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Elevated levels of nitric oxide during hypoglycaemia cause structural and functional injury to callosal white matter axons in the rodent brain

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Introduction: Nitric oxide (NO) is a free radical that can act both as a signalling molecule and a neurotoxin. Previous literature suggest that it is involved in multiple brain pathologies. The main aim of this study was to investigate the role of NO in conduction block and structural axonal injury during and following glucose deprivation (GD).

Methods: Using combined two-photon imaging and electrophysiology, we investigated the increased levels of NO during and following the injury in YFP-H transgenic mice. This was correlated with the degree of axonal structural integrity, and with axonal functional integrity through maintenance of the compound action potential (CAP). Pharmacological agents were used to elucidate the pathophysiology of this NO-induced injury.

Results: 45 mins of GD resulted in loss of axonal structural integrity concomitant with the loss of CAP. Addition of 10 micro;M 7-nitroindazole (7-NI), a neuronal nitric oxide synthase (nNOS) inhibitor did not offer any protection. On the other hand, addition of 10 µM 1400W, a selective inducible NOS (iNOS) inhibitor, offered partial protection to white matter axons.

Conclusion: In conformity with published data on the rat optic nerve, increased levels of NO during injury resulted in structural and functional axonal injury. Addition of 1400W resulted in partial protection to both YFP labelled axons and to the CAP. This suggests that the rise in NO during injury is dependent on the inducible isoform of NOS, and is most likely derived from astrocytes and microglia.

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Role of the lateral habenula in modulating the rewarding effects of nicotine

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Introduction: Existing smoking cessation therapies have not yet been proven very successful and a better understanding of the neurobiology of tobacco dependence is still needed. Nicotine, acting on the midbrain dopaminergic system, is responsible for rewarding and reinforcing properties of tobacco. The lateral habenula (LHb) is a structure known to inhibit DA neurons and encoding aversive stimuli and might represent a possible target for the action of nicotine.

Methods: Single Unit extracellular Recordings in vivo from either the LHb or VTA or rat brain.

Results: We have showed that nicotine induce anxiety-like behavior in rats and that LHb lesion reverse this effect.

Moreover, nicotine increased, medially but not laterally, VTA dopaminergic neuronal activity. Following nicotine chronic treatment, this pattern of activation was inverted, as well as when the LHb was lesioned. This increase was almost abolished following nicotine chronic treatment in LHb lesioned rats

Conclusion: Our evidences indicate that the LHb might play an important role in mediating the aversive and positive effects of nicotine in the brain and that midbrain DA system participate to its mechanism of action. Our data suggest that counteracting the LHb decreased neuronal response to nicotine, following its chronic administration, might represent a successful strategy in treating nicotine addiction.

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Management of Spontaneous Intracranial Haemorrhage – the local experience

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Introduction: Spontaneous intracerebral haemorrhage (ICH) accounts for 9-27% of strokes worldwide. Guidelines for the management of spontaneous ICH have been updated by the European Stroke Organisation in 2014 and by the American Heart Association/American Stroke Association in 2015. The aim of this study was to compare local practice to international guidelines prior to introduction of local guidelines, identifying areas of our care pathway needing most attention.

Methods: Data was collected retrospectively on 44 patients who presented to Mater Dei Hospital with spontaneous ICH throughout 2015, using admission notes, iSoft Clinical Manager, and Electronic Case Summary reports.

Results: The mean age at presentation was 65.9 years and 43.2% were female. All patients underwent CT imaging, with mean time to first CT being 145 minutes (+/- 1 S.D. 120 minutes). The average blood pressure (BP) was 156/81 mmHg at triage, and 147/81 mmHg at 6 hours. Despite a statistically significant difference between these systolic BP readings ($p=0.045$), only 66.7% of patients had a systolic BP below the recommended 140 mmHg at 6 hours, with anti-hypertensives used in only 46.2% of patients. 20.5% of patients were on warfarin, with warfarin reversal attempted in only 55.5% of patients. 25% of patients received neurosurgical review and 63.6% of these proceeded to surgical intervention in view of neurological deterioration or development of hydrocephalus. Pneumatic compression stocking use was documented in only 2 patients, both of whom were in ITU, despite international recommendations for their use.

Conclusion: Our audit indicates poor adherence with international guidelines particularly in the context of blood pressure control, warfarin reversal and DVT prophylaxis. Local guidelines were introduced in 2017, highlighting these points. We plan to repeat this audit in 2018, to identify whether local guidelines have been effective in improving patient care.