

although the glutamate-induced •NO dynamics were not significantly affected along aging, the neurovascular coupling was progressively impaired accompanying a decline in memory performance. Noteworthy, in spite of a reduced CBF response coupled to glutamatergic activation, the ΔpO_2 associated to the hemodynamic response was higher in older animals, strongly suggesting a decrease in global metabolic rate of O_2 . Furthermore, the age-dependent impairment in the neurovascular coupling was mimicked in young rats by promoting an unbalance in redox status toward oxidation via intracellular generation of superoxide radical by using the redox-active quinone. This observation strengthens the idea that oxidative stress may have a critical role in the neurovascular uncoupling underlying brain aging and dysfunction. Overall, data supports a connection of impairment of neurovascular response with cognition decline.

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S7-05 | An active lifestyle decreases the severity of prostate cancer lesions in male Wistar rats

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Background: Prostate cancer (PC) hormonal dependence is well known, as well as the effect of exercise on androgen levels. This work aims to evaluate the influence of an active lifestyle on dorsolateral prostate lesions in a rat model of chemically-induced PC.

Materials and methods: Fifty-five male Wistar Unilever rats were divided into four groups group I (sedentary), group II (sedentary-PC), group III (exercised), group IV (exercised-PC). Animals began the physical exercise in a treadmill at eight weeks of age and were trained at an intensity corresponding to 50% of the maximum speed determined in the maximum effort test performed monthly, 5 days/week,

during 53 weeks. At 12 weeks of age PC was induced by flutamide testosterone propionate, N-methyl-N-nitrosourea and crystalline testosterone implants. Animals were sacrificed at 61 weeks of age. Experiments were approved by DGAV.

Results and conclusions: At the end of the experiment, group I showed higher mean body weight than group III ($P = 0.04$); group II showed higher body weight compared to group IV ($P < 0.001$). The prostate average weights were higher in PC-induced groups ($P < 0.001$). The mean values of cholesterol were higher in groups I and II ($P < 0.05$). The creatine kinase concentration was higher in group IV than in group II ($P = 0.003$). Testosterone serum concentrations were 128.42 ± 25.53 pg/mL, 1921.55 ± 255.57 pg/mL, 256.99 ± 31.44 pg/mL and 2715.70 ± 315.18 pg/mL in groups I, II, III, and IV, respectively. Animals from group II showed 85.7% of dysplasia, 64.3% of PIN and 64.3% of microinvasive carcinomas of the dorsolateral prostate. Animals from group IV showed a slight decrease in the number of observed lesions (70% of dysplasia, 58.8% of PIN and 58.8% of invasive carcinomas). Our results suggest that exercise may have the potential to delay PC progression.

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S7-06 | The neuroprotective effect of N-acetylcysteine in the rat model of the endothelin-1-induced focal cerebral ischemia

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The increased production of reactive oxygen species (ROS) is a crucial factor aggravating cerebral ischemia. Here, we explored neuroprotective effects of the ROS scavenger N-acetylcysteine in a model of focal ischemia induced by one hour long epipial application of 10-20 μ M endothelin-1 on somatosensory rat barrel cortex. The level of suppression of sensory-evoked and spontaneous activity following three hours of endothelin-1 washout was used to estimate the level of ischemia-induced functional impairment. N-acetylcysteine (20 μ M) was epipially applied throughout one hour before and one hour during endothelin-1 application. We found that the frequency of spontaneous action potentials (AP) in the animals pretreated with N-acetylcysteine recovered to $67 \pm 32\%$ of control level three hours after endothelin-1 application ($n = 12$ rats), while in control animals, the AP frequency recovered only to $5 \pm 2\%$ of control ($n = 7$ rats, $P < 0.05$).

Also, the level of recovery of the principal whisker-evoked cortical sensory potential initial slope and amplitude was fivefold in animals pretreated with N-acetylcysteine compared to control group. Thus, N-acetylcysteine significantly improves the recovery of neuronal activity in rat barrel cortex in a model of the endothelin-1 induced focal ischemia.

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S8-O1 | Connecting the dots between a High-Fat/Cholesterol Diet and Sporadic Alzheimer's Disease

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Ample evidence from epi-clinical and pre-clinical studies suggests mid-life hypercholesterolemia is a risk factor for developing Alzheimer's disease (AD) at a later age. However, the mechanistic link between the two is poorly understood. In the present work we performed a comparative study between a transgenic model of AD (3xTgAD) and age-matched NTg mice fed a high-fat/cholesterol diet (HFCD) for an 8-week period, evaluating cognitive function, hippocampal synaptic plasticity and nitrenergic transmission as well as oxidative metabolism. We observed that the HFCD produced a modest 10% increase in serum cholesterol levels in NTg mice. Despite this, behavioral tasks (novel object recognition and Y-maze) revealed that the HFCD induced in NTg mice cognitive deficits similar to those observed in age-matched 3xTgAD mice. Similarly, evaluation of synaptic plasticity revealed compromised LTP in the CA1 subregion of hippocampal slices in HFCD-fed NTg mice similar to that observed in the genetic model of AD. Considering our previous observation of age- and genotype-dependent change in nitric oxide (NO) bioactivity in the hippocampus of NTg and 3xTgAD mice, we determined NMDAR-linked NO production in the CA1 of hippocampal slices. We found that the HFCD decreased NO production resulting from receptor activation, recapitulating the effect of age. Similarly, evaluation of mitochondrial respiration in intact hippocampal slices using high-resolution respirometry showed decreased respiratory

capacity resulting from HFCD, similar to that observed previously as a result of aging and not the 3xTg genotype. These observations suggest that NTg mice fed a HFCD develop an AD-like after that recapitulates some aspects observed in a genetic model of AD. Furthermore, a HFCD induces changes in NMDAR-linked NO dynamics as well as mitochondrial sparing capacity that we have found to be poorly expressed in the 3xTgAD model, although we have shown them to be a result of aging.

S8-O2 | Characterization and follow-up of the Coimbra cohort of Machado-Joseph disease patients

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Background: Machado–Joseph disease (MJD) is the most common of the dominantly-inherited ataxias worldwide. To date, there is no therapy to stop or slow disease progression, but potential candidates are ready for clinical studies and therefore the availability of a large cohort of patients is critical. The European Spinocerebellar ataxia type 3/Machado-Joseph disease Initiative (ESMI) is, in this context, intended to set up an international MJD cohort ready for interventional trials. Here, we characterized the Coimbra's cohort of MJD patients that integrates the ESMI project.

Methods: This study was approved by Ethics Committee of Faculty of Medicine, University of Coimbra. Patients were enrolled upon signing informed consent and characterized using clinical and functional tests at baseline and after 1 year.

Results: 39 patients were enrolled. Mean age of disease onset was 40.4 ± 11.9 years old, disease duration was 10.1 ± 6.1 years and number of CAG repeats on expanded allele was 71.7 ± 4.6 . At baseline, mean SARA (Scale for the Assessment and Rating of Ataxia) score was 13.8 ± 10.1 , whereas mean INAS count was 5.6 ± 2.3 . All patients exhibited at least one non-ataxic symptom. ADL score was 9.4 ± 9 . For CCFS scale, obtained mean scores were 2.513 ± 0.2 . Follow-up data revealed no variations from baseline in SARA and INAS. ADL scores, on the contrary, were significantly higher comparing with baseline. No statistically significant changes were observed in 9-Hole Peg and PATA tests, but a decrease in the performance of 8-meters walking test was observed.