 hours. We observed the cell death with increasing concentration of methylmercury and in particular the concentration 50 μM produces 50% mortality. Flow cytometric analysis showed that the treatment with methylmercury already at 25 μM determined apoptotic death; higher concentrations (75 and 100 μM) of methylmercury produced a late apoptosis. To confirm these data we tested the Caspase-3 expression and observed that the methylmercury, at 25 e 50 μM, caused the cleavage and activation of this protease.
Additionally we investigated the cellular cycle by flow cytometry. Surprisingly we have found that the concentrations of methylmercury 10 and 25 μM determined an arrest in phase S/G2M. Higher concentrations altered the typical profile of the cellular cycle and increased the cellular death.
With this in mind we wanted to investigate whether our results matched with other cell lines. For this reason we used the human cell line MO3.13 presenting phenotypic characteristics of oligodendrocytes. The obtained results were comparable to those previously described with cardiomyocytes. The next step in this work will be to study the effects induced by chronic doses of methylmercury.

Guallar et al. (2002)The New England Journal of Medicine. 347:1747–1754.
Yoshizawa et al. (2002) The New England Journal of Medicine. 347(22):1755–1760.
Farina et al. (2011). Toxicology and Applied Pharmacology. 25:405–417.
Furieri et al. (2011). British Journal of Pharmacology.162:1819–1831.