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Submitted abstracts

P1. EYE-GAZE TECHNOLOGY AS A COMMUNICATION DEVICE: HABILITATION PROCESS WITH THREE SUBJECTS WITH RETT SYNDROME

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Background:
Communication in girl's with Rett syndrome is a major problem. The aim of this study was to evaluate subjects´ ability to learn to use eye-gaze technology and its influence on their communication skills, their possibilities to take part in social situations as an active partner, and to find out which areas of function are most often used to describe habilitation process to gain eye-gaze technology as a communication aid.

Materials and Methods:
Three teenage girls took part in a three-year habilitation process to learn to use Tobii-I® device as a communication aid. Reports about each subject's functioning and habilitation goals written by occupational and speech therapists were classified using International Classification of Functioning, Disability and Health (ICF). Parents were interviewed, focusing on their experiences of the process.

Results:
All subjects learned to use eye-gaze technology as a communication aid, though some dyspraxia in eye-gaze-use were reported. The most common ICF-categories describing the process were products and technology for communication (e125), functions of structures adjoining the eye (b215) and undertaking a single task (d210). Parents believed that the device had a positive impact on their daughters' participation possibilities, but found the repeated evaluations stressful.

Conclusions:
ICF is a useful tool for defining meaningful concepts, when analyzing natural habilitation process. The ability to use communication devices varied depending on alertness and motivation. Dyspraxia in using gaze seemed to diminish under the habilitation period. In future it is important to offer individually motivational communication material early on, while simultaneously training the movements and fixation of the eye.

P2. Course of Tourette syndrome and comorbidities in a large prospective study

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Background:
Tourette syndrome (TS) is a childhood onset neurodevelopmental disorder characterized by frequent comorbidities and improvement of tics during adolescence. The clinical presentation is heterogeneous and can vary significantly from few tics without comorbidities to severe tics and disabling comorbidities and coexisting psychopathologies. This large prospective study describes the clinical course of tics and comorbidities in a large prospective longitudinal study, the development of phenotypes and the prevalence of comorbidities and coexisting psychopathologies in a cross-sectional view.

Materials & Methods:
The clinical cohort was recruited at the Danish National Tourette Clinic. Data was collected with uniform clinical examinations at baseline (n=314, age range 5-19 years) and at follow-up (n=227, age range 11-26) 6 years later to examine the development in expression of tics and comorbidities and of phenotypes. Additionally, a cross-sectional screening for coexisting psychopathologies with The Development and Well-Being Assessment (DAWBA) were performed at follow up reporting the presence of DSM IV diagnoses(n=146).

Results and Conclusions:
Tics, OCD and ADHD severity scores are significantly age-related and all declining during adolescence though with different rates. Although, ADHD severity declined based on DSM IV criteria, analyzed with the Danish national norm scores the adolescents aged 11-18 (n=83) had a significantly raised norm score in inattention, hyperactive- impulsivity and conduct.
The development in phenotypes changed towards less comorbidity with 40% presenting with TS-only at baseline and 55% at follow-up which can help guide patients and be used for genetic, etiological and clinical research purposes.
At baseline only 10.2% were regarded as TS pure. At follow up prevalence of comorbidities and coexistent psychopathologies was 61.2% whereas 38.2% presented pure TS. At follow up we found a broader spectrum of TS-associated comorbidities and coexistent psychopathologies in the emotional, behavioral and neurodevelopmental spectrum.
In spite of general improvement and partial remission considerable comorbidities and coexisting psychopathologies persist in adolescence and threshold symptoms and difficulties still have to be considered in clinics.

P3. NF1 and the gastrointestinal canal: A high prevalence of gastrointestinal symptoms correlated to constipation

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Background:
Gastrointestinal involvement in the NF1 population is poorly described. Our theory was that NF1 could be associated with a higher prevalence of gastrointestinal symptoms, predominantly leading to constipation. Thus, the purpose of the PhD was to gain new insight into the frequency and classification of gastrointestinal symptoms in patients with NF1 and to correlate these findings with NF1 pheno- and genotype.

Materials & Methods:
Gastrointestinal symptoms were assessed with a Rome® III diagnostic questionnaire. The patients completed a supplementary questionnaire on self- perceived conception of NF1. NF1 disease severity and visibility severity were assessed by the patient's physician. Simple and multiple logistic regressions were used and the groups were compared using odds ratio. NF1 mutational analysis was performed with targeted next-generation sequencing.

Results and Conclusions:
We compared 102 4-17-year-olds, median age 10.3, and 46 of their unaffected siblings, median age 10, and 175 adults, median age 34.2 and 91 of their unaffected relatives, median age 42.0. The overall response rate was 80%.
The overall likelihood of having gastrointestinal symptoms usually attributed to either functional dyspepsia, irritable bowel syndrome or constipation was higher among the 4-17-year-olds with NF1 (odds ratio (OR) 3.58 (95% CI: 1.30-9.79) and among the adults with NF1 (OR: 3.06; 95% CI: 1.62-5.79, adjusted).
The likelihood of functional constipation was higher among the 4-17-year-olds with NF1 (OR: 6.41 (95% CI: 1.45-28.24) and the among adults with NF1 (OR: 3.49; 95% CI: 1.14-10.64, adjusted).
Assessing the NF1 mutational spectrum in relation to constipation, there was a higher occurrence of missense mutations in cases compared to controls. NF1 severity and the patient's conception of NF1 showed no statistically significant effect on the likelihood of constipation. Even though not significant, the conception of NF1 illness burden showed the strongest association with constipation (OR: 1.83 (95% CI: 0.95-3.52).
The prevalence of gastrointestinal symptoms attributed to constipation was high in patients with NF1. No clear correlation with NF1 phenotype severity or genotype was established. The high prevalence of constipation indicates that it is not functional but part of the NF1 disorder.

P4. Everolimus treatment of medically refractory epilepsy associated with tuberous sclerosis complex – Status on the first Danish pediatric patients

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Background:
Tuberous sclerosis complex (TSC) is an autosomal dominant disease which in Denmark has an incidence of 5-10/year and a prevalence of approximately 200-400 cases. It is a multi-organ disease caused by dysfunction of the tumor suppressing hamartin/tuberin complex leading to an over-activated mTOR signaling pathway and uncontrolled cell growth. In the central nervous system characteristic lesions include cortical/subcortical tubers and subependymal giant cell astrocytomas. Epilepsy is frequent, and two-thirds of patients are refractory to anti-epileptic medication. Protocolled treatment has recently been recommended by The Danish Medicines Council. Four pediatric patients at Rigshospitalet have met the criteria for everolimus therapy.

Materials & Methods:
Criteria for starting treatment include established TSC diagnosis, medically refractory epilepsy with significant seizure burden, no contraindications to everolimus and expected good compliance. Monitoring of treatment and stop-criteria will be presented. With parental written consent data for medical history was collected from the medical records

Results and Conclusions:
Four pediatric patients have started treatment with everolimus with the indication drug-resistant epilepsy and TSC since August 2017. Age at treatment onset was 1.2-6.1 years (median 1.7 years). Gender distribution 1:1 (M:F). Weekly number of seizures before everolimus initiation was 20-160 (median 110). Three patients reached adequate p-everolimus levels in 44-72 days (median 57 days). Levels below target were frequent due to drug interactions and/or pausing of everolimus because of neutropenia. Total days of treatment as of 24th of June 2018 has been 55-314 days (median 222 days). Reduction in seizures after 4 months was >50% for three patients One patient has not reached therapeutic levels yet. Parents of all patients have reported positive psychomotor development. One of the three patients became seizure free after concomitant epilepsy surgery. Side effects observed were one case of exanthema and in another patient, mild transient neutropenia during minor infections.
In conclusion, the early data on everolimus as adjunctive treatment in TSC associated epilepsy is promising with regards to both effect and tolerability. Close monitoring is warranted.

P5. The etiology, treatment and recovery rate in acute facial palsy in children living in borrelia burgdorferi endemic area, Turku, Finland

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Background:
Facial palsy causes facial weakness with loss of taste, hyperacusis, and decrease of salivation and tear secretion. Lyme borreliosis is a common cause of acute facial palsy in children living in *Borrelia burgdorferi* endemic areas, and the empiric treatment is usually targeted on it. Other causes can be trauma, inflammation, other infection than borreliosis and neoplasia, or the etiology can remain unknown. The recovery rate of facial palsy in children has been good.

Materials & Methods:
We collected medical record and laboratory data of patients under 17 years of age (n = 94) treated for facial palsy in the Department of Paediatrics and Adolescent Medicine, Turku University Hospital, in years 2002-2016. Our aim was to investigate the incidence of borrelia infection and other etiology in facial palsy patients in borrelia endemic area of Turku. Positive antibodies against flagellar antigen, positive C6 index, positive *B. burgdorferi* PCR in CSF, or positive intrathecal antibody index were considered as definite Lyme borreliosis diagnosis. We also examined the outcome after facial palsy in borrelia and non-borrelia groups. Recovery to House-Brackmann score 1 (normal) or 2 (slight facial weakness noticeable only in near inspection and complete closure of eye with minimal effort) were noted as sufficient recovery result.

Results and Conclusions:
The etiology of facial palsy was Lyme borreliosis in 35 (37%) patients. In non-borrelia group the etiology was acute otitis in nine, other infection in head/neck area in two, tumor in one and acute polyradiculitis in one patient. In 46 patients the etiology remained unclear. The empiric treatment was doxycycline alone in 57, ceftriaxone followed by doxycycline in 19, only ceftriaxone in 6 and neither in 12 of 94 patients. Peroral steroid treatment was given to 20 patients. The overall rate of sufficient recovery was fast (under 2 months) in 74% and slow (2-9 months) in 23% of all 94 patients. The permanent facial palsy was noted in 3 (3%) patients, and the recovery rate of one patient remained unclear. The patients in borrelia group seemed to heal faster: the recovery was fast in 86% and slow in 11%. In non-borrelia group, the recovery rate was fast in 66% and slow in 29%. In both groups the facial palsy remained permanent in 3% of patients.

P6. Whole exome sequencing and rhPCR accurately resolve copy number variation in highly homologous SMN1 and SMN2 genes

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Background:
Spinal muscular atrophy (SMA) is a neuromuscular disorder characterized by progressive degeneration of spinal cord motor neurons, atrophy of skeletal muscles, and generalized weakness. The clinical phenotype ranges from a severe infantile form with a limited life expectancy to an adult-onset mild form of the disease. In the majority of cases, the disease is caused by a homozygous absence of the survival motor neuron 1 (*SMN1*) gene. Highly homologous *SMN2* gene that differs from *SMN1* only by a single coding nucleotide resulting in a splicing defect and low SMN2 function can also modify the disease severity. Patients with a higher *SMN2* copy number usually manifest a milder clinical phenotype.

Materials & Methods:
To address the clinical importance of accurate and efficient *SMN1* and *SMN2* copy number analysis, we developed a custom bioinformatic analysis based on whole exome sequencing data combined with a novel RNase H2-dependent PCR (rhPCR) for confirmation analysis. The bioinformatic method utilizes next-generation sequencing (NGS) reads at four loci differing between the genes while the rhPCR assays target two of the loci with RNA-modified primers and activating RNase H2 enzyme improving the assay specificity and sensitivity compared to traditional quantitative PCR-based methods. We validated the methods using a set of commercially available samples and patient DNA samples extracted from blood and saliva.

Results:
Both methods showed 100% sensitivity and specificity. Additionally, we applied the bioinformatic analysis to test 2196 de-identified patient samples and observed heterozygous *SMN1* deletion in 2.6% of the samples, which is in agreement with frequencies reported earlier.

Conclusions:
We have established an accurate and high-throughput approach to test for *SMN1* and *SMN2* copy numbers enabling diagnostics of SMA and application of novel therapeutic strategies.

P7. Ictal Urinary Urge in Focal Temporal Lobe Epilepsy - Case Report

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Background:
Ictal urinary urge represents a rare lateralizing sign indicating a seizure onset in the non dominant temporal lobe.

Materials & Methods:
An 8 years old patient with mild Intellectual Disability, low school performance, Hyperactive behavior, was referred from a rural area, with daily episodes, duration of 1-2 minutes, characterized by agitated behavior simulating urinary urgency, left hand catching external genitalia, decreased communication and visual contact with his surrounded, and defecation (in few episodes), preceded by unpleasant feeling in his stomach. Since 2 years, Interpreted and treated as a behavior disorder. Brain MRI interpreted as normal. First EEG without epileptic activity, started on Valproate w/o response, second prolonged EEG showed Right Temporal-Frontal and Left Central Epileptic Activity, we started him on Carbamazepine achieving good response of episodes. Few months later his father stopped treatment by his own resulting in new episodes, after reestablishment of Carbamazepine attacks were controlled.

Results and Conclusions:
Ictal urinary urgency and genital discomfort has a value for lateralization and localization of seizures onset.

* Videos of the episodes suffered by our patient are available.

P8. Morbidity and mortality in children with low muscle mass undergoing scoliosis surgery. A retrospective single-center cohort study with patients from all parts of Denmark and the Faroe Islands.

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Background:
Children with low muscle mass are at increased risk of pulmonary, circulatory, nutritional and surgical complications. Triggered by some complicated cases, we aimed at assessing morbidity and mortality in children with low muscle mass undergoing spinal surgery in our unit. We hypothesised that these patients would be at an increased risk for complications.

Materials & methods:
In this retrospective cohort study, we included consecutive patients under the age of 18 years with scoliosis due to spinal muscular atrophy type II and III, cerebral palsy, Duchenne muscular dystrophy, Ulrich muscular dystrophy or Merosin-deficient congenital muscular dystrophy, who underwent spinal surgery for scoliosis in Copenhagen University Hospital Rigshospitalet between 2012 and 2016. We registered pre-, intra, and postoperative predefined variables by means of the medical files. The primary outcome measure was 90-day mortality. Secondary outcomes were duration of mechanical ventilation, rate of pneumonia, number of red blood cell transfusions, rate of hypo/hyperglycaemia, hospital length of stay, intensive care unit length of stay, and readmission rates.

Results:
We included a total of 48 children with a median (interquartile range, IQR) age of 14 (13-15). At baseline, 46 patients were wheelchair bound, 52% received any respiratory assistance, and the median (IQR) body mass index (BMI) was 16.3 kg/m^2 (14-19) with 70 % being categorised as underweight (BMI <18). Less than 40% of the patients had their nutritional status assessed preoperatively.
All patients were alive at day 90, 12.5% of the patients developed pneumonia postoperatively, and 12.5% were re-admitted to the hospital due to infection or respiratory failure. The median (IQR) hospital length of stay was 11 (10-15) days.

Conclusion:
In this sample of consecutive children undergoing spinal surgery for scoliosis, we found a high rate of pulmonary complications and readmissions with resulting long hospital length of stay. Also, we found inadequate nutritional screening and treatment preoperatively and postoperatively. Altogether, we believe that these findings warrant a future perioperative care protocol aiming at improving the quality of care provided to this vulnerable patient population.

P9. Characterisation of children with dyskinetic cerebral palsy born between 1999-2007: a population based study

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Background:
The aim of this study was to describe the epidemiology, aetiology and clinical findings in dyskinetic cerebral palsy (CP) in a population-based study of children born between 1999-2007 and to compare finding with cases of bilateral spastic CP.

Materials & Methods:
Data has been collected from the Danish national CP register. Total number of CP cases in the period was 1165. Age at ascertainment was 5 to 6 years.

Results and Conclusions:
92 children with dyskinetic CP were included (53 males, 39 females). Prevalence of dyskinetic CP was 0.16 per 1000 live-births. The majority were born at term (75.6% vs. 51.2% for bilateral spastic CP) and had an appropriate weight for gestational age (81.3%). Compared to children with bilateral spastic CP there were more cases with APGAR level <5 at 5 minutes (21.7% vs. 11.2%), neonatal seizures (43.5% vs. 28.5%), and neonatal cerebral irritation or depression (56.5% vs. 42.6%), but less cases with respiratory deficiency, anemia, hyperbilirubinemia and sepsis. Level of impairment based on gross motor function classification system (GMFCS) was: mild GMFCS (I-II ; n=9) and severe GMFCS level (III-V ; n=81) as compared to: mild GMFCS (I-II; n=182) and severe GMFCS level (III-V; n=353) for bilateral spastic cases. The rate of reduced developmental quotient (DQ<50 in 68.1%), visual impairment (severely impaired in 39.3%) and epilepsy after the neonatal period (65.9%) increased with severity of the motor disability. MRI had been performed in 74 children with dyskinetic CP and was normal in 15 (18.1%) whereas it was performed in 439 children with bilateral spastic CP and was normal in 112 (25.5%). Basal ganglia/thalamus lesions were more prevalent in children with dyskinetic CP as compared to bilateral spastic CP, but only occurred in 27.7% of dyskinetic cases vs. 12.8% in bilateral spastic CP cases. In the remaining children a great variety of lesions was found. We conclude that dyskinetic CP is most prevalent in term-born, appropriate for gestational aged children with severe impairments. Dyskinetic CP has overlapping clinical features with cases of bilateral spastic CP, but differ significantly in several perinatal features.

P10. Diagnostic Approach to Children with Presumed Congenital Myasthenic Syndromes

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Background:
Establishing efficient methods for diagnosis of illnesses that are otherwise hard to pin down is favorable for our patients and healthcare system alike.
Congenital myasthenic syndromes (CMS) is a group of rare, inherited disorders characterized by abnormal transmission within the motor endplate. This group of syndromes is difficult to diagnose, as patients may present with a wide array of symptoms of varying severity, such as muscle weakness (hypotonia), respiratory and feeding difficulties, hanging eyelids (ptosis), joint stiffness (artrogryposis), growth problems or delayed motor development. Additionally, CMS can be difficult to differentiate from other types of neuromuscular conditions with overlapping presentations.
This study seeks to retrospectively compile clinical and paraclinical findings in a group of undiagnosed patients with aforementioned symptoms, to access whether diagnostic accuracy can be improved.

Materials & Methods:
Data was retrospectively collected from the medical records of 25 patients whom had been examined at the Dept. of Neuropediatrics at Rigshospitalet. All patients had undergone testing with single-fiber electromyography (sfEMG), a muscle biopsy and/or a wide multi-gene panel consisting of 256 genes associated with a wide spectrum of primary muscle disorders. Blinded evaluation of the sfEMG was compared with clinical findings and genetic results.

Results and Conclusions:
Patients were aged 0-17 years, with a median age of 5.3 at sfEMG testing. Gender distribution was 16:9 (M:F). A large subset of patients presented with symptoms compatible with myasthenic syndromes, such as: fatiguability (n=14), delayed motor development (n=19), ptosis (n=5) and muscle weakness (n=11). Other symptoms included: respiratory issues (n=5), hypermobility (n=12) and feeding difficulties (n=9). Patients had undergone paraclinical testing, including sfEMG (25/25 patients), muscle biopsy (19/25), a wide multi-gene panel (13/25) or other genetic tests (5/25). A diagnosis was accomplished in 13 patients and ranged from nemaline myopathy, rigid spine muscular dystrophy, *GRIN2B* mutation and myasthenia gravis. Comparative data of the diagnostic approaches will be presented at the NNPS meeting.

P11. PARENTS' EXPRESSIONS OF CONCERNS AND HOPES FOR THE FUTURE AND CONCOMITANT ASSESSMENTS OF DISABILITY IN THEIR CHILDREN

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Background:
To ask parents to freely express their concerns and hopes for the future in their children with disability and assess their children's disability as well as to analyse these data for consistency.

Materials & Methods:
Parents of 162 children with spina bifida, spinal muscular atrophy, muscular disorders, cerebral palsy, visual impairment, hearing impairment, mental disability or disability following brain tumours were asked to freely express their concerns and hopes for the future and to assess disability in their own children by employing a set of 26 ICF-CY body function (b) codes and activity and participation (d) codes. A grounded theory approach was employed to systematise parents' expressions of concerns and hopes; then, parents scored on a 5-step qualitative Likert scale. Identically, parents assessed their children's disability using the ICF-CY 5-step Likert qualifier scale.

Results:
Altogether, 119 parents freely expressed their concerns and hopes. Of those, 101 also assessed their child's disability using the 26 ICF-CY codes. A total of 475 expressions of concerns and hopes (issues) were expressed and categorized into 34 areas of concern and hopes (subsections). The most frequent issues involved education and understanding, goodwill and communication between parents and community support. Qualitative data on both 5-step qualifier scales showed good reliability. Rasch analysis maps on concerns and hopes for children as well as on ICF-CY assessment demonstrated good alignment and a clinically relevant progression from least to most disabled children.

Conclusions:
Parents can express valid and reliable data on their concerns and hopes for the future and can reliably assess disability in their own children.

Reference:
Illum NO, Bonderup M, Gradel KO. Parents' expressions of concerns and hopes for the future and their concomitant assessments of disability in their children. Clinical Medicine Insights: Pediatrics 2018;12:1-13

P12. Pulmonary Function in Patients With Advanced Duchenne Muscular Dystrophy: Eteplirsen-Treated Patients Compared With Multiple Natural History Cohorts

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Background:
Eteplirsen is approved in the US for treating Duchenne muscular dystrophy (DMD) patients with genetic mutations amenable to exon 51 skipping. We evaluated pulmonary function data from patients in a phase 2, open-label study and in multiple CINRG Duchenne Natural History Study (CINRG DNHS) cohorts.

Materials & Methods:
Study 204: males aged 7−21y with advanced DMD received once-weekly eteplirsen 30mg/kg for 96 weeks. Pulmonary function (exploratory outcome) was assessed by percent predicted forced vital capacity (FVC%p). Change from baseline analysis: FVC%p was evaluated in eteplirsen patients and a CINRG DNHS cohort aged 8−19y receiving standard-of-care treatment with glucocorticoids. Longitudinal age-based analysis: annual change in FVC%p was evaluated in eteplirsen patients and 3 CINRG DNHS cohorts (All CINRG; Genotyped CINRG; CINRG Exon 51) aged 10−<18y, where linear phase of decline is expected.

Results and Conclusions:
Change from baseline analysis: eteplirsen-treated patients (n=23) had mean change in FVC%p of −6.4 at Year 1 and −0.5 from Year 1–Year 2. CINRG cohort (n=10) had mean change in FVC%p of −8.2 over 1y. Age-based longitudinal analysis: annual rate of FVC%p change was significantly lower with eteplirsen (–3.66; n=20) versus other cohorts (All CINRG: –5.56; n=172; Genotyped CINRG: –5.67; n=148; CINRG Exon 51: –6.00; n=20).
Eteplirsen significantly attenuated FVC%p decline in DMD patients versus well-matched, steroid-treated natural history cohorts.

Author Disclosures:
Peter Rydqvist: Employee of Sarepta Therapeutics, Inc.
Heather Gordish-Dressman: No conflicts to disclose.
Erik Henricson: Consultant for Sarepta Therapeutics, Inc.
Lixin Han: Employee of Sarepta Therapeutics, Inc.
Ashish Dugar: Employee of Sarepta Therapeutics, Inc.
Craig M. McDonald: has served as a consultant for clinical trials for BioMarin, Cardero Therapeutics, Catabasis, Eli Lilly, Halo Therapeutics, Marathon, Mitokyne Pfizer, PTC Therapeutics, Santhera Pharmaceuticals, and Sarepta Therapeutics, Inc.; serves on advisory boards for Eli Lilly, Mitokyne, Marathon, PTC Therapeutics, and Sarepta Therapeutics, Inc.; and has received research grants from the US Department of Education/National Institute on Disability and Rehabilitation Research (NIDRR), the National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR), the US National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, the US Department of Defense, and the US Parent Project Muscular Dystrophy.

P13. The Mollii-suit® - A novel method using reciprocal inhibition on children with cerebral palsy, GFMCS IV-V. A 6 month prospective study.

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Background:
Spasticity is a common characteristic in children with cerebral palsy (CP). Treatment for spasticity consists of surgery, exercise and spasticity relieving drugs, which might not always be effective. This warrants new treatment for relieving and modifying their spasticity, without further impact on other daily activities. The objective of this study was to assess the effectiveness of an assistive technology. Mollii® is a two pieces suit with integrated electrodes for multifocal transcutaneous electrical stimulation(TENS) computed by personalized evaluation and utilizing the concept of reciprocal inhibition.

Materials & Methods:
Participants were recruited from three schools with disabled children in the isle of Zealand, Denmark. Thirty-one participants, 19 boys (7y-17y) and 12 girls (7y-16y), with predominantly spastic disease were included in the study and twenty completed. The participants wore the suit for one hour in school settings or at home every second day in a trial period of 6 months. Measurements were performed before and 4, 12, and 24 weeks after the treatment has started. Passive range of motion(pROM) were measured using a goniometer. Spasticity by the modified Ashworth scale and tardieu were tested in all treated joint and muscles. Furthermore, the goal attainment scale(GAS) were completed by primary physiotherapist and occupational therapist. A one sample Wilcoxon Signed Ranks test were performed for GAS, pROM and spasticity (SPSS Ver.22).

Results and Conclusions:
A statistical significantly decreased change in spasticity was measured in m. biceps femoris and m. semitendinosus (p: 0,015 and 0,014), and in m. quadriceps femoris (p: 0,046). A significant increased tardieu was measured in m. biceps femoris and m. semitendinosus (p: 0,002) and in m. flexor carpi radialis, m. palmaris longus and m.flexor carpi ulnaris (p:0,041). The pROM was not statistically significantly different in any of the treated muscles. Individualized goals(GAS) related to function and mobility improved significantly throughout the intervention (p: 0,004). In conclusion, the results of this study indicate the Mollii®-suit may affect spasticity in the individualized treated muscles, and have a positive effect on personalized therapeutic goals related to function and mobility.

P14. KIAA2022 – an epileptic encephalopathy gene: elucidating the clinical phenotype

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Background:
The *KIAA2022*-gene has recently been found to cause epileptic encephalopathy. We wanted to elucidate the clinical phenotype.

Material & Method:
We collected phenotypic data on 17 unpublished sporadic KIAA2022-probands (1male/16 females) and on a family with three affected siblings (2 males/1 female) and three unaffected female carriers. The phenotype in previously published cases was reviewed in order to give a more precise description of the phenotype.

Results and conclusion:
Mutations in the sporadic cases were predicted to result in a frameshift or premature stop. The mutation in the family was a probably pathogenic inframe deletion.
All males had moderate-severe intellectual disability and a neuropsychiatric diagnosis. Of the 17 female patients, 15 had mild-moderate intellectual disability and two had moderate-severe intellectual disability. Treatment resistant seizures affected a majority of the female patients (12/17). Subtle or evident dysmorphic features were described in half of the patients. Psychiatric disorders, regression and movement disorders were also described.
The family consisted of three unaffected adult females and three affected siblings showing a variable phenotype: the two brothers had moderate intellectual disability and autism and one had myoclonic astatic seizures. The sister had mild intellectual disability and myoclonic astatic seizures. Comparison of the new and the previously published cases showed consistency in phenotype and mutation types. In conclusion, *KIAA2022*-mutations cause both recessive and dominant X-linked treatment resistant seizures and intellectual disability. The phenotype in females and males overlap but females do generally show less severe intellectual disability.
The family cases showed both recessive and dominant X-linked inheritance. Skewed X-inactivation could be an explanation or the phenotype in the family might not be caused by the KIAA2022 variant, since it is neither a frameshift nor a stop mutation.

P15. Pre- and postoperative cognitive function and predictors of cognitive outcome in a Danish pediatric epilepsy surgery cohort

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Background:
The recurrent seizures of pediatric medically intractable epilepsy (MIE) are known to impair brain development and can lead to a loss in cognitive functioning. Surgery is increasingly being used to treat children suffering from MIE. The ultimate goals of resective epilepsy surgery are to achieve freedom from seizures and discontinue antiepileptic drug treatment, thereby stabilizing or improving developmental capacities. The aims of this study were to investigate the pre- and postoperative cognitive function in a pediatric epilepsy surgery cohort and to identify predictive determinants of delayed postoperative cognitive development.

Materials & Methods:
A consecutive series of 111 Danish children who underwent epilepsy surgery between January 1996 and December 2016 were examined. All underwent preoperative cognitive evaluation and were reevaluated at 1-year and/or 2-year follow-up. The Bayley Scales of Infant and Toddler Development or the Mullen Scale of Early Learning was used in patients up to age 70 months and in patients with severe and profound mental retardation. Older patients were evaluated using Wechsler Intelligence Tests. Multi-operated patients were examined separately from single-operated patients. Furthermore, patients who underwent callosotomy were excluded from the general analysis.

Results and Conclusions:
The cohort consisted of 90 single-operated patients, 16 multi-operated patients and five callosotomy patients. The mean preoperative IQ of the single-operated patients was 67.9. This improved to 70.7 at latest follow-up. 30% showed an IQ increase ≥10 points at latest follow-up. The multi-operated patients had a mean preoperative IQ of 60.1. IQ at latest follow-up remained stable at 60.2 and 18.8% showed an IQ increase ≥10 points. The callosotomy patients had low preoperative IQ, with a mean of 41.8 points. IQ fell to 38.8 points at latest follow-up. We conclude that epilepsy surgery has a stabilizing effect on IQ values and may allow for IQ gains in the years following surgery. Patients operated effectively with a single surgery have the best cognitive outcome while multi-operated patients may take longer to show their cognitive gains. Longer follow-up periods are needed in order to assess the extent of the beneficial effects of surgery on cognitive ability.

P16. Diagnostic value of oligoclonal bands in children: a Danish nationwide multicenter population-based cohort study

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Background:
Oligoclonal bands (OCB) are frequently positive in multiple sclerosis (MS), but MS is rare in children, and OCB are only present in 0–10% of children with acute disseminated encephalomyelitis (ADEM). Therefore, OCB may be of limited diagnostic value in children. Our aim was to evaluate the diagnostic value of OCB in children (<18 years).

Materials & Methods:
In a nationwide population-based setting, we retrieved data on 2,055 children's OCB examination including cerebrospinal fluid leucocytes and differential count, protein, albumin ratio, erythrocytes, and glucose ratio during 1994–2017. We grouped children based on hospital discharge diagnoses from 2 months before and 1 year after the date of OCB examination, and we reviewed the medical record in 321 children including those with acquired demyelinating syndromes (ADS) during 2008–15. We used Fishers exact test to explore differences of OCB positivity in incident ADS before and after 12 years of age and calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for OCB to distinguish ADS from other diagnostic groups.

Results:
Median age at OCB examination was 15.2 years (range=1.8–18.0) and 10% were OCB positive. OCB positivity was highest in ADS (52%), but it was highly age-dependent: 21% of children with incident ADS before age 12 years were OCB positive, in contrast the proportion was 68% in children aged 12–17 years ($p<0.0001$). Positive OCB were not predictive for ADS compared with CNS infections or other immune-mediated CNS diseases in children before age 12 years. However, positive OCB in children aged 12–17 years were highly predictive for ADS compared with CNS infections and other immune-mediated CNS diseases (PPV: 0.89; 95% CI=0.82–0.94; $p<0.0001$), but negative OCB were not discriminatory (NPV: $p=0.17$).

Conclusions:
Positive OCB were rare in ADEM and as this is the most common ADS before age 12 years, OCB positivity was not discriminatory between diagnostic groups at this age. However, positive OCB were frequent in children with ADS aged 12–17 due to increasing incidence of MS. In a clinical setting, OCB examination may therefore only be diagnostically valuable in children aged 12–17 years if there is clinical suspicion of MS, and here only a positive test has clinically relevant predictive value.

P17. Phosphorodiamidate Morpholino Oligomers for Treatment of Duchenne Muscular Dystrophy

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Background:
Exon skipping is a mutation-specific approach to treating patients with Duchenne muscular dystrophy (DMD). We describe clinical findings with phosphorodiamidate morpholino oligomers (PMOs), which are nucleic acid analogs that selectively redirect pre-mRNA splicing to facilitate dystrophin production.

Materials & Methods:
We describe findings from clinical studies of the PMOs eteplirsen and golodirsen.

Results and Conclusions:
In clinical studies of exon 51 skipping (eteplirsen; n=36) and exon 53 skipping (golodirsen; n=25), internally shortened dystrophin mRNA was observed in all treated patients (per reverse transcription polymerase chain reaction). Eteplirsen increased dystrophin expression 15.5-, 11.6-, and 2.4-fold vs untreated controls (assessed by percent dystrophin-positive fibers, Western blot, and immunohistochemistry intensity, respectively; all, $P \leq 0.007$) in a 180-week study, and 2.8-fold (by Western blot; $P=0.008$) in a 48-week study. Golodirsen increased dystrophin expression 10.7-fold (assessed by Western blot) over baseline following 48 weeks of treatment. Over 4 years, versus comparable external controls, eteplirsen slowed the ambulatory decline (6-minute walk test difference, 165 m; $P=0.001$) and the cumulative risk of losing ambulation (83% vs 17%). In 2 clinical studies that included nonambulatory patients, eteplirsen slowed pulmonary decline versus natural history data (assessed by spirometry).
Eteplirsen and golodirsen demonstrated clinical and biochemical effects in patients with DMD, and ongoing studies of these compounds are further characterizing effects in various patient populations.

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Peter Rydqvist: Employee of Sarepta Therapeutics, Inc.
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