Abstracts

AXONAL EXCITABILITY PROPERTIES IN DRAVET’S SYNDROME REFLECT EFFECT OF LOSS OF SODIUM CHANNELS

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Introduction Mutations in SCN1A encoding the Na+,1.1 subunit of the neuronal sodium channel underlie the devastating epilepsy of Dravet’s syndrome.1 The mechanism by which Na+,1.1 dysfunction causes seizures is not clear. In vitro and in silico channel evaluation can support mutation pathogenicity but cannot define the in vivo impact of channel dysfunction. Axonal excitability studies can show the pattern of single-channel dysfunction in disorders where the channel is peripherally expressed.2 This study was undertaken to determine whether axonal excitability studies could detect changes in Dravet’s patients related to the condition or due to medication effect.

Methods Patients with Dravet’s syndrome were recruited from clinics in Sydney and Melbourne and axonal excitability studies were performed. Excitability results were analysed in 3 age groups and compared to age-matched normal controls.

Results Twenty six patients (ages 2–46) were studied. Findings were most pronounced in patients aged 20–46 (n=7) with 6.9% greater increase in threshold during hyperpolarisation (p=0.1), 7.6% greater threshold decrease on depolarisation (p=0.005) and, in the recovery cycle, 19.7% reduction in superexcitability (p=0.002) and 26% reduction in subexcitability (p=0.03). Axonal excitability studies resembled previously published changes seen in patients with sodium channel blockade caused by acute tetrodotoxin poisoning.3

Conclusions Changes in excitability of axonal membrane in Dravet’s syndrome are consistent with a decrease in sodium channel function. As the affected channel in Dravet’s syndrome is not peripherally expressed, the effect seen is likely due to the heavy anticonvulsant regime required to control epilepsy, combined with a progressive loss of sodium channel function that occurs with age.

REFERENCES

Intruduction Neuroimaging and CSF analysis compose essential steps in evaluating patients with autoimmune encephalitis (AE). No study has compared the magnitude and prognostic implications of these findings between different subtypes. Herein we examine cases of AE with neuronal cell surface antibodies, and contrast the results of early investigations.

Methods We performed medical records search from 2008–2018 in 5 Victorian hospitals. Cases of AE were established in accordance with diagnostic criteria by Graus et al.4 Clinical and laboratory data was collected. All neuroimaging was evaluated independently by a neuroradiologist.

Results We identified 52 patients with AE with neuronal cell surface antibodies (21 NMDAR, 27 VGKC, 3 AMPAR, 1 GABAB).

We found that among patients with anti-LGI1 antibodies the presence of abnormal CSF correlated with increased rates of mortality (50% vs 0%). This effect was largely mediated by CSF lymphocytosis, which was present in 2 patients who both died within 12 months of diagnosis.

We found that the development of hippocampal atrophy was more common amongst patients with abnormal MRI findings, but in particular those with changes affecting the medial temporal lobe. This effect was evident both in the cases with anti-VGKC antibodies (60% vs 18%, 75% vs 17%) and the cohort as a whole (56% vs 15%, 83% vs 13%).

Conclusions This is the first study of its kind in Australia, and identifies some unique correlation between early investigation findings, and the clinical and radiological outcome. A larger cohort is required to determine if these findings are statistically significant.

REFERENCES

MELBOURNE MOBILE STROKE UNIT HALVES WORKFLOW FOR ACUTE STROKE REPERFUSION THERAPY

1. Henry Zhao*, 1,2,3Skyle Coot, 2Francesca Langenberg, 1Damien Easton, 1Michael Stephenson, 4Karen Smith, 5Stephen Bernard, 2Patricia Desmond, 7Peter Mitchell, 2,5Bernard Yan, 1,2Bruce CV Campbell, 1Mark Parsons, 1Geoffrey A Donnan, 1,2,3Stephen M Davis. 1The Melbourne Brain Centre and Department of Neurology, Royal Melbourne Hospital, Melbourne, VIC, Australia; 2Department of Medicine and Radiology, The University of Melbourne, Melbourne, VIC, Australia; 3Department of Radiology, Royal Melbourne Hospital, Melbourne, VIC, Australia; 4Ambulance Victoria, Melbourne, VIC, Australia.

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Background The Melbourne Mobile Stroke Unit (MSU) utilises a specialised ambulance with on-board CT scanner and multidisciplinary team to provide on-scene imaging, treatment and triage for central Melbourne, Australia. We describe the operational impact of the MSU on commencement of acute reperfusion therapy.

Methods Data from the first 12 months of operation were collected for all patients receiving reperfusion therapy from November 2017. Workflow times were compared to contemporary published Australian data and historical controls from Royal Melbourne Hospital.

NEUROIMAGING AND CSF FINDINGS IN AUTOIMMUNE ENCEPHALITIS WITH NEURONAL CELL SURFACE ANTIBODIES

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Background The Melbourne Mobile Stroke Unit (MSU) utilises a specialised ambulance with on-board CT scanner and multidisciplinary team to provide on-scene imaging, treatment and triage for central Melbourne, Australia. We describe the operational impact of the MSU on commencement of acute reperfusion therapy.

Methods Data from the first 12 months of operation were collected for all patients receiving reperfusion therapy from November 2017. Workflow times were compared to contemporary published Australian data and historical controls from Royal Melbourne Hospital.
Mechanical Thrombectomy in Pediatric Stroke: Systematic Review, Individual Participant Data Meta-Analysis, and Case Series

Introduction In adults, there is strong evidence demonstrating the superiority of mechanical thrombectomy (MT) for intracerebral hemorrhage over thrombolysis alone for the treatment of acute ischemic stroke due to large vessel occlusion (LVO). The role of MT in the pediatric stroke population is less clear. Here we present an updated systematic review addressing the use of MT in pediatric patients, including three cases from our centre in Sydney, Australia. We have also completed an individual participant data (IPD) meta-analysis of clinical and angiographic outcomes based on these results.

Method Our systematic review and IPD meta-analysis was performed according to PRISMA-IPD (Preferred Reporting Items for Systematic Reviews and Meta-Analyses: Individual Participant Data) guidelines. Primary outcomes measures were change in NIHSS (National Institute of Health Stroke Scale) score following MT, and mRS (modified Rankin Scale) score at final reported follow-up. The secondary outcome measure was functional angiographic result using the mTICI (modified Treatment in Cerebral Ischemia) scale.

Results MT resulted in good long-term neurological outcomes (mRS 0–2) in 60/67 cases (89.6%) follow-up timing μ=4.1 months: 95%CI 2.9–5.3), good short-term neurological outcomes (reduction in NIHSS by 8 or more points or post-MT NIHSS of 0–1) in 37/52 cases (71.2%), and successful recanalization (mTICI 2b/3) in 57/67 cases (85.1%).

Conclusions In paediatric patients, MT is an effective treatment for ischaemic stroke due to LVO. In the absence of a dedicated prospective registry and with randomized control trials unfeasible, this report represents the best available evidence for the use of MT in the paediatric setting.

013 The Impact of Aggressive Blood Pressure Management in the Post-Thrombolysis Setting

Introduction High blood pressure (BP) post-thrombolysis has been associated with an increased rate of bleeding and poorer outcome. We noted frequent BPs of >180 mmHg with a target of keeping BP <180. We therefore made an aggressive target of SBP <160 mmHg would result in fewer BP protocol violations.

Methods Patients were prospectively captured comparing patients thrombolysed during the 12 months before and 12 months following the introduction of a new more aggressive BP protocol, allowing for a 6 month transition period. Results were adjusted for baseline function and stroke severity using regression analysis.

Results Pre-protocol change 68 and post-100 patients were thrombolysed. Baseline characteristics were similar between groups. There was a trend for a lower rate of SBPs >180 mmHg (adjusted OR 0.49; 95% CI 0.31–1.1; p=0.097) and a significantly higher rate of SBPs <120 mmHg (adjusted OR 1.27; 95% CI 0.58–2.8; p=0.36) in the aggressive BP protocol group; although events of extreme SBPs (>200 and <100 mmHg) were similar between groups. Favourable outcomes (mRS = 0–2) at 3 months were similar between groups (adjusted OR 1.27; 95% CI 0.58–2.8; p=0.36) as was the rate of symptomatic haemorrhages (adjusted OR 1.26; 95% CI 0.28–5.7; p=0.76). Model fit was improved by adding study group to the model.

Conclusions More aggressive post-thrombolysis BP management lowered the overall BP, but did not result in improved patient outcomes. Potential explanations include a small sample size, reduced cerebral perfusion offsetting reduced bleeding risk, or high BP being merely an epiphenomenon of worse outcome rather than causative.

AvXS-101 Gene-Replacement Therapy (GRT) in Presymptomatic Spinal Muscular Atrophy (SMA): Study Update

Introduction SMA is a neurodegenerative disease caused by biallelic deletion/mutation of the survival motor neuron 1