2399 AN EARLY PHASE OPEN-LABEL TRIAL OF A NOVEL TARP INHIBITOR

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Objectives ES-481 is a novel AMPA-Transmembrane AMPA regulatory protein (TARP) inhibitor that specifically targets hippocampal excitation glutamate transmission by disrupting protein-protein interactions between the AMPA receptor and the γ-8 TARP. Preclinical data predicts that ES-481 has broad spectrum anti-seizure effects. ES-481-C201 is a Phase 2A trial in four Australian Epilepsy Clinical Trial Network (ECTN) centres assessing efficacy, safety and pharmacokinetics in adult patients with drug resistant epilepsy. It has two phases: Double-Blind Treatment (DBT) and Open-Label Extension (OLE). Here we report the early experience from the OLE.

Methods Subjects completing the DBT Phase are offered enrolment in the OLE. OLE subjects are assessed at regular intervals for anti-seizure efficacy and safety. Anti-seizure efficacy is assessed by examining mean difference in seizure frequency in OLE, subjects have to demonstrate continued efficacy, tolerability and safety measures.

Results To date, eight subjects have completed the DBT Phase and enrolled in the OLE. One subject dropped out due to a non-treatment AE, and one withdrew consent. The six remaining subjects have shown clinically significant decreases in seizure activity, good tolerability, and no adverse safety signals after 3 to 9 months.

Conclusions The data to date from the OLE Phase indicates that ES-481 is well tolerated and potentially efficacious in controlling seizures in adult subjects with drug resistant epilepsy. Confirmation of this experience is awaited from the results of the DBT Phase.

2401 LONG-TERM HEALTH BURDEN OF DEFERRED OR NO TREATMENT FOR NEWLY DIAGNOSED EPILEPSY

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Objective To assess if early treatment in newly diagnosed epilepsy is associated with lower health burden than delayed or no treatment.

Methods Adults with newly diagnosed epilepsy between 1999–2016 were linked with state-wide databases to extract hospital admission, ambulatory psychiatric care, and mortality data from 1970–2019. Data were compared between patients receiving immediate, delayed and no treatment at up to 10 years post-diagnosis, adjusted for seizure type, age at onset, baseline comorbidity and others.

Result Of 603 patients (61% male; median age 40 years) with newly diagnosed epilepsy, 422 (70%) were treated immediately, 110 (18%) received delayed treatment, and 71 (12%) were untreated at the end of follow-up (median 6.8 years). Patients immediately treated had higher proportions of epileptogenic lesions on neuroimaging, seizure clusters and more pre-diagnostic seizures.

Immediately treated patients had a higher ten-year rate of all-cause admissions or emergency department presentations than the untreated (incidence rate ratio [IRR]=2.0; 95% confidence interval [CI]:1.4–2.9) and delayed treatment groups (IRR=1.7; 95%CI:1.0–2.8).

However, mortality was similar when immediate treatment was compared with delayed (hazard ratio [HR]=0.99; 95%CI:0.56–1.76) or no treatment (HR=1.31; 95% CI:0.55–3.10). Immediately treated patients also had similar ten-year risk of developing new physical and psychiatric comorbidities compared with the delayed (p=0.68; p=0.18, respectively) and untreated groups (p=0.69; p=0.28, respectively).

Conclusions Newly diagnosed epilepsy patients with deferred or no treatment did not have worse outcomes, compared to those immediately treated. Instead, patients treated immediately had greater healthcare utilisation, which may reflect more severe underlying epilepsy.

2402 ZEBRAS, NOT HORSES: AN ATYPICAL CASE OF NEUROSARCOIDOSIS

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Objectives Sarcoïdosis isolated to peripheral nerves and/or muscles is rare.1,2 Clinical suspicion typically occurs when there are other systemic manifestations present. This case is an example of neurosarcoïdosis presenting similarly to Guillain-Barré Syndrome. It also emphasises the significant impact nerve and muscle biopsies can have on diagnosis and management.

Case A previously well 64-year-old male presented with a severe symmetric, ascending weakness and numbness of all limbs with associated areflexia progressing over two weeks and culminating in an inability to walk. His presentation was of a severe subacute onset polyneuropathy and Guillaine-Barré syndrome was therefore suspected. Tests for autoimmune, infectious, malignant, and nutritional causes were negative. Cerebrospinal fluid showed a protein level of 2100 mg/L, white cell count of 45 x10⁶/L, 99% of which were mononuclear. MRI of the brain and spine showed no nerve root enhancement or other relevant abnormality. Nerve conduction studies and electromyography demonstrated a severe axonal polyneuropathy with active denervation. The patient continued to deteriorate despite two courses of intravenous immunoglobulin and a sural nerve and vastus lateralis muscle biopsy was performed.
therefore performed. Both the nerve and muscle biopsies showed noncaseating granulomatous inflammation consistent with neurosarcoidosis. An FDG-PET scan did not show sarcoidosis involving other organs.

Conclusions This case shows that sarcoidosis can be limited to just the nerves and muscles without clear systemic manifestations. It also provides a case for neurosarcoidosis to be considered as a differential in future presentations of subacute onset polynuropathy.

REFERENCES
3. et al 2020; 2403

2004 SEVERE AXONAL NEUROPATHY FOLLOWING NITROUS OXIDE MISUSE

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Background Nitrous oxide misuse causes severe neurotoxicity due primarily to functional vitamin B12 (cobalamin) deficiency. Peripheral neuropathy is a less frequent presentation than subacute combined degeneration of the cord (SCDC).

Methods Review of a patient with severe axonal neuropathy secondary to nitrous oxide misuse.

Results An 18-year-old Chinese male presented with subacute bilateral foot drop, distal numbness and neuropathic pain. There was transient finger weakness and no proximal weakness, symptoms of CNS dysfunction or constitutional symptoms. He was misusing nitrous oxide over several months and self-initiated oral cobalamin supplementation.

On examination, there was mild abductor pollicis brevis weakness bilaterally and bilateral foot drop (2/5 power on dorsiflexion, ankle eversion and great toe extension). Ankle jerks were absent. Plantar responses were flexor. Coordination was normal. Sensation was reduced distally. Gait was high-stepping and tandem was unsteady. Romberg’s could not be performed.

Nerve conduction studies demonstrated severe axonal motor neuropathy with active denervation change on electromyography. MR spine showed subtle T2/FLAIR dorsal column hyperintensity. Somatosensory evoked potentials revealed abnormal large-fibre sensory conduction rostral to the cauda equina. Bloodwork demonstrated mild macrocytosis, low red-cell folate and normal cobalamin. Neuropathy/vasculitic screens and CSF analysis were unremarkable.

He received high-dose parenteral cobalamin and supportive care. He did not return for follow-up.

Conclusions Nitrous oxide misuse can cause severe axonal neuropathy, in addition to the more frequent SCDC, and can be the predominant clinical phenotype, even in the setting of oral supplementation. This syndrome is profoundly disabling but potentially reversible with abstinence and high-dose cobalamin replacement.

2004 THE TEMPORAL DISTRIBUTION OF INTERICAL DISCHARGES IN JUVENILE ABSENCE EPILEPSY (JAE) SHOW CYCLES DURING SLEEP WITH BURSTS SUGGESTING COUPLING TO A SLEEP-PHASE GENERATOR

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Objectives Idiopathic Generalised Epilepsy is not a benign condition with increasing evidence of enduring cognitive deficits beyond seizures. We aimed to describe the temporal distribution, duration, and relationship to sleep of interictal discharges (IEDs) using outpatient ambulatory 24-hour EEG recordings (aEEG) in juvenile absence epilepsy (JAE).

Methods We retrospectively identified 15 patients with JAE undergoing treatment adjustment with at least three aEEGs between 2012–2020. JAE was classified with onset of first or predominant absence seizures after age 9 years. We used a published automated detection algorithm to assist aEEG review and recorded the timing and length of IEDs. Following training, PH/AD independently marked IEDs with any uncertain or discordant IEDs resolved by WD. For each individual recording, the timing and length of the discharges was plotted against 24-hour clock.

Results 15 patients (onset age 9 to 16 years), had a total of 14701 IEDs (median 104; IQR 11 – 403). 9917 (67.5%) IEDs occurred between 22:00 and 07:00 (individual aEEG median 63%; IQR 49.8% – 92.3%). IEDs show an overall pattern of clustered discharges during sleep compared to a more sporadic frequency in wakefulness. In addition, during sleep IEDs oscillate between high frequency peaks and quiescent periods throughout the night.

Conclusions JAE demonstrates a cyclical pattern in the distribution of IEDs with two-thirds occurring during sleep. The oscillating pattern of IEDs during sleep has not been previously reported in humans and suggests coupling to a sleep phase generator, a critical time for memory encoding.

2007 AN INTERESTING CASE OF ATYPICAL PARKINSONISM


Objectives Functional movement disorders (FMD) are thought to account for around 10% of new patients at large movement disorder clinics. Among patients with FMD, only 5% have functional parkinsonism. Functional progressive supranuclear palsy (PSP) likely accounts for a very small proportion of these patients. Despite a literature search, I was not able to find any case description of functional PSP. I report an interesting and rare case of functional parkinsonism very closely mimicking PSP.

A 70-year-old NZ European man presented to the Emergency Department following a collapse and progression of symptoms related to his previously diagnosed PSP, making him...