B.02

Recessive mutations in ATP8A2 cause severe hypotonia, cognitive impairment, hyperkinetic movement disorders and progressive optic atrophy

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Background: *ATP8A2* mutations have only recently been associated with human disease. We present the clinical features from the largest cohort of patients with this disorder reported to date. **Methods:** An observational study of 9 unreported and 2 previously reported patients with biallelic *ATP8A2* mutations was carried out at multiple centres. **Results:** The mean age of the cohort was 9.4 years old (range: 2.5-28 yrs). All patients demonstrated developmental delay, severe hypotonia and movement disorders: chorea/choreoathetosis (100%), dystonia (27%) or facial dyskinesia (18%). Hypotonia was apparent at birth (70%) or before 6 months old (100%). Optic atrophy was observed in 75% of patients who had a funduscopic examination. MRI of the brain was normal for most patients with a small proportion showing mild cortical atrophy (30%), delayed myelination (20%) and/or hypoplastic optic nerves (20%). Epilepsy was seen in two older patients. **Conclusions:** *ATP8A2* gene mutations have emerged as a cause of a novel phenotype characterized by developmental delay, severe hypotonia and hyperkinetic movement disorders. Optic atrophy is common and may only become apparent in the first few years of life, necessitating repeat ophthalmologic evaluation. Early recognition of the cardinal features of this condition will facilitate diagnosis of this disorder.

B.03

Registered EEG technologists can accurately identify ictal and interictal epileptiform patterns on routine EEG

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Background: Registered EEG technologists (RETs) are trained in both the technical aspects of EEG and in preliminary EEG interpretation. However, there is little research evaluating the accuracy of EEG interpretation by RETs. **Methods:** Retrospective study of consecutive routine EEG recordings performed at SickKids Hospital. Preliminary reports by RETs and final reports by neurophysiologists were compared in 5 domains: background activity, focal abnormalities, ictal and inter-ictal epileptiform discharges and summary. **Results:** 500 EEG recordings were analyzed. Sensitivity and specificity of RET reports was high for the assessment of background (85%, 93%), focal slowing (84%, 93%) and inter-ictal epileptiform discharges (92%, 90%). RET reports identified ictal EEG patterns in 32 cases vs. 29 cases identified by neurophysiologists. RET reports were 100% accurate for noting no EEG change for all of 11 cases with non-epileptic events. **Conclusions:** Preliminary EEG reports by RETs were sensitive and specific for all EEG domains analyzed. In the majority of cases, the preliminary interpretation made by the RET was concordant with the final report of the neurophysiologist. Given these findings, RETs may be able to participate in the screening of routine EEG recordings in order to enhance the productivity of busy EEG laboratories.

B.04

Insight into the mesial frontal negative motor area: The girl with a very unusual interest in having her back patted

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Background: Currently, there is limited insight in to the function of the mesial frontal negative motor area (NMA) and the anatomic structures implicated in its function. **Methods:** We present a patient with a Rett-like phenotype, refractory frontal lobe epilepsy, and reflexogenic seizures in which backpatting induced atonic seizures with a semiology resembling the patient falling asleep. The patient underwent video EEG monitoring and ictal/interictal SPECT imaging capturing the reflexogenic seizures. Iterative reconstruction was performed, with images co-registered to previously acquired MRI with subtraction Ictal-Interictal imaging co-registered to MRI. **Results:** Interictally, the patient's EEG showed a slow background and right frontal spikes. Ictally, the patient had numerous subclinical frontal seizures. The reflexogenic seizures had an ictal pattern at the vertex (Cz) with the ictal SPECT imaging, showing hyperperfusion in the right mesial frontal region, both paramedian precentral and postcentral gyri, and right basal ganglia. **Conclusions:** Our findings support the hypothesis that the negative motor area may be activated by the primary sensory cortex; moreover, the ictal SPECT now suggests involvement of the basal ganglia in the NMA's function.

B.05

Nusinersen in infants who initiate treatment in a presymptomatic stage of spinal muscular atrophy (SMA): interim results from the Phase 2 NURTURE study

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Background: NURTURE (NCT02386553) is an ongoing open-label single-arm efficacy/safety study of intrathecal nusinersen in infants who initiate treatment in a presymptomatic stage of spinal muscular atrophy (SMA). **Methods:** Enrolled infants were age ≤6 weeks at first dose, clinically presymptomatic, had genetically diagnosed SMA, and 2 or 3 copies of *SMN2*. Primary endpoint is time to death or respiratory intervention (≥6 hours/day continuously for ≥7 days or tracheostomy). **Results:** As of July 5, 2017, 25 infants (2 copies *SMN2*, n=15;3 copies, n=10) were enrolled. All infants were alive. Two infants (both with 2 copies *SMN2*) required respiratory intervention (but not tracheostomy or permanent ventilation) during an acute, reversible viral infection and thus met the primary endpoint. At last

visit, 22/24 (92%) infants had achieved WHO motor milestones sitting without support and 8/16 (50%;2 *SMN2*, n=3/11;3 *SMN2*, n=5/5) on study >13 months achieved walking alone. AEs were reported in 24/25 (96%) infants; most 20/25 (80%) had AEs that were mild/moderate in severity; 9 had serious AEs. Four infants had an AE possibly related to study drug, which resolved despite continued treatment. No new safety concerns were identified. **Conclusions:** Nusinersen continued to benefit infants who initiated treatment in a presymptomatic stage of SMA.

Study Support: Biogen

B.06

Safety and efficacy of nusinersen in infants/children with spinal muscular atrophy (SMA): part 1 of the phase 2 EMBRACE study

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Background: EMBRACE (NCT02462759) Part 1 is a randomized, double-blind, sham-procedure controlled study assessing safety/tolerability of intrathecal nusinersen (12-mg equivalent dose) in symptomatic infants/children with SMA who were not eligible to participate in ENDEAR or CHERISH. **Methods:** Eligible participants had onset of SMA symptoms at ≤6 months with 3 *SMN2* copies; onset at ≤6 months, age >7 months and 2 copies; or onset at >6 months, age ≤18 months, and 2/3 copies. Safety/tolerability was the primary endpoint. Exploratory endpoints included Hammersmith Infant Neurological Examination Section 2 (HINE-2) motor milestone attainment, change in ventilator use, and growth. **Results:** EMBRACE Part 1 was terminated early based on positive results from ENDEAR. Safety/tolerability was similar to previous trials. More nusinersen-treated (11/14;79%) vs. sham–treated individuals (2/7;29%) were HINE-2 motor milestone responders. Between Day 183 and 302, mean (SD) hours of ventilator use changed by +1.236 (3.712) hours in nusinersen-treated (n=12) and +2.123 (3.023) hours in sham–treated individuals (n=7). Similar increases in weight and body length were observed in nusinersen-treated and sham–treated individuals by Day 183. **Conclusions:** In EMBRACE Part 1, nusinersen demonstrated a favorable benefit-risk profile. These results add to the aggregated efficacy, safety/tolerability data of nusinersen in SMA.

Study Supported by: Ionis and Biogen

B.07

Review of patients with Spinal Muscular Atrophy treated with Nusinersen in Ontario

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Background: Spinal Muscular Atrophy (SMA) is an autosomal recessive neurodegenerative disease. In June 2017, Health Canada approved Nusinersen, currently the only available drug for SMA. Since 2016, patients in Ontario have been treated clinically with Nusinersen through different access programs. **Methods:** Retrospective case series of patients with SMA treated clinically with Nusinersen in Ontario, describing clinical characteristics and logistics of intrathecal Nusinersen administration. **Results:** Twenty patients have been treated across four centres. To date, we have reviewed 8 cases at one centre (seven SMA Type I, one SMA Type II). Age at first dose ranged from 3-156 months and disease duration 9-166 months. Patients had received 4-7 doses at last evaluation. Three patients with scoliosis (2 with spinal rods) required fluoroscopy-guided radiologist administration, and 4 required general anesthesia. No complications/adverse events were reported. At last follow up, 5/8 families reported improved daily activities. Of 5 patients with baseline and follow up motor function testing, 3 demonstrated improved scores. One patient died due to respiratory decline at age 9 months, despite improved motor outcome scores. **Conclusions:** We describe the first Canadian post-marketing experience with Nusinersen. Timely dissemination of this information is needed to guide clinicians, hospital administrators, and policy-makers.

CNSS Chair's Select Abstracts

C.01

Endoscopic versus open microvascular decompression of trigeminal neuralgia: a systematic review and comparative meta-analysis

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Background: Microvascular decompression (MVD) is commonly used in the treatment of trigeminal neuralgia with positive clinical outcomes. Fully endoscopic microvascular decompression (E-MVD) has been proposed as a minimally invasive, effective alternative, but a comparative review of the two approaches in the literature has not been conducted. **Methods:** We performed a meta-analysis comparing patient outcome rates and complications for both techniques. From a pool of 1,039 studies, 22 articles were selected for review: 12 open MVD and 10 E-MVD. The total number of patients was 6,734. **Results:** Good pain relief was achieved in 81% of MVD and 88% of E-MVD patients, with a mean recurrence rate of 14% and 9% respectively. Average rates of complications in MVD versus E-MVD included facial paresis or weakness, 9%, 3%; hearing loss,