

Monday 27 April 2015

**Cerebral Palsy Alliance** is delighted to bring you this free weekly bulletin of the latest published research into cerebral palsy. Our organisation is committed to supporting cerebral palsy research worldwide - through information, education, collaboration and funding. Find out more at [www.cpresearch.org.au](http://www.cpresearch.org.au)

**Professor Nadia Badawi AM**

Macquarie Group Foundation Chair of Cerebral Palsy

[Subscribe to CP Research News](#)

## Interventions and Management

1. *J Biomed Opt.* 2015 Apr;20(4):46009. doi: 10.1117/1.JBO.20.4.046009.

**Evaluation of cortical plasticity in children with cerebral palsy undergoing constraint-induced movement therapy based on functional near-infrared spectroscopy.**

Cao J1, Khan B1, Hervey N1, Tian F1, Delgado MR2, Clegg NJ3, Smith L3, Roberts H3, Tulchin-Francis K3, Shierk A3, Shagman L4, MacFarlane D4, Liu H1, Alexandrakis G1.

PMID: [25900145](#) [PubMed - in process]

2. *Drug Des Devel Ther.* 2015 Apr 1;9:1913-1926.

**Clinical and pharmacological properties of incobotulinumtoxinA and its use in neurological disorders.**

Jost WH1, Benecke R2, Hauschke D3, Jankovic J4, Kaňovský P5, Roggenkämper P6, Simpson DM7, Comella CL8.

**BACKGROUND:** IncobotulinumtoxinA (Xeomin®) is a purified botulinum neurotoxin type A formulation, free from complexing proteins, with proven efficacy and good tolerability for the treatment of neurological conditions such as blepharospasm, cervical dystonia (CD), and post-stroke spasticity of the upper limb. This article provides a comprehensive overview of incobotulinumtoxinA based on randomized controlled trials and prospective clinical studies. **SUMMARY:** IncobotulinumtoxinA provides clinical efficacy in treating blepharospasm, CD, and upper-limb post-stroke spasticity based on randomized, double-blind, placebo-controlled trials with open-label extension periods (total study duration up to 89 weeks). Adverse events were generally mild or moderate. The most frequent adverse events, probably related to the injections, included eyelid ptosis and dry eye in the treatment of blepharospasm, dysphagia, neck pain, and muscular weakness in patients with CD, and injection site pain and muscular weakness when used for treating spasticity. In blepharospasm and CD, incobotulinumtoxinA was investigated in clinical trials permitting flexible intertreatment intervals based on the individual patient's clinical need; the safety profile of intervals shorter than 12 weeks was comparable to intervals of 12 weeks and longer. There were no cases of newly formed neutralizing antibodies during the Phase III and IV incobotulinumtoxinA trials. Phase III head-to-head trials of incobotulinumtoxinA versus onabotulinumtoxinA for the treatment of blepharospasm and CD have demonstrated therapeutic equivalence of both formulations. Additional Phase III trials of incobotulinumtoxinA in conditions such as lower-limb spasticity, spasticity in children with cerebral palsy, and sialorrhea in various neurological disorders are ongoing. **CONCLUSION:** IncobotulinumtoxinA is an effective, well-tolerated botulinum neurotoxin type A formulation. Data from randomized clinical trials and further observational studies are expected to help physicians to optimize treatment by tailoring the choice of formulation, dose, and treatment intervals to the patient's clinical needs.

[PMID: 25897202](#) [PubMed - as supplied by publisher] PMCID: PMC4389813 Free PMC Article

### 3. Orthopedics. 2015 Apr 1;38(4):e248-52. doi: 10.3928/01477447-20150402-50.

#### Treatment of hip subluxation in skeletally mature patients with cerebral palsy.

Oetgen ME, Ayyala H, Martin BD.

Hip subluxation is common in children with spastic cerebral palsy. Most physicians favor intervention to treat hip subluxation in skeletally immature patients with cerebral palsy. However, treatment in skeletally mature patients with cerebral palsy is controversial. The goal of this study was to evaluate radiographic and clinical outcomes after hip reconstruction in skeletally mature patients with cerebral palsy. The authors performed a retrospective review of all skeletally mature patients (n=20) with cerebral palsy who underwent hip surgery for subluxation at the authors' institution between 2005 and 2011. Charts were reviewed for demographic characteristics, procedure, follow-up, and complications. Acetabular index, migration index, and neck-shaft angle were measured on preoperative and most recent radiographs. Average follow-up was 2.2 years. Average migration index for the entire group improved from 57% to 20% (P<.0001). Of patients who had all radiographic abnormalities addressed at surgery (varus derotational femoral osteotomy for neck-shaft angle >135°, open reduction for migration index >50%, and acetabular osteotomy for acetabular index >25°), 91% had a final migration index of less than 25%. In patients who did not have all radiographic abnormalities addressed, 33% had a migration index of less than 25% at final follow-up. No intraoperative complications occurred; however, 13 patients had at least 1 postoperative complication. Hip subluxation in skeletally mature patients with cerebral palsy is difficult to treat and is associated with a high incidence of complications. The likelihood of a successful outcome appears to be related to the appropriateness of the surgical procedure. When all radiographic abnormalities were addressed during surgery, a successful radiographic outcome at final follow-up was much more likely than when intervention was less comprehensive. [Orthopedics. 2015; 38(4):e248-e252].

Copyright 2015, SLACK Incorporated.

[PMID: 25901615](#) [PubMed - in process]

### 4. Phys Ther. 2015 Apr 23. [Epub ahead of print]

#### Therapist-Designed Adaptive Riding in Children With Cerebral Palsy: Results of a Feasibility Study.

Angsupaisal M1, Visser B2, Alkema A3, Meinsma M4, Maathuis CG5, Reinders-Messelink H6, Hadders-Algra M7.

**BACKGROUND:** It is debatable whether adaptive riding (AR) in children with cerebral palsy (CP) does improve postural control and gross motor development. **OBJECTIVE:** To explore feasibility of an extensive assessment protocol for a randomized controlled trial on therapist designed AR in children with CP aiming to assess effects on child outcomes and working mechanisms of sitting postural control. **DESIGN:** Pre-Post group design with two baseline measurements. **METHODS:** Six children (one girl, five boys; 6-12 years; median 8 years 9 months) with bilateral spastic CP, GMFCS level III participated. Outcome was evaluated three times (T0, T1, T2) at 6 weeks intervals. T0 and T1 were baseline measurements; between T1 and T2 therapist designed AR-intervention including an integrated program of postural challenge exercises (2x per week during 1 hour) was applied. The complex protocol included GMFM-88 and EMG-recording of postural muscle activity during reaching while sitting (EMG at T1 and T2 only). **RESULTS:** The protocol was feasible. Median GMFM scores changed from 64.4 (T0) to 66.7 (T1; p=0.075) and from 66.7 (T1) to 73.2 (T2; p=0.028). The change scores of all children exceeded the minimal clinically important differences (MCIDs) of the GMFM-88. Five out of six children showed a decrease in stereotyped top-down recruitment between T1 and T2 (p=0.173). **LIMITATIONS:** Lack of control group, small sample size and potential assessor bias for all but the EMG parameters, are study limitations. **CONCLUSION:** Feasibility of the complex protocol was established. The data suggest that 6-week therapist designed AR-intervention may improve gross motor function and may reduce stereotyped postural adjustments in children with CP. The limited results beg for replication in a well-powered RCT.

© 2015 American Physical Therapy Association.

[PMID: 25908525](#) [PubMed - as supplied by publisher]

#### 5. *Pediatr Surg Int.* 2015 Apr 17. [Epub ahead of print]

##### **Percutaneous endoscopic gastrostomy (PEG) does not worsen vomiting in children.**

Kakade M1, Coyle D, McDowell DT, Gillick J.

**PURPOSE:** We aimed to evaluate the rate and examine potential predictors of subsequent anti-reflux procedures in a population undergoing percutaneous endoscopic gastrostomy (PEG) insertion. **MATERIALS:** We retrospectively reviewed the pre- and post-operative clinical course of patients undergoing PEG insertion over a 10-year period with respect to indication, underlying co-morbidity, and GER investigation and management. **RESULTS:** We reviewed data on 170 patients. Neurological disability (e.g., cerebral palsy) was the most common underlying condition in those undergoing PEG insertion (n = 104) followed by cystic fibrosis (n = 29). Oropharyngeal dysphagia and failure to thrive were the commonest indications for PEG. Eight patients (4.7 %) reported increased frequency of vomiting after PEG, 6 (75 %) of whom had a pre-operative diagnosis of GER. Two (25 %) patients from this subgroup subsequently required anti-reflux surgery. Patient's with neurological disease were not at increased risk of new-onset GER or increased vomiting following PEG insertion compared to those with non-neurological conditions (p = 0.259). In total, 8 (4.7 %) and 7 (4.1 %) patients underwent fundoplication and gastrojejunal tube insertion, respectively. **CONCLUSIONS:** PEG insertion does not appear to induce symptomatic gastro-oesophageal reflux in the majority of children, suggesting that in the majority of cases, a concurrent anti-reflux procedure is unnecessary. Parents should be counseled accordingly.

[PMID: 25895072](#) [PubMed - as supplied by publisher]

#### 6. *J Physiol Anthropol.* 2015 Apr 24;34(1):17. [Epub ahead of print]

##### **Effects of seat surface inclination on respiration and speech production in children with spastic cerebral palsy.**

Shin HK1, Byeon EJ2, Kim SH3.

**BACKGROUND:** Respiratory and speech problems are commonly observed in children with cerebral palsy (CP). The purpose of this study was to identify if inclination of seat surface could influence respiratory ability and speech production in children with spastic diplegic CP. **METHODS:** Sixteen children with spastic diplegic CP, ages 6 to 12 years old, participated in this study. The subjects' respiratory ability (forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), peak expiratory flow (PEF), and maximum phonation time (MPT)) were measured in three sitting conditions: a seat surface inclined 0°, anterior 15°, and posterior 15°. **RESULTS:** FVC was significantly different across three inclinations of seat surface,  $F(2, 45) = 3.81, P = 0.03$ . In particular, the subjects' FVC at a seat surface inclined anterior 15° was significantly greater than at a seat surface inclined posterior 15° ( $P < 0.05$ ). However, FEV1, PEF, and MPT were not significantly affected by seat surface inclination ( $P > 0.05$ ). **CONCLUSIONS:** The results suggest that anterior inclination of seat surface may provide a positive effect on respiratory function in children with spastic diplegic CP.

[PMID: 25907023](#) [PubMed - as supplied by publisher] Free full text

#### 7. *Dev Neurorehabil.* 2015 Apr 23:1-13. [Epub ahead of print]

##### **Interarticular coordination in children with and without cerebral palsy.**

Nip IS1.

The current study investigates how interarticular coordination changes across speaking tasks varying in articulatory and linguistic demands for children with CP and their typically-developing peers. Articulatory movements from 12 children with spastic CP (7M, 5F, 4-15 years of age) and 12 typically-developing age- and sex-matched peers were cross-correlated to determine the degree of spatial and temporal coupling between the upper lip and jaw, lower lip and jaw, and upper and lower lips. Spatial and temporal coupling were also correlated with

intelligibility. Results indicated that children with CP have reduced spatial coupling between the upper and lower lips and reduced temporal coupling between all articulators as compared to their typically-developing peers. For all participants, sentences were produced with the greatest degree of interarticulator coordination when compared to the diadochokinetic and syllable repetition tasks. Measures of interarticulator coordination were correlated with intelligibility for the speakers with CP.

[PMID: 25905558](#) [PubMed - as supplied by publisher]

#### **8. Augment Altern Commun. 2015 Apr 22:1-12. [Epub ahead of print]**

##### **Designing AAC Research and Intervention to Improve Outcomes for Individuals with Complex Communication Needs.**

Light J1, Mcnaughton D.

There is a rapidly growing body of research that demonstrates the positive effects of augmentative and alternative communication (AAC) intervention on the communication of children and adults with complex communication needs. Despite the positive impact of many AAC interventions, however, many individuals with complex communication needs continue to experience serious challenges participating in educational, vocational, healthcare, and community environments. In this paper, we apply the framework proposed by the International Classification of Functioning, Disability and Health (ICF) to illustrate the need to re-think AAC intervention to improve outcomes for individuals with complex communication needs, and to foster a new generation of intervention research that will provide a solid foundation for improved services. Specifically, the paper emphasizes the need to take a more holistic view of communication intervention and highlights the following key principles to guide AAC intervention and research: (a) build on the individual's strengths and focus on the integration of skills to maximize communication, (b) focus on the individual's participation in real-world contexts, (c) address psychosocial factors as well as skills, and (d) attend to extrinsic environmental factors as well as intrinsic factors related to the individual who requires AAC.

[PMID: 25904008](#) [PubMed - as supplied by publisher]

## **Prevention and Cure**

#### **9. BMC Res Notes. 2015 Apr 23;8(1):166. [Epub ahead of print]**

##### **Cerebral palsy in children in Kampala, Uganda: clinical subtypes, motor function and co-morbidities.**

Kakooza-Mwesige A1,2, Forssberg H3, Eliasson AC4, Tumwine JK5.

**BACKGROUND:** Cerebral palsy (CP) is a common chronic childhood disorder worldwide. There is limited information about the CP panorama in sub-Saharan Africa. Our aim was to describe the clinical subtypes, gross and fine motor functions and presence of co-morbidities in a group of children with CP attending a tertiary hospital in Uganda. **METHODS:** Children with CP in the age range of 2-12 years visiting the paediatric CP clinic at Mulago Hospital, Kampala, were enrolled. Screening and inclusion were based on a three-stage procedure: i) Two screening questions from the Ten Question Screen; ii) Clinical assessments adapted from the Surveillance for Cerebral Palsy in Europe (SCPE); iii) Clinical examinations and diagnoses of subtype, severity level and co-morbidities. Caregivers were interviewed using questionnaires to provide information on child's medical history and co-morbidities. Co-morbidity scores were calculated for each child. **RESULTS:** One hundred and thirty five children with CP were enrolled (72 males, 63 females, median age 3 years 5 months, IQR-2 years 4 months-5 years 6 months). Bilateral spastic type was commonest (45%); moderate impairment in gross motor function was present in 43%, with comparable numbers (37%) in the mild and severely impaired fine motor function groups. The severe gross and fine motor function levels were seen in the bilateral spastic and dyskinetic CP subtypes. Signs of learning disability (75%) and epilepsy (45%) were the commonest co-morbidities. Higher co-morbidity scores were obtained in children with dyskinetic CP and severe levels of gross and fine motor function. There was a significant difference in distribution of the co-morbidity scores between the CP subtypes, gross motor and fine motor function levels (p

<0.001). Signs of speech and language impairments were associated with bilateral spastic CP and severe gross and fine motor dysfunction ( $p < 0.05$ ). CONCLUSIONS: Bilateral spastic CP was the main clinical subtype, with signs of learning disability and epilepsy as major causes of co-morbidity. The severity of gross and fine motor function levels was related to severity of clinical CP subtypes. Our findings imply a higher occurrence of birth asphyxia or post natively acquired infections. Improvement in emergency obstetric and postnatal care may reduce this burden.

[PMID: 25902796](#) [PubMed - as supplied by publisher] Free full text

**10. Dev Med Child Neurol. 2015 Apr 21. doi: 10.1111/dmcn.12772. [Epub ahead of print]**

**Disentangling racial and ethnic disparities in cerebral palsy.**

Oskoui M1.

[PMID: 25900384](#) [PubMed - as supplied by publisher]

**11. Arch Dis Child Fetal Neonatal Ed. 2015 Apr 20. pii: fetalneonatal-2014-307655. doi: 10.1136/archdischild-2014-307655. [Epub ahead of print]**

**Antenatal magnesium sulfate: Neuro-protection for preterm infants.**

Oddie S1, Tuffnell DJ2, McGuire W3.

The neuro-protective effect of antenatal magnesium sulfate on very preterm infants has been demonstrated in good-quality randomised controlled trials and meta-analyses. Magnesium administered prior to preterm delivery crosses over to the foetal circulation and acts via several pathways to reduce perinatal neuronal damage. Meta-analysis of the trial data indicates that antenatal magnesium sulfate reduces the risk of cerebral palsy by one-third, and results in one fewer case in every 50 women treated. Treatment is associated with discomfort and flushing in some women, but maternal side-effects are mostly transient and manageable. Magnesium sulfate has also been found to be without any serious adverse consequences in newborn infants. Consensus recommendations and guidelines have been developed and implemented internationally, and endorsed by the UK Royal College of Obstetricians and Gynaecologists. However, magnesium sulfate for neuro-protection of very preterm infants has not yet become established widely in UK practice. Paediatricians, neonatologists and advocacy groups for preterm infants and their families could contribute to raising awareness and engage in dissemination activities and implementation initiatives to develop local protocols for adoption of this safe, effective and cost-effective intervention to reduce the burden of cerebral palsy in children born very preterm.

Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to <http://group.bmj.com/group/rights-licensing/permissions>.

[PMID: 25896966](#) [PubMed - as supplied by publisher]

**12. J Matern Fetal Neonatal Med. 2015 Apr 20:1-4. [Epub ahead of print]**

**Antenatal magnesium sulfate and neurodevelopmental outcome of preterm infants born to preeclamptic mothers.**

Bozkurt O1, Eras Z, Canpolat FE, Oguz SS, Uras N, Dilmen U.

OBJECTIVE: Previous studies demonstrated that magnesium sulfate is associated with better neurological outcome and decreased cerebral palsy rates in preterm newborns. The aim of this study is to assess the effects of antenatal magnesium sulfate on neurodevelopmental outcomes of preterm infants. METHODS: Preterm newborns with a gestational age of <32 weeks whose mothers were diagnosed with preeclampsia were extracted from the hospital records and files retrospectively. The neurodevelopmental assessment was performed at 2 years of age by developmental pediatrician. The results of the infants exposed to antenatal magnesium sulfate were compared with the control group. RESULTS: Between the years 2010 and 2012, 387 preterm babies were born to preeclamptic

mothers. Fifty-nine (15.2%) of them were exposed to antenatal magnesium sulfate. The main clinical characteristics did not differ between the groups. On the other hand, cerebral palsy was significantly lower in preterm infants exposed to magnesium sulfate compared to the control group (3.3% and 12.2%, respectively,  $p = 0.004$ ). On multinomial logistic regression analysis, magnesium sulfate was not an independent significant factor to reduce CP on its own. **CONCLUSION:** Antenatal magnesium sulfate can be used as a neuroprotective strategy especially for the prevention of cerebral palsy in preterm infants. Future studies should be designed to support the positive effect of antenatal magnesium sulfate on neurologic development.

[PMID: 25893546](#) [PubMed - as supplied by publisher]

### **13. Pediatrics. 2015 Apr 20. pii: peds.2014-1520. [Epub ahead of print]**

#### **Incidence and Outcomes of Symptomatic Neonatal Arterial Ischemic Stroke.**

Grunt S1, Mazenauer L2, Buerki SE2, Boltshauser E3, Mori AC4, Datta AN5, Fluss J6, Mercati D7, Keller E8, Maier O9, Poloni C10, Ramelli GP11, Schmitt-Mechelke T12, Steinlin M2.

**BACKGROUND AND OBJECTIVES:** Neonatal arterial ischemic stroke (NAIS) is associated with considerable lifetime burdens such as cerebral palsy, epilepsy, and cognitive impairment. Prospective epidemiologic studies that include outcome assessments are scarce. This study aimed to provide information on the epidemiology, clinical manifestations, infarct characteristics, associated clinical variables, treatment strategies, and outcomes of NAIS in a prospective, population-based cohort of Swiss children. **METHODS:** This prospective study evaluated the epidemiology, clinical manifestations, vascular territories, associated clinical variables, and treatment of all full-term neonates diagnosed with NAIS and born in Switzerland between 2000 and 2010. Follow-up was performed 2 years (mean 23.3 months, SD 4.3 months) after birth. **RESULTS:** One hundred neonates (67 boys) had a diagnosis of NAIS. The NAIS incidence in Switzerland during this time was 13 (95% confidence interval [CI], 11-17) per 100 000 live births. Seizures were the most common symptom (95%). Eighty-one percent had unilateral (80% left-sided) and 19% had bilateral lesions. Risk factors included maternal risk conditions (32%), birth complications (68%), and neonatal comorbidities (54%). Antithrombotic and antiplatelet therapy use was low (17%). No serious side effects were reported. Two years after birth, 39% were diagnosed with cerebral palsy and 31% had delayed mental performance. **CONCLUSIONS:** NAIS in Switzerland shows a similar incidence as other population-based studies. About one-third of patients developed cerebral palsy or showed delayed mental performance 2 years after birth, and children with normal mental performance may still develop deficits later in life.

Copyright © 2015 by the American Academy of Pediatrics.

[PMID: 25896840](#) [PubMed - as supplied by publisher]

### **14. Gynecol Obstet Fertil. 2015 Apr 17. pii: S1297-9589(15)00091-0. doi: 10.1016/j.gyobfe.2015.03.017. [Epub ahead of print]**

[C. Racinet et al. in reply to the correspondence by D. Philopoulos concerning their article: Can caesarean delivery prevent cerebral palsy?

Medico-legal implications of a French ecological study. *Gynecol Obstet Fertil* 2015;43:8-12 [Article in French] Racinet C1.

[PMID: 25899116](#) [PubMed - as supplied by publisher]

### **15. Gynecol Obstet Fertil. 2015 Apr 16. pii: S1297-9589(15)00086-7. doi: 10.1016/j.gyobfe.2015.03.012. [Epub ahead of print]**

D. Philopoulos in reply to the article by C. Racinet et al.: Can cesarean delivery prevent cerebral palsy? Medico-legal implications of a French ecological study. *Gynecol Obstet Fertil* 2015;43:8-12 [Article in French] Philopoulos D1.

[PMID: 25892106](#) [PubMed - as supplied by publisher]