Cerebral Palsy ALLIANCE

NEWS
Cerebral Palsy Research

Monday 6 February 2012

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. This free weekly bulletin is just one of our activities. Please find out more at www.cpresearch.org.au

Professor Nadia Badawi
Macquarie Group Foundation Chair of Cerebral Palsy
PO Box 560, Darlinghurst, New South Wales 2010 Australia

Interventions and Management

1. J Neurosurg Pediatr. 2012 Feb;9(2):209-15.

Effects of intrathecal baclofen therapy on motor and cognitive functions in a rat model of cerebral palsy.

Nomura S, Kagawa Y, Kida H, Maruta Y, Imoto H, Fujii M, Suzuki M.

Departments of Neurosurgery.

Object: Cerebral palsy (CP) arises in the early stages of brain development and manifests as spastic paresis that is often associated with cognitive dysfunction. Available CP treatments are aimed at the management of spasticity and include botulinum toxin administration, selective dorsal rhizotomy, and intrathecal baclofen (ITB). In this study, the authors investigated whether the management of spasticity with ITB therapy affected motor function and whether the release of spasticity was associated with an improvement in intellectual function. Methods: Newborn Sprague-Dawley rats were divided into the following groups: control, CP model, and CP model with ITB therapy. For the CP model, postnatal Day 7 (P7) rats were exposed to hypoxic conditions (8% O(2)) for 150 minutes after ligation of the right common carotid artery. In the groups receiving ITB therapy, a spinal catheter was connected to an osmotic pump filled with baclofen and placed in the spinal subarachnoid space on P21 in the early group and on P35 in the late group. A daily dose of 12 μg of baclofen was continuously administered until P49, resulting in 28 days of therapy in the early group and 14 days in the late group. Changes in spasticity in the CP and CP with ITB treatment groups were confirmed by assessing the motor evoked potential in the plantar muscle. Results: In the CP group, the time required to complete a beam-walking test on P49 was significantly longer than that in the control and ITB treatment groups (4.15 ± 0.60 vs 2.10 ± 0.18 and 2.22 ± 0.22 seconds, respectively). Results of the beam-walking test are expressed as the mean ± SD. Radial arm maze performance on P49 indicated that spatial reference memory had significantly deteriorated in the CP group compared with controls (2.33 ± 0.87 vs 0.86 ± 0.90 points); moreover, working memory was also negatively affected by CP (0.78 ± 1.09 vs 0.14 ± 0.38 points). Results of the memory tests are expressed as the mean ± SE. These memory functions did not recover after ITB treatment. Conclusions: Management of spasticity with ITB therapy improved the walking ability in the rat CP model. Intrathecal baclofen therapy-which reduces harmful sensory and motor stimulations caused by spasticity to more optimal levels-contributed to motor function recovery; however, it had no effect on intellectual recovery as assessed by memory performance in the rat CP model.

PMID: 22295929 [PubMed - in process]

2. Arch Dis Child Educ Pract Ed. 2012 Jan 31. [Epub ahead of print]

Feeding difficulties in children with cerebral palsy.

Andrew MJ, Parr JR, Sullivan PB.

Department of Paediatrics, John Radcliffe Hospital, University of Oxford, Oxford, UK.

Feeding difficulties are common in children with cerebral palsy and have an effect on growth, nutritional state, general health, social interaction and behaviour and developmental outcomes. Many factors have an effect on feeding ability. Identification of these factors and amelioration of their impact on feeding difficulties is essential to promote adequate growth and nutrition. Appropriate assessment and management is best achieved by a multiprofessional team skilled in the care of children with cerebral palsy and feeding impairments. Feeding difficulties must be considered within the wider context of family and social circumstance.

PMID: 22293504 [PubMed - as supplied by publisher]

3. Ther Clin Risk Manag. 2012;8:15-23. Epub 2012 Jan 25.

Randomized Phase III evaluation of the efficacy and safety of a novel glycopyrrolate oral solution for the management of chronic severe drooling in children with cerebral palsy or other neurologic conditions.

Zeller RS, Lee HM, Cavanaugh PF, Davidson J.

Blue Bird Circle Clinic for Pediatric Neurology at Texas Children's Hospital and Baylor College of Medicine, Houston, TX, USA.

AIM: To evaluate the efficacy of glycopyrrolate oral solution (1 mg/5 mL) in managing problem drooling associated with cerebral palsy and other neurologic conditions. METHOD: Thirty-eight patients aged 3-23 years weighing at least 27 lb (12.2 kg) with severe drooling (clothing damp 5-7 days/week) were randomized to glycopyrrolate (n = 20), 0.02-0.1 mg/kg three times a day, or matching placebo (n = 18). Primary efficacy endpoint was responder rate, defined as percentage showing ≥3-point change on the modified Teacher's Drooling Scale (mTDS). RESULTS: Responder rate was significantly higher for the glycopyrrolate (14/19; 73.7%) than for the placebo (3/17; 17.6%) group (P = 0.0011), with improvements starting 2 weeks after treatment initiation. Mean improvements in mTDS at week 8 were significantly greater in the glycopyrrolate than in the placebo group (3.94 ± 1.95 vs 0.71 ± 2.14 points; P < 0.0001). In addition, 84% of physicians and 100% of parents/caregivers regarded glycopyrrolate as worthwhile compared with 41% and 56%, respectively, for placebo (P ≤ 0.014). Most frequently reported treatment-emergent adverse events (glycopyrrolate vs placebo) were dry mouth, constipation, and vomiting. INTERPRETATION: Children aged 3-16 years with problem drooling due to neurologic conditions showed a significantly better response, as assessed by mTDS, to glycopyrrolate than to placebo. CLINICALTRIALS.GOV IDENTIFIER: NCT00425087.

PMID: 22298950 [PubMed - in process] PMCID: PMC3269347

4. Ther Clin Risk Manag. 2012;8:25-32. Epub 2012 Jan 25.

Safety and efficacy of glycopyrrolate oral solution for management of pathologic drooling in pediatric patients with cerebral palsy and other neurologic conditions.

Zeller RS, Davidson J, Lee HM, Cavanaugh PF.

Texas Children's Hospital, Baylor College of Medicine, Houston, TX.

BACKGROUND: The purpose of this study was to assess the safety and efficacy of oral glycopyrrolate solution 1 mg/5 mL for 24 weeks in pediatric patients with chronic moderate-to- severe drooling associated with cerebral palsy and other neurologic conditions. METHODS: In this multicenter, open-label, 24-week study, males and females aged 3-18 years weighing at least 27 lb received oral glycopyrrolate solution, starting at 0.02 mg/kg three times

daily and titrated in increments of 0.02 mg/kg every 5-7 days for 4 weeks to an optimal maintenance dose or a maximum dose of 0.1 mg/kg, but not exceeding 3 mg three times daily. Safety was assessed by description and tabulation of all adverse events. The primary efficacy endpoint was response, defined as at least a three-point change from baseline to week 24 on the modified Teacher's Drooling Scale. RESULTS: Of 137 intent-to-treat participants, 10 (7.3%) received the maximum dose of 0.1 mg/kg three times daily; 122 (89%) had at least one treatment-emergent adverse event, 47% related to oral glycopyrrolate solution, with most being mild-to-moderate in intensity. The most commonly reported treatment-emergent adverse events were constipation (20.4%), vomiting (17.5%), diarrhea (17.5%), pyrexia (14.6%), dry mouth (10.9%), flushing (10.9%), and nasal congestion (10.9%). Nineteen patients (13.9%) discontinued treatment due to an adverse event, but no adverse event was specifically associated with discontinuation. Two patients had clinically significant toxicity grade shifts, one each in platelet count and calcium concentration. No deaths occurred on treatment; deaths of three patients (multisystem organ failure, anoxic encephalopathy, and aspiration pneumonia) within 30 days of their last dose were not considered to be treatment-related. At 24 weeks, 52.3% (95% confidence interval 43.7-60.9) of patients were responders, with at least a three-point decrease in modified Teacher's Drooling Scale from baseline, with 83.5% of parents/caregivers and 85.8% of investigators rating oral glycopyrrolate solution as being worthwhile. CONCLUSION: Oral glycopyrrolate solution 1 mg/5 mL for chronic moderate-to-severe drooling associated with cerebral palsy or other neurologic conditions was well tolerated over 24 weeks by pediatric patients aged 3-18 years.

PMID: 22298951 [PubMed - in process] PMCID: PMC3269348

5. Dev Med Child Neurol. 2012 Jan 28. doi: 10.1111/j.1469-8749.2011.04199.x. [Epub ahead of print]

The effect of virtual reality interventions on physical activity in children and adolescents with early brain injuries including cerebral palsy.

Mitchell L, Ziviani J, Oftedal S, Boyd R.

Queensland Cerebral Palsy and Rehabilitation Research Centre, School of Medicine, Faculty of Health Sciences, The University of Queensland, Queensland. Royal Children's Hospital, Herston, Brisbane, Queensland. Queensland Children's Medical Research Institute, Royal Children's Hospital, Brisbane. School of Health and Rehabilitation Sciences, The University of Queensland, Queensland, Australia.

PMID: 22283557 [PubMed - as supplied by publisher]

6. Technol Health Care. 2012 Jan 1;20(1):1-9.

A combination of Botulinum Toxin A therapy and Functional Electrical Stimulation in children with cerebral palsy - A pilot study.

Galen S, Wiggins L, McWilliam R, Granat M.

Bioengineering Unit, University of Strathclyde, Glasgow, UK.

Background: Among the ambulant population of children with spastic cerebral palsy (CP), dynamic equinus is one of the most common form of gait deviation that is encountered. Objective: To investigate the combined effects of Functional Electrical Stimulation (FES) and Botulinum Toxin A (BTXA) therapy in children with spastic CP, and to demonstrate the feasibility of this combination therapy. Methods: A single-subject design with repeated measures was adopted. Eight children (six males, two females; mean age 7 y 9 mo, SD 1 y 5 mo; range 7 y to 11 y) diagnosed with hemiplegic (n=6) or diplegic (n=2) spastic CP completed the study. Each subject participated in the study for twenty weeks. This period consisted of baseline (one week), BTXA phase (three weeks), first FES phase (four weeks), first control phase (four weeks), second FES phase (four weeks) and second control phase (four weeks). Subjects were assessed at the end of each phase. The ankle angle at the end of swing phase was selected as the primary outcome measure. The secondary outcome measure recorded was the foot contact pattern. Results: There was an increase in ankle dorsiflexion at the end of the combined intervention in most subjects (n=6), accompanied by an improvement in foot contact pattern. Conclusions: This pilot study demonstrated that it is feasible to combine BTXA therapy with FES in ambulant children with spastic CP.

PMID: 22297709 [PubMed - in process]

7. Dev Neurorehabil. 2012 Feb 1. [Epub ahead of print]

Short- and long-term effects of synchronized metronome training in children with hemiplegic cerebral palsy: A two case study.

Johansson AM, Domellöf E, Rönnqvist L.

Department of Psychology, Umeå University , Umeå , Sweden.

Background: Children with cerebral palsy (CP) require individualized long-term management to maintain and improve motor functions. The objective of this study was to explore potential effects of synchronized metronome training (SMT) on movement kinematics in two children diagnosed with spastic hemiplegic CP (HCP). Method: Both children underwent 4-weeks/12 sessions of SMT by means of the Interactive Metronome (IM). Optoelectronic registrations of goal-directed uni- and bimanual upper-limb movements were made at three occasions; pre-training, post completed training and at 6-months post completed training. Results: Significant changes in kinematic outcomes following IM training were found for both cases. Findings included smoother and shorter movement trajectories in the bimanual condition, especially for the affected side. In the unimanual condition, Case I also showed increased smoothness of the non-affected side. Conclusions: The observed short- and long-term effects on the spatio-temporal organization of upper-limb movements need to be corroborated and extended by further case-control studies.

PMID: 22296344 [PubMed - as supplied by publisher]

8. Gait Posture. 2012 Jan 31. [Epub ahead of print]

Automated method to distinguish toe walking strides from normal strides in the gait of idiopathic toe walking children from heel accelerometry data.

Pendharkar G, Percival P, Morgan D, Lai D.

Department of Electrical and Computer Systems Engineering, Monash University, Clayton Campus, Melbourne, Australia.

Toe walking mainly occurs in children due to medical condition or physical injury. When there are no obvious signs of any medical condition or physical injury, a diagnosis of Idiopathic Toe Walking (ITW) is made. ITW children habitually walk on their toes, however can modify their gait and walk with a heel-toe gait if they want to. Correct gait assessment in ITW children therefore becomes difficult. To solve this problem, we have developed an automated way to assess the gait in ITW children using a dual axis accelerometer. Heel acceleration data was recorded from the gait of ITW children using boots embedded with the sensor in the heel and interfaced to a handheld oscilloscope. An innovative signal processing algorithm was developed in IgorPro to distinguish toe walking stride from normal stride using the acceleration data. The algorithm had an accuracy of 98.5%. Based on the statistical analysis of the heel accelerometer data, it can be concluded that the foot angle during mid stance in ITW children tested, varied from 36° to 11.5° while as in normal children the foot stance angle is approximately zero. This algorithm was later implemented in a system (embedded in the heel) which was used remotely to differentiate toe walking stride from normal stride. Although the algorithm classifies toe walking stride from normal stride in ITW children, it can be generalized for other applications such as toe walking in Cerebral Palsy or Acquired Brain Injury subjects. The system can also be used to assess the gait for other applications such as Parkinson's disease by modifying the algorithm.

PMID: 22300731 [PubMed - as supplied by publisher]

9. J Pediatr Orthop B. 2012 Mar;21(2):167-9.

A hip resurfacing implant in an adolescent with cerebral palsy.

Roche AJ, Davies GR, Sampath J.

Alder Hey Childrens NHS Foundation Trust, Liverpool, UK.

Pain or skin irritation due to the femoral stump after proximal femoral resection for chronic spastic hip dislocation in children with severe cerebral palsy may be encountered. We describe a technique that, to our knowledge, has been unreported earlier and can deal with this phenomenon to improve the patient's comfort level and help the patient to sit more comfortably.

PMID: 22301430 [PubMed - in process]

10. Clin Orthop Relat Res. 2012 Jan 31. [Epub ahead of print]

50 Years Ago in CORR: The Role of the Orthopaedic Surgeon in the Management of Cerebral Palsy S. Ralph Terhune MD, Paul W. Shannon MD, Fred H. Devane MD, J. Carter Denton MD CORR 1958;11:132-173.

Brand RA, Dabney KW.

Clinical Orthopaedics and Related Research, 1600 Spruce Street, Philadelphia, PA, 19103, USA, eic@clinorthop.org.

PMID: 22290133 [PubMed - as supplied by publisher]

11. Dev Neuropsychol. 2012 Jan;37(1):30-50.

Specific memory impairment following neonatal encephalopathy in term-born children.

van Handel M, de Sonneville L, de Vries LS, Jongmans MJ, Swaab H.

Child and Adolescent Psychiatry , University Medical Center Utrecht , Utrecht , Netherlands.

This study examines short-term memory, verbal working memory, episodic long-term memory, and intelligence in 32 children with mild neonatal encephalopathy (NE), 39 children with moderate NE, 10 children with NE who developed cerebral palsy (CP), and 53 comparison children, at the age of 9 to 10 years. Results: in addition to a global effect on intelligence, NE had a specific effect on verbal working memory, verbal and visuo-spatial long-term memory, and learning, which was associated with degree of NE. Although these memory problems occurred in children without CP, they were more pronounced when children had also developed CP.

PMID: 22292830 [PubMed - in process]

12. Psychosomatics. 2012 Jan 31. [Epub ahead of print]

Recurrent Self-Limited Hyperthermia Following ECT for Catatonia in a Young Man with Cerebral Palsy.

Bation R, Devic P, Lambrinidis A, Damasceno C, D'Amato T, Poulet E.

Université de Lyon, Lyon, F-69003, France; Université Lyon 1, Lyon, EA4166, France; CH Le Vinatier, Bron, F-69677, France; Institut Fédératif des Neurosciences de Lyon (IFNL), Hôpital neurologique, Bron, F-69394, France.

PMID: 22300947 [PubMed - as supplied by publisher]

13. J Paediatr Child Health. 2011 Sep;47(9):599-602. doi: 10.1111/j.1440-1754.2011.02159.x.

Ethical considerations in paediatric neurology: neuromuscular disease and epilepsy.

Bodensteiner JB, Ng YT.

Division of Pediatric Neurology, Barrow Neurological Institute/St. Joseph's Children's Health Center, Phoenix, Arizona, United States.

The pace of developing technology with respect to many diagnostic tests, as well as available treatments including artificial ventilation, may have progressed at a faster rate than our ethical, humane ability to decide on the optimal choices for our patients. In fact, who should make these choices; physicians or patients and families? Certain ethical aspects of neuromuscular disorders and epilepsy are reviewed. For neuromuscular disease, the example of Duchenne muscular dystrophy (DMD) with regards to genetic testing, relatively early wheelchair placement and individualised invasive ventilation is discussed. In epilepsy, performing neurosurgery in severely impaired children is probably appropriate in some cases if desired by the family. Financial and human costs restrict therapies and testing for epilepsy as well as other neurological and medical diseases. Whether it is ethical to consider costs in medical treatment or not, it is certainly a reality.

PMID: 21951440 [PubMed - indexed for MEDLINE]

14. Endocr Pract. 2012 Jan 31:1-9. [Epub ahead of print]

Sitagliptin in GAD antibody positive diabetes mellitus.

Kandasamy N, Lennox G, Annamalai AK, Maguire G, Adler AI.

Wolfson Diabetes and Endocrine Clinic, Institute of Metabolic Science.

Background: Sitagliptin, an inhibitor of dipeptidyl peptidase 4 (DPP-4), is currently approved for the treatment of type 2 diabetes mellitus. We describe a case illustrating the use of sitagliptin in anti- gamma amino butyric acid (GAD) antibody positive diabetes mellitus in association with a rare ataxic variant of stiff person syndrome (SPS).Case report: A 68 year old Japanese female presented with poorly controlled "type 2" diabetes mellitus, cerebral palsy, cerebellar ataxia and hypothyroidism. She complained of stiffness and spasms. Antidiabetic medications included gliclazide, rosiglitazone and acarbose; different insulins had been tried but stopped as they worsened her stiffness and spasms. The glycosylated haemoglobin (HbA1c) remained above 9% despite maximum doses of the above-listed oral hypoglycaemic agents. After starting sitagliptin, her HbA1c decreased from 9.3% (78mmol/mol) to 7.3% (56mmol/mol) in five months. Investigations confirmed an ataxic variant of SPS. 18 months later her anti-GAD antibody levels had fallen by approximately 85%.Conclusions: Apart from the well known mechanism of an increase in GLP-1 sitagliptin may exert its glucose lowering effect by other mechanisms in patients with autoimmune diabetes. Further studies are required to address the utility of DPP4-inhibitors in non-type 2 diabetes.

PMID: 22297059 [PubMed - as supplied by publisher]

Prevention and Cure

15. J Obstet Gynaecol. 2012 Feb;32(2):135-40.

Treatment with magnesium sulphate in pre-term birth: A systematic review and meta-analysis of observational studies.

Wolf HT, Hegaard HK, Greisen G, Huusom L, Hedegaard M.

Department of Abdominal Surgery , Nykøbing Falster Sygehus.

Premature birth increases a child's risk of cerebral palsy and death. The aim of this work is to investigate the association between treatment with magnesium sulphate during premature deliveries and infants' cerebral palsy and mortality through a meta-analysis of observational studies. A comprehensive search of the Cochrane Library, EMBASE and the PubMed database from their inceptions to 1 October, 2010 using the keywords 'magnesium sulphate, children/infant/pre-term/premature and cerebral palsy/mortality/morbidity/adverse effects/outcome' identified 11 reports of observational studies. Two authors working independently extracted the data. A meta-analysis of the data found an association between magnesium sulphate treatment and a significantly reduced risk of mortality (RR 0.73; 95% CI 0.61-0.89) and cerebral palsy (OR 0.64; 95% CI 0.47-0.89). Antenatal treatment with magnesium sulphate during premature deliveries seems to be associated with health benefits for the infants. The effective dose and timing, however, is not defined and given the lack of mechanistic understanding of the effect of MgSO(4), a reasonable alternative is a large-scale pragmatic clinical trial.

PMID: 22296422 [PubMed - in process]

16. Am J Hum Genet. 2011 Dec 9;89(6):745-50. Epub 2011 Nov 17.

Recessive mutations in ELOVL4 cause ichthyosis, intellectual disability, and spastic quadriplegia.

Aldahmesh MA, Mohamed JY, Alkuraya HS, Verma IC, Puri RD, Alaiya AA, Rizzo WB, Alkuraya FS.

Department of Genetics, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia.

Very-long-chain fatty acids (VLCFAs) play important roles in membrane structure and cellular signaling, and their contribution to human health is increasingly recognized. Fatty acid elongases catalyze the first and rate-limiting step in VLCFA synthesis. Heterozygous mutations in ELOVL4, the gene encoding one of the elongases, are known to cause macular degeneration in humans and retinal abnormalities in mice. However, biallelic ELOVL4 mutations have not been observed in humans, and murine models with homozygous mutations die within hours of birth as a result of a defective epidermal water barrier. Here, we report on two human individuals with recessive ELOVL4 mutations revealed by a combination of autozygome analysis and exome sequencing. These individuals exhibit clinical features of ichthyosis, seizures, mental retardation, and spasticity-a constellation that resembles Sjögren-Larsson syndrome (SLS) but presents a more severe neurologic phenotype. Our findings identify recessive mutations in ELOVL4 as the cause of a neuro-ichthyotic disease and emphasize the importance of VLCFA synthesis in brain and cutaneous development.

PMID: 22100072 [PubMed - indexed for MEDLINE] PMCID: PMC3234380 [Available on 2012/6/9]

17. BMC Pediatr. 2012 Feb 1;12(1):11. [Epub ahead of print]

Developmental outcome of very low birth weight infants in a developing country.

Ballot DE, Potterton J, Chirwa T, Hilburn N, Cooper PA.

BACKGROUND: Advances in neonatal care allow survival of extremely premature infants, who are at risk of

handicap. Neurodevelopmental follow up of these infants is an essential part of ongoing evaluation of neonatal care. The neonatal care in resource limited developing countries is very different to that in first world settings. Follow up data from developing countries is essential; it is not appropriate to extrapolate data from units in developed countries. This study provides follow up data on a population of very low birth weight (VLBW) infants in Johannesburg, South Africa. METHODS: The study sample included all VLBW infants born between 01/06/2006 and 28/02/2007 and discharged from the neonatal unit at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). Bayley Scales of Infant and Toddler Development Version 111 (BSID 111) were done to assess development. Regression analysis was done to determine factors associated with poor outcome. RESULTS: 178 infants were discharged, 26 were not available for follow up, 9 of the remaining 152 (5.9%) died before an assessment was done; 106 of the remaining 143 (74.1%) had a BSID 111 assessment. These 106 patients form the study sample; mean birth weight and mean gestational age was 1182 grams (SD: 197.78) and 30.81 weeks (SD: 2.67) respectively. The BSID (111) was done at a median age of 16.48 months. The mean cognitive subscale was 88.6 (95% CI: 85.69 - 91.59), 9 (8.5%) were < 70, mean language subscale was 87.71 (95% CI: 84.85 - 90.56), 10 (9.4%) < 70, and mean motor subscale was 90.05 (95% CI: 87.0 - 93.11), 8 (7.6%) < 70. Approximately one third of infants were identified as being at risk (score between 70 and 85) on each subscale. Factors associated with poor outcome included cystic periventricular leukomalacia (PVL), resuscitation at birth, maternal parity, prolonged hospitalisation and duration of supplemental oxygen. PVL was associated with poor outcome on all three subscales. Birth weight and gestational age were not predictive of neurodevelopmental outcome. CONCLUSION: Although the neurodevelopmental outcome of this group of VLBW infants was within the normal range, with a low incidence of cerebral palsy, these results may reflect the low survival of babies with a birth weight below 900 grams. In addition, mean subscale scores were low and one third of the babies were identified as "at risk", indicating that this group of babies warrants long-term follow up into school going age.

PMID: 22296705 [PubMed - as supplied by publisher]

18. Childs Nerv Syst. 2012 Jan 28. [Epub ahead of print]

Polymicrogyria: correlation of magnetic resonance imaging and clinical findings.

Mavili E, Coskun A, Per H, Donmez H, Kumandas S, Yikilmaz A.

Department of Radiology, Faculty of Medicine, Erciyes University, 38039 Melikgazi, Kayseri, Turkey, ertmavili@yahoo.com.

AIM: The aim of this study is to evaluate the correlation between clinical presentation and the extent of cortical involvement in patients with polymicrogyria. MATERIALS AND METHODS: The magnetic resonance imaging findings of 26 patients were evaluated for the location and distribution of polymicrogyria. Presence of asphyxia at birth and serological tests for TORCH infections, the presence and type (spastic, flaccid) of motor deficits, mental development, microcephaly, and epilepsy were noted. RESULTS: Nineteen patients had bilateral, whereas seven had unilateral involvement. Patients with unilateral polymicrogyria presented later with milder symptoms. The most encountered symptom in patients with bilateral involvement was mental motor retardation (MMR) (89%) and speech problems (84%). The clinical presentations of patients with asphyxia and positive serological tests for cytomegalovirus (CMV) were worse. All patients with positive serological tests for CMV had bilateral involvement. The perisylvian region was affected in five (71%) patients with unilateral involvement. The most encountered presenting symptom in these patients was epilepsy. Cerebral palsy was seen in three (43%) of the patients, and all of them had left hemiparesis. Microcephaly, MMR, and speech delay were detected in one (14%) of the patients. CONCLUSIONS: Late presenting epilepsy may be a predictor of a unilateral polymicrogyria and is associated with relatively good prognosis. CMV infection and the presence of asphyxia are predictors of worse prognosis.

PMID: 22286201 [PubMed - as supplied by publisher]

19. Eur J Clin Invest. 2011 Dec 30. doi: 10.1111/j.1365-2362.2011.02644.x. [Epub ahead of print]

Methylation capacity in children with severe cerebral palsy.

Schoendorfer NC, Obeid R, Moxon-Lester L, Sharp N, Vitetta L, Boyd RN, Davies PS.

Children's Nutrition Research Centre, School of Medicine, The University of Queensland, Herston, Queensland,

Australia Clinical Chemistry Department, Saarland University Medical School, Homburg, Germany Perinatal Research Centre, University of Queensland Centre for Clinical Research Centre for Integrative Clinical and Molecular Medicine, School of Medicine, The University of Queensland Queensland Cerebral Palsy and Rehabilitation Research Centre, School of Medicine, The University of Queensland, Herston, Queensland Australia.

Background: Methylation cycle and folate-mediated one-carbon metabolism maintenance is important for many physiological processes including neurotransmitter regulation, nerve myelination and DNA synthesis. These processes play an indispensible role in growth and development, as well as in cognitive function and neuromuscular stability, which are key issues in children with severe cerebral palsy (CP). Methods: Blood samples were collected from children with severe CP (n = 24) and age-matched typically developing healthy controls (n = 24), as an exploratory study. The CP group was divided into orally (O) or enterally fed via percutaneous endoscopic gastrostomy (E). Concentrations of red cell folate (RCF), methylmalonic acid (MMA), mean cell volume (MCV), homocysteine (Hcy), cystathionine, choline, betaine and urate were assayed. Results: Homocysteine was increased in both O mean (±SD) = 6·28 (±1·81 μM) and E = 6·03 (±1·28), vs. controls = 5·07 (±0·98) P = 0·02. Higher MMA was found in controls = 157 (±54) and O = 141 (±101), vs. E = 88(±21) P = 0·05. RCF was higher in E = 1422 (±70 nM) vs. O = 843 (±80) and controls = 820 (±43) P < 0·001. MCV z-scores were elevated in E = 3·1 (±1·8) and O = 1·1 (±1·1) compared with controls = -0·2 (±1·1) P < 0·001. Urate was significantly reduced in O = -0·64 (±1·38) and E = -0·87 (±0·71), vs. controls = 0·18 (±0·62) P = 0·006. Conclusions: Raised MCV in the presence of elevated red cell folate, adequate B12 status and low plasma urate suggest potential methyltetrahydrofolate trapping and impaired purine synthesis. Well-documented malnutrition issues in O may explain differences between CP groups. These data support the hypothesis of possible dysregulation in methylation capacity and/or folate one-carbon metabolism, although more research is needed to elucidate a precise mechanism.

PMID: 22299647 [PubMed - as supplied by publisher]

20. J Neurotrauma. 2012 Jan 20;29(2):313-21.

Mild hyperthermia worsens the neuropathological damage associated with mild traumatic brain injury in rats.

Sakurai A, Atkins CM, Alonso OF, Bramlett HM, Dietrich WD.

The Department of Neurological Surgery and the Miami Project to Cure Paralysis, University of Miami Miller School of Medicine , Miami, Florida.

The effects of slight variations in brain temperature on the pathophysiological consequences of acute brain injury have been extensively described in models of moderate and severe traumatic brain injury (TBI). In contrast, limited information is available regarding the potential consequences of temperature elevations on outcome following mild TBI (mTBI) or concussions. One potential confounding variable with mTBI is the presence of elevated body temperature that occurs in the civilian or military populations due to hot environments combined with exercise or other forms of physical exertion. We therefore determined the histopathological effects of pre- and post-traumatic hyperthermia (39°C) on mTBI. Adult male Sprague-Dawley rats were divided into 3 groups: pre/post-traumatic hyperthermia, post-traumatic hyperthermia alone for 2 h, and normothermia (37°C). The pre/post-hyperthermia group was treated with hyperthermia starting 15 min before mild parasagittal fluid-percussion brain injury (1.4-1.6 atm), with the temperature elevation extending for 2 h after trauma. At 72 h after mTBI, the rats were perfusion-fixed for quantitative histopathological evaluation. Contusion areas and volumes were significantly larger in the pre/post-hyperthermia treatment group compared to the post-hyperthermia and normothermic groups. In addition, pre/post-traumatic hyperthermia caused the most severe loss of NeuN-positive cells in the dentate hilus compared to normothermia. These neuropathological results demonstrate that relatively mild elevations in temperature associated with peri-traumatic events may affect the long-term functional consequences of mTBI. Because individuals exhibiting mildly elevated core temperatures may be predisposed to aggravated brain damage after mTBI or concussion, precautions should be introduced to target this important physiological variable.

PMID: 22026555 [PubMed - in process] PMCID: PMC3261791 [Available on 2013/1/20]

21. Pediatrics. 2012 Feb;129(2):e414-e423. Epub 2012 Jan 30.

Fetal and Maternal Candidate Single Nucleotide Polymorphism Associations With Cerebral Palsy: A Case-Control Study.

O'Callaghan ME, Maclennan AH, Gibson CS, McMichael GL, Haan EA, Broadbent JL, Goldwater PN, Painter JN, Montgomery GW, Dekker GA; for the Australian Collaborative Cerebral Palsy Research Group.

BSc (Hons), 72 King William Rd, Level 1 Queen Victoria Building, Women's and Children's Hospital, University of Adelaide Discipline of Obstetrics and Gynaecology, North Adelaide, Australia, 5006. michael.ocallaghan@student.adelaide.edu.au.

OBJECTIVE: Previous studies have suggested associations between certain genetic variants and susceptibility to cerebral palsy (CP). This study was designed to assess established and novel maternal and child genetic and epidemiologic risk factors for CP along with their interactions.
METHODS: DNA from 587 case and 1154 control mother-child pairs was analyzed. A panel of 35 candidate single nucleotide polymorphisms (SNPs) were examined and included SNPs in genes associated with (1) thrombophilia, (2) inflammation, and (3) risk factors for CP (eg, preterm birth). Comparisons were specified a priori and made by using a $\chi(2)$ test. RESULTS: There were 40 fetal and 28 maternal associations with CP when analyzed by CP subtype, gestational age, genotypes of apolipoprotein E, and haplotypes of mannose-binding-lectin. After Bonferroni correction for multiple testing, no fetal or maternal candidate SNP was associated with CP or its subtypes. Only fetal carriage of prothrombin gene mutation remained marginally associated with hemiplegia in term infants born to mothers with a reported infection during pregnancy. Odds ratio directions of fetal SNP associations were compared with previously reported studies and confirmed no trend toward association. CONCLUSIONS: Except for the prothrombin gene mutation, individual maternal and fetal SNPs in our candidate panel were not found to be associated with CP outcome. Past reported SNP associations with CP were not confirmed, possibly reflecting type I error from small numbers and multiple testing in the original reports.

PMID: 22291124 [PubMed - as supplied by publisher]

22. PLoS One. 2011;6(10):e25404. Epub 2011 Oct 7.

Iron insufficiency compromises motor neurons and their mitochondrial function in Irp2-null mice.

Jeong SY, Crooks DR, Wilson-Ollivierre H, Ghosh MC, Sougrat R, Lee J, Cooperman S, Mitchell JB, Beaumont C, Rouault TA.

Eunice Kennedy Shriver National Institute of Child Health and Development, National Institutes of Health, Bethesda, Maryland, United States of America.

Genetic ablation of Iron Regulatory Protein 2 (Irp2, Ireb2), which post-transcriptionally regulates iron metabolism genes, causes a gait disorder in mice that progresses to hind-limb paralysis. Here we have demonstrated that misregulation of iron metabolism from loss of Irp2 causes lower motor neuronal degeneration with significant spinal cord axonopathy. Mitochondria in the lumbar spinal cord showed significantly decreased Complex I and II activities, and abnormal morphology. Lower motor neurons appeared to be the most adversely affected neurons, and we show that functional iron starvation due to misregulation of iron import and storage proteins, including transferrin receptor 1 and ferritin, may have a causal role in disease. We demonstrated that two therapeutic approaches were beneficial for motor neuron survival. First, we activated a homologous protein, IRP1, by oral Tempol treatment and found that axons were partially spared from degeneration. Secondly, we genetically decreased expression of the iron storage protein, ferritin, to diminish functional iron starvation. These data suggest that functional iron deficiency may constitute a previously unrecognized molecular basis for degeneration of motor neurons in mice.

PMID: 22003390 [PubMed - indexed for MEDLINE] PMCID: PMC3189198