face validity for the proposed model of social vulnerability, which allows us to approach its target validity.

0533 - FASTING INDUCES REMODELING OF THE OREXIGENIC PROJECTIONS FROM THE ARCUATE NUCLEUS TO THE HYPOTHALAMIC PARAVENTRICULAR NUCLEUS IN A GROWTH HORMONE SECRETAGOGUE RECEPTOR-DEPENDENT MANNER

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Abstract/Resumen: Some hypothalamic circuits are known to undergo morphological and functional remodeling in order to ensure the control of the body homeostasis. Ghrelin is a stomach-derived hormone that acts on the growth hormone secretagogue receptor (GHSR), and is known to play a key regulatory role on the energy balance. Here, we hypothesized that the up-regulation of the GHSR system during fasting at the orexigenic Agouti-related peptide (AgRP)/neuropeptide Y (NPY)-producing neurons of the arcuate nucleus (ARC) would promote a morphological remodeling of the ARC projections to the hypothalamic paraventricular nucleus (PVH) in adult mice, and that such structural changes mediate the fasting-induced activation of the PVH neurons. We showed through immunostaining analysis that the total amount of the orexigenic neuropeptides AgRP and NPY (mean intensity), the density of fibers containing these neuropeptides (area) and the amount of AgRP and NPY per fiber (integrated density) were increased in the PVH of fasted mice. Similarly, analysis of fluorescent signal in the PVH of NPY-GFP mice also showed that ARCnpy-->PVH projections increase under fasting. In addition, tracing studies confirmed that ARC-->PVH projections increase under fasting. Importantly, fasting-induced activation of PVH neurons was impaired in ARC-ablated mice in which the density and strength of ARCagrp/npy-->PVH projections is not increased under fasting. Additionally, we show that fasting-induced remodeling of these projections from the ARC to the PVH and the fasting-induced activation of the PVH neurons is impaired in mice with pharmacological or genetic blockage of the GHSR signaling suggesting that ghrelin signaling controls these adaptations. To our knowledge, these are the first evidence that the connectivity between hypothalamic circuits controlling food intake can be remodeled in the adult brain, depending on the energy balance conditions, and that GHSR activity is a key regulator of this phenomenon.

0545 - ACUTE FE-DEXTRAN TREATMENT AND REDOX BALANCE IN RAT WHOLE BRAIN AND CORTEX

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Abstract/Resumen: An acute Fe-dextran treatment produced oxidative stress in rat brain that lead to the translocation of Nrf2 to the cell nucleus, producing the activation of genes involved in the glutathione metabolism in the cellular environment. Previous reports have shown that the acute Fe overload produced by a single injection of Fe-dextran resulted in a significant decrease in total thiol and glutathione content in rat cortex area after 6 and 8 h post injection (p.i.). In the whole brain, enzymatic activities of glutathione-S-transferase (GST) and glutathione peroxidase (GPx), and total thiol content were increased as compared to control tissues at 6 or 8 h p.i., respectively. The aim of this study was to determine the effect of acute Fe overload on glutathione-dependent enzymatic metabolism in cortex rat brain. A single dose of 500 mg Fe-dextran/kg body weight was administrated intraperitoneally to male Sprague Dawley rats. Total brain samples or cortex area were obtained from control and treated animals after 6 or 8 h p.i.. Glutathione reductase (GR) was determined spectrophotometrically. Reduced glutathione (GSH), oxidized glutathione (GSSG) and malondialdehyde (MDA) content were determined by reverse phase HPLC. MDA content showed a significant increased ($p<0.05$) at 8 h p.i. in whole brain. A significant decrease in cortical GSH ($p<0.05$), and a significant increase in cortical GSSG ($p<0.05$) was observed at 8 h p.i. A slight but non-significant reduction in the activity of the enzyme GR was seen at 6 and 8 h p.i. in brain cortex. Taking as a whole, these results suggested that the increase in the GSSG/GSH ratio could be associated to the increase in the activities of GST and GPx without any change in GR activity in brain cortex. Moreover, it seems that the alteration in the redox status caused by the Fe treatment in the cortex could contribute to the lipid peroxidation changes detected in the whole brain.

0546 - EXPRESSION OF CCL2 BY REACTIVE ASTROCYTES AFTER COMPLETE SPINAL CORD INJURY

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Abstract/Resumen: As it is known, spinal cord injury (SCI) involves different degrees of disruption in the sensitive, autonomic and motor systems. Therefore, the goal in this field is finding some therapeutic approach that could promote the recovery of the previously lost functions. Keeping this in mind, the main research carried out by our group, is focused on the design of a treatment that promotes different kind of locomotor recovery (using a transection SCI rat model). One of these treatments involves the intra-spinal administration of Netrin-1, an embryological chemoattractant protein proved to participate in axonal navigation. Netrin-1 treated animals showed a significant improvement in the recovery of locomotion, as well as their autonomic functions. In line with this, the present project focuses on the study on how the inflammation at the lesion site evolves during a complete SCI. For this matter, each specimen was studied sequentially day to day after the injury, observing the evolution of the inflammatory process. CCL2, a chemokine secreted by astrocytes that promotes the activation of macrophages after the SCI, is one of the main markers for inflammation in this pathology. Histologically, we detected and quantified CCL2's localization and expression in reactive astrocytes. We also measured the number of macrophages at the lesion site. These results were obtained by performing an immunofluorescence microscopy each day after the SCI, starting at day 1 until day 20. Our results show a scar healing at the lesion site; a sharp increase in the number of macrophages, with a maximum reached at the third day after the SCI and a following decrease of them. CCL2 expression varies among days after SCI. CCL2 increases as days go by, upstream of the lesion site. However, its expression starts to decrease at the epicenter of the lesion coinciding with macrophage's migration. Finally, our results show an increase of the inflammation at the lesion site after SCI. This process significantly decreases in rats treated with Netrin-1, whose number of macrophages, expression of CCL2 and scar area are significantly lower.

0549 - AUTOPHAGY PROTECTS BV-2 MICROGLIAL CELLS FROM MANGANESE-INDUCED CELL DEATH