NEWS
Cerebral Palsy Research

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Interventions and Management

1. Hand function in children with unilateral spastic cerebral palsy.
Hadžagić Ćatibušić F, Užičanin S, Bulja D, Gasal Gvozdenović E.

Med Glas (Zenica). 2019 Feb 1;16(1). doi: 10.17392/967-19. [Epub ahead of print]

Aim To assess hand function and explore the relationship between hand function and neuroimaging findings in children with unilateral spastic cerebral palsy (US CP). Methods Hand function was assessed using Manual Ability Classification System (MACS, I-V). Brain lesions were divided into five groups: brain maldevelopment (MAL), periventricular white matter lesions (PV WM), cortical/subcortical gray matter lesions (C/SC GM), nonspecific and normal findings. Results Of 114 children with US CP (77 boys and 37 girls), 56 were with right-sided and 58 with left-sided involvement. MACS I was found in 49 (42.9%), MACS II in 19 (16.7%), MACS III in 19 (16.7 %), MACS IV in 9 (7.9%) and MACS V in 18 (15.8%) children (p=0.002). Computed tomography (CT) as the only neuroimaging has been done in 18 (15.8%), magnetic resonance imaging (MRI) at 94 (82.5%) children, whereas 2 (1.7%) children had neither CT nor MRI. The CT showed PV WM in eight (44.4%), C/SC GM lesions in 6 (33.3%), and normal findings in 4 (22.2%) children (p=0.709). The MRI showed MAL in 8 (8.5%), PV WM in 46 (48.9%), C/SC GM in 28 (29.8%), miscellaneous in 2 (2.1%), and normal finding in 10 (10.7%) children (p=0.0001). Mild hand dysfunction (MACS I and II) was assessed in 68 (59.7%) children, of which 33 had PV WM lesions (p=0.001). Conclusion Mild hand dysfunction in children with US CP has been significantly associated with PV WM lesions. The type of brain lesion may help to identify its timing and predict the level of hand dysfunction.

PMID: 30256057

2. Contracture formation in the upper limb in cerebral palsy starts early.
Pontén E.

Dev Med Child Neurol. 2018 Sep 23. doi: 10.1111/dmcn.14047. [Epub ahead of print]

PMID: 30246329

3. Trunk and pelvic alignment in relation to postural control in children with cerebral palsy.
Abd El-Nabie WAE, Mustafa Saleh MS.

J Back Musculoskelet Rehabil. 2018 Sep 14. doi: 10.3233/BMR-181212. [Epub ahead of print]

BACKGROUND: Trunk pelvic mal-alignment and postural control deficit are common problems facing children with

cerebral palsy. OBJECTIVE: The aim of this study was to investigate the relation of trunk and pelvic alignment with postural control in children with diplegic cerebral palsy. METHODS: Seventy seven children with spastic diplegic cerebral palsy (CP), aged 6 to 8 years with level II on Gross Motor Function Classification System, participated in this study. Trunk imbalance, lateral deviation of the spine and pelvic tilt were evaluated by using Formetric instrumentation system while postural control was assessed by using Pediatric Balance Scale. RESULTS: The results showed that there is a moderate negative correlation of trunk imbalance, lateral deviation of the spine and pelvic tilt with postural control (-0.44, -0.59 and -0.57, respectively). CONCLUSIONS: Increased trunk imbalance, lateral deviation of the spine and pelvic tilt may be associated with decreased postural control ability in children with diplegic CP.

PMID: 30248038

4. [S2 Alar-Iliac Screws in Fixation and Correction of Combined Neuromuscular Spinal and Pelvic Deformities].
Repko M, Filipovič M, Leznar M, Šprláková-Puková A, Heger J.

Acta Chir Orthop Traumatol Cech. 2018;85(3):194-198. [Article in Czech]

PURPOSE OF THE STUDY Neuromuscular deformities of the spine represent surgically uneasy to solve problems as well as serious handicaps causing sitting instability, pressure ulcers as well as pain. The aim of our study is to conduct a retrospective clinical analysis of the results of surgical correction of these deformities. This paper presents the use of a recent technique of sacral-alar-iliac (S2AI) screws and its comparison with other techniques of pelvic stabilisation. MATERIAL AND METHODS The group of 41 patients treated surgically with S2AI screws technique and transpedicular or hybrid instrumentation of the spine consisted of patients with the primary diagnosis of muscular dysthrophy, spinal muscular atrophy, cerebral palsy and some other neuromuscular diseases. The results of pelvic obliquity correction and scoliotic correction in combined neuromuscular deformities of the spine and pelvis were analysed. The technique of S2AI screws implantation and the possibility of their free-hand technique implementation were presented. RESULTS In the followed-up group of patients an average correction of pelvic obliquity by 81% (from 29.1 degrees before the operation to 5.6 degrees after the operation) was reported. On average, 74% correction of scoliotic spine deformity was achieved (from 83.3 degrees before the operation to 22.5 degrees after the operation). In both the cases neither a significant loss of correction at the minimum one-year follow-up nor any serious complications associated with grappling of pelvic fixation were observed. DISCUSSION The S2AI screws offer at least the same stability and ability of correction as iliac screws and at the same time they provide significantly better results compared with the older methods of pelvic fixation such as the Galvestone technique. With a good knowledge of the surgical technique and anatomical aspects this technique can be applied in the form of a free-hand technique. Navigation as well as robotic techniques can help with the accurate positioning of the S2AI screw. Transfixation of sacroiliacal syndesmosis in patients with a neuromuscular handicap does not lead to deterioration of their mobility. CONCLUSIONS Simultaneous stabilisation of spine and pelvis makes it possible to achieve a good quality correction of the deformity and good clinical results over a long period of time. It allows for stability of the sitting position of the patients and improves the quality of their lives. Nowadays, the S2AI screws are considered to be biomechanically the best quality pelvic fixation, eliminating subcutaneous prominence of the instrumentation and reducing the risk of skin decubitus.

PMID: 30257778

5. Reversible Spasticity Suppression and Locomotion Change After Pulsed Radiofrequency on the Dorsal Root Ganglia of Rats With Spinal Cord Injury.
Chang CH, Lu KH, Lin WT, Chen SC, Shih WP, Lin CW.

Neuromodulation. 2018 Sep 25. doi: 10.1111/ner.12853. [Epub ahead of print]

OBJECTIVES: Radiofrequency has been used to suppress spasticity affecting motion in patients with cerebral palsy and spinal cord injury. This study tested spasticity suppression and locomotion change after pulsed radiofrequency (PRF) at the dorsal root ganglion of rats with spasticity. MATERIALS AND METHODS: Twenty-four rats that survived for 28 days after thoracic spinal cord injury and showed spasticity in the right hind limb were separated randomly to a PRF group or Sham operation group. PRF consisted of 2 Hz biphasic 25 msec trains of PRF (500 kHz, 5 V intensity) applied on the right L5 dorsal root ganglion for 300 sec. Muscle tension of the right triceps surae was measured at 450 deg/sec of passive ankle dorsiflexion on the day before and 3, 7, and 14 days after PRF or sham operation. Locomotive function was evaluated by obtaining Basso, Beattie, and Bresnahan (BBB) scores. RESULTS: Muscle tension of the triceps surae decreased significantly three days after PRF, and gradually returned to baseline 14 days later. In the sham operation group, muscle tension increased significantly more than 14 days. The BBB scores declined from 10 to 8 after PRF and returned to pre-PRF levels 14 days later, while scores remained constant after sham operation. CONCLUSIONS: PRF produced significant and reversible suppression in spasticity, but this was accompanied by deterioration in locomotive function. Thus, caution should be exercised in considering the benefits and

costs in suppressing spasticity in ambulatory patients, and implanted devices that apply titratable doses of PRF may be best to optimize patients' needs.

PMID: 30253013

6. Supracondylar femoral rotation osteotomy affects frontal hip kinetics in children with bilateral cerebral palsy.
Thielen M, Wolf SI, Klotz MC, Geisbüsch A, Putz C, Krautwurst B, Dreher T.

Dev Med Child Neurol. 2018 Sep 25. doi: 10.1111/dmcn.14035. [Epub ahead of print]

AIM: To evaluate the influence of supracondylar femoral derotation osteotomy (FDO) on hip abduction muscle force and frontal hip moments in children with bilateral cerebral palsy. METHOD: For this retrospective cohort study 79 children (36 females, 43 males; mean age at surgery 11y [SD 3y]; range 4-17y) with bilateral cerebral palsy and preoperatively and 1-year postoperatively documented frontal hip moments who received supracondylar FDO in 134 limbs were included. The control group consisted of eight children (two females, six males; mean age 11y [SD 4y]; range 5-17y) who received single-event multi -level surgery without FDO. RESULTS: Hip joint impulse ($p<0.001$) and the first peak of frontal hip moments ($p=0.003$) increased, whereas the second peak decreased ($p<0.001$) from preoperatively to postoperatively. Hip abductor strength improved ($p=0.001$) from preoperatively to postoperatively. INTERPRETATION: Despite the compensatory mechanism, frontal hip moments are decreased preoperatively. Supracondylar FDO results in increased frontal hip moments. Changes in anteversion directly influence hip kinetics, although no direct change of the proximal bony geometry is performed. WHAT THIS PAPER ADDS: Internal rotation gait cannot fully restore the frontal hip moment. Supracondylar femoral derotation osteotomy (FDO) influences frontal hip kinetics in children with bilateral cerebral palsy. Supracondylar FDO changes the curve progression of frontal hip moments. Supracondylar FDO restores the hip abductor moment arm. Supracondylar FDO leads to an increase in hip abductor muscle force.

PMID: 30255540

7. Measuring levels of muscle fatigue in spastic cerebral palsy.
Ratel S, Doré E, Duché P.

Dev Med Child Neurol. 2018 Sep 23. doi: 10.1111/dmcn.14046. [Epub ahead of print]

PMID: 30246367

8. Using a cost function based on kinematics and electromyographic data to quantify muscle forces.
Wen J, Raison M, Achiche S.

J Biomech. 2018 Sep 11. pii: S0021-9290(18)30723-1. doi: 10.1016/j.jbiomech.2018.09.002. [Epub ahead of print]

A reliable evaluation of muscle forces in the human body is highly desirable for several applications in both clinical and research contexts. Several models of muscle force distribution based on non-invasive measurements have been proposed since 1836 (Weber and Weber, 1836), amongst which Crowninshield's model (Crowninshield and Brand, 1981), which maximizes a cost-function representing the muscle fiber endurance, is the most popular. It is worth noting that Crowninshield's model is the most widely adopted notwithstanding its major limitations of physiological coherence. Forster et al. (2004) pointed out that "these (conventional) criteria however do not predict co-contraction adequately". Besides, electromyographic (EMG)-driven models have been proposed to assess individual muscle forces, which have not been broadly adopted due to their complexity and the need for a calibration before each test. In this context, a cost function based on kinematic and electromyographic data could provide the advantage of being physiologically more coherent with muscle activations compared to conventional cost-functions based on kinematics solely, and easier to use than the EMG-driven models. The objective of this study is to propose the first cost-function based on kinematics and electromyographic data to quantify muscle forces. When applying this new cost-function on a database of upper limb motions data of 17 subjects, healthy or with cerebral palsy, the muscle force prediction of the proposed model was 17.74% more coherent with the EMG pattern than the prediction of Crowninshield's model. And on average, these results were more consistent whether the subjects were healthy or with cerebral palsy. In conclusion, we propose this cost-function for the quantification of muscle forces.

PMID: 30243496

9. Usefulness of a Qualitative Ultrasound Evaluation of the Gastrocnemius-Soleus Complex with the Heckmatt Scale for Clinical Practice in Cerebral Palsy.
Battisti N, Milletti D, Miceli M, Zenesini C, Cersosimo A.

Ultrasound Med Biol. 2018 Sep 22. pii: S0301-5629(18)30356-9. doi: 10.1016/j.ultrasmedbio.2018.08.006. [Epub ahead of print]

Ultrasound is increasingly used for the evaluation of spastic muscles in cerebral palsy. Increased echo intensity is considered indicative of a muscle fibrous involution. The aim of this study was to highlight any correlation between increased echo intensity of the gastrocnemius-soleus complex and clinical tests for stiffness evaluation, age and functional level measured with the Gross Motor Function Classification System. We used the qualitative echo intensity grading system of the Heckmatt scale (HS) and tested its inter-rater reliability. The study group comprised 60 patients with cerebral palsy. We found a weak significant correlation between HS scores and clinical stiffness measures and between HS and age for all muscles studied, and between the HS and Gross Motor Function Classification System only for the soleus muscle. The study indicated moderate inter-rater reliability, with κ values between 0.60 and 0.73, for almost all muscles studied. Ultrasound provides a useful complementary survey of stiffness tests in cerebral palsy.

PMID: 30253885

10. The responsiveness and validity of the Early Clinical Assessment of Balance in toddlers with cerebral palsy: Brief report.
Pierce SR, Skorup J, Miller A, Paremski AC, Prosser LA.

Dev Neurorehabil. 2018 Sep 25:1-3. doi: 10.1080/17518423.2018.1523244. [Epub ahead of print]

PURPOSE: The Early Clinical Assessment of Balance (ECAB) is a measure of postural stability for children with cerebral palsy (CP). The purpose of this research was to investigate the relationship between the ECAB and Gross Motor Function Measure-66 (GMFM-66) and to determine the responsiveness of the ECAB in children with CP under three years of age. METHODS: Twenty seven children (mean age of 25 months) participated. Data were collected before and after 3 and 6 months of physical therapy. Responsiveness was calculated using standardized response means (SRM). RESULTS: Significant relationships were observed between the ECAB, GMFM-66 score (r = 0.87), and GMFM subscales (r = 0.63-0.86). A moderate effect size (SRM = 0.62) and a large effect size (SRM = 0.92) for the ECAB were found over the 3- and 6-month intervention periods, respectively. CONCLUSION: These results support the validity and responsiveness of the ECAB in young children with CP.

PMID: 30252589

11. Nutritional status in cerebral palsy: A Cross-sectional comparative survey of children in Kano, Nigeria.
Adamu AS, Sabo UA, Gwarzo GD, Belonwu RO.

Niger Postgrad Med J. 2018 Jul-Sep;25(3):156-160. doi: 10.4103/npmj.npmj_67_18.

BACKGROUND: Cerebral palsy (CP) is a common neurodevelopmental motor disorder resulting from early childhood brain insult. Nutrition in children is very important for growth and development. This is more so in those with chronic illnesses such as CP. This study was conducted with the aim of assessing the anthropometry and anthropometric indices of CP children. MATERIALS AND METHODS: This comparative, cross-sectional study recruited 150 children with CP matched for age and sex, with 150 children without CP (as controls). The participants' socio-demographic and CP-related data were collected using a pre-tested questionnaire designed for the study. The weight and height of the subjects were measured. Nutritional status was determined using the World Health Organization Z-scores. RESULTS: Overall prevalence of malnutrition in CP subjects was 86%. This was significantly higher than in controls, whose prevalence was 55.3% ($\chi 2 = 34.027, P < 0.0001$). The prevalence of stunting, wasting and underweight in CP subjects was 53.3%, 57.5% and 66.9%, respectively. These were also significantly higher than those of controls who had prevalence of stunting being 16.7%, wasting 8.5% and underweight 14.8%. CONCLUSION: This study found a high prevalence of malnutrition (especially under-nutrition) and therefore underscores the need for more emphases on nutritional assessment, counselling and management in CP patients.

PMID: 30264766

12. Parental Perspectives on Diagnosis and Prognosis of Neonatal Intensive Care Unit Graduates with Cerebral Palsy.
Guttmann K, Flibotte J, DeMauro SB.

J Pediatr. 2018 Sep 21. pii: S0022-3476(18)31088-6. doi: 10.1016/j.jpeds.2018.07.089. [Epub ahead of print]

OBJECTIVES: To describe how parents of neonatal intensive care unit (NICU) graduates with cerebral palsy (CP) perceive both the accuracy of prognoses provided in the NICU and the timing of their child's diagnosis of CP, and to assess the influence of functional outcome on these perceptions. STUDY DESIGN: We surveyed parents of NICU graduates with CP about timing and benefit of diagnosis, accuracy of prognosis, and functional abilities of their children. After piloting and validation, CP parent support groups circulated the survey on social media, websites, and email lists. Bivariate relationships between categorical responses to survey questions were assessed with the $\chi 2$ test, and multivariable logistic regression was performed to identify independent factors associated with perceptions about the timing of diagnosis. RESULTS: Parents of 463 children were included. Two-thirds (67%) of the children were diagnosed with CP before age 2 years, yet 40% of the respondents felt that diagnosis was made late, and only 11% categorized diagnosis as early. More than one-half (59%) perceived a benefit to diagnosis. There was a significant association between earlier age at diagnosis and greater functional limitations; 24% of parents who recalled being given a prognosis reported that their child functioned as predicted, and 46% reported that their child exceeded expectations. Parents were more likely to believe that children with fewer functional limitations had exceeded expectations. CONCLUSION: Parents remember prognostic discussions about children who develop CP as underestimating functional outcome. Diagnosis is rarely seen as early and is associated with benefits. These observations suggest that clinicians should aim to diagnose CP early and to maintain guarded optimism about future outcomes. Tools for improved communication are urgently needed.

PMID: 30244983

13. A support programme for caregivers of children with disabilities in Ghana: Understanding the impact on the wellbeing of caregivers.
Zuurmond M, Nyante G, Baltussen M, Seeley J, Abanga J, Shakespeare T, Collumbien M, Bernays S.

Child Care Health Dev. 2018 Sep 27. doi: 10.1111/cch.12618. [Epub ahead of print]

BACKGROUND: Four fifths of the estimated 150 million children with disability in the world live in resource poor settings where the role of the family is crucial in ensuring that these children survive and thrive. Despite their critical role, evidence is lacking on how to provide optimal support to these families. This study explores the impact of a participatory training programme for caregivers delivered through a local support group, with a focus on understanding caregiver wellbeing. METHODS: A qualitative longitudinal study was conducted to investigate the impact of a training programme, "getting to know cerebral palsy," with caregivers on their wellbeing. Eighteen caregivers, from four districts, were interviewed up to three times over 14 months, to assess impact and the reasons for any changes. RESULTS: Low levels of knowledge, high levels of stigma, physical and emotional exhaustion, and often difficult family relationships with social exclusion of the child and caregiver were common themes at the outset. Caregivers struggled to combine their caring and economic activities. This was exacerbated by the common absence of the father. Two months after completion of the training, their reported wellbeing had improved. The reasons for this were an improved understanding about their child's condition, positive attitudinal change towards their child, feelings of hope, and through the group support, a profound realisation that they are "not on their own." While relationships within the family remained complex in many cases, the support group offered an important and alternative social support network. CONCLUSIONS: This study illustrates the many benefits of a relatively simple caregiver intervention, which has the potential to offer a mechanism to provide sustainable social support for caregivers and children with cerebral palsy. Any future programme needs to also address more structural issues, including stigma and discrimination, and strengthen approaches to family engagement.

PMID: 30259548

14. Bladder changes after catheterizable channel creation in adults with cerebral palsy who are in chronic urinary retention.
Narayan VM, Pariser JJ, Gor RA, Katorski J, Elliott SP.

Neurourol Urodyn. 2018 Sep 24. doi: 10.1002/nau.23818. [Epub ahead of print]

AIMS: Cerebral palsy (CP) is characterized by motor impairments as a result of brain injury during development. Patients can

have neurogenic bladder dysfunction and are often unable to catheterize through their native urethra. Catheterizable channel (CC) creation can facilitate clean intermittent catheterization (CIC). We have observed that patients with large capacity, low-pressure bladders can develop de novo neurogenic detrusor overactivity (NDO) postoperatively. We sought to better characterize this finding. METHODS: We reviewed the charts of patients 17 years or older with CP seen between 2006 and 2017. Patients undergoing creation of any type of CC without augmentation cystoplasty, due to adequate storage on pre-operative urodynamics (UDS), were included. Pre- and post-operative UDS were reviewed. Frequency of incontinence and use of anticholinergics or intravesical injections of onabotulinum toxin A (Btx) were reviewed. RESULTS: Eight patients with CP underwent CC creation without augmentation. Preoperatively, six of eight patients were in chronic retention with two others performing CIC. Following CC creation, patients in retention required additional NDO management with anticholinergics, mirabegron, or onabotulinumtoxin A. Among those with complete UDS data, 67% demonstrated lower maximum cystometric capacity postoperatively. Median follow-up was 25 months. CONCLUSIONS: CC creation facilitates CIC in adults with CP who are in chronic retention due to pseudodyssynergia. Despite preoperative UDS suggesting an adequate capacity, low-pressure bladder, such patients often manifest de novo NDO and worsening incontinence upon initiation of CIC after surgery. These findings should be considered when determining whether to perform augmentation at the time of CC in adults with CP.

PMID: 30248183

15. Detection of Infantile Movement Disorders in Video Data Using Deformable Part-Based Model.
Khan MH, Schneider M, Farid MS, Grzegorzek M.

Sensors (Basel). 2018 Sep 21;18(10). pii: E3202. doi: 10.3390/s18103202.

Movement analysis of infants' body parts is momentous for the early detection of various movement disorders such as cerebral palsy. Most existing techniques are either marker-based or use wearable sensors to analyze the movement disorders. Such techniques work well for adults, however they are not effective for infants as wearing such sensors or markers may cause discomfort to them, affecting their natural movements. This paper presents a method to help the clinicians for the early detection of movement disorders in infants. The proposed method is marker-less and does not use any wearable sensors which makes it ideal for the analysis of body parts movement in infants. The algorithm is based on the deformable part-based model to detect the body parts and track them in the subsequent frames of the video to encode the motion information. The proposed algorithm learns a model using a set of part filters and spatial relations between the body parts. In particular, it forms a mixture of part-filters for each body part to determine its orientation which is used to detect the parts and analyze their movements by tracking them in the temporal direction. The model is represented using a tree-structured graph and the learning process is carried out using the structured support vector machine. The proposed framework will assist the clinicians and the general practitioners in the early detection of infantile movement disorders. The performance evaluation of the proposed method is carried out on a large dataset and the results compared with the existing techniques demonstrate its effectiveness.

PMID: 30248968

16. Movement intention detection in adolescents with cerebral palsy from single-trial EEG.
Jochumsen M, Shafique M, Hassan A, Niazi IK.

J Neural Eng. 2018 Sep 27. doi: 10.1088/1741-2552/aae4b8. [Epub ahead of print]

Objectives: As for stroke rehabilitation, brain-computer interfaces could potentially be used for inducing neural plasticity in patients with cerebral palsy by pairing movement intentions with relevant somatosensory feedback. Therefore, the aim of this study was to investigate if movement intentions from children with cerebral palsy can be detected from single-trial EEG. Moreover, different feature types and electrode setups were evaluated. Approach: Eight adolescents with cerebral palsy performed self-paced dorsiflexions of the ankle while nine channels of EEG were recorded. The EEG was divided into movement intention epochs and idle epochs. The data were pre-processed and temporal, spectral and template matching features were extracted and classified using a random forest classifier. The classification accuracy of the 2-class problem was used as an estimation of the detection performance. This analysis was repeated using a single EEG channel, a Large Laplacian filtered channel and nine channels. Results: A classification accuracy of ~70% was obtained using only a single channel. This increased to ~80% for the Laplacian filtered data, while ~75% of the data were correctly classified when using nine channels. In general, the highest accuracies were obtained using temporal features or using all of them combined. Significance: The results indicate that it is possible to detect movement intentions in patients with cerebral palsy; this may be used in the development of a brain-computer interface for motor rehabilitation of patients with cerebral palsy.

PMID: 30260322

17. Neuromodulation of lumbosacral spinal networks enables independent stepping after complete paraplegia.
Gill ML, Grahn PJ, Calvert JS, Linde MB, Lavrov IA, Strommen JA, Beck LA, Sayenko DG, Van Straaten MG, Drubach DI, Veith DD, Thoreson AR, Lopez C, Gerasimenko YP, Edgerton VR, Lee KH, Zhao KD.

Nat Med. 2018 Sep 24. doi: 10.1038/s41591-018-0175-7. [Epub ahead of print]

Spinal sensorimotor networks that are functionally disconnected from the brain because of spinal cord injury (SCI) can be facilitated via epidural electrical stimulation (EES) to restore robust, coordinated motor activity in humans with paralysis. Previously, we reported a clinical case of complete sensorimotor paralysis of the lower extremities in which EES restored the ability to stand and the ability to control step-like activity while side-lying or suspended vertically in a body-weight support system (BWS). Since then, dynamic task-specific training in the presence of EES, termed multimodal rehabilitation (MMR), was performed for 43 weeks and resulted in bilateral stepping on a treadmill, independent from trainer assistance or BWS. Additionally, MMR enabled independent stepping over ground while using a front-wheeled walker with trainer assistance at the hips to maintain balance. Furthermore, MMR engaged sensorimotor networks to achieve dynamic performance of standing and stepping. To our knowledge, this is the first report of independent stepping enabled by task-specific training in the presence of EES by a human with complete loss of lower extremity sensorimotor function due to SCI.

PMID: 30250140

18. Usefulness of Magnetoinertial Wearable Devices in Neurorehabilitation of Children with Cerebral Palsy.
Iosa M, de Sanctis M, Summa A, Bergamini E, Morelli D, Vannozzi G.

Appl Bionics Biomech. 2018 Sep 4;2018:5405680. doi: 10.1155/2018/5405680. eCollection 2018.

BACKGROUND: Despite the increasing use of wearable magnetoinertial measurement units (MIMUs) for gait analysis, the efficacy of MIMU-based assessment for planning rehabilitation has not been adequately documented yet. METHODS: The usefulness of a MIMU-based assessment was evaluated comparing the data acquired by three MIMUs located at the pelvis, sternum, and head levels in 12 children with cerebral palsy (CP, age: 2-9 years) and 12 age-matched children with typical development (TD). Gait stability was quantified in terms of acceleration attenuation coefficients from pelvis to head, pelvis to sternum, and sternum to head. Children with CP were randomly divided in two groups: in the first group (CPI), MIMU-based parameters were used by therapists for planning patient-tailored rehabilitation programs, whereas in the second group (CPB), therapists were blind to the MIMU-based assessment results. Both CPI and CPB were tested before and after the relevant neurorehabilitation program. Ad hoc questionnaires were also administered to therapists of the CPI group to assess the degree of usefulness perceived about the information provided by the MIMU-based assessment. RESULTS: Significant differences were found between children with CP and those with TD for the acceleration attenuation coefficient from pelvis to head ($p = 0.048$) and from pelvis to sternum ($p = 0.021$). After neurorehabilitation, this last parameter increased more in CPI (35%) than in CPB (6%, $p = 0.017$ for the interaction group per time). The results of the questionnaires showed that therapists agreed with the usability (100% judged it as "easy to use") and usefulness of the MIMU-based assessment in defining patient-oriented interventions (87%). CONCLUSIONS: There is a large debate in literature about the efficacy of classical gait analysis that should be enlarged to new technological approaches, such as that based on MIMUs. This study is a first proof of concept about the efficacy of this approach for neurorehabilitation of children with CP.

PMID: 30254691

19. Eyes on communication: trialling eye-gaze control technology in young children with dyskinetic cerebral palsy.
Karlsson P, Bech A, Stone H, Vale C, Griffin S, Monbaliu E, Wallen M.

Dev Neurorehabil. 2018 Sep 25:1-7. doi: 10.1080/17518423.2018.1519609. [Epub ahead of print]

PURPOSE: This study aims to identify eye-gaze control technology outcomes, parent perception of the technology and support received, and gauge the feasibility of available measures. METHODS: Five children with dyskinetic cerebral palsy, mean age 4 years, 4 months (1 year, 0 months); n = 4 males; trialled two eye-gaze control technology systems, each for six weeks. Parents completed pre- and post-questionnaires. RESULTS: Parents found the 6-week home-based trial period to be the right length. Written guidelines and instructions about set-up, calibration, and play and learning activities were perceived as important. Children demonstrated improvements in goal achievement and performance. Parents found questionnaires on quality of life, participation, behaviours involved in mastering a skill and communication outcomes challenging to complete resulting in substantial missing data. CONCLUSION: Eye-gaze control technology warrants further investigation for young children with

dyskinetic cerebral palsy in a large international study.

PMID: 30252561

20. Meeting brain-computer interface user performance expectations using a deep neural network decoding framework.
Schwemmer MA, Skomrock ND, Sederberg PB, Ting JE, Sharma G, Bockbrader MA, Friedenberg DA.

Nat Med. 2018 Sep 24. doi: 10.1038/s41591-018-0171-y. [Epub ahead of print]

Brain-computer interface (BCI) neurotechnology has the potential to reduce disability associated with paralysis by translating neural activity into control of assistive devices. Surveys of potential end-users have identified key BCI system features, including high accuracy, minimal daily setup, rapid response times, and multifunctionality. These performance characteristics are primarily influenced by the BCI's neural decoding algorithm, which is trained to associate neural activation patterns with intended user actions. Here, we introduce a new deep neural network decoding framework for BCI systems enabling discrete movements that addresses these four key performance characteristics. Using intracortical data from a participant with tetraplegia, we provide offline results demonstrating that our decoder is highly accurate, sustains this performance beyond a year without explicit daily retraining by combining it with an unsupervised updating procedure, responds faster than competing methods, and can increase functionality with minimal retraining by using a technique known as transfer learning. We then show that our participant can use the decoder in real-time to reanimate his paralyzed forearm with functional electrical stimulation (FES), enabling accurate manipulation of three objects from the grasp and release test (GRT). These results demonstrate that deep neural network decoders can advance the clinical translation of BCI technology.

PMID: 30250141

21. The Effects of a 5-Day Virtual-Reality Based Exercise Program on Kinematics and Postural Muscle Activity in Youth with Cerebral Palsy.
Mills R, Levac D, Sveistrup H.

Phys Occup Ther Pediatr. 2018 Sep 28:1-16. doi: 10.1080/01942638.2018.1505801. [Epub ahead of print]

AIMS: To determine the effects of a 5-day virtual reality (VR)-based intervention on anticipatory and reactive mechanisms of postural control in children and adolescents with cerebral palsy (CP). METHODS: Eleven youth with CP (GMFCS levels I and II), ages 7-17, were allocated to intervention (N = 5) and control (N = 6) groups. Both groups attended balance assessment sessions 1 week apart. Participants in the intervention group received 1-hour one-on-one physiotherapist-supervised VR balance games for 5 consecutive days between assessments. For balance assessments, participants stood erect with eyes open on a movable platform that translated progressively through four speeds in the anterior/posterior direction. Participants performed two trials each of experimenter-triggered and self-triggered perturbations. Postural muscle activity and kinematics were recorded. The Anchoring Index and body segment cross-correlations were calculated as an indication of body stabilization, and the number of steps taken to regain balance/avoid falling were counted. Mann-Whitney U tests for between group differences in change scores were undertaken with an accepted significance level of 0.01. RESULTS: No consistent differences in change scores were identified between groups. CONCLUSIONS: There was no effect of a 5-day VR-based intervention on postural control mechanisms used in response to oscillating platform perturbations. Subsequent studies will further tailor VR interventions to patients' functional balance needs.

PMID: 30265609

22. Vaginal Ureaplasma species increase chorioamnionitis in very preterm infants with preterm premature rupture of the membranes at < 28 weeks of gestation.
Suzuki Y, Horie K, Yada Y, Kono Y, Hirashima C, Usui R, Matsubara S, Ohkuchi A.

Eur J Clin Microbiol Infect Dis. 2018 Sep 22. doi: 10.1007/s10096-018-3385-5. [Epub ahead of print]

Our aim was to investigate the association between vaginal Ureaplasma species (spp.) and the subsequent occurrence of chorioamnionitis (CAM), perinatal death, neonatal morbidity, and long-term neurodevelopmental impairments (NDIs) at 3 years of age. We analyzed 55 pregnant women with singleton pregnancy who had preterm premature rupture of the membranes (pPROM) at < 28+0 weeks of gestation, and delivered between 22+0 and 31+6 weeks at our tertiary hospital in 2007-2016.

NDIs were defined as either cerebral palsy or developmental delay evaluated at 1.5 and/or 3 years old. The presence of Ureaplasma spp. and Mycoplasma hominis were evaluated using urea-arginine broth and Mycoplasma PPLO Agar. The presence of Ureaplasma spp. in the vagina was positive in 41%. Vaginal Ureaplasma spp. was a significant risk factor for CAM; however, it was not significantly associated with the occurrence of perinatal death, pulmonary hypoplasia, respiratory distress syndrome, transient tachypnea of the newborn, intraventricular hemorrhage, periventricular leukomalacia, bronchopulmonary dysplasia defined as oxygen required and occasional ventilatory assistance required at week 36 as modified (BPD36), or NDIs. The crude odds ratio (95% confidence interval) of Ureaplasma spp. for the occurrence of CAM was 9.5 (1.10-82) ($p = 0.041$). In very preterm birth infants with pPROM, CAM, BPD36, and NDIs occurred in 78, 60, and 36%, respectively. Vaginal Ureaplasma spp. was a significant risk factor for CAM in very preterm birth infants with pPROM. The incidences of BPD36 and NDIs in such infants were very high, nearing 3/5 and 1/3, respectively.

PMID: 30244363

23. Prospective research in infants with mild encephalopathy identified in the first six hours of life: neurodevelopmental outcomes at 18-22 months.
Chalak LF, Nguyen KA, Prempunpong C, Heyne R, Thayyil S, Shankaran S, Laptook AR, Rollins N, Pappas A, Koclas L, Shah B, Montaldo P, Techasaensiri B, Sánchez PJ, Sant'Anna G.

Pediatr Res. 2018 Sep 13. doi: 10.1038/s41390-018-0174-x. [Epub ahead of print]

BACKGROUND: Studies of early childhood outcomes of mild hypoxic-ischemic encephalopathy (HIE) identified in the first 6 h of life are lacking. OBJECTIVE: To evaluate neurodevelopmental outcomes at 18-22 months of PRIME study. STUDY DESIGN: Multicenter, prospective study of mild HIE defined as ≥1 abnormality using the modified Sarnat within 6 h of birth and not meeting cooling criteria. Primary outcome was disability with mild: Bayley III cognitive 70-84 or ≥85 and either Gross Motor Function Classification System (GMFCS) 1 or 2, seizures, or hearing deficit; moderate: cognitive 70-84 and either GMFCS 2, seizures, or hearing deficit; severe: cognitive <70, GMFCS 3-5. RESULTS: Of the 63 infants enrolled, 51 (81%) were evaluated at 19 ± 2 months and 43 (68%) completed Bayley III. Of the 43 infants, 7 (16%) were diagnosed with disability, including 1 cerebral palsy and 2 autism. Bayley scores < 85 in either cognition, motor, or language were detected in 17 (40%): 14 (32%) language, 7 (16%) cognitive, and 6 (14%) motor domain. Infants with disability had more abnormalities on discharge examination and brain MRI, with longer hospital stay ($p < 0.001$). CONCLUSIONS: In this contemporary untreated cohort of mild HIE, disability occurred in 16% of infants at 18-22 months.

PMID: 30250303

24. Autism Spectrum Disorder and Neonatal Serum Magnesium Levels in Preterm Infants.
Bakian AV, Bilder DA, Korgenski EK, Bonkowsky JL.

Child Neurol Open. 2018 Sep 18;5:2329048X18800566. doi: 10.1177/2329048X18800566. eCollection 2018.

Premature birth is associated with increased risk of autism spectrum disorder. Antenatal maternal magnesium administration is known to reduce subsequent risk of cerebral palsy including among premature infants, suggesting a potentially broader neuroprotective role for magnesium. Our objective was to determine whether magnesium could be protective against autism spectrum disorders in premature infants. A cohort of 4855 preterm children was identified, magnesium levels from 24 to 48 hours of life recorded, and subsequent autism spectrum disorder status determined. Adjusted relative risk of autism spectrum disorder with each 1 mg/dL increase in neonatal magnesium level was 1.15 (95% confidence interval: 0.86-1.53). Analysis of variance indicated that magnesium levels varied by gestational age and maternal antenatal magnesium supplementation, but not autism spectrum disorder status ($F1,4824 = 1.43$, $P = .23$). We found that neonatal magnesium levels were not associated with decreased autism spectrum disorder risk. Future research into autism spectrum disorder risks and treatments in premature infants is needed.

PMID: 30246047

25. High versus low dose caffeine in preterm infants: A systematic review and meta-analysis.
Brattström P, Russo C, Ley D, Bruschettini M.

Acta Paediatr. 2018 Sep 22. doi: 10.1111/apa.14586. [Epub ahead of print]

AIM: Though caffeine is a consolidated treatment in preterm infants, the efficacy and safety of a higher dose have not been systematically appraised. METHODS: A systematic review was conducted to compare high (loading dose >20 mg/kg and maintenance >10 mg/kg/day) versus low dose of caffeine. MEDLINE, EMBASE, Central, and conference proceedings for randomized controlled trials (RCTs) and quasi-RCTs were searched. Two authors independently screened the records, extracted the data and assessed the risk of bias. RESULTS: As only six RCTs enrolling a total of 816 preterm infants were included, the required information size was not reached. The loading and maintenance doses varied between 20-80 mg/kg/day and 3-20 mg/kg/day, respectively. The use of high dose had no impact on mortality (RR: 0.85; 95% CI: 0.53-1.38; RCTs = 4) or bronchopulmonary dysplasia (RR: 0.93; 95% CI: 0.72-1.20; studies = 4), however it resulted in fewer cases of extubation failure and apneas and shorter duration of mechanical ventilation. The quality of the evidence was low due (imprecision of the estimates). CONCLUSION: Due to imprecision it is not possible to determine whether high dose caffeine is more effective and safe than a low dose. High dose might improve short-term respiratory function without reducing bronchopulmonary dysplasia.

PMID: 30242903

26. Modulation of Microglial Activation by Adenosine A2a Receptor in Animal Models of Perinatal Brain Injury.
Colella M, Zinni M, Pansiot J, Cassanello M, Mairesse J, Ramenghi L, Baud O.

Front Neurol. 2018 Sep 11;9:605. doi: 10.3389/fneur.2018.00605. eCollection 2018.

Neuroinflammation has a key role in the pathogenesis of perinatal brain injury. Caffeine, a nonspecific antagonist of adenosine receptors (ARs), is widely used to treat apnea of prematurity and has been linked to a decrease in the incidence of cerebral palsy in premature infants. The mechanisms explaining its neuroprotective effect have not yet been elucidated. The objective of this study was to characterize the expression of adenosine and ARs in two neonatal rat models of neuroinflammation and to determine the effect of A2aR blockade on microglial activation assessed through inflammatory cytokine gene expression. We have used two rat models of microglial activation: the gestational low protein diet (LPD) model, associated with chronic brain injury, and postnatal ibotenate intracerebral injections, responsible for acute excitotoxicity injury. Adenosine blood levels have been measured by Tandem Mass Spectrometry. The expression of ARs in vivo was assessed using qPCR and immunohistochemistry. In vivo models have been replicated in vitro on primary microglial cell cultures exposed to A2aR agonist CGS-21680 or antagonist SCH-58261. The effects of these treatments have been assessed on the M1/M2 cytokine expressions measured by RT-qPCR. LPD during pregnancy was associated with higher adenosine levels in pups at postnatal day 1 and 4. A2aR mRNA expression was significantly increased in both cortex and magnetically sorted microglial cells from LPD animals compared to controls. CD73 expression, responsible for extracellular production of brain adenosine, was significantly increased in LPD cortex and sorted microglia cells. Moreover, CD73 protein level was increased in ibotenate treated animals. In vitro experiments confirmed that LPD or control microglial cells exposed to ibotenate display an increased expression, at both protein and molecular levels, of A2aR and M1 markers (IL-1β, IL-6, iNOS, TNFα). This pro-inflammatory profile was significantly reduced by SCH-58261, which reduces M1 markers in both LPD and ibotenate-exposed cells, with no effect on control cells. In the same experimental conditions, a partial increased of M1 cytokines was observed in response to A2aR agonist CGS-21680. These results support the involvement of adenosine and particularly of its receptor A2aR in the regulation of microglia in two different animal models of neuroinflammation.

PMID: 30254599

27. Glycopyrrolate.
AuthorsGallanosa A, Bhimji SS.

SourceStatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018-. 2018 Sep 12.

Glycopyrrolate, also known as glycopyrronium, is an anticholinergic drug. It is a synthetically created quaternary amine with both a pyridine and a cyclopentane moiety within the compound's structure. Glycopyrrolate has been widely used as a preoperative medication to inhibit salivary gland and respiratory secretions. The most frequent reasons for administering anticholinergics include producing an antisialagogue effect, creating a sedative and amnesic effect, and preventing reflex bradycardia. Anticholinergics are not predictably effective in increasing gastric fluid pH or decreasing gastric fluid volume. Glycopyrrolate is among the more common anticholinergic medications. It used perioperatively as a muscarinic receptor antagonist.[1] Other commonly used anticholinergics include atropine and scopolamine. Most frequently, glycopyrrolate is used to reduce pharyngeal, tracheal, bronchial, and sialagogue effects preoperatively; decreased secretions are the desired effect during anesthesia when a tracheal tube is in place. A blockade of reflexive vagal cardiac inhibition reflexes during both intubation and anesthetic induction may also occur. Glycopyrrolate may be administered to reverse the neuromuscular blockade due to nondepolarizing muscle relaxants postoperatively and is frequently used in conjunction with neostigmine, a

cholinesterase inhibitor.[2] It is also used to reduce severe or chronic drooling in pediatric patients with neurologic conditions, such as cerebral palsy. The intravenous formulation of glycopyrrolate is classically used to reverse vagal reflexes and bradycardia intraoperatively, as well as to reverse the muscarinic effects of cholinergic agents such as neostigmine or pyridostigmine.[3]

PMID: 30252291

28. Decline in severe spastic cerebral palsy at term in Denmark 1999-2007.
Hoei-Hansen CE, Laursen B, Langhoff-Roos J, Rackauskaite G, Uldall P.

Eur J Paediatr Neurol. 2018 Sep 6. pii: S1090-3798(18)30030-8. doi: 10.1016/j.ejpn.2018.08.010. [Epub ahead of print]

AIM: To analyse trends in prevalence and severity of cerebral palsy (CP) in Denmark in birth years 1999-2007 and compare with previous periods. METHOD: Data has been collected uniformly in the Danish cerebral palsy national register nationwide since 1995. Rates in the time periods 1999-2001, 2002-2004 and 2005-2007 covering 585,393 births were analysed by gestational age and subtypes. RESULTS: Total number of CP cases in the period was 1165. The overall prevalence of CP decreased significantly from 2.1 in 1999-2001 to 1.8 in 2005-2007 per 1000 livebirths ($p = 0.022$). The decline was only significant for children born at term ($p = 0.007$) but not for the preterm ($p = 0.44$). The decline in children born at term was based on a decrease in bilateral spastic CP ($n = 117$ in years 1999-2001 and $n = 59$ in 2005-2007). Multidisciplinary obstetric skills training with neonatal resuscitation in Denmark was initiated in 2003 and timely associated with the decrease. The prevalence of unilateral spastic CP the prevalence did not change, but in the two last time periods more children had a right-sided than left-sided unilateral spastic CP. CONCLUSION: The decline in rate of CP seen in 2005-2007 as compared to 1999-2001 was mainly based on fewer cases of severe spastic CP in term infants. We hypothesize that improved neonatal resuscitation in the delivery room may be partly responsible for the decrease. In premature children the decline was not significant in this time period, but has been dramatically decreasing in the years before the time period here analysed.

PMID: 30241693

Prevention and Cure

29. A unique de novo gain-of-function variant in CAMK4 associated with intellectual disability and hyperkinetic movement disorder.
Zech M, Lam DD, Weber S, Berutti R, Poláková K, Havránková P, Fečíková A, Strom TM, Růžička E, Jech R, Winkelmann J.

Cold Spring Harb Mol Case Stud. 2018 Sep 27. pii: mcs.a003293. doi: 10.1101/mcs.a003293. [Epub ahead of print]

Calcium/calmodulin-dependent protein kinases (CaMKs) are key mediators of calcium signaling and underpin neuronal health. Although widely studied, the contribution of CaMKs to Mendelian disease is rather enigmatic. Here, we describe an unusual neurodevelopmental phenotype, characterized by milestone delay, intellectual disability, autism, ataxia, and mixed hyperkinetic movement disorder including severe generalized dystonia, in a proband who remained etiologically undiagnosed despite exhaustive testing. We performed trio-whole-exome sequencing to identify a de novo essential splice-site variant (c.981+1G>A) in CAMK4, encoding CaMKIV. Through in silico evaluation and cDNA analyses, we demonstrated that c.981+1G>A alters CAMK4 pre-mRNA processing and results in a stable mRNA transcript containing a 77-nt out-of-frame deletion and a premature termination codon within the last exon. The expected protein, p.Lys303Serfs*28, exhibits selective loss of the C-terminal regulatory domain of CaMKIV and bears striking structural resemblance to previously reported synthetic mutants that confer constitutive CaMKIV activity. Biochemical studies in proband-derived cells confirmed an activating effect of c.981+1G>A and indicated that variant-induced excessive CaMKIV signaling is sensitive to pharmacological manipulation. Additionally, we found that variants predicted to cause selective depletion of CaMKIV`s regulatory domain are unobserved in diverse catalogs of human variation, thus revealing that c.981+1G>A is a unique molecular event. We propose that our proband`s phenotype is explainable by a dominant CAMK4 splice-disrupting mutation that acts through a gain-of-function mechanism. Our findings highlight the importance of CAMK4 in human neurodevelopment, provide a foundation for future clinical research of CAMK4, and suggest the CaMKIV signaling pathway as a potential drug target in neurological disease.

PMID: 30262571