AXONAL EXCITABILITY PROPERTIES IN DRAVET SYNDROME

Abstracts

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AXONAL EXCITABILITY PROPERTIES IN DRAVET'S SYNDROME REVEAL EFFECT OF LOSS OF SODIUM CHANNELS

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Introduction Mutations in SCN1A encoding the Na1.1 subunit of the neuronal sodium channel underlie the devastating epilepsy of Dravet’s syndrome.1 The mechanism by which Na1.1 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 hyperpolarization (p=0.1), 7.6% greater threshold decrease on depolarization (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 block caused by acute tetrodotoxin poisoning.

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

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

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Introduction 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.1 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.

REFERENCE

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MELBOURNE MOBILE STROKE UNIT HALVES WORKFLOW FOR ACUTE STROKE REPERFUSION THERAPY

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Introduction The Melbourne Mobile Stroke Unit (MSU) utilises a specialised ambulance with on-board CT scanner and multi-disciplinary 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.