

Monday 28 May 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. *Dev Med Child Neurol.* 2012 May;54(5):429-35. doi: 10.1111/j.1469-8749.2012.04258.x. Epub 2012 Mar 21.

Motor function after selective dorsal rhizotomy: a 10-year practice-based follow-up study.

Josenby AL, Wagner P, Jarnlo GB, Westbom L, Nordmark E.

Division of Physiotherapy, Department of Health Sciences, Health Sciences Centre, Lund University, Lund, Sweden. annika.lundkvist@med.lu.se

AIM: The aim of this study was to explore changes in motor function up to 10 years after selective dorsal rhizotomy (SDR). **METHOD:** The participants comprised 29 children (20 males, nine females) with bilateral spastic diplegia who were consecutively operated on at a median age of 4 years and 3 months and followed until a median age of 15 years. SDR was combined with physiotherapy and regular follow-up visits. The distribution of preoperative Gross Motor Function Classification System (GMFCS) levels was as follows: I, n=1; II, n=7; III, n=8; IV, n=12; and V, n=1. Muscle tone in hip flexors, hip adductors, knee flexors, and plantar flexors was assessed with the modified Ashworth scale, passive range of motion in hip abduction, popliteal angle, maximum knee extension, dorsiflexion of the foot was measured with a goniometer, and gross motor function was assessed using the Gross Motor Function Measure (GMFM-66). The results were compared with preoperative values, taking into account age at the time of SDR. **RESULTS:** After 10 years, muscle tone in hip flexors, hip adductors, knee flexors and plantar flexors was normalized in 19, 24, 13 and 23 participants respectively; mean change in passive range of motion ranged from -2.0° to 8.6°, and the mean increase in GMFM-66 was 10.6. Changes in GMFM-66 were associated with preoperative GMFCS level and GMFM-66 scores. **INTERPRETATION:** Children who underwent SDR and physiotherapy and were regularly followed up by an experienced team showed improved gross motor function for up to 10 years postoperatively.

© The Authors. *Developmental Medicine & Child Neurology* © 2012 Mac Keith Press.

Comment in

Dev Med Child Neurol. 2012 May;54(5):389-90.

[PMID: 22435543](https://pubmed.ncbi.nlm.nih.gov/22435543/) [PubMed - indexed for MEDLINE]

2. Dev Med Child Neurol. 2012 May;54(5):389-90. doi: 10.1111/j.1469-8749.2012.04255.x. Epub 2012 Mar 21.

Motor function after dorsal rhizotomy.

McLaughlin J.

Neurodevelopmental Program, Seattle Children's Hospital Seattle, WA, USA.

Comment on

Dev Med Child Neurol. 2012 May;54(5):429-35.

[PMID: 22435527](#) [PubMed - indexed for MEDLINE]

3. Clin Rehabil. 2012 May 18. [Epub ahead of print]

Study of the therapeutic effects of a hippotherapy simulator in children with cerebral palsy: a stratified single-blind randomized controlled trial.

Herrero P, Gomez-Trullen EM, Asensio A, Garcia E, Casas R, Monserrat E, Pandyan A.

Faculty of Health Sciences, San Jorge University, Spain.

Objective: To investigate whether hippotherapy (when applied by a simulator) improves postural control and balance in children with cerebral palsy. **Design:** Stratified single-blind randomized controlled trial with an independent assessor. Stratification was made by gross motor function classification system levels, and allocation was concealed. **Subjects:** Children between 4 and 18 years old with cerebral palsy. **Interventions:** Participants were randomized to an intervention (simulator ON) or control (simulator OFF) group after getting informed consent. **Treatment** was provided once a week (15 minutes) for 10 weeks. **Main measures:** Gross Motor Function Measure (dimension B for balance and the Total Score) and Sitting Assessment Scale were carried out at baseline (prior to randomization), end of intervention and 12 weeks after completing the intervention. **Results:** Thirty-eight children participated. The groups were balanced at baseline. Sitting balance (measured by dimension B of the Gross Motor Function Measure) improved significantly in the treatment group (effect size = 0.36; 95% CI 0.01-0.71) and the effect size was greater in the severely disabled group (effect size = 0.80; 95% CI 0.13-1.47). The improvements in sitting balance were not maintained over the follow-up period. Changes in the total score of the Gross Motor Function Measure and the Sitting Assessment Scale were not significant. **Conclusion:** Hippotherapy with a simulator can improve sitting balance in cerebral palsy children who have higher levels of disability. However, this did not lead to a change in the overall function of these children (Gross Motor Function Classification System level V).

[PMID: 22610128](#) [PubMed - as supplied by publisher]

4. Int J Pediatr. 2012;2012:583249. Epub 2012 May 7.

Factors influencing physical activity in children and youth with special health care needs: a pilot study.

Feehan K, O'Neil ME, Abdalla D, Fragala-Pinkham M, Kondrad M, Berhane Z, Turchi R.

Drexel School of Public Health, Drexel University, 245 N. 15th Street, Mail Stop 660, Philadelphia, PA 19102, USA.

Background. Evidence suggests that children and youth with special health care needs (CYSHCN) have decreased physical activity compared to peers. This study describes weight status and physical activity in CYSHCN and identifies factors associated with physical activity and community resources to promote physical activity. **Methods.** Parents (n = 21) and CYSHCN (n = 23) were recruited from a pediatric clinic. The most prevalent diagnoses were autism (n = 7, 30%) and cerebral palsy (n = 3, 13%). Interviews were conducted with parents for information on physical activity and community resources. Children's height and weight were measured to calculate body mass index (BMI). **Results.** The majority of CYSHCN (n = 13, 59%) were obese. CYSHCN did not meet recommended levels of 60 minutes of daily physical activity and engaged in more screen time than recommended. More children

with cognitive/behavioral/emotional diagnoses were obese compared to children with physical/medical diagnoses. A majority of parents (n = 16, 73%) indicated their CYSHCN need more supervision to participate in physical activity in community programs. Conclusion. The majority of CYSHCN in this study were obese and sedentary. Resources to promote physical activity are needed for this population.

[PMID: 22611411](#) [PubMed - in process]

3. Dev Med Child Neurol. 2012 May 19. doi: 10.1111/j.1469-8749.2012.04343.x. [Epub ahead of print]

Stationary cycling for children with cerebral palsy: does it get them anywhere?

Taylor NF.

Department of Physiotherapy, La Trobe University; Allied Health Clinical Research Office, Eastern Health, Victoria, Australia.

[PMID: 22607398](#) [PubMed - as supplied by publisher]

4. Dev Med Child Neurol. 2012 May;54(5):477-9; author reply 479-81. doi: 10.1111/j.1469-8749.2012.04240.x. Epub 2012 Mar 12.

Caution is warranted in interpreting data from a recent trial of modified constraint-induced therapy.

Ramey SL, Deluca SC, Case-Smith J, Stevenson R.

Comment on

Dev Med Child Neurol. 2011 Dec;53(12):1091-9.

[PMID: 22409421](#) [PubMed - indexed for MEDLINE]

5. Dev Med Child Neurol. 2012 May;54(5):424-8. doi: 10.1111/j.1469-8749.2012.04252.x. Epub 2012 Mar 5.

Further evidence of validity of the Modified Melbourne Assessment for neurologically impaired children aged 2 to 4 years.

Randall M, Imms C, Carey L.

Department of Occupational Therapy, The Royal Children's Hospital, Parkville, Victoria, Australia.

AIM: This paper reports the second phase of a study to extend the Melbourne Assessment for use with children with neurological impairment aged 2 to 4 years. The aim was to establish if (1) children's scores on the Modified Melbourne Assessment (MMA) and the Quality of Upper Extremity Skills Test (QUEST) showed a moderate to high, positive relation, (2) children had comparable behaviours for task and time demands on both tools, and (3) scores on the MMA could discriminate between children with mild, moderate, and severe levels of upper limb impairment. **METHOD:** An observational study of 30 children (19 males, 11 females) with neurological impairment aged 2 to 4 years. Twenty-four children had spasticity (20 with a unilateral and four with a bilateral impairment) and two children presented with athetosis, two with ataxia, and two with hypotonia. **RESULTS:** A high, positive relation was found between children's scores on the MMA and the QUEST ($p=0.90$; $p=0.001$). The clinical use of the MMA was comparable to the QUEST. MMA scores were able to discriminate between children's levels of upper limb impairment as determined by clinicians' ratings ($F(2,27) = 67.76$, $p=0.001$). **INTERPRETATION:** These findings suggest the MMA can be clinically useful for children as young as 2.5 years and has the advantage of being valid for use with older children. Scores from the tool can also provide therapists with a quantitative means of consistently reporting level of upper limb impairment.

© 2012 The Authors. Developmental Medicine & Child Neurology © 2012 Mac Keith Press.

[PMID: 22390189](#) [PubMed - indexed for MEDLINE]

6. J Med Assoc Thai. 2011 Dec;94 Suppl 7:S139-44.

Inter-rater and intra-rater reliability of the gross motor function measure (GMFM-66) by Thai pediatric physical therapists.

Mahasup N, Sritipsukho P, Lekskulchai R, Keawutan P.

Postgraduate Studies Program, Faculty of Medicine, Thammasat University, Pathumthani, Thailand.

OBJECTIVE: The present study aimed to determine inter-rater reliability and intra-rater reliability of the 66-item version of the Gross Motor Function Measure (GMFM-66) in assessing motor ability of Thai children with cerebral palsy. **MATERIAL AND METHOD:** Ten children, aged 2-10 years, were recruited in the present study. Eight children with spastic diplegia from an outpatient department of Thammasat University Hospital, and two normal children were recruited. The motor abilities of the subjects were recorded on a video camera. Three pediatric physical therapists independently watched the video recordings and scored each child according to the GMFM assessment. The video clips often children were assessed on two occasions at an interval of one week by the same therapists. The inter-rater and intra-rater reliability were analyzed using an intraclass correlation coefficient (ICC). **RESULTS:** The inter-rater reliability and intra-rater reliability of the GMFM-66 were both high. The ICC for inter-rater reliability was 0.93 and for intra-rater reliability were 0.99-1.00 for the total scores. **CONCLUSION:** The present study confirms high inter-rater and intra-rater reliability of the GMFM-66 measured by Thai pediatric physical therapists. Therefore, in clinical practice, we recommend Thai pediatric physical therapists to use the GMFM-66 in assessing motor ability of cerebral palsy patients.

[PMID: 22619920](#) [PubMed - in process]

7. Dev Med Child Neurol. 2012 May;54(5):388-9. doi: 10.1111/j.1469-8749.2012.04253.x. Epub 2012 Mar 30.

Promoting wellness is achievable in rehabilitation--but what are the critical ingredients for success?

Majnemer A.

School of Physical and Occupational Therapy, McGill University, Montreal, Quebec, Canada.

Comment on

Dev Med Child Neurol. 2012 May;54(5):415-23.

[PMID: 22469309](#) [PubMed - indexed for MEDLINE]

8. Dev Neuropsychol. 2012 May;37(4):317-32.

Short-term memory in young adults with spastic diplegic cerebral palsy.

Toomela A.

Institute of Psychology, Tallinn University, Tallinn, Estonia.

We examined short-term memory activation processes and task-relevant, task-irrelevant, and dynamic inhibitory processes in a group of young adults with hypoxic-ischaemic prenatal spastic diplegic cerebral palsy (HI-CP, N = 27) with group-level and person-oriented methods of data analysis. Performance was compared with age, sex, and education of a matched control group (N = 135). We found that HI-CP is accompanied with low level of correct answers and high levels of task-relevant and task-irrelevant intrusions and repetitions on the Memory with Pause and Homogeneous Interference short-term memory tasks. Person-oriented analyses revealed several different configurations of dysfunction in the HI-CP group.

[PMID: 22612544](#) [PubMed - in process]

9. **Strabismus.** 2012 Jun;20(2):78-83.

Diagnosing cerebral visual impairment in children with good visual acuity.

van Genderen M, Dekker M, Pilon F, Bals I.

Department of Ophthalmology, Bartiméus Institute for the Visually Impaired.

Purpose: To identify elements that could facilitate the diagnosis of cerebral visual impairment (CVI) in children with good visual acuity in the general ophthalmic clinic. **Methods:** We retrospectively investigated the clinical characteristics of 30 children with good visual acuity and CVI and compared them with those of 23 children who were referred with a suspicion of CVI, but proved to have a different diagnosis. Clinical characteristics included medical history, MRI findings, visual acuity, crowding ratio (CR), visual field assessment, and the results of ophthalmologic and orthoptic examination. We also evaluated the additional value of a short CVI questionnaire. **Results:** Eighty-three percent of the children with an abnormal medical history (mainly prematurity and perinatal hypoxia) had CVI, in contrast with none of the children with a normal medical history. Cerebral palsy, visual field defects, and partial optic atrophy only occurred in the CVI group. 41% of the children with CVI had a CR ≥ 2.0 , which may be related to dorsal stream dysfunction. All children with CVI, but also 91% of the children without CVI gave ≥ 3 affirmative answers on the CVI questionnaire. **Conclusion:** An abnormal pre- or perinatal medical history is the most important risk factor for CVI in children, and therefore in deciding which children should be referred for further multidisciplinary assessment. Additional symptoms of cerebral damage, i.e., cerebral palsy, visual field defects, partial optic atrophy, and a CR ≥ 2 may support the diagnosis. CVI questionnaires should not be used for screening purposes as they yield too many false positives.

[PMID: 22612357](#) [PubMed - in process]

10. **J Transl Med.** 2012 May 18;10(1):100. [Epub ahead of print]

Treatment of one case of cerebral palsy combined with posterior visual pathway injury using autologous bone marrow mesenchymal stem cells.

Li M, Yu A, Zhang F, Dai G, Cheng H, Wang X, An Y.

BACKGROUND: Cerebral palsy is currently one of the major diseases that cause severe paralysis of the nervous system in children; about 9-30% of cerebral palsy patients also have visual impairment, which has no effective treatment thus far. Bone marrow mesenchymal stem cells (BMSCs) have very strong self-renewal, proliferation, and pluripotent differentiation potentials. Therefore, autologous BMSC transplantation has become a novel method for treating cerebral palsy. **METHODS:** An 11-year-old boy had a clear history of dystocia and asphyxia after birth; at the age of 6 months, the family members observed his gaze casting around and noted that he displayed a lack of attention. A brain MRI examination at the age of 7 years showed that the child had cerebral palsy with visual impairment (i.e., posterior visual pathway injury). The patient was hospitalized for 20 days and was given four infusions of intravenous autologous BMSCs. Before transplantation and 1, 6, and 12 months after transplantation, a visual evoked potential test, an electrocardiogram, routine blood tests, and liver and kidney function tests were performed. **RESULTS:** The patient did not have any adverse reactions or abnormal consequences during hospitalization or postoperative follow-up. After discharge, the patient could walk more smoothly than he could before transplantation; his vision significantly improved 6 months after transplantation, which was also supported by the electrophysiological examinations. **CONCLUSIONS:** The clinical application of BMSCs is safe and effective for improving vision in the treatment of cerebral palsy combined with visual impairment.

[PMID: 22607263](#) [PubMed - as supplied by publisher]

11. Sleep Med Rev. 2012 May 18. [Epub ahead of print]**Interventions with a sleep outcome for children with cerebral palsy or a post-traumatic brain injury: A systematic review.**

Galland BC, Elder DE, Taylor BJ.

Department of Women's & Children's Health, University of Otago, PO Box 913, Dunedin 9016, New Zealand.

The purpose of this study was to conduct a systematic literature review on interventions for sleep problems in children (aged 0-12 years) with cerebral palsy (CP) or traumatic brain injury (TBI). The literature describes sleep disorders as common in both conditions. Criteria were expanded to include interventions for other medical conditions where sleep was measured as an outcome. No interventions specifically designed to improve sleeping in children with CP or TBI were found. A literature search was conducted of five databases (Ovid MEDLINE, EMBASE, PsychINFO, CINAHL, and the Cochrane Database) from January 1 1990, to June 2011. The search terms [infant (age 0-23 months) or child, preschool (age 2-5 years) or child (age 6-12 years)] were used, with key terms related to CP and TBI. The search yielded 491 articles; 19 were relevant for CP, one for TBI. For CP, if the intervention improved the symptom/s targeted as primary outcome/s, sleep (measured as a secondary outcome) also improved. Few studies used objective measures of sleep, so efficacy could not be assessed. Only four studies were randomized controlled trials. Interventions were diverse. Where melatonin was used for CP patients with sleep problems/disorders, several related to phase or sleep maintenance disorders, improvements in sleep latency and night waking were consistently found, and in some subjects, improvements in total sleep time. No studies using melatonin studied CP patients exclusively. The one study where sleep was measured as a secondary outcome for TBI was of limited value. In conclusion, more well-designed studies are necessary to advance evidence-based treatments in the area of sleep problems for these chronic pediatric conditions.

Copyright © 2012 Elsevier Ltd. All rights reserved.

[PMID: 22609124](#) [PubMed - as supplied by publisher]

Prevention and Cure

12. J Immunol. 2012 May 18. [Epub ahead of print]**Magnesium Decreases Inflammatory Cytokine Production: A Novel Innate Immunomodulatory Mechanism.**

Sugimoto J, Romani AM, Valentin-Torres AM, Luciano AA, Ramirez Kitchen CM, Funderburg N, Mesiano S, Bernstein HB.

Department of Reproductive Biology, Case Western Reserve University School of Medicine, Cleveland, OH 44106;

MgSO₄ exposure before preterm birth is neuroprotective, reducing the risk of cerebral palsy and major motor dysfunction. Neonatal inflammatory cytokine levels correlate with neurologic outcome, leading us to assess the effect of MgSO₄ on cytokine production in humans. We found reduced maternal TNF- α and IL-6 production following in vivo MgSO₄ treatment. Short-term exposure to a clinically effective MgSO₄ concentration in vitro substantially reduced the frequency of neonatal monocytes producing TNF- α and IL-6 under constitutive and TLR-stimulated conditions, decreasing cytokine gene and protein expression, without influencing cell viability or phagocytic function. In summary, MgSO₄ reduced cytokine production in intrapartum women, term and preterm neonates, demonstrating effectiveness in those at risk for inflammation-associated adverse perinatal outcomes. By probing the mechanism of decreased cytokine production, we found that the immunomodulatory effect was mediated by magnesium and not the sulfate moiety, and it was reversible. Cellular magnesium content increased rapidly upon MgSO₄ exposure, and reduced cytokine production occurred following stimulation with different TLR ligands as well as when magnesium was added after TLR stimulation, strongly suggesting that magnesium acts intracellularly. Magnesium increased basal I κ B α levels, and upon TLR stimulation was associated with reduced NF- κ B activation and nuclear localization. These findings establish a new paradigm for innate immunoregulation, whereby magnesium plays a critical regulatory role in NF- κ B activation, cytokine production, and disease

pathogenesis.

[PMID: 22611240](#) [PubMed - as supplied by publisher]

13. JPEN J Parenter Enteral Nutr. 2012 May 18. [Epub ahead of print]

Micronutrient, Antioxidant, and Oxidative Stress Status in Children With Severe Cerebral Palsy.

Schoendorfer NC, Vitetta L, Sharp N, Digeronimo M, Wilson G, Coombes JS, Boyd R, Davies PS.

The University of Queensland, Brisbane, Australia.

BACKGROUND: Markers indicative of micronutrient and antioxidant status in children with cerebral palsy (CP) were explored due to these children's well-documented issues with food intake and the limited biochemical literature. **Materials and METHODS:** Children aged 4 to 12 years with marked CP (n = 24) and controls (n = 24) were recruited. The CP group represented orally (O) or enterally fed (E) children. Concentrations of red cell folate (RCF), magnesium, superoxide dismutase (SOD), glutathione reductase, and peroxidase were measured, as well as serum methylmalonic acid and vitamin C. Plasma hemoglobin, C-reactive protein, α -tocopherol, cholesterol, zinc, protein carbonyls, and total antioxidant capacity were also quantified. **RESULTS:** Data are reported as mean (SD) and z scores where values differ with age. Many similarities existed, but zinc z scores were reduced in O (-1.10 [0.83]) vs controls (-0.54 [0.54]) (P < .05), as well as for glutathione reductase in O (10.15 [1.69]) vs E (12.22 [2.41]) and controls (11.51 [1.67]) (P < .05). RCF was greatly increased in E (1422 [70]) vs O (843 [80]) and controls (820 [43]) (P < .001). SOD was decreased in E (24.3 [1.4]) vs controls (27.0 [2.8]) (P < .05). **Conclusion:** Considering their vast impact on physiology, micronutrients should be routinely monitored in orally fed children with swallowing disorders and dietary limitations. Excessive intakes, particularly long term in enterally fed children, should also be monitored in view of their potential for competitive inhibition, particularly at high levels.

[PMID: 22610980](#) [PubMed - as supplied by publisher]

14. Lancet Neurol. 2012 Jun;11(6):556-66. Epub 2012 May 16.

Tertiary mechanisms of brain damage: a new hope for treatment of cerebral palsy?

Fleiss B, Gressens P.

Centre for the Developing Brain, Institute of Reproductive and Developmental Biology, Department of Surgery and Cancer, Imperial College, Hammersmith Campus, London, UK; INSERM, U676, Paris, France; Université Paris Diderot, Faculté de Médecine, Paris, France; PremUP, Paris, France.

Cerebral palsy is caused by injury or developmental disturbances to the immature brain and leads to substantial motor, cognitive, and learning deficits. In addition to developmental disruption associated with the initial insult to the immature brain, injury processes can persist for many months or years. We suggest that these tertiary mechanisms of damage might include persistent inflammation and epigenetic changes. We propose that these processes are implicit in prevention of endogenous repair and regeneration and predispose patients to development of future cognitive dysfunction and sensitisation to further injury. We suggest that treatment of tertiary mechanisms of damage might be possible by various means, including preventing the repressive effects of microglia and astrocyte over-activation, recapitulating developmentally permissive epigenetic conditions, and using cell therapies to stimulate repair and regeneration. Recognition of tertiary mechanisms of damage might be the first step in a complex translational task to tailor safe and effective therapies that can be used to treat the already developmentally disrupted brain long after an insult.

Copyright © 2012 Elsevier Ltd. All rights reserved.

[PMID: 22608669](#) [PubMed - in process]

15. Nature. 2012 Apr 29;485(7399):517-21. doi: 10.1038/nature11007.

Glycolytic oligodendrocytes maintain myelin and long-term axonal integrity.

Fünfschilling U, Supplie LM, Mahad D, Boretius S, Saab AS, Edgar J, Brinkmann BG, Kassmann CM, Tzvetanova ID, Möbius W, Diaz F, Meijer D, Suter U, Hamprecht B, Sereda MW, Moraes CT, Frahm J, Goebbels S, Nave KA.

Max Planck Institute of Experimental Medicine, Department of Neurogenetics, Hermann-Rein-Strasse 3, D-37075 Göttingen, Germany.

Oligodendrocytes, the myelin-forming glial cells of the central nervous system, maintain long-term axonal integrity. However, the underlying support mechanisms are not understood. Here we identify a metabolic component of axon-glia interactions by generating conditional Cox10 (protoheme IX farnesyltransferase) mutant mice, in which oligodendrocytes and Schwann cells fail to assemble stable mitochondrial cytochrome c oxidase (COX, also known as mitochondrial complex IV). In the peripheral nervous system, Cox10 conditional mutants exhibit severe neuropathy with dysmyelination, abnormal Remak bundles, muscle atrophy and paralysis. Notably, perturbing mitochondrial respiration did not cause glial cell death. In the adult central nervous system, we found no signs of demyelination, axonal degeneration or secondary inflammation. Unlike cultured oligodendrocytes, which are sensitive to COX inhibitors, post-myelination oligodendrocytes survive well in the absence of COX activity. More importantly, by in vivo magnetic resonance spectroscopy, brain lactate concentrations in mutants were increased compared with controls, but were detectable only in mice exposed to volatile anaesthetics. This indicates that aerobic glycolysis products derived from oligodendrocytes are rapidly metabolized within white matter tracts. Because myelinated axons can use lactate when energy-deprived, our findings suggest a model in which axon-glia metabolic coupling serves a physiological function.

[PMID: 22622581](#) [PubMed - in process]

16. Stem Cells Dev. 2012 May 24. [Epub ahead of print]

Use of human umbilical cord blood mononuclear cells to prevent perinatal brain injury: a pre-clinical study.

Dalous J, Pansiot J, Pham H, Chatel P, Nadaradja C, d'agostino I, Vottier G, Schwendimann L, Vanneaux V, Charriaut-Marlangue C, Titomanlio L, Gressens P, Larghero J, Baud O.

INSERM, U676, Paris, France; jeremie.dalous@inserm.fr.

Cerebral palsy (CP) is the most frequent neurological disorder associated with perinatal injury of the developing brain. Major brain lesions associated with CP are white matter damage (WMD) in preterm infants and cortico-subcortical lesions in term newborns. Cell therapy is considered promising for the repair of brain damage. Human umbilical cord blood mononuclear cells (hUCB-MNCs) are a rich source of various stem cells that could be of interest in repairing perinatal brain damage. Our goal was to investigate the potential of hUCB-MNCs to prevent or repair brain lesions in an animal model of excitotoxic brain injury. We induced neonatal brain lesions using intracranial injections of ibotenate, a glutamate agonist, in 5-day-old rat pups. hUCB-MNCs were injected either intraperitoneally (i.p.) or intravenously (i.v.) soon or 24h after ibotenate injection, and their neurological effects assessed using histology and immunohistochemistry. hUCB-MNCs injected i.p. did not reach the systemic circulation but high amounts induced a significant systemic inflammatory response and increased the WMD induced by the excitotoxic insult. This effect was associated with a significant 40% increase in microglial activation around the white matter lesion. hUCB-MNCs injected i.v. soon or 24h after the excitotoxic insult did not affect lesion size, microglial activation, astroglial cell density or cell proliferation within the developing white matter or cortical plate at any concentration used. We demonstrated that hUCB-MNCs could not integrate into the developing brain or promote subsequent repair. We found that the i.p. injection of high amounts of hUCB-MNCs was associated with systemic inflammation that aggravated WMD.

[PMID: 22621245](#) [PubMed - as supplied by publisher]