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Neurogenesis in the developing brain: alterations after platinum compounds

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Several chemotherapeutic agents have significant side effects and acquired or intrinsic drug resistance that limit their clinical application. One such agent is cisplatin, a cytostatic drug widely used in the treatment of testicular, ovarian, head and neck cancers and a variety of other solid tumours both in adults and children. In general, relatively little is known about the effects of cisplatin on the cells of the Central Nervous System (CNS). Therefore much attention has been focused on designing platinum compounds with improved pharmacological properties, whose activity may not necessarily require reaction with DNA.

In our research we compared the effects of platinum complexes on developing cerebellum and hippocampus, two significant areas from a neurogenic viewpoint. The aim is to evaluate the neurotoxicity of these drugs and to study the regenerative capability of CNS in response to neuronal injury. To this purpose we considered the process of cell death and proliferation and we analysed the expression of morphological, functional (e.g. calcium-binding proteins, neurotransmitter receptors) and neurogenic markers (e.g. GFAP, nestin, PSA-NCAM, DCX, NeuN).

The results we have obtained so far, confirm the early neurotoxic action of cisplatin, followed by considerable events of recovery and remodelling of CNS cytoarchitecture; moreover, the other new platinum compounds induce less severe damages on the developing brain[1].

In our next researches, attention will be paid to the action mechanisms of new platinum complexes that encompasses neurotoxicity and drug resistance.

References

1. **Cerri S.**, Calabriso N., Pisu M., Bernocchi G., Muscella A., Fanizzi F.P., Ciccarese A., Marsigliante S.; *Neurotoxicity of platinum compounds: comparison of the effects of cisplatin and [Pt (O,O'-acac) (γ-acac) (DMS)]*. 10th International Symposium on Platinum Coordination Compounds in Cancer Chemotherapy and Satellite symposium "Molecular aspects of metal-anticancer drugs", Verona, 30 Novembre- 3 Dicembre 2007