

## P6.15

### L-lactate reduces ischemic white matter injury and modulates HCA1 oligodendrocyte expression in an in vivo mouse model of focal ischemia

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**Introduction:** L-lactate is a metabolite that is oxidized preferentially to glucose under conditions of high metabolic stress. The discovery and localization of the lactate receptor HCA1 in various brain regions suggests that lactate is additionally an important signaling molecule in the brain. Lactate is neuroprotective in various ischemia paradigms, reduces axonal injury in vitro and is avidly utilized by oligodendrocytes (OLs). The protective potential of L-lactate to reduce white matter (WM) injury in a mouse stroke model was investigated.

**Methods:** A single dose of L-lactate (250mg/kg-1) or vehicle was administered intraperitoneally shortly before or following a transient 60-minute middle cerebral artery occlusion (MCAO) in mice. Integrity of WM was assessed using histological and immunohistochemical methods at 24 hours and 7 days of reperfusion. Modulation of the lactate receptor HCA1 on WM OLs with or without L-lactate treatment was investigated by immunofluorescence.

**Results:** Treatment with L-lactate resulted in improved histological staining in affected WM, reduced ischemia-induced OL loss and attenuated apoptotic signaling in OLs compared to vehicle at acute and subacute stages. Further to previously reported neuronal expression, HCA1 was found to be localized on WM OLs. Ischemia elicited an increase in HCA1 fluorescence expression on WM OLs, particularly in regions proximal to the occluded artery. HCA1 expression was further amplified by exogenous L-lactate at acute and subacute stages.

**Conclusion:** These data suggest that protection by L-lactate extends beyond gray matter in a clinically relevant rodent focal ischemia model. Modulation of the HCA1 receptor on OLs presents a novel role for lactate signaling in WM which could be involved in OL injury and survival pathways.

## P6.16

### Role of the cannabinoid system in absence epilepsy

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**Introduction:** Absence epilepsy is a paediatric neurological condition characterised by recurrent generalised non-convulsive seizures. Currently, pharmacological intervention for the management of epilepsy aims to achieve total seizure control, and is sometimes successful. However, at present, there exists no medication to prevent epileptogenesis from occurring in the first place. Research has shown various key players in the regulation of neuronal hyperexcitability. Some highlighted neurotransmitters include monoamines,

serotonin, as well as endocannabinoids. Phyto- and synthetic-cannabinoids (CB), and endocannabinoids have shown to have anti-epileptic effects; however, their effects on comorbid memory impairment, anxiety and depression are not known.

**Methods:** The aim of this study is to investigate the effect of endocannabinoid neuronal systems on seizure control, development of depression and anxiety in the Genetic Absence Epilepsy Rat from Strasbourg (GAERS) and in their Non Epileptic Control (NEC) rats. EEG recording and behavioral tests such as hole board, elevated plus maze and forced swimming test will be used to evaluate the effect of cannabinoid compounds.

**Results:** This has been carried out by using low doses of the cannabinoid agonist WIN 55, 212-2s (WIN) at 2mg/kg IP, compared to its vehicle. The use of drugs blocking the cannabinoid receptor CB1-antagonist AM251 (1mg/kg IP) will also be investigated to verify whether WIN effects are mediated by this receptor.

**Conclusion:** We will provide evidence for CB dysfunction in this disease and identify potential targets that may, in the medium term, lead to novel anti-absence drugs.

## P6.17

### The European Audit of seizure management in hospitals: the local experience

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**Introduction:** Seizures remain a common important neurological presentation to all acute hospitals worldwide. The National Audit of Seizure Management in Hospitals (NASH) collected data on about 9000 patients presenting with seizures to over 150 hospitals in the UK, identifying an unacceptable variation in the quality of care. The European Audit of Seizure Management in Hospitals (EuroNASH) is currently being undertaken in a number of European countries, including Malta.

**Methods:** The aim of EuroNASH is to establish the first European benchmark for the management of seizures. Anonymous data was collected retrospectively on acute management, prior care and onward care for 50 patients who presented to Mater Dei with seizures between August 2016 and 2017, by reviewing the clinical notes. While the results from EuroNASH are yet to be published, we can compare local data with that from NASH.

**Results:** The median age was 47, and 60% were male, (NASH: median age 44, 57% male). 54% of Maltese patients and 61% of NASH patients had a known prior diagnosis of epilepsy (p=0.33). Of these, 63% of Maltese patients were seen by an epilepsy specialist during the previous year compared to only 37% of patients in the UK (p< 0.05). Ninety-eight percent (98%) of our patients were reviewed by a specialist during admission or got early referral, compared to 53.9% of NASH patients (p<0.05). Ninety-four percent (94%) of Maltese patients were seen by a doctor within 4 hours of presentation to the emergency