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## Interventions and Management

### 1. Postural mechanisms in moderate-to-severe cerebral palsy

Adam David Goodworth, Sandra L Saavedra

J Neurophysiol. 2021 Mar 31. doi: 10.1152/jn.00549.2020. Online ahead of print.

People with moderate-to-severe cerebral palsy (CP) have the greatest need for postural control research yet are usually excluded from research due to deficits in sitting ability. We use a support system that allows us to quantify and model postural mechanisms in non-ambulatory children with CP. A continuous external bench tilt stimulus was used to evoke trunk postural responses in 7 sitting children with CP (ages 2.5 to 13 years) in several test sessions. Eight healthy adults were also included. Postural sway was analyzed with root mean square (RMS) sway and RMS sway velocity, along with frequency response functions (FRF, gain and phase) and coherence functions across two different stimulus amplitudes. A feedback model (including sensorimotor noise, Passive, Reflexive, and Sensory Integration mechanisms) was developed to hypothesize how postural control mechanisms are organized and function. Experimental results showed large RMS sway, FRF gains, and variability compared to adults. Modeling suggested that many subjects with CP adopted "simple" control with major contributions from a Passive and Reflexive mechanism and only a small contribution from active sensory integration. In contrast, mature trunk postural control includes major contributions from sensory integration and sensory reweighting. Relative to their body size, subjects with CP showed significantly lower damping, 3-5 times larger corrective torque, and much higher sensorimotor noise compared to the healthy mature system. Results are the first characterization of trunk postural responses and the first attempt at system identification in moderate-to-severe CP, an important step toward developing and evaluating more targeted interventions.

PMID: [33788612](#)

### 2. Effects of Inspiratory Muscle and Balance Training in Children with Hemiplegic Cerebral Palsy: A Randomized Controlled Trial

Büşra Kepenek-Varol, Hülya Nilgün Gürses, Dilara Füsün İçağasıoğlu

Dev Neurorehabil. 2021 Apr 1;1-9. doi: 10.1080/17518423.2021.1905727. Online ahead of print.

The aim of the study was to investigate the effects of inspiratory muscle and balance training on pulmonary function, respiratory muscle strength (RMS), functional capacity, and balance in children with hemiplegic cerebral palsy (CP). Thirty children with hemiplegic CP (Gross Motor Function Classification System I-II) included in this study. The control group (n = 15) underwent conventional physiotherapy rehabilitation program (CPRP) that included balance exercises, and the training group's (n = 15) program included inspiratory muscle training (IMT) in addition to CPRP for 8 weeks. The outcome measures were pulmonary function test, RMS measurement, the six-minute walk test (6MWT), and balance tests. There were no significant differences in the score changes of pulmonary function, balance, and 6MWT distance between groups ( $p > .05$ ),

whereas maximum inspiratory and expiratory pressure further increased in the training group ( $p > .05$ ). RMS assessment and the identification of children who need it, and adding IMT to CPRP will contribute greatly to the rehabilitative approach of children with CP.

PMID: [33792496](#)

### **3. Pharmacological and neurosurgical interventions for individuals with cerebral palsy and dystonia: a systematic review update and meta-analysis**

Emma Bohn, Katherine Goren, Lauren Switzer, Yngve Falck-Ytter, Darcy Fehlings

Review Dev Med Child Neurol. 2021 Mar 27. doi: 10.1111/dmcn.14874. Online ahead of print.

**Aim:** To update a systematic review of evidence published up to December 2015 for pharmacological/neurosurgical interventions among individuals with cerebral palsy (CP) and dystonia. **Method:** Searches were updated (January 2016 to May 2020) for oral baclofen, trihexyphenidyl, benzodiazepines, clonidine, gabapentin, levodopa, botulinum neurotoxin (BoNT), intrathecal baclofen (ITB), and deep brain stimulation (DBS), and from database inception for medical cannabis. Eligible studies included at least five individuals with CP and dystonia and reported on dystonia, goal achievement, motor function, pain/comfort, ease of caregiving, quality of life (QoL), or adverse events. Evidence certainty was evaluated using GRADE. **Results:** Nineteen new studies met inclusion criteria (two trihexyphenidyl, one clonidine, two BoNT, nine ITB, six DBS), giving a total of 46 studies (four randomized, 42 non-randomized) comprising 915 participants when combined with those from the original systematic review. Very low certainty evidence supported improved dystonia (clonidine, ITB, DBS) and goal achievement (clonidine, BoNT, ITB, DBS). Low to very low certainty evidence supported improved motor function (DBS), pain/comfort (clonidine, BoNT, ITB, DBS), ease of caregiving (clonidine, BoNT, ITB), and QoL (ITB, DBS). Trihexyphenidyl, clonidine, BoNT, ITB, and DBS may increase adverse events. No studies were identified for benzodiazepines, gabapentin, oral baclofen, and medical cannabis. **Interpretation:** Evidence evaluating the use of pharmacological and neurosurgical management options for individuals with CP and dystonia is limited to between low and very low certainty.

PMID: [33772789](#)

### **4. Perioperative Botulinum Toxin Injections to Enhance Surgical Outcomes in Patients With Spasticity: Preoperative, Intraoperative, and Postoperative Case Reports**

Geoffrey Frost, Heather Finlayson, Sepehr Saeidiborjani, Philippe Lagnau, Rajiv Reebye

Case Reports Arch Rehabil Res Clin Transl. 2021 Jan 12;3(1):100101. doi: 10.1016/j.arrct.2021.100101. eCollection 2021 Mar.

Spasticity causes an array of disabilities, which in turn may lead to the need for surgical intervention. Spasticity itself may also negatively affect surgical outcomes. This report reviews the potential benefit of perioperative (before, during, or after surgery) botulinum toxin (BoNT) injections for 3 patients with spasticity due to spinal cord injury, stroke, or multiple sclerosis. We discuss perioperative BoNT in 3 time periods: preoperatively, intraoperatively, and postoperatively. The cases demonstrate the use of perioperative BoNT in decreasing pain, improving wound healing, and improving surgical outcomes. We conclude by discussing the potential use of perioperative BoNT for surgical interventions in patients with spasticity and the need for further high-quality research in this field.

PMID: [33778474](#)

### **5. Effect of Action Observation Therapy in the Rehabilitation of Neurologic and Musculoskeletal Conditions: A Systematic Review**

Deirdre Ryan, Brona Fullen, Ebonie Rio, Ricardo Segurado, Diarmiad Stokes, Cliona O'Sullivan

Review Arch Rehabil Res Clin Transl. 2021 Jan 27;3(1):100106. doi: 10.1016/j.arrct.2021.100106. eCollection 2021 Mar.

**Objective:** To investigate the effect of action observation therapy (AOT) in the rehabilitation of neurologic and musculoskeletal conditions. **Data sources:** Searches were completed until July 2020 from the electronic databases Allied and Complementary Medicine Database (via OVID SP), Cumulative Index to Nursing and Allied Health Literature, Cochrane Library, EMBASE, MEDLINE, and the Physiotherapy Evidence Database. **Study selection:** Randomized controlled trials comparing AOT with standard care were assessed. Musculoskeletal (amputee, orthopedic) and neurologic (dementia, cerebral palsy, multiple sclerosis, Parkinson disease, stroke) conditions were included. There were no age limitations. Articles had to be available in English. **Data extraction:** Two reviewers independently screened titles, abstracts and full extracts of studies for eligibility and assessed the risk of bias of each study using the Cochrane Risk of Bias Tool. Data extraction included participant characteristics and intervention duration, frequency, and type. **Results:** The effect of AOT in different outcome measures (OMs) was referenced in terms of body structures and functions, activities and participation, and environmental factors as outlined by the International Classification of Functioning, Disability, and Health (ICF). Of the 3448 articles identified, 36 articles with 1405 patients met the inclusion criteria. Seven of the 11 meta-analyses revealed a significant effect of intervention, with results presented using the mean difference and 95% CI. A best evidence synthesis was used across all OMs. Strong evidence supports the use of AOT in the rehabilitation of individuals with stroke and Parkinson disease; moderate evidence supports AOT in the rehabilitation of populations with orthopedic and multiple sclerosis diagnoses. However, moderate evidence is provided for and against the effect of AOT in persons with Parkinson disease and cerebral palsy. **Conclusions:** This review suggests that AOT is advantageous in the rehabilitation of certain conditions in improving ICF domains. No conclusions can be drawn regarding treatment parameters because of the heterogeneity of the intervention. AOT has been considerably less explored in musculoskeletal conditions.

PMID: [33778479](#)

## **6. The Effect of Bilateral Anodal Transcranial Direct Current Stimulation versus Treadmill Training on Brain Activities, Gait Functions, Level of Participation and Enjoyment of Children with Cerebral Palsy: A Randomized Controlled Trial Protocol**

Hikmat Hadoush, Nihad A Almasri, Nasim Alnuman

Dev Neurorehabil. 2021 Mar 27;1-7. doi: 10.1080/17518423.2021.1905730. Online ahead of print.

**Background:** Cerebral palsy (CP) possesses bilateral sensory-motor cortical excitability alterations. In past studies, researchers have applied unilateral anodal transcranial direct stimulation (tDCS) with inconsistent findings. **Objective:** Examining the effects of treadmill training with either unilateral or bilateral anodal tDCS stimulation on brain activities, gait, and body functions of children with CP. **Design:** Randomized-clinical-trial. **Participants:** Eighty children with CP will be allocated into: treadmill/bilateral-tDCS, treadmill/unilateral-tDCS, treadmill/sham-tDCS, and treadmill groups. Additional 20 neurotypical children will be recruited for comparison. **Intervention:** Planned intervention will implement ten-sessions of treadmill training (50% of maximum-ground speed) either with unilateral-tDCS over left sensory-motor, or bilateral-tDCS over left/right sensory-motor areas. **Brain activities, gait, body functions, and participation will be assessed at pre-intervention, post-intervention, and at one-month follow-up. Result and Discussion:** This study would contribute to extant findings on the use of tDCS stimulation in children with CP and to our understanding of the appropriateness of the planned outcome measures.

PMID: [33775198](#)

## **7. Associations of inter-segmental coordination and treadmill walking economy in youth with cerebral palsy**

Gregor Kuntze, Shane Esau, Leticia Janzen, Laura Brunton, Kate Nuique, Elizabeth Condliffe, Carolyn Emery

J Biomech. 2021 Mar 20;120:110391. doi: 10.1016/j.jbiomech.2021.110391. Online ahead of print.

This study investigated associations of thigh-shank coordination deficit severity and metabolic demands of walking in youth with cerebral palsy (CP) and their typically developing (TD) peers. Youth (ages 8-18 years) with hemiplegic and diplegic CP [Gross Motor Classification System (GMFCS) I-III] and their age (within 12 months) and sex-matched peers performed a modified six-minute-walk-test on a treadmill. Kinematics (Motion Analysis, USA, 240 Hz) and mass-specific gross metabolic rate (GMR; COSMED, Italy) were analyzed for minute two of treadmill walking. Thigh-shank coordination was determined using continuous relative phase (CRP) analysis. GMR was normalized using participant specific Froude numbers (i.e. GMREq). Maximum and minimum CRP deficit angles (CRPMax, CRPMin) were analysed in SPSS (IBM, USA) using paired samples t-tests with Bonferroni correction ( $p = 0.0125$ ). Associations of knee extension angle deficit (KEDMax) and coordination outcomes with GMREq (log) were assessed using multiple linear regression. Twenty-eight matched pairs were

included, demonstrating significantly larger CRPMax for youth with CP [GMFCS I mean pair difference (98.75%CI) 8.2 (-0.1,16.5),  $P = 0.013$ ; GMFCS II/III 26.1 (2.3,50.0),  $P = 0.008$ ]. Joint kinematics and coordination outcomes were significantly associated with GMREq ( $P < 0.001$ ), primarily due to CRPMax ( $P < 0.001$ ), leading to a 1.7 (95%CI; 1.1, 2.4)% increase in GMREq for every degree increase in CRPMax. These findings indicate an association of thigh-shank coordination deficit severity and increasing metabolic demands of walking in youth with CP. CRP may be a clinically useful predictor of metabolic demands of walking in CP. Future work will evaluate the sensitivity of CRP to coordination and walking economy changes with surgical and non-surgical management.

PMID: [33774436](#)

### 8. [Treatment of equinus with serial casting][Article in Spanish]

A Fernández Gómez, D Hermoso de Mendoza Pi, J A Conejero Casares, M B Romero Romero, M Rodríguez-Piñero Durán

Rehabilitacion (Madr). 2021 Mar 23;S0048-7120(21)00006-2. doi: 10.1016/j.rh.2021.01.003. Online ahead of print.

Introduction: Equinus in children produces a pattern of unsteady gait and inefficient and inadequate positioning in the wheelchair. Treatment with a serial casting cycle maintains range of motion and facilitates the development of normal movement patterns. Its use in combination with botulinum toxin has proven benefits, but there is a lack of guidance on the optimal management protocol. Objective: The aim of this study were to describe the characteristics of the population with equinus of diverse aetiology and to determine the effectiveness of treatment with serial casting. We also aimed to assess its use in conjunction with botulinum toxin in patients with spastic cerebral palsy. Material and method: This longitudinal retrospective study included a sample of 95 Achilles tendons of children attended in a children's rehabilitation clinic between 2012 and 2018, with ankle dorsal flexion less than  $10^\circ$ , treated by a cycle of serial casts with or without botulinum toxin. The variables analysed were sex, year when treatment started, age, BMI, diagnosis, previous and/or later treatment, spasticity (modified Ashworth), laterality, active and passive joint range of dorsal and plantar flexion along with R1 (Tardieu). Measurements were carried out with a mechanical inclinometer prior to the first, second and third cast, after the third cast and at 2, 8 and 14 months. The statistical analysis was performed with SPSS®. Results: There was a statistically significant improvement of  $10.02^\circ$  between passive dorsal flexion prior to the first cast and after the third cast, which remained at  $6.66^\circ$  ( $P=.02$ ) between the former and after 14 months. Conclusions: Serial casting is an effective method in the management of equinus of any aetiology and has a minimal complication rate.

PMID: [33771381](#)

### 9. Systematic Review of Fatigue in Individuals With Cerebral Palsy

Luca Puce, Ilaria Pallecchi, Karim Chamari, Lucio Marinelli, Tiziano Innocenti, Riccardo Pedrini, Laura Mori, Carlo Trompetto

Front Hum Neurosci. 2021 Mar 15;15:598800. doi: 10.3389/fnhum.2021.598800. eCollection 2021.

In this systematic review, we collected and analyzed literature works comparing self-reported fatigue and objectively-measured fatigue in individuals with cerebral palsy (CP) and in age-matched typically developing/typically developed (TD) controls (Healthy). The search was conducted on four electronic databases/platforms (PubMed, Web of Science, Cochrane Library, and Scopus) using the key words "cerebral palsy" combined with "fatig\*," where the asterisk was used as a wildcard. As a critical appraisal tool, the Joanna Briggs Institute Critical Appraisal Checklist for Quasi-Experimental Studies (2017) was used. A total of 22 studies passed the critical appraisal rating and were included in both narrative and quantitative analyses. The overall evidence quality of the findings was considered very good. Data of objectively-measured fatigue in performing maximal fatiguing tasks indicated lower fatigue levels in participants with CP, possibly due to their pathological inability to recruit highly fatigable muscle fibers. Highly trained individuals with CP and TD controls performing maximal fatiguing tasks seem to be an exception to this, as they exhibited similar levels of fatigue. In submaximal fatiguing tasks, including daily physical activities, either objectively-measured or self-reported fatigue was higher in participants with CP than in TD controls, indicating a lower ability for development of neurophysiological compensation for fatigue among participants with CP. Further studies on fatigue are needed to gain an insight into the multifold mechanisms of fatigue in individuals with CP. Understanding fatigue mechanisms could help in setting up strategies for effective intervention programs, with benefits in healthcare and improved quality of life of individuals with CP. Systematic Review Registration: [PROSPERO 2019], identifier [CRD42019143524].

PMID: [33790748](#)

### **10. White Paper by the European Society for Swallowing Disorders: Screening and Non-instrumental Assessment for Dysphagia in Adults**

Renée Speyer, Reinie Cordier, Daniele Farneti, Weslania Nascimento, Walmari Pilz, Eric Verin, Margaret Walshe, Virginie Woisard

Dysphagia. 2021 Mar 31;1-17. doi: 10.1007/s00455-021-10283-7. Online ahead of print.

This White Paper by the European Society for Swallowing Disorders (ESSD) reports on the current state of screening and non-instrumental assessment for dysphagia in adults. An overview is provided on the measures that are available, and how to select screening tools and assessments. Emphasis is placed on different types of screening, patient-reported measures, assessment of anatomy and physiology of the swallowing act, and clinical swallowing evaluation. Many screening and non-instrumental assessments are available for evaluating dysphagia in adults; however, their use may not be warranted due to poor diagnostic performance or lacking robust psychometric properties. This white paper provides recommendations on how to select best evidence-based screening tools and non-instrumental assessments for use in clinical practice targeting different constructs, target populations and respondents, based on criteria for diagnostic performance, psychometric properties (reliability, validity, and responsiveness), and feasibility. In addition, gaps in research that need to be addressed in future studies are discussed. The following recommendations are made: (1) discontinue the use of non-validated dysphagia screening tools and assessments; (2) implement screening using tools that have optimal diagnostic performance in selected populations that are at risk of dysphagia, such as stroke patients, frail older persons, patients with progressive neurological diseases, persons with cerebral palsy, and patients with head and neck cancer; (3) implement measures that demonstrate robust psychometric properties; and (4) provide quality training in dysphagia screening and assessment to all clinicians involved in the care and management of persons with dysphagia.

PMID: [33787994](#)

### **11. Dental age and skeletal maturity assessment in patients with cerebral palsy**

Nemanja Marinkovic, Ksenija Zelic, Petar Milovanovic, Jovana Milutinovic, Marija Djuric, Angelina Nikodijevic Latinovic, Nenad Nedeljkovic

Eur J Oral Sci. 2021 Mar 30:e12780. doi: 10.1111/eos.12780. Online ahead of print.

The aims of this study were to calculate the estimated dental age and the degree of skeletal maturity in patients with cerebral palsy and control patients (i.e., without a diagnosis of cerebral palsy) and to compare the findings with the chronological age of patients in both study groups. In this cross-sectional study, the European formula and the Willems method were used to estimate the dental age of 52 patients with cerebral palsy and 104 control patients, all aged between 7 and 15 years. For all patients, their estimated dental age was compared with their chronological age. The degree of skeletal maturity of 35 patients with cerebral palsy and 104 control patients was estimated according to Baccetti's method. There was no statistically significant difference in the deviation of the estimated dental age from the chronological age between patients with cerebral palsy and control patients when the European formula or the Willems method was applied. No difference was found in the frequency of Baccetti's stages between patients with cerebral palsy and control patients in the same age category, for both sexes. To estimate dental age in patients with cerebral palsy, the European formula is preferable for orthodontic purposes and the Willems method is preferable for forensic purposes. Using Baccetti's method it was not possible to detect potential differences in skeletal maturity between patients with cerebral palsy and controls.

PMID: [33786880](#)

### **12. Cerebral palsy and the data of pain**

Amanda K Greene

Dev Med Child Neurol. 2021 Mar 31. doi: 10.1111/dmcn.14877. Online ahead of print.

PMID: [33786830](#)

### 13. Caregiver-Reported Pain Management Practices for Individuals With Cerebral Palsy

Abigail M Raiter, Chantel C Burkitt, Alyssa Merbler, Lisa Lykken, Frank J Symons

Arch Rehabil Res Clin Transl. 2021 Jan 18;3(1):100105. doi: 10.1016/j.arrct.2021.100105. eCollection 2021 Mar.

**Objective:** To investigate types and intensity of pain experienced by individuals with cerebral palsy (CP) and common pain-relieving approaches used by caregivers. **Design:** The approach was cross-sectional, using standardized interviews. **Setting:** Individuals with CP were recruited from a specialty health care hospital. **Participants:** Eighty-six individuals (N=86; mean age, 17.2 years; male, 58%) with CP and complex communication needs participated. **Interventions:** Not applicable. **Main outcome measures:** Pain type, mean pain intensity (MPI) (graded on a scale of 0=no pain to 10=worst possible pain), and mean pain relief (MPR) (graded on a scale of 0=intervention did not help at all to 10=intervention completely relieved pain) were assessed by caregiver report as part of the Dalhousie Pain Interview for each type of pain experienced in the previous 7 days. **Results:** Caregivers reported that 58 participants (67%) had experienced pain in the previous 7 days. MPI was  $7.7 \pm 1.8$  when the pain was worst in the previous 7 days. The 2 most common types of pain included musculoskeletal pain (n=70) and gastrointestinal pain (n=11). The most frequent treatment to relieve musculoskeletal pain was changing positions (n=27, MPI= $5.1 \pm 2.3$ , MPR= $6.6 \pm 2.1$ ), medication (n=25, MPI= $7.4 \pm 1.6$ , MPR= $5.3 \pm 1.9$ ), and massage (n=19, MPI= $6.7 \pm 1.9$ , MPR= $5.2 \pm 1.7$ ). To treat gastrointestinal pain, medication was typically used (n=4, MPI= $4.8 \pm 1.4$ , MPR= $5.5 \pm 1.0$ ), although no treatment was just as common (n=4, MPI= $4.5 \pm 2.3$ ). **Conclusions:** The results indicate that musculoskeletal pain is prevalent in individuals with CP, and changing physical positions and providing medication are strategies most used by caregivers.

PMID: [33778478](#)

### 14. Repeated onabotulinum neurotoxin A injections for drooling in children with neurodisability

Stijn Bekkers, Theresa Ys Leow, Karen Van Hulst, Lynn B Orriëns, Arthur Rt Scheffer, Frank Ja Van Den Hoogen

Dev Med Child Neurol. 2021 Mar 27. doi: 10.1111/dmcn.14872. Online ahead of print.

**Aim:** To evaluate the effect of repeated onabotulinum neurotoxin A injections for the treatment of drooling in children with neurodisabilities. **Method:** This was a retrospective cohort study, in which the first, second, and third onabotulinum neurotoxin A injection were compared within children treated between 2000 and 2020. Primary outcomes included drooling quotient, visual analogue scale (VAS), and treatment success defined as  $\geq 50\%$  reduction in drooling quotient and/or VAS 8 weeks after treatment. Each outcome was obtained at baseline and 8 weeks posttreatment. **Results:** Seventy-seven children were included (mean age at first injection: 8y 3mo, SD 3y 7mo, range 3-17y; 44 males, 33 females; 51.9% with cerebral palsy, 45.5% wheelchair-bound). The objective (drooling quotient) and subjective (VAS) effect after the second injection was lower compared to the first injection. The third injection showed less objective and significantly less subjective effect compared to the first injection. An overall success rate of 74.0%, 41.6%, and 45.8% were found for the first, second, and third injection respectively. **Interpretation:** Although onabotulinum neurotoxin A remained effective throughout the entire treatment course, there is less effect of subsequent onabotulinum neurotoxin A injections compared to the first. Although there might be a loss of effect after repeated injections, there is continued improvement for most children.

PMID: [33772779](#)

### 15. The Role of Cognitive Control and Emotion Regulation in Predicting Mental Health Problems in Children with Neurodevelopmental Disorders

Diana Tajik-Parvinchi, Linda Farmus, Paula Tablon Modica, Robert A Cribbie, Jonathan A Weiss

Child Care Health Dev. 2021 Mar 27. doi: 10.1111/cch.12868. Online ahead of print.

**Background:** Many youth with neurodevelopmental disorders experience mental health problems such as anxiety, depression, or anger and these are often associated with impairments of cognition and emotion regulation. The mechanisms that may be

linking cognitive difficulties, emotion regulation, and mental health are not known. Aims: The current study examined whether adaptive and maladaptive (dysregulated) emotion regulation mediated the link between different cognitive control processes (working memory, inhibition, and shifting) and internalizing/externalizing symptoms in children with neurodevelopmental disorders. Methods: Participants included 48 children (8-13 years of age) with one or more diagnoses of autism, attention deficit hyperactivity disorder, cerebral palsy, and learning disability, who were enrolled in a larger study of cognitive behaviour therapy targeting emotion regulation. Multiple mediation analyses were implemented using the PROCESS macro. The mediation effects of adaptive and maladaptive emotion regulation were examined on the relationships between (1) working memory and internalizing/externalizing symptoms, (2) inhibition and internalizing/externalizing symptoms, and (3) shifting and internalizing/externalizing symptoms. All data was collected prior to intervention, at baseline. Results: Shifting, inhibitory control, and working memory predicted increased emotion dysregulation, which functioned as a full mediator to both internalizing and externalizing problems in children with NDD. Conclusion: In the presence of emotionally triggering situations, children with greater cognitive challenges experience greater maladaptive emotion regulation, which results in both internalizing and externalizing problems. For youth with neurodevelopmental disorders, therapeutic plans that include strengthening of working memory, inhibition, and shifting abilities in addition to emotion regulation skills training may be helpful in alleviating externalizing and internalizing behaviour.

PMID: [33772823](#)

### **16. Performance Variability During Motor Learning of a New Balance Task in a Non-immersive Virtual Environment in Children With Hemiplegic Cerebral Palsy and Typically Developing Peers**

Minxin Cheng, Michael Anderson, Danielle E Levac

Front Neurol. 2021 Mar 15;12:623200. doi: 10.3389/fneur.2021.623200. eCollection 2021.

Background: Motor impairments contribute to performance variability in children with cerebral palsy (CP) during motor skill learning. Non-immersive virtual environments (VEs) are popular interventions to promote motor learning in children with hemiplegic CP. Greater understanding of performance variability as compared to typically developing (TD) peers during motor learning in VEs may inform clinical decisions about practice dose and challenge progression. Purpose: (1) To quantify within-child (i.e., across different timepoints) and between-child (i.e., between children at the same timepoint) variability in motor skill acquisition, retention and transfer in a non-immersive VE in children with CP as compared to TD children; and (2) To explore the relationship between the amount of within-child variability during skill acquisition and learning outcomes. Methods: Secondary data analysis of 2 studies in which 13 children with hemiplegic CP and 67 TD children aged 7-14 years undertook repeated trials of a novel standing postural control task in acquisition, retention and transfer sessions. Changes in performance across trials and sessions in children with CP as compared to TD children and between younger (7-10 years) and older (11-14 years) children were assessed using mixed effects models. Raw scores were converted to z-scores to meet model distributional assumptions. Performance variability was quantified as the standard deviation of z-scores. Results: TD children outperformed children with CP and older children outperformed younger children at each session. Older children with CP had the least between-child variability in acquisition and the most in retention, while older TD children demonstrated the opposite pattern. Younger children with CP had consistently high between-child variability, with no difference between sessions. Within-child variability was highest in younger children, regardless of group. Within-child variability was more pronounced in TD children as compared to children with CP. The relationship between the amount of within-child variability in performance and performance outcome at acquisition, retention and transfer sessions was task-specific, with a positive correlation for 1 study and a negative correlation in the other. Conclusions: Findings, though preliminary and limited by small sample size, can inform subsequent research to explore VE-specific causes of performance variability, including differing movement execution requirements and individual characteristics such as motivation, attention and visuospatial abilities.

PMID: [33790848](#)

### **17. Home Use of a Percutaneous Wireless Intracortical Brain-Computer Interface by Individuals With Tetraplegia**

John D Simeral, Thomas Hosman, Jad Saab, Sharlene N Flesher, Marco Vilela, Brian Franco, Jessica Kelemen, David M Brandman, John G Ciancibello, Paymon G Rezaei, Emad N Eskandar, David M Rosler, Krishna V Shenoy, Jaimie M Henderson, Arto V Nurmikko, Leigh R Hochberg

IEEE Trans Biomed Eng. 2021 Mar 30;PP. doi: 10.1109/TBME.2021.3069119. Online ahead of print.

Objective: Individuals with neurological disease or injury such as amyotrophic lateral sclerosis, spinal cord injury or stroke

may become tetraplegic, unable to speak or even locked-in. For people with these conditions, current assistive technologies are often ineffective. Brain-computer interfaces are being developed to enhance independence and restore communication in the absence of physical movement. Over the past decade, individuals with tetraplegia have achieved rapid on-screen typing and point-and-click control of tablet apps using intracortical brain-computer interfaces (iBCIs) that decode intended arm and hand movements from neural signals recorded by implanted microelectrode arrays. However, cables used to convey neural signals from the brain tether participants to amplifiers and decoding computers and require expert oversight, severely limiting when and where iBCIs could be available for use. Here, we demonstrate the first human use of a wireless broadband iBCI. Methods: Based on a prototype system previously used in pre-clinical research, we replaced the external cables of a 192-electrode iBCI with wireless transmitters and achieved high-resolution recording and decoding of broadband field potentials and spiking activity from people with paralysis. Two participants in an ongoing pilot clinical trial completed on-screen item selection tasks to assess iBCI-enabled cursor control. Results: Communication bitrates were equivalent between cabled and wireless configurations. Participants also used the wireless iBCI to control a standard commercial tablet computer to browse the web and use several mobile applications. Within-day comparison of cabled and wireless interfaces evaluated bit error rate, packet loss, and the recovery of spike rates and spike waveforms from the recorded neural signals. In a representative use case, the wireless system recorded intracortical signals from two arrays in one participant continuously through a 24-hour period at home. Significance: Wireless multi-electrode recording of broadband neural signals over extended periods introduces a valuable tool for human neuroscience research and is an important step toward practical deployment of iBCI technology for independent use by individuals with paralysis. On-demand access to high-performance iBCI technology in the home promises to enhance independence and restore communication and mobility for individuals with severe motor impairment.

PMID: [33784612](#)

### **18. Exploration of multimodal alternative access for individuals with severe motor impairments: Proof of concept**

Kelsey Mandak, Janice Light, Savanna Brittlebank-Douglas

Assist Technol. 2021 Mar 29. doi: 10.1080/10400435.2021.1910375. Online ahead of print.

Many individuals with complex communication needs and severe motor impairments are unable to control technologies through conventional means and require alternative access techniques to achieve accurate and efficient access. With current alternative access techniques, individuals with severe motor impairments are limited in that they can only use one access technique at a time. The purpose of this project was to test proof of concept of a new multimodal access technique which integrated eye gaze and single switch scanning selection techniques. The aims were to investigate the learning patterns of two adults with severe cerebral palsy when first introduced to the multimodal access technique and then to compare the accuracy and efficiency of multimodal to single-modality access when selecting targets on an AAC visual scene display. The participants learned to use the multimodal access technique; they demonstrated improvements in their accuracy of selection across sessions and attained at least 80% accuracy within 3-15 training sessions. Both participants achieved similar accuracy with multimodal access compared to single-modality, but took longer to select targets with multimodal access compared to single-modality. The potential utility of multimodal access is explored as well as important avenues for future research.

PMID: [33780326](#)

### **19. Data linkage and pain medication in people with cerebral palsy: a cross-sectional study**

Elena Guiomar García Jalón, Aideen Maguire, Oliver Perra, Anna Gavin, Dermot O'Reilly, Allen Thurston

Dev Med Child Neurol. 2021 Mar 31. doi: 10.1111/dmcn.14854. Online ahead of print.

Aim: To explore data linkage and pain medication as a proxy for pain, to assess differences in pain medication between the cerebral palsy (CP) and the general populations, and to identify factors associated with pain medication in CP. Method: This cross-sectional study linked the Northern Ireland CP Register and two administrative health care databases for people resident in Northern Ireland born between 1981 and 2008. Pain medication as a proxy was validated by replicating analyses from the Study of Participation of Children with Cerebral Palsy Living in Europe (SPARCLE) studies. Logistic regression compared pain medication in the CP and general populations. Multi-level regression models assessed factors associated with pain medication in the CP cohort. Results: The sample size was 701 075, of whom 1430 (0.2%) were people with CP. There were 358 969 males and 340 677 females in the general population, and 810 males and 620 females in the CP population, with an age range of 4 to 31 years in both groups. The validation exercise produced results similar to the SPARCLE studies. More people with CP received pain medication (61% vs 50.9%) and had twice the odds of being prescribed opioid analgesics (odds



ratio [OR]=2.81, 95% confidence interval [CI] 2.32-3.40). Among those with CP, the odds of being prescribed pain medication were higher for: females (OR=1.34, 95% CI 1.06-1.70), younger age (OR=1.60, 95% CI 1.02-2.51), Gross Motor Function Classification System level V (OR=2.60, 95% CI 1.52-4.47), seizures (OR=2.55, 95% CI 1.68-3.87), and higher deprivation score (OR=2.06, 95% CI 1.41-3.24). Interpretation: Pain medication is an effective proxy for pain. More people with CP were prescribed pain medication than the general population. Pain medication for people with CP is not only dependent on physiological and clinical characteristics, but also environmental factors.

PMID: [33786820](#)

## **20. Changes in walking ability, intellectual disability, and epilepsy in adults with cerebral palsy over 50 years: a population-based follow-up study**

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Dev Med Child Neurol. 2021 Mar 27. doi: 10.1111/dmcn.14871. Online ahead of print.

**Aim:** To determine if walking ability and presence of intellectual disability and epilepsy change from childhood to 50 years of age in individuals with cerebral palsy (CP), and if such changes are related to age, sex, or CP subtype. **Method:** This was a population-based follow-up study of 142 adults born from 1959 to 1978 (82 males, 60 females; mean age 48y 4mo, range 37-58y; 44% unilateral, 35% bilateral, 17% dyskinetic, and 4% ataxic CP) listed in the CP register of western Sweden. We compared childhood data with a follow-up assessment in 2016. **Results:** At follow-up, walking ability had changed significantly ( $p < 0.001$ ). The proportion of participants walking without aids had decreased from 71% to 62%, and wheelchair ambulation increased from 18% to 25%. Walking ability was related to subtype ( $p = 0.001$ ), but not to age, sex, pain, fatigue, or body mass index. The proportion classified as having intellectual disability had increased from 16% to 22% ( $p = 0.039$ ) and the proportion with epilepsy from 9% to 18% ( $p = 0.015$ ). Of those with childhood epilepsy, 46% were seizure-free without medication. **Interpretation:** Walking ability and the presence of intellectual disability and epilepsy had changed significantly since childhood. Life-long access to specialized health care is warranted for re-evaluation of impairments, treatment, and assistance.

PMID: [33772773](#)

## **21. Perspectives of children and adolescents with cerebral palsy about involvement as research partners: a qualitative study**

C Cavens, C Imms, G Drake, N Garrity, M Wallen

Disabil Rehabil. 2021 Mar 28;1-10. doi: 10.1080/09638288.2021.1900927. Online ahead of print.

**Purpose:** Children and adolescents with cerebral palsy have diverse needs and often engage with healthcare services, including paediatric rehabilitation. Partnering with these children and adolescents on research projects to inform practice has the potential to ensure services continue to remain relevant and appropriate. This study aimed to identify what children and adolescents with cerebral palsy suggest are effective ways for researchers to involve them as partners in research. **Materials and methods:** This qualitative study was guided by interpretive description. Children and adolescents with cerebral palsy between 8 and 18 years participated in semi-structured, activity-based focus groups or interviews. Verbatim transcripts were coded and analysed using thematic analysis. One member of the research team was a young woman with cerebral palsy. **Results:** Seventeen children and adolescents with cerebral palsy from NSW and Victoria (Australia) were involved. Participants were between 8 and 18 years (mean = 12 years), male ( $n = 11$ ) and female ( $n = 6$ ). Analysis identified four nested themes: "insider knowledge", "reasons for involvement", "roles in research" and "facilitating partnership". **Conclusion:** This study identified perspectives of children and adolescents on their involvement as research partners, and considerations for researchers to facilitate involvement of children and adolescents with cerebral palsy as partners in research. **IMPLICATIONS FOR REHABILITATION** The commitment in healthcare to client-centred practice requires that consumers, including children and young people with cerebral palsy, have opportunities to influence the direction of research which impacts them. Children and young people with cerebral palsy are interested in research partnerships and motivated to be involved in various areas of research. Effective research partnerships with younger populations can be facilitated by researchers acknowledging a child or young person's expertise, and employing strategies relating to open communication, flexibility and support.

PMID: [33779451](#)

## 22. Comparing multi-attribute utility instruments: CP-6D, a Cerebral palsy specific instrument, vs AQoL-4D

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Expert Rev Pharmacoecon Outcomes Res. 2021 Mar 28. doi: 10.1080/14737167.2021.1909477. Online ahead of print.

**Background:** Economic-evaluations of Cerebral palsy (CP) were based on utility estimates of health-related quality of life (HRQoL) from generic multi-attribute utility instruments (MAUIs). However, generic instruments had limited use as they could not capture some of the important aspects of living with CP. The Cerebral palsy 6 Dimension (CP-6D) is a disease specific MAUI. In this study, we compared the results of CP-6D with the Assessment of Quality of Life (AQoL-4D), a generic MAUI, and tested the criterion validity of the CP-6D in the general population. **Methods:** An online survey of the Australian general population (n=2002), who completed both the AQoL-4D and CP-6D MAUIs, was conducted. Validity was assessed from the correlations between the domains, items and instruments. ANOVA and t-tests were used to assess the instrument's discrimination in different social demographic categories. **Results:** There was a moderate correlation between the instruments (0.64). Differences in socio-demographic characteristics showed a medium effect size ( $p < 0.001$ ) in both instruments and had a similar effect on utility weights in both instruments. Although, the CP-6D was more sensitive to changes in income and education. **Conclusions:** Our results suggest that CP-6D and AQoL-4D were measuring a similar underlying construct. Both instruments responded similarly to socio-demographic differences.

PMID: [33779449](#)

## 23. The predictive value of 'red flags' as milestones of psychomotor development of premature babies - preliminary study

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Ann Agric Environ Med. 2021 Mar 18;28(1):183-188. doi: 10.26444/aaem/126746. Epub 2020 Sep 11.

**Introduction:** Premature babies are a special group at risk of persistent brain damage caused by diseases, the most serious of which are cerebral palsy (CP), autism spectrum disorders (ASD) and mental retardation, among others. These conditions may occur concurrently, but appear more often as separate disease syndromes in the same group of at-risk children. Long-term observation of psychomotor development by an interdisciplinary medical team closely cooperating with parents is necessary. It is important to detect the risk of developing these diseases as soon as possible in all development spheres. **Material and methods:** The research was conducted to demonstrate the prognostic value of 'red flags' of developmental milestones and the ability to detect early signs of risk of developing CP and ASD in extremely premature babies. In this preliminary study, 42 preterm babies, born after less than 32 weeks pregnancy participated. **Results:** The occurrence of 'red flags' in the spheres: gross motor, fine motor and cognitive at 9 months was strongly associated with their presence at 24 months. The sensitivity and specificity were: gross motor - 0.91 (95% CI: 0.59, 1.00) and 0.94 (95% CI: 0.79, 0.99); fine motor - 0.83 (95% CI: 0.36-1.00) and 1.00 (95% CI: 0.90-1.00); cognitive - 1.00 (0.40, 1.00) and 0.97 (0.86, 1.00). Other spheres had lower sensitivity but high specificity. **Conclusions:** The conclusion is that the 'red flags' at the 9 months milestones already predict the normal or developmental delay of premature babies, and predict the risk of CP and ASD. Due to the availability and lack of the need for specialized and costly training, it is worth considering their use in everyday life medical practice.

PMID: [33775086](#)

## 24. Surviving and Thriving: Early Intervention for Neonatal Survivors With Developmental Disability in Uganda

Cally J Tann, Maya Kohli-Lynch, Ruth Nalugya, Samantha Sadoo, Karen Martin, Rachel Lassman, Carol Nanyunja, Margaret Musoke, Margaret Sewagaba, Margaret Nampijja, Janet Seeley, Emily L Webb

Infants Young Child. 2021 Jan;34(1):17-32. doi: 10.1097/IYC.000000000000182. Epub 2020 Nov 20.

Global attention on early child development, inclusive of those with disability, has the potential to translate into improved action for the millions of children with developmental disability living in low- and middle-income countries. Nurturing care is crucial for all children, arguably even more so for children with developmental disability. A high proportion of survivors of

neonatal conditions such as prematurity and neonatal encephalopathy are affected by early child developmental disability. The first thousand days of life is a critical period for neuroplasticity and an important window of opportunity for interventions, which maximize developmental potential and other outcomes. Since 2010, our group has been examining predictors, outcomes, and experiences of neonatal encephalopathy in Uganda. The need for an early child intervention program to maximize participation and improve the quality of life for children and families became apparent. In response, the "ABAaNA early intervention program," (now re-branding as 'Baby Ubuntu') a group participatory early intervention program for young children with developmental disability and their families, was developed and piloted. Piloting has provided early evidence of feasibility, acceptability, and impact and a feasibility trial is underway. Future research aims to develop programmatic capacity across diverse settings and evaluate its impact at scale.

PMID: [33790497](#)

### **25. A connectome-based approach to assess motor outcome after neonatal arterial ischemic stroke**

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Ann Clin Transl Neurol. 2021 Mar 30. doi: 10.1002/acn3.51292. Online ahead of print.

**Objective:** Studies of motor outcome after Neonatal Arterial Ischemic Stroke (NAIS) often rely on lesion mapping using MRI. However, clinical measurements indicate that motor deficit can be different than what would solely be anticipated by the lesion extent and location. Because this may be explained by the cortical disconnections between motor areas due to necrosis following the stroke, the investigation of the motor network can help in the understanding of visual inspection and outcome discrepancy. In this study, we propose to examine the structural connectivity between motor areas in NAIS patients compared to healthy controls in order to define the cortical and subcortical connections that can reflect the motor outcome. **Methods:** Thirty healthy controls and 32 NAIS patients with and without Cerebral Palsy (CP) underwent MRI acquisition and manual assessment. The connectome of all participants was obtained from T1-weighted and diffusion-weighted imaging. **Results:** Significant disconnections in the lesioned and contra-lesioned hemispheres of patients were found. Furthermore, significant correlations were detected between the structural connectivity metric of specific motor areas and manuality assessed by the Box and Block Test (BBT) scores in patients. **Interpretation:** Using the connectivity measures of these links, the BBT score can be estimated using a multiple linear regression model. In addition, the presence or not of CP can also be predicted using the KNN classification algorithm. According to our results, the structural connectome can be an asset in the estimation of gross manual dexterity and can help uncover structural changes between brain regions related to NAIS.

PMID: [33787079](#)

### **26. Intra-amniotic inflammatory complications in preterm prelabor rupture of membranes and long-term neurodevelopmental outcomes of infants: a systematic review**

Hana Burckova, Jaroslav Stranik, Ivana Musilova, Jana Matulova, Bo Jacobsson, Marian Kacerovsky

J Matern Fetal Neonatal Med. 2021 Mar 29;1-6. doi: 10.1080/14767058.2021.1903859. Online ahead of print.

**Objective:** To perform a systematic review of the literature available on the association between the presence of microbial invasion of the amniotic cavity (MIAC) and/or intra-amniotic inflammation and long-term neurodevelopmental outcomes of infants from pregnancies complicated by preterm prelabor rupture of membranes (PPROM). **Methods:** A literature search, from their earliest entries to May 2020, was performed by employing three electronic databases (Web of Science, PubMed, and Scopus). The selection criteria were as follows: (1) singleton pregnancies with PPRM; (2) available information regarding MIAC and/or intra-amniotic inflammation; (3) long-term (at least one year of the corrected age) neurodevelopmental outcomes of respective infants. **Results:** The initial search identified 10,953 articles, of which 8 were selected for full-text reading; however, none were included in the review owing to the following reasons: (i) spontaneous preterm labor with intact membranes and/or indicated (iatrogenic) preterm delivery were included in the studies without providing separate data for PPRM (n = 5); (ii) long-term, at least one year of the corrected age, neurodevelopmental outcomes of infants were not assessed (n = 1); (iii) the presence of both the abovementioned reasons (n = 1); (iv) amniotic fluid was not assessed, and a long-term neurodevelopmental outcome was not evaluated (n = 1). **Conclusion:** The literature search provides evidence of a knowledge gap in the association between the presence of MIAC and/or intra-amniotic inflammation and long-term neurodevelopmental outcomes in infants with PPRM.

PMID: [33781152](#)

### 27. Extracellular Vesicles and Preeclampsia: Current Knowledge and Future Research Directions

Carlos Palma, Jessica Jellins, Andrew Lai, Alexis Salas, America Campos, Shayna Sharma, Gregory Duncombe, Jon Hyett, Carlos Salomon

Subcell Biochem. 2021;97:455-482. doi: 10.1007/978-3-030-67171-6\_18.

Preeclampsia (PE) is associated with long-term morbidity in mothers and lifelong morbidities for their children, ranging from cerebral palsy and cognitive delay in preterm infants, to hypertension, diabetes and obesity in adolescents and young adults. There are several processes that are critical for development of materno-fetal exchange, including establishing adequate perfusion of the placenta by maternal blood, and the formation of the placental villous vascular tree. Recent studies provide persuasive evidence that placenta-derived extracellular vesicles (EVs) represent a significant intercellular communication pathway, and that they may play an important role in placental and endothelial cell (both fetal and maternal) function. These functions are known to be altered in PE. EVs can carry and transport a wide range of bioactive molecules that have potential to be used as biomarkers and therapeutic delivery tools for PE. EV content is often parent cell specific, thus providing an insight or "thumbprint" of the intracellular environment of the originating cell (e.g., human placenta). EVs have been identified in plasma under both normal and pathological conditions, including PE. The concentration of EVs and their content in plasma has been reported to increase in association with disease severity and/or progression. Placenta-derived EVs have been identified in maternal plasma during normal pregnancy and PE pregnancies. They contain placenta-specific proteins and miRNAs and, as such, may be differentiated from maternally-derived EVs. The aim of this review, thus, is to describe the potential roles of EVs in preeclampsia pregnancies, focussing on EVs secreted from placental cells. The biogenesis, specificity of placental EVs, and methods used to characterise EVs in the context of PE pregnancies will be also discussed.

PMID: [33779928](#)

### 28. Folic acid alleviates jaundice of phenylhydrazine (PHA)-induced neonatal rats by reducing Lys-homocysteinylation of albumin

Hong-Qian Wang, Er-Liang Kong, Xia Zhang, Xiao-Yan Meng, Jin-Min Zhang, Wei-Feng Yu, Fei-Xiang Wu

Cell Biol Toxicol. 2021 Mar 31. doi: 10.1007/s10565-021-09602-3. Online ahead of print.

Neonatal jaundice is a common symptom that occurs in neonates during the first month of their life and is generally divided into physiological and pathological subtypes. In serious cases, pathological neonatal jaundice frequently shows complications including seizures, cerebral palsy, and kernicterus. However, due to the unclear pathogenesis of pathological neonatal jaundice, effective drugs for this disease remain unsatisfied. In the present study, we first estimated the protective effects of folic acid (FA) on phenylhydrazine (PHA) or homocysteine (Hcy)-injected neonatal rats (2-3 days aged). Intriguingly, we found that FA significantly decreased the elevated total bilirubin (TBIL) and direct bilirubin (DBIL) concentration, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) activity in PHA- or Hcy-injected rats, indicating that FA improves liver functions. Meanwhile, our results also showed that the plasma Hcy level and N-homocysteinylation (N-Hcy) modification of albumin were significantly elevated in the jaundice rats, which were obviously reversed after FA administration. Furthermore, we identified a novel N-Hcy modification site K545 of human serum albumin (HSA) using LC-MS/MS, and the mutagenesis assay in HEK293 further validated these observations. Besides, we demonstrated that the N-Hcy modification of albumin functionally inhibits the bilirubin-binding ability of albumin without altering its protein level both in vitro and in vivo. Altogether, we highlight a mechanism that FA reduces the plasma Hcy level and thereby enhance the bilirubin-binding ability of albumin, which may provide a novel therapeutic strategy for the treatment of pathological neonatal jaundice.

PMID: [33788065](#)

### 29. Clinical and biochemical footprints of inherited metabolic disease. V. Cerebral palsy phenotypes

Gabriella A Horvath, Nenad Blau, Carlos R Ferreira

Review Mol Genet Metab. 2021 Mar 13;S1096-7192(21)00071-8. doi: 10.1016/j.ymgme.2021.03.008. Online ahead of print.

Cerebral palsy is the most common physical disability of childhood describing a heterogeneous group of neurodevelopmental disorders that cause activity limitation, but often are accompanied by disturbances of sensation, perception, cognition, communication and behavior, or by epilepsy. Inborn errors of metabolism have been reported in the literature as presenting with features of cerebral palsy. We reviewed and updated the list of metabolic disorders known to be associated with symptoms suggestive of cerebral palsy and found more than 150 relevant IEMs. This represents the fifth of a series of articles attempting to create and maintain a comprehensive list of clinical and metabolic differential diagnosis according to system involvement.

PMID: [33775522](#)

### **30. Can we delineate brain injury in full-term neonates using serum biomarkers?**

Nikolaos Efstathiou, Aristidis Slavakis, Vasiliki Drossou, Katerina Kantziou, Vasiliki Dermetzoglou, Vasiliki Soubasi

Brain Inj. 2021 Mar 29;1-10. doi: 10.1080/02699052.2021.1907862. Online ahead of print.

**OBJECTIVE:** Early identification of neonates at risk of neurological impairment is particularly important for the bedside clinician. Clinical value of S100b and neuron-specific enolase in neonates has not been yet established. We investigated their kinetics and possible early clinical utility in neonatal encephalopathy (NE). **STUDY DESIGN:** 36 full-term neonates (13 with moderate/severe encephalopathy, 11 with mild encephalopathy, 12 controls) were enrolled and studied prospectively. Serum S100b and neuron-specific enolase (NSE) were measured serially on days(d) 1, 3, 9 and 18 of life. Brain MRI and long-term neurodevelopmental outcome were also assessed. **RESULT:** Neonates with moderate/severe encephalopathy had significantly increased S100b (d1) and NSE levels (d1, d3, d9) compared to controls. Neuron-specific enolase significantly correlated with the degree of encephalopathy, and a cutoff of 38.8 µg/l (d1) accurately predicted moderate/severe encephalopathy. S100b (d1) cutoff points of 1.6 µg/l and 11.4 µg/l prognosticated severe encephalopathy and death/cerebral palsy, respectively. Both biomarkers correlated well with neuroimaging and Bayley-III scores. **CONCLUSION:** Combined clinical, laboratory, imaging and neurodevelopmental data indicate that serum S100b and NSE can be useful biomarkers for the diagnosis and prognosis of neonatal brain injury, providing useful information to the bedside clinician.

PMID: [33780304](#)