Network connectivity following a single unprovoked seizure using 7 Tesla resting-state fMRI


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Background: Predicting epilepsy following a first seizure is difficult. Network abnormalities are observed in patients with epilepsy using resting-state functional MRI (rs-fMRI), which worsen with duration of epilepsy. We use rs-fMRI to identify network abnormalities in patients after a first seizure that can be used as a biomarker to predict development of epilepsy. Methods: Patients after a single, unprovoked seizure and age/sex matched healthy controls underwent 7 Tesla structural and resting-state functional MRI. Data were analyzed using graph theory measures. Patients were followed for development of epilepsy. Results: Nine patients and nine control subjects were analyzed. There were no differences in baseline characteristics. No patients developed epilepsy (average follow-up 3 months). No differences between groups occurred on a whole-brain network level. At a 20% threshold, significant differences occurred in the default mode network (DMN). Patients demonstrated an increased local efficiency (p=0.02) and clustering coefficient (p=0.04), and decreased path length (p=0.02) and betweenness centrality (p=0.02). Conclusions: No whole-brain network changes occur after a single unprovoked seizure. No patient has developed epilepsy suggesting this group does not have network alterations after a single seizure. In the DMN, the alterations noted indicate increased segregation of network function.

CACN CHAIR’S SELECT ABSTRACTS

A.01

The relationship between fatigue and health-related quality of life in a clinical trial population of Duchenne muscular dystrophy patients


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Background: Fatigue was recently reported to be the largest contributor to poor health-related quality of life (HRQOL) in paediatric Duchenne muscular dystrophy (DMD). Additional studies are necessary to confirm the generalizability of this finding. Our objective was to explore the longitudinal relationship between fatigue and HRQOL in an additional cohort of DMD patients. Methods: We performed a secondary analysis of data from a clinical trial (NCT00592553), which enrolled patients with nonsense mutation DMD, aged 5–20 years, from 37 sites in 11 countries (N=174). Fatigue and HRQOL were assessed using the PedsQL Multidimensional Fatigue Scale and Generic Core Scales, respectively, by patient- and parent-report at baseline and over 48 weeks. Results: Patients reported greater fatigue than healthy controls from published data. There was no significant difference between patient- and parent-reported fatigue. Fatigue was significantly correlated with worse HRQOL at baseline, by patient-report (r=0.70, P<0.001) and parent-report (r=0.70, P<0.001); and at 48 weeks, by patient-report (r=0.79, P<0.001) and parent-report (r=0.74, P<0.001). Change in fatigue was significantly correlated with change in HRQOL over 48 weeks, by patient-report (r=0.64, P<0.001) and parent-report (r=0.67, P<0.001). Conclusions: Fatigue is a major contributor to HRQOL in DMD. The strong association between fatigue and HRQOL corroborates previous studies, and suggests that reducing fatigue may improve HRQOL.

A.02

Assessing visual functions in children with an optic pathway glioma using steady-state visual evoked potentials

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Background: Optic pathway gliomas (OPG) represent 5% of pediatric brain tumours. Visual acuity measures are used to evaluate treatment response. Current clinical tests to assess visual field integrity are subjective and require verbal cooperation. Thus, the objective of this study was to evaluate the clinical effectiveness of Steady State Visual Evoked Potentials (ssVEPs) to measure visual field integrity.
in a non-invasive and objective manner. Methods: SsVEPs were obtained in ten children with OPGs and 42 controls ages 3 to 21. The stimuli consisted of two circular dartboard patterns stimulating fovea and peripheral zones at two flickering frequencies, so that central and peripheral visual fields could be assessed simultaneously. The test consisted of eight stimuli presentations of 10 seconds. Results: Results indicate significantly lower ssVEP amplitudes in children with OPGs ($M = 2.52, 95\% CI [1.13, 3.92]$) compared to controls ($M = 13.26, 95\% CI [8.85, 17.67]$) in the central visual field ($p = .021$). However, no between group differences were detected in the peripheral field ($p > .05$). There were no significant differences between age groups ($p > 0.05$). Conclusions: This objective, affordable, and non-invasive method appears to be effective in detecting central visual field deficits in children with OPGs rapidly and consistently.

A.03

Analyses of surgical and MRI factors associated with cerebellar mutism
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Background: The surgical risk factors and neuro-imaging characteristics associated with cerebellar mutism (CM) remain unclear and require further investigation. We aimed to examine surgical and MRI findings associated with CM in children following posterior fossa tumor resection. Methods: Using our data registry, we retrospectively collected data from pediatric patients who acquired CM and were matched based on age and pathology type with patients not acquiring CM after posterior fossa surgery. The strength of association between surgical and MRI variables and CM were examined using odds ratios (ORs) and corresponding 95% confidence intervals (CIs). Results: A total of 22 patients were included. Medulloblastoma was the most common pathology among CM patients (91%). Tumor attachment to the floor of the fourth ventricle (OR, 6; 95% CI, 0.7-276), calcification/hemosiderin deposition (OR 7; 95% CI 0.9-315.5), and post-operative peri-ventricular ischemia on MRI (OR, 5; 95% CI, 0.5-236.5) were found to have the highest association with CM. Conclusions: Our results may suggest that tumor attachment to the floor of the fourth ventricle, pathological calcification, and post-operative ischemia are relatively more prevalent in patients with CM. Collectively, our work calls for a larger multi-institutional study of CM patients to further investigate the determinants and management of CM to potentially minimize its development and predict onset.

A.04

Functional investigations of CIC and ATXN1L in Oligodendroglioma
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Background: Oligodendroglioma (ODG), a molecularly defined subtype of glioma, is a treatment responsive, slow growing tumour strongly associated with IDH mutation and 1p19q co-deletion. Mutations in Capicua (CIC), located on chromosome 19q, have been found in up to 70% of IDH mutated, 1p19q co-deleted ODGs; suggesting that loss or altered function of CIC may be crucially associated with ODG’s unique biology. CIC and ATXN1L have previously been implicated in neurodegeneration, however, this interaction has not been studied in cancer. Methods: Transcriptome profiling of CIC knockout HEK293 cell lines generated using CRISPR was performed using microarray. CIC and ATXN1L interaction was confirmed using immunoprecipitation and immunofluorescence. Transcript and protein changes of CIC targets were tested using RT-qPCR and Western blot following ATXN1L siRNA knockdown. Results: Transcriptomic profiling of CIC knockout cell lines resulted in a list of candidate CIC target genes validated against clinical samples. Immunoprecipitation and immunofluorescence confirmed CIC and ATXN1L interaction. Derepression of candidate CIC targets at transcript and protein levels was seen upon siRNA knockdown of ATXN1L. Conclusions: The interaction between CIC and ATXN1L is necessary for the repression of CIC target genes, including known oncogenes. Further research into the relationship between CIC and ATXN1L may lead potentially novel avenues of therapeutic approaches for less favorable gliomas.

A.05

An epidemiologic study of SLC52A2-related Riboflavin Transport Deficiency
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Background: Riboflavin transporter deficiency (RTD), formerly known as Brown-Vialetto-van Laere syndrome, is an early-onset neurodegenerative disorder with distinctive phenotypes. RTD is caused by mutations in either the SLC52A2 or SLC52A3 genes that encode riboflavin transporters RFVT-2 and RFVT-3, respectively. Methods: This was a 3-year retrospective case review from the Cure RTD International Registry. Results: 73 individuals (~60% female, 14 deceased) from 56 families had genetically confirmed RTD Type 2, including 30 novel SLC52A2 mutations (24 missense, 2 nonsense, 4 deletion). The mean ages at symptom onset and at diagnosis were 2.4 years (SD 1.5, range 0.25 – 8, n=63) and 12.0 years (SD 10.2, range 0.75 – 52, n=56) respectively. Most common presenting symptoms were sensory ataxia (n=43), sensorineural hearing loss (n=22), nystagmus/visual loss secondary to optic atrophy (n=14), upper limb weakness (n=11), and respiratory insufficiency (n=9). Treatment included high dose riboflavin, other supplements, and supportive care; 7 individuals required transfusions for anemia pre-riboflavin treatment and 17 (25%) received a cochlear implant. The minimum prevalence of RTD was estimated to be 1 per million, with >100 new