This free weekly bulletin lists the latest research on cerebral palsy (CP), as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases. These articles were identified by a search using the key term “cerebral palsy”.

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Interventions


Foreword.

Novak I, Kerr Graham H.

Head of Research, Cerebral Palsy Institute University Notre Dame Australia.

PMID: 20633175 [PubMed - as supplied by publisher]


Centre for Musculoskeletal Studies, University of Western Australia, Princess Margaret Hospital, Western Australia.

Botulinum neurotoxin type-A (BoNT-A) has been used in association with other interventions in the management of spasticity in children with cerebral palsy (CP) for almost two decades. This consensus statement is based on an extensive review of the literature by an invited international committee. The use of BoNT-A in the lower limbs of children with spasticity caused by CP is reported using the American Academy of Neurology Classification of Evidence for therapeutic intervention. Randomized clinical trials have been grouped into five areas of management, and the outcomes are presented as treatment recommendations. The assessment of children with CP and evaluation of outcomes following injection of BoNT-A are complex, and therefore, a range of measures and the involvement of a multidisciplinary team is recommended. The committee concludes that injection of BoNT-A in children with CP is generally safe although systemic adverse events may occur, especially in children with more physical limitations (GMFCS V). The recommended dose levels are intermediate between previous consensus statements. The committee further concludes that injection of BoNT-A is effective in the management of lower limb spasticity in children with CP, and when combined with physiotherapy and the use of orthoses, these interventions may improve gait and goal attainment.

PMID: 20633177 [PubMed - as supplied by publisher]

Botulinum toxin assessment, intervention and aftercare for cervical dystonia and other causes of hypotonia of the neck: international consensus statement.

Novak I, Campbell L, Boyce M, Fung VS.

Cerebral Palsy Institute, School of Medicine, University of Notre Dame Australia, Darlinghurst, Sydney, NSW.

Dystonia in the neck region can be safely and effectively reduced with injections of Botulinum neurotoxin-A and B. People with idiopathic cervical dystonia have been studied the most. Benefits following injection include increased range of movement at the neck for head turning, decreased pain, and increased functional capacity (Class I evidence, level A recommendation). The evidence for efficacy and safety in patients with secondary dystonia in the neck is unclear based on the lack of rigorous research conducted in this heterogeneous population (level U recommendation). Psychometrically sound assessments and outcome measures exist to guide decision-making (Class I evidence, level A recommendation). Much less is known about the effectiveness of therapy to augment the effects of the injection (Class IV, level U recommendation). More research is needed to answer questions about safety and efficacy in secondary spastic neck dystonia, effective adjunctive therapy, dosing and favourable injection techniques.

PMID: 20633181 [PubMed - as supplied by publisher]


Botulinum toxin assessment, intervention and aftercare for paediatric and adult drooling: international consensus statement.

Reddihough D, Erasmus CE, Johnson H, McKellar GM, Jongerius PH.

Developmental Medicine, Royal Children's Hospital, Parkville, Victoria, Australia, Murdoch Children's Research Institute, & University of Melbourne, Melbourne.

Many individuals with neurological problems or anatomical abnormalities of the jaw, lips or oral cavity may drool, which can impact on health and quality of life. A thorough evaluation of the patient's history, examination of the oral region by a speech pathologist and, in individuals over 3 years, a dental examination is warranted. Questionnaires with established validity such as the Drooling Impact Scale are useful assessment tools. A hierarchical approach to treatment is taken from least invasive therapies, such as speech pathology, to more invasive, such as injection of botulinum neurotoxin type-A (BoNT-A) into the salivary glands (parotid and submandibular). The wishes of the individual and their carer are crucial considerations in determining the suitability of the intervention for the patient. In the presence of dysphagia and cerebral palsy (CP), careful assessment is required prior to the injection of BoNT-A. Favourable responses to intervention include a reduction in the secretion of saliva and in drooling, as well as psychosocial improvements. BoNT-A is usually well tolerated, although potential side effects should be discussed with the patient and carer.

PMID: 20633182 [PubMed - as supplied by publisher]


Effect of hinged ankle-foot orthoses on standing balance control in children with bilateral spastic cerebral palsy.

Rha DW, Kim DJ, Park ES.

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Purpose: To identify the characteristics of static standing balance and its postural control mechanisms during quiet side-by-side standing and the changes in these measures whilst wearing hinged ankle-foot orthoses (AFOs) in chil-
Children with bilateral spastic cerebral palsy (CP). Materials and Methods: Twenty-one children with bilateral spastic CP (6.10 +/- 1.09 year-old) and 22 typically developing (TD) children (5.64 +/- 0.49 year-old) were recruited. Pressure data were recorded while subjects with or without AFOs stood on dual force platforms and net body center of pressure (CoP) coordinates were calculated from this data. Net body CoP was traced for measuring mediolateral (ML) and anteroposterior (AP) displacement and path length per second. Correlation coefficients between parameters representing ankle, hip, and transverse body rotation strategies were also analyzed. Results: ML and AP displacement and path length per second of the CoP trajectory were higher in children with CP compared to TD children (p < 0.05). There were no significant improvements in these parameters whilst wearing hinged AFOs. Compared to TD children, children with CP used less ankle strategy though more hip and transverse rotation strategies for postural control during quiet standing. Whilst wearing hinged AFOs, the contribution of ankle strategy was significantly increased for ML balance control in children with CP (p < 0.05). Conclusion: Hinged AFOs for children with CP may be helpful in improving the postural control mechanisms but not the postural stability in quiet side-by-side standing.

PMID: 20635451 [PubMed - in process]


Interictal Epileptiform Discharges in Persons Without A History of Seizures: What Do They Mean?

So EL.

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Interictal epileptiform discharge (IED) is rarely observed in healthy volunteers without a history of seizures, but higher rates of occurrence are reported in children than in adults. Higher rates are also observed among neurologic inpatients and outpatients without a seizure history, but the risk of subsequent unprovoked seizures or epilepsy is low in healthy volunteers and patients. An exception is the patients with autism spectrum disorders, attention deficit/hyperactivity disorder, or cerebral palsy, who are predisposed to epilepsy development. However, it is currently unclear whether epilepsy risk is higher for patients with incidentally detected IED than for the patients without IED. Hospitalized patients with IED but no prior seizures often have underlying acute or progressive brain disorders. Although they have increased risk of acute seizures, the risk for subsequent unprovoked seizures or epilepsy is unknown and requires assessment on an individual basis. For patients who have psychogenic spells but no seizure history, the rate of IED detection is low, similar to that of healthy volunteers. The association between IED and transient cognitive impairment has not been established in nonepileptic persons. Evidence thus far does not suggest that routine EEG screening of pilot candidates reduces risk of flight-related accidents.

PMID: 20634716 [PubMed - as supplied by publisher]


Functional gains after surgical procedures in spastic upper extremity: a comparative study between children and adults.

Malizos KN, Liantsis AK, Varitimidis SE, Dailiana ZH, Rigopoulos NS.

Hand Surgery and Microsurgery Unit, Department of Orthopaedics and Trauma Surgery, School of Health Sciences, University of Thessalia, Larissa, Greece.

Thirty-four patients with spastic upper extremity secondary to cerebral palsy underwent operative treatment with bony and soft tissue procedures including osteotomies, capsulotomies, tendon transfers, lengthening and releases. The follow-up ranged from 24 months to 9 years with a mean of 52 months. For the evaluation of the surgical outcome patients were classified into two age groups, one younger (4-14 years) and one older (15-34 years). All patients in both the groups presented with significant improvement postoperatively. Patients who were operated early (first group) had statistically better results in a series of tasks that were used for evaluation. We suggest early intervention with all necessary surgical steps which should be individualized depending on patient's situation and needs.

Maggot Debridement Therapy for Postsurgical Wound Infection in Scoliosis: A Case Series in Five Patients.

Hwang JH, Modi HN, Suh SW, Hong JY, Yang JH, Park JH.

From the *Department of Orthopedics, Korea University Guro Hospital, Scoliosis Research Institute, Seoul, South Korea; daggerDepartment of Orthopedics, Konkuk University Medical School, Seoul, South Korea; and double daggerDepartment of Orthopedics, Korea University Anam Hospital, Seoul, South Korea.

STUDY DESIGN.: Case series of 5 patients who developed resistant wound infection after scoliosis surgery. OBJECTIVE: To present maggot debridement therapy (MDT) as an effective alternative to the conventional treatment in postsurgical infection in scoliosis. SUMMARY OF BACKGROUND DATA: Numerous clinical reports have been published that describe outstanding effects of MDT, most notable on debridement, cleansing, disinfection, and healing of indolent wounds, many of which have previously failed to respond to conventional treatment. However, till date no reports have been found in the literature describing its use for the treatment of wound infection after scoliosis surgery, which has relatively longer and deeper wound. METHODS: A total of 5 patients (2 females and 3 males) who developed wound infection after scoliosis correction surgery were included in this study. All were operated for neuromuscular scoliosis using posterior approach with pedicle screw fixation. All developed deep wound infection within 2 to 6 weeks of surgery, which was resistant to all kinds of conventional therapy. MDT applied in all using prepared commercially available maggot bags, and dressing was changed twice a week till wound shows signs of healing. After confirming negative culture, MDT was stopped and routine dressings or secondary closure was done. During the treatment, wound appearance, size, and development of healing were observed. RESULTS: There were 1 patient with paralytic scoliosis and 4 with cerebral palsy. All wound healed completely within 5.2 +/- 1.8 weeks of MDT or 8.8 +/- 3.8 cycles of MDT. There was no recurrence on final follow-up of 21.6 +/- 5.9 months. Wound size was also decreased from 24.2 +/- 3.3 cm of pre-MDT to 11.8 +/- 4.5 cm post-MDT showing 51.2% reduction in wound size. There was partial implant removal in 2 cases before MDT; however, no further implant extraction was needed in any case after MDT. Treatment was tolerated well by all patients without any obvious complications due to MDT. CONCLUSION: We would propose to use MDT for the treatment of wound infection after scoliosis surgery as an effective alternative to conventional treatment. In this way, implant extraction could be avoided without losing any correction.

PMID: 20634782 [PubMed - as supplied by publisher]


Self-Injury among a Community Cohort of Young Children at Risk for Intellectual and Developmental Disabilities.

Maclean WE Jr, Tervo RC, Hoch J, Tervo M, Symons FJ.

University of Wyoming, Laramie, Wyoming, Minnesota.

OBJECTIVE: To identify risk factors for self-injurious behavior in young children with developmental delay and to determine whether that group is also more likely to exhibit other challenging behaviors. STUDY DESIGN: A retrospective chart review of 196 children <6 years of age referred for comprehensive neurodevelopmental evaluations. We analyzed child developmental level, receptive and expressive communication level, mobility, visual and auditory impairment, and co-morbid diagnoses of cerebral palsy, seizure disorders, and autism. RESULTS: Sixty-three children (32%; mean age = 42.7 mo, 63% male) were reported to engage in self-injurious behavior at the time of the evaluation. Children with and without self-injurious behavior did not differ on overall developmental level, expressive or receptive language level, mobility status or sensory functioning, or in rates of identification with cerebral palsy, seizure disorders, or autism. However, the self-injurious behavior group was rated significantly higher by parents on destructive behavior, hurting others, and unusual habits. CONCLUSIONS: Although self-injurious behavior was reported to occur in 32% of the cohort, the modal frequency was monthly/weekly and the severity was low. No significant differences were found for risk markers reported for adults, adolescents, and older children with intellectual and developmental disabilities. However, self-injurious behavior was comorbid with other behavior problems in this
Levels of empathy in undergraduate occupational therapy students.

Brown T, Williams B, Boyle M, Molloy A, McKenna L, Molloy L, Lewis B.

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Empathy is an important attribute for occupational therapists in establishing rapport and in better understanding their clients. However, empathy can be compromised by high workloads, personal stressors and pressures to demonstrate efficacy. Occupational therapists also work with patients from a variety of diagnostic groups. The objective of this study was to determine the extent of empathy and attitudes towards clients amongst undergraduate occupational therapy students at one Australian University. A cross-sectional study was undertaken using a written survey of the Jefferson Scale of Physician Empathy (JSPE) and the Medical Condition Regard Scale. Overall, a strong level of empathy was reported amongst students. Four medical conditions that occupational therapists work with (stroke, cerebral palsy, traumatic brain injury and depression) were held in high regard. Substance abuse, however, was held in comparatively low regard. Overall, the year of study appeared to have no significant impact on the students' empathy. Despite having a lower reported empathy level than found in health professions from other studies using the JSPE, occupational therapy students were found to have a good level of empathy. Of concern, however, was the bias reported against the medical condition of substance abuse, highlighting that there may be a need to reinforce that patients from this diagnostic group are equally deserving of quality care irrespective of their clinical condition. Recommendations for future research include completing a longitudinal study of occupational therapy students' empathy levels and investigating the empathy levels of occupational therapists working with different client groups. Limitations of the study include the convenience sampling of occupational therapy students enrolled at one university which limits the generalizability of the results to groups of participants with similar characteristics.

Effect of spastic cerebral palsy on jaw-closing muscles during clenching.

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The motor effort of jaw-closing muscles during maximal voluntary clenching (MVC) was compared between individuals with spastic cerebral palsy (CP) and nondisabled control subjects (CG). Bilateral electromyographic (EMG) activity of the anterior temporalis (AT) and masseter (MS) muscles was obtained during MVC in 22 subjects with CP and 29 nondisabled subjects. The oral functional status of the group with CP was evaluated using the Orofacial Motor Function Assessment Scale. The group with CP presented lower bilateral EMG activity during MVC compared to the control group for both AT and MS muscles. Subgroups with CP who were only slightly and very slightly orally impaired had a higher bilateral AT EMG activity compared to individuals with CP who were severely and moderately compromised. A statistically significant positive correlation was found between the oral motor function and EMG activity of the group with CP in all the muscles evaluated. Individuals with CP had motor weakness in the jaw-closing muscles, a condition that may compromise their masticatory function.

Gait compensations caused by foot deformity in cerebral palsy.

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Cerebral palsy (CP) is a complex syndrome, with multiple interactions between joints and muscles. Abnormalities in movement patterns can be measured using motion capture techniques, however determining which abnormalities are primary, and which are secondary, is a difficult task. Deformity of the foot has anecdotally been reported to produce compensatory abnormalities in more proximal lower limb joints, as well as in the contralateral limb. However, the exact nature of these compensations is unclear. The aim of this paper was to provide clear and objective criteria for identifying compensatory mechanisms in children with spastic hemiplegic CP, in order to improve the prediction of the outcome of foot surgery, and to enhance treatment planning. Twelve children with CP were assessed using conventional gait analysis along with the Oxford Foot Model prior to and following surgery to correct foot deformity. Only those variables not directly influenced by foot surgery were assessed. Any that spontaneously corrected following foot surgery were identified as compensations. Pelvic rotation, internal rotation of the affected hip and external rotation of the non-affected hip tended to spontaneously correct. Increased hip flexion on the affected side, along with reduced hip extension on the non-affected side also appeared to be compensations. It is likely that forefoot supination occurs secondary to deviations of the hindfoot in the coronal plane. Abnormal activity in the tibialis anterior muscle may be consequent to tightness and overactivity of the plantarflexors. On the non-affected side, increased plantarflexion during stance also resolved following surgery to the affected side. Copyright © 2010 Elsevier B.V. All rights reserved.

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The convex wrapping algorithm: A method for identifying muscle paths using the underlying bone mesh.

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Associating musculoskeletal models to motion analysis data enables the determination of the muscular lengths, lengthening rates and moment arms of the muscles during the studied movement. Therefore, those models must be anatomically personalized and able to identify realistic muscular paths. Different kinds of algorithms exist to achieve this last issue, such as the wired models and the finite elements ones. After having studied the advantages and drawbacks of each one, we present the convex wrapping algorithm. Its purpose is to identify the shortest path from the origin to the insertion of a muscle wrapping over the underlying skeleton mesh while respecting possible non-sliding constraints. After the presentation of the algorithm, the results obtained are compared to a classically used wrapping surface algorithm (obstacle set method) by measuring the length and moment arm of the semitendinosus muscle during an asymptomatic gait. The convex wrapping algorithm gives an efficient and realistic way of identifying the muscular paths with respect to the underlying bones mesh without the need to define simplified geometric forms. It also enables the identification of the centroid path of the muscles if their thickness evolution function is known. All this presents a particular interest when studying populations presenting noticeable bone deformations, such as those observed in cerebral palsy or rheumatic pathologies. Copyright © 2010 Elsevier Ltd. All rights reserved.

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Sport participation by physically and cognitively challenged young athletes.

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Many physically and cognitively challenged athletes participate in organized and recreational sports. Health benefits of sport participation by athletes with disabilities have been well recognized. A careful preparticipation evaluation and proper classification of athletes ensures safe sports participation by athletes with disabilities. Some conditions in these athletes, such as problems with thermoregulation, autonomic control, neurogenic bladder and bowel, latex allergy, and many associated and secondary complications deserve special consideration. This article reviews common medical issues that relate to sport participation by athletes with physical and cognitive disabilities.

PMID: 20538157 [PubMed - indexed for MEDLINE]


A case for customized seating.

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Each custom seating referral is a puzzle. By gathering the various pieces of client and caregiver input, client assessment, and trial equipment, the seating professional can create an overall plan that successfully meets client needs. Using a combination of commercial seating products, custom seating products, and creative hardware combinations has proven to be a successful model of care for the OrthoSEAT program at Mary Free Bed Rehabilitation Hospital. Through communication, interaction, and construction, a seating professional can successfully match products and fabrication methods to each individual's need for function and comfort.

PMID: 20527631 [PubMed - indexed for MEDLINE]


From case to case: nursing patients with a tracheostomy [Article in German]

Messer M.

PMID: 20521467 [PubMed - indexed for MEDLINE]


Further evidence of validity of the Gait Deviation Index.

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In this paper, the relationship of the Gait Deviation Index (GDI) to gross motor function and its ability to distinguish between different Gross Motor Function Classification System (GMFCS) levels was determined. A representative sample of 184 ambulant children with CP in GMFCS levels I (n=57), II (n=91), III (n=22) and IV (n=14) were recruited as part of a population-based study. Representative gait cycles were selected following a 3D gait analysis and gross motor function was assessed using the Gross Motor Function Measure (GMFM). GDI scores were calcu-
lated in Matlab. Valid 3D kinematic data were obtained for 173 participants and both kinematic and GMFM data were obtained for 150 participants. A substantial relationship between mean GDI and GMFM-66 scores was demonstrated (r=0.70; p<0.001) with significant differences in mean GDI scores between GMFCS levels (p<0.001) indicating increasing levels of gait deviation in subjects less functionally able. The relationship between the GDI, GMFM and GMFCS in a representative sample of ambulators, lends further weight to the validity of the GDI scoring system. Furthermore it suggests that the subtleties of gait may not be wholly accounted for by gross motor function evaluation alone. Gait specific tools such as the GDI more likely capture both the functional and aesthetic components of walking. Copyright 2010 Elsevier B.V. All rights reserved.

PMID: 20226675 [PubMed - indexed for MEDLINE]


Selective motor control of the lower extremities in children with cerebral palsy: Inter-rater reliability of two tests.

Smits DW, van Groenestijn AC, Ketelaar M, Scholtes VA, Becher JG, Gorter JW.

Center of Excellence for Rehabilitation Medicine Utrecht, Rehabilitation Center De Hoogstraat Utrecht, The Netherlands.

Purpose: The purpose of this study was to examine the inter-rater reliability of two tests measuring selective motor control (SMC) of the lower extremities in children with cerebral palsy (CP). Methods: Two testers independently assessed 21 children (13 boys, eight girls; mean age 6 years 5 months, SD 12 months) with spastic CP (14 unilateral and seven bilateral) using the Boyd and Graham SMC test (with an existing protocol) and the modified Trost SMC test (with a newly developed protocol). Inter-rater reliability was analysed using Cohen's Kappa. Results: For the Boyd and Graham SMC test for ankle dorsiflexion, Kappa was 0.55 (95% CI = 0.36-0.74). For the modified Trost SMC test for ankle dorsiflexion, knee extension, hip abduction and hip flexion, Kappas were 0.65 (0.47-0.84), 0.69 (0.49-0.88), 0.57 (0.37-0.78) and 0.71 (0.51-0.91), respectively. Conclusion: The SMC tests showed moderate (Boyd and Graham SMC test) to good (modified Trost SMC test) inter-rater reliability.

PMID: 20629592 [PubMed - in process]


A balancing act: children’s experience of modified constraint-induced movement therapy.

Gilmore R, Ziviani J, Sakzewski L, Shields N, Boyd R.

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OBJECTIVE: This qualitative study explored the experiences of children participating in modified constraint-induced movement therapy (CIMT) within a circus-themed day camp. METHODS: Individual semi-structured interviews were performed with 32 children (15 girls, 17 boys; mean age 10.1 years) to gain insights into their experience of CIMT. Interviews were audio recorded, transcribed verbatim and independently read by two authors to identify common themes. RESULTS: Three themes emerged from the data: children's experience of wearing the glove employed in the modified CIMT, their reactions to the camp format and the gains they made during the camp. CONCLUSION: The results highlighted the need to achieve a balance between the frustration of participating in modified CIMT and what was seen as motivators to sustain involvement. Findings are interpreted in the context of self-determination theory and remind clinicians to ensure interventions consider autonomy, competence and relatedness.

PMID: 20222769 [PubMed - indexed for MEDLINE]

Toilet training in mental retardation; approach to diurnal enuresis in a 12-year-old boy with hemiparesis. [Article in Dutch]
de Moor JH, Frielink N, Roijen LE.
St Radboud Universiteit, Nijmegen.

A 12-year-old boy with hemiparesis, severe mental retardation, reduced mobility and behavioural problems was not yet toilet trained. He was successfully trained using a behavioural treatment. The training program was based on gradual prolongation of urine retention, the introduction of behaviour restrictions, rewards for using the toilet and overcorrection using repeated exercises if diurnal enuresis occurred. A third of 4- to 18-year-olds with a cerebral palsy do not have diurnal bladder control at the age of 6, in contrast to 1-3% in the general population. An important cause of this difference is the believe that bladder control is dependent on the time of development of bladder control muscles and that it cannot be affected by external methods. This case study shows that even in a relatively older and severely and multiply disabled boy diurnal enuresis can be solved.

PMID: 20619035 [PubMed - in process]


Robotic assisted treadmill therapy in children with cerebral palsy [Article in German]
Borggräfe I, Meyer-Heim A, Heinen F.
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PMID: 20623939 [PubMed - in process]

Epidemiology / Aetiology / Diagnosis & Early Treatment

Please note: This is not yet a comprehensive outline of cerebral palsy prevention literature. It is expected that more research will be included when the search terms are expanded to include key terms other than "cerebral palsy". It is a work-in-progress and it will be expanded in coming months.


Neurological and developmental disabilities in ELBW and VLBW: follow-up at 2 years of age.
Stoinska B, Gadzinowski J.
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Objective: To establish the prevalence of neurodevelopmental disabilities among premature infants born in western Poland. Study Design: From 1999 to 2003, 640 extremely low birth weight (ELBW) and 777 very low birth weight (VLBW) infants were admitted to the tertiary care center in Poland. Discharged home were 302 and 671 of them, respectively. At 2 years corrected age, 165 ELBW and 285 VLBW children were diagnosed with neurosensory abnormality including cerebral palsy (CP) and evaluated with Bayley Scales of Infant Development II. Result: Mental developmental index (MDI) score <70 was recorded in 104 children (23.1%). There were 75 (16.7%) cases of CP, 8 (1.7%) deafness/hearing loss, 22 (4.8%) blindness and 14 (3.1%) of epilepsy. Patients with abnormal neurosensory status had significantly lower MDI compared with those with normal development (83.8+/−9 vs 54.7+/−10). Severe intraventricular haemorrhage, periventricular leucomalacia, ventricular dilatation and hydrocephalus were the most important risk factors for neurologic abnormality. Conclusion: Severe disability is more common among ELBW com-
pared with VLBW infants and remains a major challenge for health-care providers. Journal of Perinatology advance online publication, 15 July 2010; doi:10.1038/jp.2010.75.

PMID: 20634795 [PubMed - as supplied by publisher]


Angiotensin II sustains brain inflammation in mice via TGF-beta.

Lanz TV, Ding Z, Ho PP, Luo J, Agrawal AN, Srinagesh H, Axtell R, Zhang H, Platten M, Wyss-Coray T, Steinman L.

The renin-angiotensin-aldosterone system (RAAS) is a key hormonal system regulating blood pressure. However, expression of RAAS components has recently been detected in immune cells, and the RAAS has been implicated in several mouse models of autoimmune disease. Here, we have identified Ang II as a paracrine mediator, sustaining inflammation in the CNS in the EAE mouse model of MS via TGF-beta. Ang II type 1 receptors (AT1Rs) were found to be primarily expressed in CNS-resident cells during EAE. In vitro, astrocytes and microglia responded to Ang II treatment by inducing TGF-beta expression via a pathway involving the TGF-beta-activating protease thrombospondin-1 (TSP-1). TGF-beta upregulation in astrocytes and microglia during EAE was blocked with candesartan (CA), an inhibitor of AT1R. Treatment of EAE with CA ameliorated paralysis and blunted lymphocyte infiltration into the CNS, outcomes that were also seen with genetic ablation of AT1Ra and treatment with an inhibitor of TSP-1. These data suggest that AT1R antagonists, frequently prescribed as antihypertensives, may be useful to interrupt this proinflammatory, CNS-specific pathway in individuals with MS.

PMID: 20628203 [PubMed - as supplied by publisher]


Combinatorial techniques for enhancing neuroprotection.

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Brain and spinal cord (CNS) trauma typically kill a number of neurons, but even more neurons are killed by secondary causes triggered by the initial trauma. Thus, a minor insult may rapidly cause the death of a vastly larger number of neurons and complete paralysis. The best mechanism for reducing the extent of neurological deficits is to minimize the number of neurons killed by post-trauma sequela. Neuroprotection techniques take many diverse forms with a breadth too great for a short review. Therefore, this review focuses on the neuroprotection provided by hypothermia and a number of other neuroprotective techniques, when administered singly or in combination, because it is generally found that combinations of applications lead to significantly better neuroprotection than is achieved by any one alone. The combinatorial approach to neuroprotection holds great promise for enhancing the degree of neuroprotection following trauma, leading to maximum maintenance of neurological function.

PMID: 20633122 [PubMed - in process]


POLG1 p.R722H mutation associated with multiple mtDNA deletions and a neurological phenotype.


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BACKGROUND: The c.2447G>A (p.R722H) mutation in the gene POLG1 of the catalytic subunit of human mitochondrial polymerase gamma has been previously found in a few occasions but its pathogenicity has remained un-
We set out to ascertain its contribution to neuromuscular disease. METHODS: Proband from two families with probable mitochondrial disease were examined clinically, muscle and buccal epithelial DNA were analyzed for mtDNA deletions, and the POLG1, POLG2, ANT1 and Twinkle genes were sequenced. RESULTS: An adult proband presented with progressive external ophthalmoplegia, sensorineural hearing impairment, diabetes mellitus, dysphagia, a limb myopathy and dementia. Brain MRI showed central and cortical atrophy, and 18F-deoxyglucose PET revealed reduced glucose uptake. Histochemical analysis of muscle disclosed ragged red fibers and cytochrome c oxidase-negative fibers. Electron microscopy showed subsarcolemmal aggregates of morphologically normal mitochondria. Multiple mtDNA deletions were found in the muscle, and sequencing of the POLG1 gene revealed a homozygous c.2447G>A (p.R722H) mutation. His two siblings were also homozygous with respect to the p.R722H mutation and presented with dementia and sensorineural hearing impairment. In another family the p.R722H mutation was found as compound heterozygosity with the common p.W748S mutation in two siblings with mental retardation, ptosis, epilepsy and psychiatric symptoms. The estimated carrier frequency of the p.R722H mutation was 1:135 in the Finnish population. No mutations in POLG2, ANT1 and Twinkle genes were found. Analysis of the POLG1 sequence by homology modeling supported the notion that the p.R722H mutation is pathogenic. CONCLUSIONS: The recessive c.2447G>A (p.R722H) mutation in the linker region of the POLG1 gene is pathogenic for multiple mtDNA deletions in muscle and is associated with a late-onset neurological phenotype as a homozygous state. The onset of the disease can be earlier in compound heterozygotes.

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