Oxidative stress and neuroinflammation effects in hippocampal development, ageing, and disease

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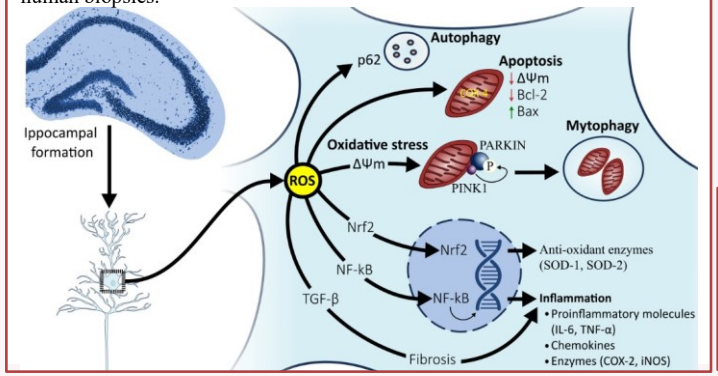
INTRODUCTION

Prolidase deficiency (PD) is a rare genetic disorder caused by mutations in PEPD gene. Prolidase enzyme can selectively cut proline dimers located at the C-terminal end of a polypeptide, crucially participating in collagen turnover. Recently, cerebellar morphological alterations in PD mice have been demonstrated, characterized by extracellular matrix disorganization, tissue damage and cell migration anomalies. Ageing is a physiological condition closely related to oxidative stress and a chronic inflammatory state called "inflammaging". A broad consensus exists that medicinal mushroom Hericium erinaceus (He1) exerts antioxidant activity also promoting cell proliferation in some brain areas of aged individuals. Eating Disorders are complex and difficult-to-cure diseases, mostly arising during adolescence. Among them, Anorexia Nervosa (AN) is characterized by insufficient energy supply for survival with severe consequences affecting the whole organism.

AIM

The purpose of this work was to evaluate inflammation and oxidative stress, as a common thread in three different pathologies, using both animal models and human biopsies.



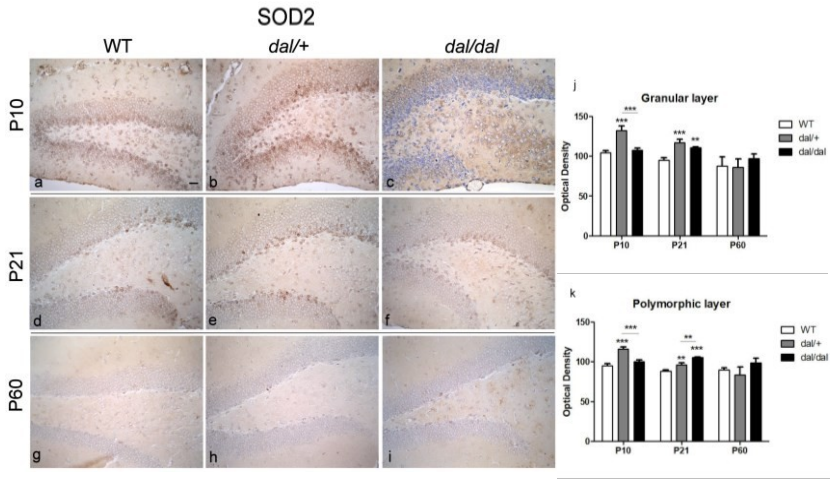
MATERIALS AND METHODS

To investigate onset and progression of inflammation and oxidative stress in the above reported pathological conditions, a battery of complementary techniques was used, followed by statistical evaluations. Morphological and immunohistochemical reactions were conducted on mouse and human hippocampal specimens considering different markers: superoxide dismutase 1 and 2 (SOD1, SOD2), cyclooxygenase 2 (COX2), nitric oxide synthase 2 (NOS2), interleukin 6 (IL-6), and transforming growth factor β (TGF-β). Parallely, Bax, Bcl-2, p62, PINK1 and PARKIN were employed to investigate cell death pathways. Haematoxylin & eosin and Nissl staining were performed for histological and cytoarchitectural analyses.

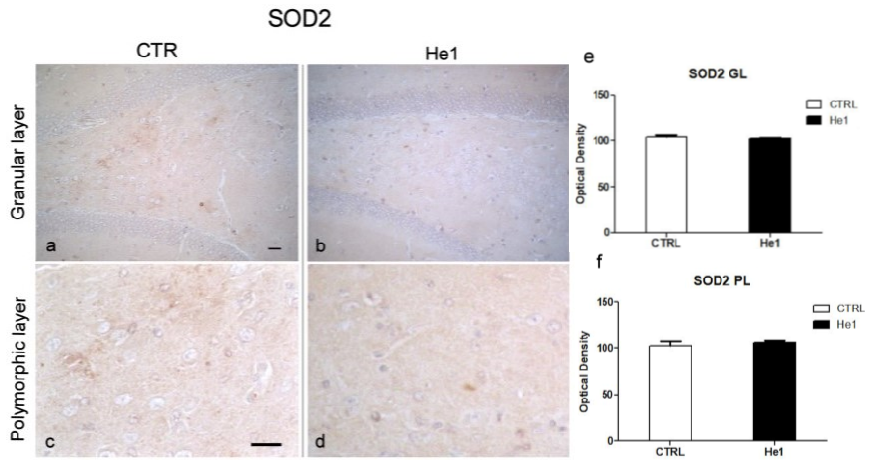
CONCLUSIONS

The results demonstrated that, in the presence of high inflammation/oxidative stress levels, the cells undertake different response mechanisms aimed at cell survival or death. Therefore, these data could provide novel insight allowing to develop new therapeutic protocols targeting inflammatory/oxidative stress pathway through activation of programmed cell death for cell survival.

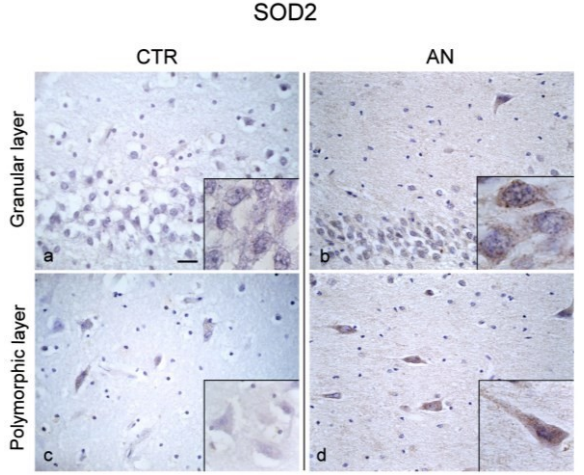
RESULTS



Strong SOD2 immunopositivity in granular cells of *dal* mice at P10 and P21 compared to WT animals.



Slight and no significant increase of SOD2 immunolabelling in He1 mice compared to control animals.



Increased SOD2 immunopositivity in AN granular and mossy hippocampal neurons compared to control condition.

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