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Professor Nadia Badawi AM

Macquarie Group Foundation Chair of Cerebral Palsy

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Interventions and Management

1. Static postural data shows a strong correlation with kinematic data in children with cerebral palsy.

Schranz C, Kruse A, Belohlavek T, Steinwender G, Tilp M, Svehlik M.

Gait Posture. 2018 Jul 29. pii: S0966-6362(18)31075-0. doi: 10.1016/j.gaitpost.2018.07.021. [Epub ahead of print]

PMID: [30087019](#)

2. Effects of Botulinum Toxin A Injection on Ambulation Capacity in Patients with Cerebral Palsy.

Çağlar Okur S, Uğur M, Şenel K.

Dev Neurorehabil. 2018 Aug 10:1-4. doi: 10.1080/17518423.2018.1502832. [Epub ahead of print]

PURPOSE: The purpose of the study is to assess the change in their ambulatory capacity and spasticity in children with cerebral palsy (CP) who received botulinum toxin A (BoNT-A) injection and underwent rehabilitation therapy. **METHODS:** Thirty patients with CP, 3-13 years who had varied functional levels and lower extremity spasticity, were randomized in two groups. In Group 1 (n = 15), BoNT-A was administered to the affected extremity and underwent rehabilitation. In Group 2 (n = 15), the patients underwent only rehabilitation protocol. The Visual Analogue Scale (VAS), Tardieu Scale (TS), Gross Motor Function Classification System (GMFCS), Selective Motor Control, and Goal Attainment Scale were evaluated 4 and 12 weeks after baseline. **RESULTS:** The mean scores of the TS ($p < 0.001$) GMFCS, GAS, and VAS ($p < 0.05$) significantly improved in Group 1. **CONCLUSION:** We think that implementation of rehabilitation protocols with BoNT-A injection is superior to alone rehabilitation therapy and increasing ambulatory capacity in patients with CP.

PMID: [30095354](#)

3. Quantifying the separate effects of Botulinum Toxin-A and lower leg casting on ankle joint hyper-resistance in children with cerebral palsy.

Bar-On L, Hanssen B, Peeters N, Schless SH, Van Campenhout A, Desloovere K.

Gait Posture. 2018 Aug 2. pii: S0966-6362(18)31001-4. doi: 10.1016/j.gaitpost.2018.06.215. [Epub ahead of print]

PMID: [30078754](#)

4. Muscle and tendon lengthening behaviour of the medial gastrocnemius during ankle joint rotation in children with cerebral palsy.

Kalkman BM, Bar-On L, Cenni F, Maganaris CN, Bass A, Holmes G, Desloovere K, Barton GJ, O'Brien TD.

Exp Physiol. 2018 Aug 9. doi: 10.1113/EP087053. [Epub ahead of print]

NEW FINDINGS: What is the central question of this study? Which structures of the medial gastrocnemius muscle tendon unit contribute to its lengthening during joint rotation and thus receive the stretching stimulus? What is the main finding and its importance? We show for the first time, that muscle and tendon lengthen differently between children with CP and TD children during a similar amount of muscle tendon unit lengthening or joint rotation. This indicates possible differences in mechanical muscle and tendon properties due to CP, which is not evident by assessment of muscle function on a joint level. **ABSTRACT:** Children with cerebral palsy (CP) commonly present with reduced ankle range of motion (ROM) partly due to changes in mechanical properties of the muscle-tendon-unit (MTU). Detailed information about how muscle and tendon interact to contribute to joint rotation is currently lacking, but may provide essential information to explain the limited effectiveness of stretching interventions in children with CP. The purpose of this study was to quantify which structures contribute to MTU lengthening and thus receive the stretch during passive ankle joint rotation. Fifteen children with CP (age: 11.4 ± 3 y) and 16 typically developing (TD) children (age: 10.2 ± 3 y) participated. Ultrasound was combined with motion tracking, joint torque and electromyography to record fascicle, muscle and tendon lengthening of the medial gastrocnemius during passive ankle joint rotations over the full and a common ROM. In children with CP, relative to MTU lengthening, muscle and fascicles lengthened less (CP: 50.4%, TD: 63% of MTU lengthening; $p < 0.04$) and tendon lengthened more (CP: 49.6%, TD: 37% of MTU lengthening, $p < 0.01$) regardless of the ROM studied. Differences between groups in the amount of lengthening of the underlying structures during a similar amount of joint rotation and MTU displacement indicate possible differences in tissue mechanical properties due to CP, which are not evident by assessment on a joint level. These factors should be considered when assessing and treating muscle function in children with CP, for example during stretching exercises as the muscle may not receive much of the applied lengthening stimulus. This article is protected by copyright. All rights reserved.

PMID: [30091806](#)

5. Is the maximum functional performance a meaningful parameter in children with cerebral palsy?

Schranz C, Kruse A, Belohlavek T, Steinwender G, Tilp M, Svehlik M.

Gait Posture. 2018 Aug 1. pii: S0966-6362(18)30986-X. doi: 10.1016/j.gaitpost.2018.06.200. [Epub ahead of print]

PMID: [30077518](#)

6. Impact of ankle-foot orthoses on gait 1 year after lower limb surgery in children with bilateral cerebral palsy.

Skaaret I, Steen H, Terjesen T, Holm I.

Prosthet Orthot Int. 2018 Aug 7:309364618791615. doi: 10.1177/0309364618791615. [Epub ahead of print]

BACKGROUND: Different types of ankle-foot orthoses are commonly used following lower limb surgery in children with bilateral spastic cerebral palsy. After three-dimensional gait analysis 1 year postoperatively, many children are recommended continued use of ankle-foot orthoses. **OBJECTIVES:** Our aims were to quantify the impact of ankle-foot orthoses on gait 1 year postoperatively and evaluate predictors for clinically important improvement. **STUDY DESIGN:** Prospective cohort study. **METHODS:** A total of 34 ambulating children with bilateral cerebral palsy, with mean age 11 years (range 6-17), comprising 12 girls and 22 boys, were measured with three-dimensional gait analysis preoperatively (barefoot) and 1 year postoperatively (barefoot and with ankle-foot orthoses). Outcome was evaluated using gait profile score, key kinematic, kinetic and temporal-spatial variables in paired sample comparisons. Logistic regression was used to evaluate predictors for clinically important improvement with orthoses ($\geq 1.6^\circ$ change in gait profile score). **RESULTS:** Walking barefoot 1 year postoperatively, major improvements were seen in gait profile score and key variables. With ankle-foot orthoses, there were significantly improved step length and velocity, additional moderate reduction/improvement in gait profile score and knee moments and decreased stance ankle dorsiflexion compared to barefoot. Children using ground reaction ankle-foot orthoses ($n = 14$) decreased stance knee flexion from 13.9° walking barefoot to 8.2° with orthoses. High gait profile score and more gait dysfunction preoperatively were significant predictors of clinically important improvement walking with orthoses. **CONCLUSION:** The results indicate improved gait function walking with ankle-foot orthoses versus barefoot 1 year after lower limb surgery. Stronger impact of ankle-foot orthoses was found in children with more pronounced gait dysfunction preoperatively. Clinical relevance The 1-year postoperative three-dimensional gait analysis is a useful method to assess treatment outcome after lower limb surgery in children with bilateral cerebral palsy and could also guide clinicians whether further treatment with ankle-foot orthoses is indicated, using clinically important differences as thresholds to evaluate their impact on gait.

PMID: [30084755](#)

7. How abnormal is normal? Stride-to-stride variability and effects of age on the gait of typically developing children.

Oudenhoven L, Booth A, Buizer A, van der Krogt M.

Gait Posture. 2018 Jul 26. pii: S0966-6362(18)30888-9. doi: 10.1016/j.gaitpost.2018.06.131. [Epub ahead of print]

PMID: [30082114](#)**8. Influence of equinus correction on mechanical advantage of the plantarflexors during gait in children with cerebral palsy.**

Carruth H, Barton G, Trinca D, Holmes G, Bass A, Baltzopoulos V, Maganaris C, O'Brien TD.

Gait Posture. 2018 Jul 18. pii: S0966-6362(18)31003-8. doi: 10.1016/j.gaitpost.2018.06.217. [Epub ahead of print]

PMID: [30076061](#)**9. Intramuscular Botulinum toxin prior to comprehensive rehabilitation has no added value for improving motor impairments, gait kinematics and goal attainment in walking children with spastic cerebral palsy.**

Schasfoort F, Pangalila R, Sneekes EM, Catsman C, Becher J, Horemans H, Stam HJ, Dallmeijer AJ, Bussmann JBJ.

J Rehabil Med. 2018 Aug 6. doi: 10.2340/16501977-2369. [Epub ahead of print]

OBJECTIVE: Botulinum toxin (BoNT-A) is widely used in combined treatment for spastic cerebral palsy, but its added value preceding comprehensive rehabilitation for motor impairments, gait, and goal attainment has not been studied. **DESIGN:** A comparative multi-centre trial, in which two groups underwent comprehensive rehabilitation (i.e. high-intensive functional physiotherapy, and indicated casting/orthoses). One group received intramuscular BoNT-A prior to rehabilitation, and the other group did not receive BoNT-A. **SUBJECTS/PATIENTS:** Children with spastic cerebral palsy, Gross Motor Function Classification System (GMFCS) levels I-III, age range 4-12 years, indicated for BoNT-A treatment regarding mobility problems. **METHODS:** Sixty-five children participated (37 boys), mean age 7.3 years (standard deviation (SD) 2.3, range 4-12 years), equally distributed across GMFCS levels. Forty-one children received BoNT-A+ comprehensive rehabilitation and 24 received comprehensive rehabilitation only. Functional leg muscle strength, passive range of motion, angle of catch, cerebral palsy-related pain, walking speed, kinematic gait parameters, goal attainment, and proxy-reported general functioning were assessed at baseline, primary end-point (12 weeks) and 24-week follow-up. Statistical analyses were performed with linear mixed models. **RESULTS:** At the primary end-point there were no statistically significant differences in treatment effects between the groups, except for the angle-of-catch of the rectus femoris, which was in favour of comprehensive rehabilitation without BoNT-A (12° difference, 95% confidence interval (95% CI) 2:23, $p = 0.025$). Results at follow-up were similar. **CONCLUSION:** At the group level, treating with BoNT-A prior to comprehensive rehabilitation did not add to the clinical effectiveness of rehabilitation. Thus, BoNT-A prescription and use should be critically reconsidered in this cerebral palsy age- and GMFCS-subgroup.

PMID: [30080235](#)**10. Muscle fatigue during a short walking exercise in children with cerebral palsy who walk with a jump gait.**

Parent A, Pouliot-Laforte A, Dal Maso F, Marois P, Ballaz L.

Gait Posture. 2018 Jul 18. pii: S0966-6362(18)30982-2. doi: 10.1016/j.gaitpost.2018.06.196. [Epub ahead of print]

PMID: [30076062](#)**11. Influence of stance phase shifts in the movement analysis profile and the Gait Profile Score for cerebral palsy patients.**

Pobatschnig B, Dumphart B, Kranzl A.

Gait Posture. 2018 Aug 1. pii: S0966-6362(18)31115-9. doi: 10.1016/j.gaitpost.2018.07.051. [Epub ahead of print]

The Gait Profile Score (GPS) is used as a summary index to interpret gait abnormalities compared to a reference group, but stance phase shifts in gait cycles are not considered. The aim of this work is to point out, if stance phase shifts affects the GPS

estimations and lead clinically relevant changes.

PMID: [30077513](#)

12. Post-treatment muscle coordination patterns during gait are highly similar to pre-treatment ones in CP children.
Pitto L, Kaat D, Guy M, Catherine H, Friedl DG, Ilse J.

Gait Posture. 2018 Jul 26. pii: S0966-6362(18)30901-9. doi: 10.1016/j.gaitpost.2018.06.144. [Epub ahead of print]

Musculoskeletal models and computational simulations could be of help to clinicians in assessing the most appropriate treatment for a patient with Cerebral Palsy (CP). Simulations trying to predict the functional outcome face the challenge of defining a reliable model of the subject's motor control in the POST-treatment condition, with only the pre-treatment EMG patterns being available to inform about the patient's control.

PMID: [30077516](#)

13. Biomechanical effects and quality of life when using a FES-system in subjects with neuromuscular gait disorders.
Block J, Putz C, Weichold C, Heitzmann D, Kaib T, Wolf SI, Alimusaj M.

Gait Posture. 2018 Jul 24. pii: S0966-6362(18)31164-0. doi: 10.1016/j.gaitpost.2018.07.090. [Epub ahead of print]

PMID: [30087018](#)

14. A Novel Approach for the Management and Prevention of Self-Induced Masticatory Lingual Trauma in the Neurologically Injured Patient.

Avashia Y, Bittar P, Suresh V, Powers DB.

Craniomaxillofac Trauma Reconstr. 2018 Sep;11(3):242-248. doi: 10.1055/s-0037-1606300. Epub 2017 Sep 19.

Self-induced masticatory trauma is an unfortunate complication of a variety of neurologic disorders, including epileptic seizures, cerebral palsy, mental retardation, psychiatric disease, and brain trauma, in addition to other described etiologies. While single or occasional occurrences of tongue biting are relatively benign, recurrent self-injury can pose major issues and predispose a patient to chronic, severe complications. To prevent the complications associated with ongoing trauma to the tongue, steps must be taken to protect individuals from chronic self-injurious behavior. Often, these interventions cause significant morbidity to the patient, such as elective removal of the dentition or complications in gaining access to the oral cavity/airway associated with maxillomandibular fixation. In the neurologically impaired patient, immobilization of the jaws is frequently associated with higher rates of agitation, aspiration, or development of complicating infections of the gingival tissues. We report a case of self-induced masticatory trauma managed with the fabrication of a custom-fabricated oral appliance. This treatment modality successfully prevents the recurrence or incidence of self-induced masticatory trauma to the tongue. The benefits of this modality are that it allows access to the oral cavity, prevents immobilization of the jaws, has minimal to no morbidity, and is completely reversible.

PMID: [30087756](#)

15. Voluntary Cough and Clinical Swallow Function in Children with Spastic Cerebral Palsy and Healthy Controls.
Mishra A, Malandraki GA, Sheppard JJ, Gordon AM, Levy ES, Troche MS.

Dysphagia. 2018 Aug 7. doi: 10.1007/s00455-018-9933-4. [Epub ahead of print]

Dysphagia and resulting pulmonary sequelae are frequently observed in children with spastic cerebral palsy (SCP). However, physiological evidence regarding airway protective behaviors (specifically swallowing and cough function) in these children is sparse. The aim of this investigation was to quantify specific feeding, swallowing, and cough impairments in children with SCP compared to controls. Eleven children with SCP (mean age: 7 ± 2 years; GMFCS: I-V; MACS: I-V) and 10 age-matched controls participated. Clinical feeding and swallowing performance was evaluated with the dysphagia disorder survey (DDS) using standardized liquid, puree, and chewable solid consistencies. Suprahyoid muscle activity and respiratory-swallow patterns were assessed with simultaneous surface electromyography and respiratory inductance plethysmography as children

swallowed the various consistencies. Voluntary cough airflow measures were also obtained. Nonparametric tests were used for group comparisons and correlational analyses. Compared to controls, children with SCP demonstrated more signs of clinical feeding and swallowing impairment ($p < 0.0001$, $\eta^2 = 0.771$), heightened suprahyoid muscle activity for puree ($p = 0.014$, $\eta^2 = 0.305$) and chewable solids ($p = 0.001$, $\eta^2 = 0.528$), more frequent post-swallow inhalation across liquid ($p = 0.005$, $\eta^2 = 0.401$), puree ($p = 0.014$, $\eta^2 = 0.304$), and chewable solids ($p = 0.035$, $\eta^2 = 0.223$), and lower cough volume acceleration ($p = 0.019$, $\eta^2 = 0.289$). Post-swallow inhalation for chewable solids was correlated with the DDS Part 1 ($r_s = 0.734$, $p = 0.010$), DDS Part 2 ($r_s = 0.610$, $p = 0.046$) and the DDS Total scores ($r_s = 0.673$, $p = 0.023$). This study is the first to provide evidence of specific physiological deficits of both swallowing and voluntary cough in children with SCP. Potential hypotheses explaining these deficits and implications for physiologically driven management are explored.

PMID: [30088088](#)

16. Vocal Fold Paralysis, Unilateral.

Singh JM, Kwartowitz G.

StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018. 2018 Jul 29.

Vocal fold immobility is a broad term that can be used to describe the abnormal movement of the true vocal folds. It can be unilateral, where only one true vocal fold is affected, or bilateral, in which both true vocal folds are affected. The abnormal movement can be characterized as being paretic, meaning some movement is present, albeit reduced or paralyzed, with complete cessation of vocal fold movement. If a true vocal fold is paralyzed, it can be described as being paralyzed in a midline, paramedian, or lateral position. This review will focus specifically on unilateral vocal fold paralysis. It is imperative to understand the neuroanatomy of the true vocal folds to understand vocal fold paralysis. The vagus nerve innervates the larynx and its associated muscles. The vagus nerve is comprised of nerve fibers that arise from the nucleus ambiguus in the medulla portion of the brainstem. Upper-motor cortico-bulbar neurons originate from the cerebral cortex and descend to synapse onto these lower-motor vagal nerve fibers, which originate from the nucleus ambiguus. After arising from the brainstem, the vagus nerve then exits the skull base at the jugular foramen and descends into the neck to give off three main branches (the pharyngeal branch, the superior laryngeal nerve [SLN], and the recurrent laryngeal nerve [RLN]). The SLN supplies sensation to the larynx above the glottis and innervates the cricothyroid muscle. The RLN descends further into the neck, loops around the subclavian artery (on the right) or the aortic arch (on the left), and ascends back up into the neck in the tracheoesophageal groove, where it enters the larynx posteriorly, near the cricothyroid joint. The RLN innervates all remaining intrinsic muscles of the larynx including the posterior cricoarytenoid, interarytenoid, lateral cricoarytenoid, and thyroarytenoid muscles.

PMID: [30085602](#)

17. The Study of Visual-Auditory Interactions on Lower Limb Motor Imagery.

Yu Z, Li L, Song J, Lv H.

Front Neurosci. 2018 Jul 24;12:509. doi: 10.3389/fnins.2018.00509. eCollection 2018.

In order to improve the activation of the mirror neuron system and the ability of the visual-cued motor imagery further, the multi-stimuli-cued unilateral lower limb motor imagery is studied in this paper. The visual-auditory evoked pathway is proposed and the sensory process is studied. To analyze the visual-auditory interactions, the kinesthetic motor imagery with the visual-auditory stimulus, visual stimulus and no stimulus are involved. The motor-related rhythm suppression is applied on quantitative evaluation. To explore the statistical sensory process, the causal relationships among the functional areas and the event-related potentials are investigated. The results have demonstrated the outstanding performances of the visual-auditory evoked motor imagery on the improvement of the mirror neuron system activation and the motor imagery ability. Besides, the abundant information interactions among functional areas and the positive impacts of the auditory stimulus in the motor and the visual areas have been revealed. The possibility that the sensory processes evoked by the visual-auditory interactions differ from the one elicited by kinesthetic motor imagery, has also been indicated. This study will promisingly offer an efficient way to motor rehabilitation, thus favorable for hemiparesis and partial paralysis patients.

PMID: [30087594](#)

18. Quality of care provided to children with cerebral palsy, Alexandria, Egypt.

Khalil M, Elweshahy H, Abdelghani H, Omar T, Ahmed S.

East Mediterr Health J. 2018 Jul 29;24(6):522-531. doi: 10.26719/2018.24.6.522.

BACKGROUND: Assessing the quality of care has become increasingly important to health care providers, regulators and purchasers of care. **AIMS:** This study assessed the quality of care provided to children with cerebral palsy attending Alexandria University Children's Hospital, Egypt. **METHODS:** Paediatric neurology residents (n = 15) who provided care to children with cerebral palsy at the hospital completed a structured checklist assessing their compliance with generic care standards. The medical records of 84 children with cerebral palsy who received care at the hospital were reviewed using the same checklist. Another checklist was completed by the head of the paediatric neurology unit, medical director of the hospital, head of physical medicine and head nurse to assess adherence to process and service improvement standards. Face-to-face interviews were conducted with the caregivers/parents of the children using a client satisfaction questionnaire. **RESULTS:** Based on what was reported by health care providers, most did not adhere to the recommended practices in the care of children with cerebral palsy. Review of the medical records also showed a lack of compliance with standards. The mean total satisfaction percentage score of parents/caregivers was 55.43% (SD 18.16). Satisfaction was particularly low for waiting time, waiting area and availability of required facilities for their child's care. **CONCLUSIONS:** There is a wide gap between the actual care provided to children with cerebral palsy and the recommended standards. Moreover, the documentation system in the hospital is poor. A quality improvement plan is needed for the provision of care to children with cerebral palsy.

PMID: [30079947](#)

19. ViEW: a wheelchair simulator for driving analysis.

Morère Y, Bourhis G, Cosnuau K, Guilmois G, Rumilly E, Blangy E.

Assist Technol. 2018 Aug 7. doi: 10.1080/10400435.2018.1503204. [Epub ahead of print]

The powered wheelchair (PW) has become an essential mobility assistive technology for people with motor disabilities. A critical step involved in maximizing the end-user experience is evaluating individual functional abilities to identify driving difficulties PW users experience during their daily activities. There are certain limitations, however, associated with on-road driving assessments, such as the practical concern of safety. And while extracting quantitative parameters such as joystick control or trajectory tracking from real wheelchairs is feasible, it requires modifications to the PW hardware architecture and, in some cases, to the physical test environment. Using powered wheelchair simulation for driving analysis offers flexibility for safely evaluating the individual's driving performance in a variable environment and situations ranging in difficulty. Additionally, it makes it possible to measure numerous variables involved in the driving process, which can then be used for computing driving performance indicators. The main objectives of this pilot study were to assess PW users' outdoor driving abilities (functional motor skills, smoothness of control, subjective driving behavior) to study how the simulator can improve outdoor driving task performance, and to define new objective criteria for evaluating the overall driving process. The study took place in the Centre of Physical Medicine and Rehabilitation for Children of Flavigny sur Moselle (France) and involved a group of 12 children and young adults diagnosed with cerebral palsy. Simulations were conducted using ViEW (Virtual Electrical Wheelchair), a 3D wheelchair simulator designed in our laboratory. In this context, we describe here an experiment to assess how driving training using a simulator can potentially improve everyday driving skills. A customized virtual environment was designed to immerse the user in a life-like driving experience and the simulation was divided into seven levels of increasing difficulty. We defined a functional evaluation rating scale for PW driving performance adapted to outdoor navigation behavior, which occupational therapists involved in the study used to assess the subjects' qualitative performance. In parallel, we used the data collected on the simulator to define driving skills indicators. The driving simulator as a training tool proved to be a promising method for teaching driving behavior in a safe environment and beneficial to users' driving performance. The acquired skills during simulations were transferable to on-road wheelchair driving (hereto referred to as real driving). The participants' performance indicators computed from motion trajectories and joystick control analysis (distance, smoothness/jerkiness, mean amplitude of control) produced positive results. Based on our findings, we believe that computed performance indicators can be a valuable decision-making tool for occupational therapists evaluating their subjects' driving abilities.

PMID: [30085901](#)

20. Maternal obesity and risk of cerebral palsy in children: a systematic review and meta-analysis.

Zhang J, Peng L, Chang Q, Xu R, Zhong N, Huang Q, Zhong M, Yu Y.

Dev Med Child Neurol. 2018 Aug 7. doi: 10.1111/dmcn.13982. [Epub ahead of print]

AIM: Several studies have examined the links between maternal obesity and the risk of cerebral palsy (CP) in children, with inconsistent results. The aim of our study was to investigate whether maternal obesity is associated with increased risk of CP in offspring by using meta-analysis. **METHOD:** PubMed and Web of Science were searched until August 2017. Observational studies relevant to the maternal obesity and risk of CP in children were extracted and compiled. Meta-analyses were performed for different obesity levels and pooled odds ratios (ORs) and 95% confidence intervals (CIs) were reported. **RESULTS:** A total of five cohort studies involving 12 324 cases and 7 919 288 participants were included in our meta-analysis. The pooled crude

and adjusted ORs (95% CIs) were 1.65 (1.38-1.98) and 1.51 (1.24-1.84) respectively. Additionally, the pooled OR (95% CI) for CP in offspring in relation to maternal obesity class I (body mass index [BMI] 30.0-34.9), class II (BMI 35.0-39.9), and class III (BMI \geq 40.0) compared with normal weight during prepregnancy or pregnancy was 1.31 (1.15-1.50), 1.65 (1.34-2.02), and 2.37 (1.91-2.94) respectively. INTERPRETATION: This meta-analysis demonstrated that increasing grades of maternal obesity are associated with a higher risk of CP in offspring.

PMID: 30084489

Prevention and Cure

21. Fas-ligand and interleukin-6 in the cerebrospinal fluid are early predictors of hypoxic-ischemic encephalopathy and long-term outcomes after birth asphyxia in term infants.

Leifsdottir K, Mehmet H, Eksborg S, Herlenius E.

J Neuroinflammation. 2018 Aug 8;15(1):223. doi: 10.1186/s12974-018-1253-y.

BACKGROUND: Cerebral ischemia generates neuroinflammation that can induce neural cell death. This cohort study assessed whether Fas-ligand (FasL) and interleukin (IL)-6 levels in the cerebrospinal fluid (CSF) after hypoxic-ischemic encephalopathy (HIE) can serve as biomarkers of hypoxic brain injury in neonates. **METHODS:** Term infants (> 37-week gestational age) who were admitted to the neonatal intensive care unit of Karolinska University Hospital in years 2002 to 2004 with perinatal asphyxia were enrolled prospectively. Control infants without brain pathology underwent lumbar puncture for suspected infection. FasL and IL-6 levels were measured in the CSF, by enzyme-linked immunosorbent assays. All patients underwent neurological assessment at 18 months. HIE was classified as mild, moderate, or severe (HIE I-III). Adverse neurological outcome at 18 months was defined as a mental developmental index < 85, deafness, blindness, cerebral palsy, or seizure disorder. **RESULTS:** Of the 44 HIE patients, 14, 16, and 14 had HIE-I, HIE-II, and HIE-III, respectively. HIE-II and HIE-III patients had higher FasL and IL-6 levels than HIE-I patients and the 20 controls (all $p < 0.0001$). Patients with adverse outcomes had higher FasL and IL-6 levels than patients with normal outcomes and controls (both $p < 0.0001$). On receiver-operator curve analyses, FasL and IL-6 (alone and together) were highly predictive of HIE grade and outcome (areas under the curve range 0.86-0.94) and showed high sensitivity (66.7-100%). These biomarkers performed better than cord blood pH (areas under the curve: HIE grade = 0.80, adverse outcomes = 0.86). **CONCLUSION:** CSF biomarkers FasL and IL-6 predicted severity of encephalopathy and long-term outcomes in post-asphyxiated infants better than a standard biomarker.

PMID: [30089504](#)

22. Perinatal Hypoxic-Ischemic Encephalopathy and Neuroprotective Peptide Therapies: A Case for Cationic Arginine-Rich Peptides (CARPs).

Edwards AB, Anderton RS, Knuckey NW, Meloni BP.

Brain Sci. 2018 Aug 7;8(8). pii: E147. doi: 10.3390/brainsci8080147.

Perinatal hypoxic-ischemic encephalopathy (HIE) is the leading cause of mortality and morbidity in neonates, with survivors suffering significant neurological sequelae including cerebral palsy, epilepsy, intellectual disability and autism spectrum disorders. While hypothermia is used clinically to reduce neurological injury following HIE, it is only used for term infants (>36 weeks gestation) in tertiary hospitals and improves outcomes in only 30% of patients. For these reasons, a more effective and easily administrable pharmacological therapeutic agent, that can be used in combination with hypothermia or alone when hypothermia cannot be applied, is urgently needed to treat pre-term (\leq 36 weeks gestation) and term infants suffering HIE. Several recent studies have demonstrated that cationic arginine-rich peptides (CARPs), which include many cell-penetrating peptides [CPPs; e.g., transactivator of transcription (TAT) and poly-arginine-9 (R9; 9-mer of arginine)], possess intrinsic neuroprotective properties. For example, we have demonstrated that poly-arginine-18 (R18; 18-mer of arginine) and its D-enantiomer (R18D) are neuroprotective in vitro following neuronal excitotoxicity, and in vivo following perinatal hypoxia-ischemia (HI). In this paper, we review studies that have used CARPs and other peptides, including putative neuroprotective peptides fused to TAT, in animal models of perinatal HIE. We critically evaluate the evidence that supports our hypothesis that CARP neuroprotection is mediated by peptide arginine content and positive charge and that CARPs represent a novel potential therapeutic for HIE.

PMID: [30087289](#)