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Cerebral palsy research news

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Interventions and Management

1. Influence of Chest and Diaphragm Manual Therapy on the Spirometry Parameters in Patients with Cerebral Palsy: A Pilot Study
Magdalena Rutka, Andrzej Myśliwiec, Tomasz Wolny, Anna Gogola, Paweł Linek

Biomed Res Int. 2021 Feb 12;2021:6263973. doi: 10.1155/2021/6263973. eCollection 2021.

Objective: To evaluate the influence of manual therapy of the chest and diaphragm on the spirometry parameters in patients with cerebral palsy (CP). Method: The study was carried out on 20 youths with CP. All participated in 6 sessions (3 sham and 3 actual), with measurements of spirometry at baseline, postsham therapies 1 and 3, before actual therapy, and postactual therapy sessions 1 and 3. Two manual techniques were included: soft tissue mobilization of the chest and the diaphragm. Results: After the first actual therapy, there was a significant ($p < 0.01$) improvement in forced vital capacity (FVC) by 0.23 L (8% of the average predicted value) and forced expiratory volume in one second (FEV1) by 0.18 L (7% of the average predicted value) as compared to results before the therapy. Change in FVC parameter was clinically significant, whereas change in FEV1 was not clinically significant. After sham therapy, there was no improvement in spirometry parameters as compared to baseline results. Conclusion: Single-time manual therapy of the chest and diaphragm has a positive effect on FVC and FEV1.

PMID: 33628791

2. Validity and reliability of the Turkish version of the pediatric motor activity log-revised (PMAL-R) for 2-17 year old children with hemiparetic cerebral palsy
Mintaze Kerem Günel, Kübra Seyhan, Kıvanç Delioğlu, Tuba Derya Doğan, Turgay Altunalan, Yasemin Kala, Edward Taub, Gitendra Uswatte

Disabil Rehabil. 2021 Feb 24;1-8. doi: 10.1080/09638288.2021.1887375. Online ahead of print.

Purpose: The Pediatric Upper-extremity Motor Activity Log-Revised (PMAL-R) is a structured interview that measures use of the more-affected arm in daily life in children with cerebral palsy (CP). This study investigated the concurrent validity and test -retest reliability of a Turkish version of the PMAL-R. Materials and methods: The PMAL-R was translated and cross-culturally adapted to Turkish and administered to parents of eighty children with hemiplegic CP between 2-17 years. Its concurrent validity was examined by correlating scores on the PMAL-R How Well and How Often scales with ABILHAND-Kids scores. Fifty parents were re-interviewed after three weeks to establish test-retest reliability. Results: PMAL-R scores were strongly correlated with ABILHAND-Kids scores (How Well scale, $r = 0.78$, $p < 0.001$; How Often scale, $r = 0.59$, $p < 0.001$). PMAL-R test-retest reliability (Intraclass correlation; How Often = 0.98, How Well = 0.99) and internal consistency (Cronbach's α; How Often = 0.96, How Well = 0.97) were high. Conclusions: This translation of the PMAL-R has good reliability and validity for measuring everyday use of the more-affected arm in Turkish children with hemiparesis due to CP between 2-17 years. Implications for rehabilitationAn instrument that evaluates real-world arm use in Turkish children with

CP.Reliability and concurrent validity of the Turkish PMAL-R is established in 2-17-year old with upper-extremity hemiparesis.Systematic replication of the clinimetric properties of the English PMAL-R is demonstrated in a wider age range than previously, 2-17 years vs. 2-8 years.Reliability and concurrent validity of the PMAL-R is shown in both children with right and left hemiparesis.

PMID: 33625932

3. Effect of Home-based Bimanual Training in Children with Unilateral Cerebral Palsy (The COAD-study): A Case Series
Lwme Beckers, Eaa Rameckers, Pbm Aarts, Jjw van der Burg, Rjem Smeets, Mlap Schnackers, B Steenbergen, Ijm de Groot, Ach Geurts, Yjm Janssen-Potten

Dev Neurorehabil. 2021 Feb 20;1-12. doi: 10.1080/17518423.2021.1886189. Online ahead of print.

Purpose: To explore the child- and parent-related effects of home-based bimanual training in children with unilateral cerebral palsy. Methods: Case series of 14 children (2-7 years) who completed goal-oriented task-specific training for 3.5 hours/week for 12 weeks by a program adopting implicit (n = 5) or explicit (n = 9) motor learning. A therapist and remedial educationalist coached parents. Progression on bimanual goals (Canadian Occupational Performance Measure (COPM)) and therapy-related parental stress (interviews) were of primary interest. Data were collected at baseline (T0), halfway through and at the end of training (T1 and T2), and after 12 weeks (T3).Results: On the COPM performance scale a clinically relevant change was seen in 50% (7/14), 86% (12/14), and 85% (11/13) of the children, at T1, T2, and T3, respectively. Some parents indicated that they had experienced stress because of the training intensity. Conclusion: The child- and parent-related effects of the home-based bimanual training programs are encouraging.

PMID: 33615975

4. Tracheal stenosis due to cervicothoracic hyperlordosis in patients with cerebral palsy treated with posterior spinal fusion: a report of the first two cases
Yuki Taniguchi, Yoshitaka Matsubayashi, So Kato, Fumihiko Oguchi, Ayato Nohara, Toru Doi, Yasushi Oshima, Sakae Tanaka

BMC Musculoskelet Disord. 2021 Feb 23;22(1):217. doi: 10.1186/s12891-021-04094-y.

Background: Spinal deformity is frequently identified in patients with cerebral palsy (CP). As it progresses, tracheal stenosis often develops due to compression between the innominate artery and anteriorly deviated vertebrae at the apex of the cervicothoracic hyperlordosis. However, the treatment strategy for tracheal stenosis complicated by spinal deformity in patients with CP remains unknown. Case presentation: This study reports two cases: a 19-year-old girl (case 1) and a 17-year-old girl (case 2), both with CP at Gross Motor Function Classification System V. Both patients experienced acute oxygen desaturation twice within the past year of their first visit to our department. X-ray and computed tomography revealed severe scoliosis and cervicothoracic hyperlordosis causing tracheal stenosis at T2 in case 1 and at T3-T4 in case 2, suggesting that their acute oxygen desaturation had been caused by impaired airway clearance due to tracheal stenosis. After preoperative halo traction for three weeks, both patients underwent posterior spinal fusion from C7 to L5 with Ponte osteotomy and sublaminar taping at the proximal thoracic region to correct cervicothoracic hyperlordosis and thoracolumbar scoliosis simultaneously. Postoperative X-ray and computed tomography revealed that the tracheal stenosis improved in parallel with the correction of cervicothoracic hyperlordosis. Case 1 did not develop respiratory failure 1.5 years after surgery. Case 2 required gastrostomy postoperatively due to severe aspiration pneumonia. However, she developed no respiratory failure related to impaired airway clearance at one-year follow-up. Conclusions: We present the first two cases of CP that developed tracheal stenosis caused by cervicothoracic hyperlordosis concomitant with progressive scoliosis and were successfully treated by posterior spinal fusion from C7 to L5. This enabled us to relieve tracheal stenosis and correct the spinal deformity at the same time. Surgeons must be aware of the possibility of coexisting tracheal stenosis in treating spinal deformity in patients with neurological impairment because the surgical strategy can vary in the presence of tracheal stenosis. This study demonstrated that some patients with CP with acquired tracheal stenosis can be treated with spinal surgery.

PMID: 33622297

5. How I do it: Selective dorsal rhizotomy, using interlaminar approaches, for spastic diplegia/quadriplegia in children with cerebral palsy
Marc Sindou, Anthony Joud, George Georgoulis

Acta Neurochir (Wien). 2021 Feb 24. doi: 10.1007/s00701-021-04770-x. Online ahead of print.

Background: Dorsal rhizotomy is considered the gold standard for treating spastic diplegia/quadriplegia in children with cerebral palsy, when rehabilitation programs reveal insufficient to control excess of spasticity. Method: The Keyhole Interlaminar Dorsal rhizotomy modality has been developed to access-individually-all L2-S2 roots, intradurally at the corresponding dural sheath, and preserve the posterior spine architecture. Intraoperative neuromonitoring consists of stimulating each ventral root, to verify its myotomal innervation, and dorsal roots, to explore their reflexive muscular responses in order to help determination of the proportion of rootlets to be cut. Conclusion: This modality, which requires 5 ± 1 h duration, offers tailored accuracy.

PMID: 33624116

6. Effectiveness comparison between carbon spring and hinged ankle-foot orthoses in crouch gait treatment of children with diplegic cerebral palsy: a randomized crossover trial
Corrado Borghi, Stefania Costi, Debora Formisano, Rita Neviani, Daniela Pandarese, Adriano Ferrari

Eur J Phys Rehabil Med. 2021 Feb 23. doi: 10.23736/S1973-9087.21.06566-7. Online ahead of print.

Background: Children with cerebral palsy (CP) often present a loss of effectiveness of the plantarflexors/knee-extensors couple that leads to crouch gait. When treating a child with crouch gait by means of ankle foot orthoses, preserving or restoring push off power is a key issue. Aim: To compare carbon-fiber spring (Carbon Ankle Seven® = CAFO) and hinged anklefoot orthoses (HAFO) effectiveness in improving functionality and walking ability in children with diplegic CP and crouch gait. Design: Randomized crossover trial. Setting: Hospital center. Population: Ten children with diplegic CP and crouch gait, 5 males and 5 females, aged 11 (4) years. Methods: The gait of each child was evaluated by means of instrumental gait analysis with both CAFO and HAFO, in a randomized order and after a 4-week adaptation period. The primary outcome measure was the change in ankle power generation. As secondary outcome measures, knee joint kinematics, stride length, walking speed, Observational Gait Scale, and preferred orthosis were considered. Results: The median of the energy produced in stance was superior with CAFO (+2.2 J/kg, IQR 4.7, p=0.006), and the energy absorbed inferior (-3.3 J/kg, IQR 4.3, p=0.011). No statistically significant difference was found for any other parameter. Preference of the children was equally distributed between the two orthoses. Conclusions: No evident superiority of CAFO with respect to HAFO was found in improving gait performance of children with CP and crouch gait. Nevertheless, the results suggest the possibility that CAFO permits an energy saving and reduction of the more compromising deficits. Clinical rehabilitation impact: The final choice of the participants indicates that CAFOs are preferred by older and heavier children, but the preference does not correlate with the performance of the orthoses during gait.

PMID: 33619943

7. Long-term follow-up after multilevel surgery in cerebral palsy
Rosa Visscher, Nadine Hasler, Marie Freslier, Navrag B Singh, William R Taylor, Reinald Brunner, Erich Rutz

Arch Orthop Trauma Surg. 2021 Feb 23. doi: 10.1007/s00402-021-03797-0. Online ahead of print.

Introduction: Single-event multilevel surgery (SEMLS) is frequently used to correct pathological gait patterns in children with bilateral spastic cerebral palsy (BSCP) in a single session surgery. However, in-depth long-term evaluation reports of gait outcomes are limited. Therefore, we investigated if SEMLS is able to correct lower extremity joint and pelvic angles during gait towards typically developing gait patterns (TDC) in children with BSCP, and if so, if this effect is durable over a 10-year period. Materials and methods: In total 13 children with BSCP GMFCS level II at time of index-surgery between the ages of 7.7-18.2 years at the time of SEMLS were retrospectively recruited. Three-dimensional gait data were captured preoperatively, as well as at short-, mid-, and long-term post-operatively, and used to analyze: movement analysis profile (MAP), gait profile score (GPS), and lower extremity joint and pelvic angles over the course of a gait cycle using statistical parametric mapping.

Results: In agreement with previous studies, MAP and GPS improved towards TDCs after surgery, as did knee extension during the stance phase ($\eta 2 = 0.67$; $p < 0.001$), while knee flexion in the swing phase ($\eta 2 = 0.67$; $p < 0.001$) and pelvic tilt over the complete gait cycle ($\eta 2 = 0.36$; $p < 0.001$) deteriorated; no differences were observed between follow-ups. However, further surgical interventions were required in 8 out of 13 of the participants to maintain improvements 10 years post-surgery. Conclusions: While the overall gait pattern improved, our results showed specific aspects of the gait cycle actually deteriorated post-SEMLS and that a majority of the participants needed additional surgery, supporting previous statements for the use of multilevel surgery rather than SEMLS. The results highlight that the field should not only focus on the overall gait scores when evaluating treatment outcomes but should offer additional long-term follow-up of lower extremity function.

PMID: 33620528

8. Interventional Approaches to Pain and Spasticity Related to Cerebral Palsy
Jacquelin Peck, Ivan Urits, Hisham Kassem, Christopher Lee, Wilton Robinson, Elyse M Cornett, Amnon A Berger, Jared Herman, Jai Won Jung, Alan D Kaye, Omar Viswanath

Review Psychopharmacol Bull. 2020 Oct 15;50(4 Suppl 1):108-120.

Purpose of review: This review will cover seminal and emerging evidence on interventional therapy chronic pain in cerebral palsy (CP). It will cover the background and burden of disease, present the current options, and then weigh the evidence that is available to support interventional therapy and the current indications. Recent findings: CP is a permanent posture and movement disorder from in-utero brain development defects with a 3-4/1,000 incidence in the US. The cost of care for each child is estimated at $921,000. Pain in CP is attributed to musculoskeletal deformities, spasticity, increased muscle tone, dislocations, and GI dysfunction. First-line treatments include physical and occupational therapy and oral pharmacological agents; however, a significant amount of patients remain refractory to these and require further therapy. Injection therapy includes botulinum toxin A (BTA) injections and intrathecal baclofen. BTA injections were shown to control chronic pain effectively and are FDA approved for spastic pain; intra-thecal baclofen, in contrast, was only shown to improve comfort and quality of life with a focus on the pain. Surgical intervention includes selection dorsal rhizotomy (SDR). It may increase range of motion and quality of life and reduce spasticity and pain; however, most evidence is anecdotal, and more research is required. Summary: Interventional therapy, including injection and surgical, is the last line of therapy for chronic pain in CP. It extends the possibility of therapy in hard-to-treat individuals; however, more data is required to provide strong evidence to the efficacy of these treatments and guide proper patient selection.

PMID: 33633421

9. Oral Muscle Relaxants for the Treatment of Chronic Pain Associated with Cerebral Palsy
Jacki Peck, Ivan Urits, Joshua Crane, Alexandra McNally, Nazir Noor, Megha Patel, Amnon A Berger, Elyse M Cornett, Hisham Kassem, Alan D Kaye, Omar Viswanath

Purpose of review: This is a comprehensive literature review of the available for treatment of oral muscle relaxants for cerebral palsy (CP) and associated chronic pain. It briefly describes the background and etiology of pain in CP and proceeds to review and weigh the available evidence for treatment for muscle relaxants. Recent findings: CP is a permanent, chronic, non-progressive neuromuscular and neurocognitive disorder of motor dysfunction that is diagnosed in infancy and is frequently (62% of patients) accompanied by chronic or recurrent muscular pain. Treatment of pain is crucial, and focuses mostly on treatment of spasticity through non-interventional techniques, surgery and medical treatment. Botulinum toxin injections provide temporary denervation, at the cost of repeated needle sticks. More recently, the use of oral muscle relaxants has gained ground and more evidence are available to evaluate its efficacy. Common oral muscle relaxants include baclofen, dantrolene and diazepam. Baclofen is commonly prescribed for spasticity in CP; however, despite year-long experience, there is little evidence to support its use and evidence from controlled trials are mixed. Dantrolene has been used for 30 years, and very little current evidence exists to support its use. Its efficacy is usually impacted by non-adherence due to difficult dosing and side-effects. Diazepam, a commonly prescribed benzodiazepine carries risks of CNS depression as well as addiction and abuse. Evidence supporting its use is mostly dated, but more recent findings support short-term use for pain control as well as enabling non-pharmacological interventions that achieve long term benefit but would otherwise not be tolerated. More recent options include cyclobenzaprine and tizanidine. Cyclobenzaprine carries a more significant adverse events profile, including CNS sedation; it was found to be effective, possible as effective as diazepam, however, it is not currently FDA approved for CP -related spasticity and further evidence is required to support its use. Tizanidine was shown to be very effective in a handful of small studies. Summary: Muscle relaxants are an important adjunct in CP therapy and are crucial in treatment of pain, as well as enabling participation in other forms of treatments. Evidence exist to support their use, however, it is not without risk and

further research is required to highlight proper dosing, co-treatments and patient selection.

PMID: 33633423

10. Effectiveness of Physical Therapy for Improving Constipation In Spastic Cerebral Palsy
Waqar Ahmed Awan, Tahir Masood, Raheela Kanwal

Altern Ther Health Med. 2021 Feb 20;AT6256. Online ahead of print.

Background: Bowel and bladder problems in children with cerebral palsy (CP) negatively affect both the children and their families. Routine physical therapy (PT) may contribute to relieving constipation in children with CP by reducing spasticity. Objective: To determine the effectiveness of PT in relieving constipation in children with spastic CP. Design: This was a single -blinded randomized crossover trial (Clinical Trail # NCT03379038) that included 35 children with spastic CP. The children who fulfilled the inclusion criteria were randomly assigned to one of two groups: the progressive physical therapy (PPT) or the maintenance physical therapy (MPT) group. Methods: Data was collected via general demographic questionnaire, defecation frequency (DF) questionnaire, Constipation Assessment Scale (CAS) and the Modified Ashworth Scale (MAS) at baseline and at the 2nd, 4th, and 6th week before and after crossover. The Mann Whitney U-test was used for between-group comparisons and the Friedman and Wilcoxon signed-rank test for post hoc analysis tests were used for within-group changes. To determine the relationship between spasticity and constipation, simple linear regression was used. Setting: National Institute of Rehabilitation Medicine, Islamabad, Pakistan. Results: Neither group showed a significant difference in spasticity level or DF at baseline or at the end of the 2nd week. However, at the end of the 4th week (PPT = 4[1] vs MPT = 2[1]; U = 192; P < .001) and 6th week (PPT = 4[1] vs 3(1); U = 158; P < .001) DF was significantly better in the PPT group than in the MPT group. Regarding constipation severity, the PPT group showed significantly better results on all items of the Constipation Assessment Scale (CAS) compared with the MPT group after intervention (P < .001). The results showed that spasticity was significantly correlated with DF (r = -0.81; P < .001) and constipation severity (r = 0.45; P < .001). Conclusion: Physical therapy significantly improves DF and reduces constipation severity in children with spastic CP.

PMID: 33609343

11. Microsurgical DREZotomy in spastic cerebral palsy: Poor man's baclofen pump
MCh Nishant Goyal, Shobha Arora, Poorvi Kulsheshtra, Priyanka Gupta

World Neurosurg. 2021 Feb 19;S1878-8750(21)00248-5. doi: 10.1016/j.wneu.2021.02.055. Online ahead of print.

Background: Intra-thecal baclofen pump(ITB)for severe refractory spastic cerebral palsy is not a viable option in resource-constraint settings. Therefore, authors assessed the role of microsurgical DREZotomy(MDT) as an alternative for patients in whom the circumstances did not allow ITB placement. Methods: A prospective clinical study was conducted from August2016 to July2020.All patients of spastic cerebral palsy(with III-IV Ashworth grade)who underwent MDT were included. Pre-operative and post-operative Ashworth grade and GMFCS level were assessed along with any change in power,sensation and bladder functions post-operatively. At last follow-up, patients' main care-provider was asked to rate the effect of surgery(on scale of 0-5)on ease of providing care related to six activities of daily living. Results: Seven patients(5 males,2 females)of spastic cerebral palsy with age range 6-21 years underwent MDT over the study period. Six patients had spastic diplegia and one had spastic hemiplegia. Preoperative Ashworth grade in all patients was 3-4 in various involved muscle groups. Four patients with spastic diplegia underwent MDT at L3-S1 level bilaterally, two patients with spastic diplegia and spastic bladder underwent MDT at L3-S4 level bilaterally whereas one patient with right-sided spastic hemiplegia underwent MDT at C5-T1 level and L3-S1 level on the right side. Post-operative Ashworth grade in all patients improved to 0-1.The improvement in mean Ashworth grade was from 3.14+0.378 preoperatively to 0.29+0.488(p-value=0.000).Most care-providers reported improvement in their ability to do physiotherapy, positioning, clothing, ambulation and to maintain patient's personal hygiene. Care-providers of six patients reported that they were likely to recommend MDT to another similar patient. Conclusion: MDT is a cost-effective tool in deceasing limb spasticity in spastic cerebral palsy especially for those who cannot afford ITB placement.

PMID: 33618044

12. The paradoxical relationship between severity of cerebral palsy and renal function in middle-aged adults: better renal function or inappropriate clinical assessment?
Daniel G Whitney, Ellen M Wolgat, Elie C Ellenberg, Edward A Hurvitz, Mary Schmidt

Disabil Rehabil. 2021 Feb 26;1-7. doi: 10.1080/09638288.2021.1890841. Online ahead of print.

Purpose: To determine the association between severity of cerebral palsy with serum creatinine (sCr) and sCr-based equations to estimate glomerular filtration rate (eGFR), a marker of renal function. Methods: A clinic-based sample of 30-64 year-olds with cerebral palsy was examined and stratified by motor impairment: gross motor function classification system (GMFCS) I/II (n = 79), GMFCS III (n = 78), and GMFCS IV/V (n = 137). sCr, which is influenced by muscle mass, was obtained and sCr-based eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. Results: sCr was lower with increasing GMFCS. The opposite pattern was observed for eGFR: GMFCS IV/V had significantly higher eGFR derived from MDRD compared to other GMFCS groups; GMFCS III had significantly higher eGFR compared to GMFCS I/II. The pattern was similar for CKD-EPI derived eGFR. Conclusions: According to widely used clinical assessment methods for renal function, higher severity of cerebral palsy among adults is associated with better renal function, which is incongruent with their other biological systems. This paradoxical relationship is likely driven by lower muscle rather than true renal function, and thus, sCr-based eGFR may overestimate renal function, especially for GMFCS IV/V. Further prospective studies are needed.Implications for rehabilitationCommon methods of clinical assessment may over-estimate renal function for adults with cerebral palsy (CP), potentially giving a false positive for normal renal health due to their reliance on muscle mass.This study of a clinic-based sample of middle-aged adults with CP highlights the paradoxical relationship between severity of CP and renal function, which is likely driven by methodological limitations in the presence of low muscle mass rather than actual better renal function.It is recommended that clinicians have a high suspicion of abnormal renal function and the need for a nephrology consultation, especially with changes in creatinine levels, even within the normal range.Rehabilitation for adults with CP must have a strong focus on muscle and kidney health, especially for patients with more severe forms of CP.

PMID: 33635734

13. Development of an ICF Core Set for adults with cerebral palsy: capturing their perspective on functioning
Suzie Noten, Lorenzo A A Troenosemito, Chonnanid Limsakul, Melissa Selb, Vincent de Groot, Manin Konijnenbelt, Daniëlle M F Driessen, Sander R Hilberink, Marij E Roebroeck, ICF Core Set for Adults with Cerebral Palsy Study Group

Dev Med Child Neurol. 2021 Feb 26. doi: 10.1111/dmcn.14841. Online ahead of print.

Aim: To examine the most relevant aspects of functioning of adults with cerebral palsy (CP) from their perspective, in order to develop an International Classification of Functioning, Disability and Health (ICF) Core Set for adults with CP. Method: We conducted six focus group discussions with adults with CP without intellectual disability and seven interviews with adults with CP with intellectual disability and caregivers, addressing all ICF components. Meaningful concepts were identified from verbatim transcripts and linked to ICF categories by two independent researchers. Results: In total, 31 adults with CP without intellectual disability (mean [SD] age 46y 1mo [14y 1mo]; 20 females, 11 males; Gross Motor Function Classification System [GMFCS] levels I-IV) and seven adults with CP and intellectual disability (mean [SD] age 25y 8mo [6y 8mo]; four females, three males; GMFCS levels III-V) participated. We identified 132 unique second-level categories: 47 body functions, seven body structures, 43 activities and participation, and 35 environmental factors. The most frequently mentioned categories were emotional function, pain, muscle tone function, support of family, products and technology, and health services. Interpretation: Adults with CP experienced problems in a broad range of body functions and activities and indicated the importance of environmental factors for functioning. The identified categories will be added to the list of candidate items to reach consensus on an ICF Core Set for adults with CP.

PMID: 33634853

14. Stakeholder perspectives of pediatric powered wheelchair standing devices: a qualitative study
Lisa K Kenyon, Kelsey L Harrison, Megan K Huettner, Sarah B Johnson, William C Miller

Dev Med Child Neurol. 2021 Feb 19. doi: 10.1111/dmcn.14842. Online ahead of print.

Aim: To explore and describe the experiences and perspectives of various stakeholders regarding the use of powered wheelchair standing devices (PWSDs). Method: The purposive sample included: children aged 6 to 18 years who used a PWSD (n=8; diagnoses: cerebral palsy, spinal muscular atrophy, spina bifida, spinal cord injury), parents of children 18 years of age or younger who used a PWSD (n=12), rehabilitation professionals working with children who used a PWSD (n=12), and professionals working at companies manufacturing PWSDs (n=3). Data were gathered via face-to-face interviews conducted either in person or via Zoom® and analyzed using the constant comparative method. Results: Three main themes emerged in the data: (1) 'Stand-on-demand' revealed how participants perceived PWSDs as allowing children to stand whenever and wherever they wanted, thereby increasing participation; (2) 'It's more than weight-bearing' uncovered participants' perceptions of psychological and physical benefits from PWSD use; and (3) 'Ecosystems influencing PWSD acquisition and use' revealed child- and non-child-related factors perceived as influencing children's procurement and use of a PWSD. Interpretation: Use of a PWSD was perceived as providing a unique opportunity for children to stand whenever and wherever they desired. Findings suggest the possible transdiagnostic application of PWSDs.

PMID: 33608892

15. "Your Child Has Cerebral Palsy": Parental Understanding and Misconceptions
Mugdha Mohanty, Forrest Beaulieu, Spoorthi Sampath, Dimira Tambunan, Shivangi Kataria, N Paul Rosman

J Child Neurol. 2021 Feb 23;883073821991300. doi: 10.1177/0883073821991300. Online ahead of print.

Importance: Caregivers of children with cerebral palsy can best help their child if they understand the disorder and the correct terminology. Objective: To assess caregiver understanding of cerebral palsy. Design: This was a cross-sectional study from a large tertiary medical center in Boston, to assess understanding of the term cerebral palsy by primary caregivers of children and adolescents with cerebral palsy. All cases were obtained from hospital electronic medical records. Telephone surveys were conducted. Caregiver understanding of cerebral palsy was assessed by open-ended responses (50%) and success in answering true/false questions about cerebral palsy (50%). Participants: Primary caregivers of children 18 years and younger with cerebral palsy. Results: Thirty-three percent of caregivers denied ever being told that their child had cerebral palsy. Most caregivers identified cerebral palsy as a brain problem (79%), lifelong condition (73%), often caused by a perinatal (60%) or gestational (40%) insult. Fifty-two percent knew that cerebral palsy was nonprogressive. Sixty-two percent of caregivers believed they had a good, very good, or excellent understanding of cerebral palsy, whereas the investigators found 69% of caregivers had a good, very good, or excellent understanding of cerebral palsy ($P = .006$). Most caregivers rated very good or excellent the setting where cerebral palsy was discussed (58%), the explanations provided (55%), and the amount of time spent (45%), yet using a Pearson correlation coefficient, most important was the time spent ($r = 0.53$). Conclusions: Following discussion with their child's physician, most primary caregivers of children with cerebral palsy have a good, very good, or excellent understanding of cerebral palsy. Most critical to a good understanding of cerebral palsy was the time spent in explaining the diagnosis.

PMID: 33620264

16. Being adults with cerebral palsy: results of a multicenter Italian study on quality of life and participation
Emanuela Pagliano, Tiziana Casalino, Sara Mazzanti, Elisa Bianchi, Elisa Fazzi, Odoardo Picciolini, Andrea Frigerio, Andrea Rossi, Francesca Gallino, Ambra Villani, Nerina Landi, Luisa Roberti, Roberto Militerni, Carlo Di Brina, Lorella Tornetta, Michela Martielli, Margherita Brizio, Marina Rodocanachi, Valeria Tessarollo, Jessica Galli, Elvira Dusi, Leonora Meschini, Elena Malinconico, Giovanni Baranello, Adriana Anderloni, Ermellina Fedrizzi

Neurol Sci. 2021 Feb 23. doi: 10.1007/s10072-021-05063-y. Online ahead of print.

Cerebral palsy (CP) is still the most common cause of disability developing in infancy. How such a complex disorder affects adult life raises important questions on the critical issues to consider and the most appropriate care pathway right from early childhood. We conducted a multicenter study on a sample of 109 individuals with CP followed up from infancy and recalled for an assessment at ages ranging between 18 and 50 years (mean age 26 years). Semi-structured interviews and specific questionnaires (SF36, LIFE-H and Hollingshead Index) were conducted to assess general psychological state, quality of life, and socio-economic conditions. Our findings showed a globally positive perception of quality of life, albeit with lower scores for physical than for mental health. Our cases generally showed good scores on participation scales, though those with more severe forms scored lower on parameters such as mobility, autonomy, and self-care. These findings were investigated in more depth in interviews, in which our participants painted a picture showing that gradual improvements have been made in several aspects over the years, in the academic attainment and employment, for instance. On the downside, our sample reported

persistent limitations on autonomy in daily life. As for the more profound psychological domain, there was evidence of suffering due to isolation and relational difficulties in most cases that had not emerged from the questionnaires. Our data have possible implications for the management of CP during childhood, suggesting the need to avoid an exclusive focus on motor function goals, and to promote strategies to facilitate communication, participation, autonomy, and social relations.

PMID: 33624178

17. Cortical oscillations that underlie working memory are altered in adults with cerebral palsy
Rashelle M Hoffman, Michael P Trevarrow, Hannah R Bergwell, Christine M Embury, Elizabeth Heinrichs-Graham, Tony W Wilson, Max J Kurz

Clin Neurophysiol. 2021 Feb 11;132(4):938-945. doi: 10.1016/j.clinph.2020.12.029. Online ahead of print.

Objective: This investigation used magnetoencephalography (MEG) to identify the neurophysiological mechanisms contributing to the altered cognition seen in adults with cerebral palsy (CP). Methods: Adults with CP (GMFCS levels I-IV) and demographically-matched controls completed a Sternberg-type working memory task during MEG. Secondarily, they completed the National Institutes of Health (NIH) cognitive toolbox. Beamforming was used to image the significant MEG oscillatory responses and the resulting images were examined using statistical parametric mapping to identify cortical activity that differed between groups. Results: Both groups had a left-lateralized decrease in alpha-beta (11-16 Hz) power across the occipital, temporal, and prefrontal cortices during encoding, as well as an increase in alpha (9-13 Hz) power across the occipital cortices during maintenance. The strength of alpha-beta oscillations in the prefrontal cortices were weaker in those with CP during encoding. Weaker alpha-beta oscillation within the prefrontal cortex was associated with poorer performance on the NIH toolbox and a higher GMFCS level. Conclusions: Alpha-beta aberrations may impact the basic encoding of information in adults with CP, which impacts their overall cognition. Altered alpha-beta oscillation might be connected with gross motor function. Significance: This experimental work highlights the aberrant alpha-beta during encoding as possible neurophysiological mechanism of the cognitive deficiencies.

PMID: 33636609

18. Ethics of providing clinically assisted nutrition and hydration: current issues
Andrew Rochford

Review Frontline Gastroenterol. 2020 Mar 26;12(2):128-132. doi: 10.1136/flgastro-2019-101230. eCollection 2021.

The provision of clinically assisted nutrition and hydration (CANH) often presents clinicians with ethical dilemmas. As the population grows there is increasing prevalence of patients with conditions such as stroke, dementia, advanced malignancy, cerebral palsy and eating disorders and a greater demand for CANH. It is important that healthcare professionals are familiar with the ethical and legal position for the provision of CANH. In addition, it is important to be aware of the clinical indications, relative contraindications and alternative means of supporting patients for whom CANH is not appropriate; this includes education and training for staff, patients, carers and relatives. The lack of high-quality evidence around clinical outcomes, particularly in the form of randomised clinical trials, and the challenges of accurate prognostication in patients who are approaching the end of life make decisions around the provision of CANH difficult for healthcare professionals.

PMID: 33613944

19. Children with Cerebral Palsy Have Altered Occipital Cortical Oscillations during a Visuospatial Attention Task
Jacy R VerMaas, Brandon J Lew, Michael P Trevarrow, Tony W Wilson, Max J Kurz

Cereb Cortex. 2021 Feb 22;bhab016. doi: 10.1093/cercor/bhab016. Online ahead of print.

Dynamically allocating neural resources to salient features or objects within our visual space is fundamental to making rapid

and accurate decisions. Impairments in such visuospatial abilities have been consistently documented in the clinical literature on individuals with cerebral palsy (CP), although the underlying neural mechanisms are poorly understood. In this study, we used magnetoencephalography (MEG) and oscillatory analysis methods to examine visuospatial processing in children with CP and demographically matched typically developing (TD) children. Our results indicated robust oscillations in the theta (4-8 Hz), alpha (8-14 Hz), and gamma (64-80 Hz) frequency bands in the occipital cortex of both groups during visuospatial processing. Importantly, the group with CP exhibited weaker cortical oscillations in the theta and gamma frequency bands, as well as slower response times and worse accuracy during task performance compared to the TD children. Furthermore, we found that weaker theta and gamma oscillations were related to greater visuospatial performance deficits across both groups. We propose that the weaker occipital oscillations seen in children with CP may reflect poor bottom-up processing of incoming visual information, which subsequently affects the higher-order visual computations essential for accurate visual perception and integration for decision-making.

PMID: 33611348

20. Cortical oscillations that underlie visual selective attention are abnormal in adolescents with cerebral palsy
Rashelle M Hoffman, Christine M Embury, Brandon J Lew, Elizabeth Heinrichs-Graham, Tony W Wilson, Max J Kurz

Sci Rep. 2021 Feb 25;11(1):4661. doi: 10.1038/s41598-021-83898-3.

Adolescence is a critical period for the development and refinement of several higher-level cognitive functions, including visual selective attention. Clinically, it has been noted that adolescents with cerebral palsy (CP) may have deficits in selectively attending to objects within their visual field. This study aimed to evaluate the neural oscillatory activity in the ventral attention network while adolescents with CP performed a visual selective attention task. Adolescents with CP (N = 14; Age = 15.7 ± 4 years; MACS I-III; GMFCS I-IV) and neurotypical (NT) adolescents (N = 21; Age = 14.3 ± 2 years) performed the Eriksen flanker task while undergoing magnetoencephalographic (MEG) brain imaging. The participants reported the direction of a target arrow that was surrounded by congruent or incongruent flanking arrows. Compared with NT adolescents, adolescents with CP had slower responses and made more errors regarding the direction of the target arrow. The MEG results revealed that adolescents with CP had stronger alpha oscillations in the left insula when the flanking arrows were incongruent. Furthermore, participants that had more errors also tended to have stronger alpha oscillatory activity in this brain region. Altogether these results indicate that the aberrant activity seen in the left insula is associated with diminished visual selective attention function in adolescents with CP.

PMID: 33633169

21. Serious Game Platform as a Possibility for Home-Based Telerehabilitation for Individuals With Cerebral Palsy During COVID-19 Quarantine - A Cross-Sectional Pilot Study
Talita Dias da Silva, Paula Lumy da Silva, Elisa de Jesus Valenzuela, Eduardo Dati Dias, Amanda Orasmo Simcsik, Mariana Giovanelli de Carvalho, Anne Michelli Gomes Gonçalves Fontes, Camila Aparecida de Oliveira Alberissi, Luciano Vieira de Araújo, Murilo Vinícius da Costa Brandão, Helen Dawes, Carlos Bandeira de Mello Monteiro

Front Psychol. 2021 Feb 2;12:622678. doi: 10.3389/fpsyg.2021.622678. eCollection 2021.

Introduction: There is a need to maintain rehabilitation activities and motivate movement and physical activity during quarantine in individuals with Cerebral Palsy (CP). Objective: This paper sets out to evaluate the feasibility and potential benefits of using computer serious game in a non-immersive virtual reality (VR) implemented and evaluated completely remotely in participants with CP for Home-Based Telerehabilitation during the quarantine period for COVID-19. Methods: Using a cross-sectional design, a total of 44 individuals participated in this study between March and June 2020, 22 of which had CP (14 males and 8 females, mean age = 19 years, ranging between 11 and 28 years) and 22 typically developing individuals, matched by age and sex to the individuals with CP. Participants practiced a coincident timing game1 and we measured movement performance and physical activity intensity using the rating of perceived exertion Borg scale. Results: All participants were able to engage with the VR therapy remotely, reported enjoying sessions, and improved performance in some practice moments. The most important result in this cross-sectional study was the significant increasing in rating of perceived exertion (through Borg scale) in both groups during practice and with CP presenting a higher rating of perceived exertion. Conclusion: Children with CP enjoyed participating, were able to perform at the same level as their peers on certain activities and increased both their performance and physical activity intensity when using the game, supporting the use of serious games for this group for home therapy and interactive games. Clinical trials registration: https://Clinicaltrials.gov, NCT04402034.

Registered on May 20, 2020.

PMID: 33633648

22. [Research progress of contralateral C 7 nerve root transfer via prevertebral pathway] [Article in Chinese]
Tao Chen, Shaoying Gao, Zairong Wei

Review Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi. 2021 Feb 15;35(2):265-268. doi: 10.7507/1002-1892.202006088.

Objective: To review the research progress on the establishment of prevertebral pathway in the treatment of unilateral total brachial plexus injury, cerebral palsy, stroke, and traumatic brain injury by contralateral C 7 nerve root transfer. Methods: The literature about contralateral C 7 nerve root transfer via prevertebral pathway at home and abroad was extensively reviewed, and the development, changes, advantages and disadvantages of various operation methods were analyzed and summarized. Results: After unilateral total brachial plexus injury, cerebral palsy, stroke, and traumatic brain injury, it can be repaired by a variety of surgical methods of the contralateral C 7 nerve root transfer via prevertebral pathway, which include the anterior subcutaneous tissue tunnel of the vertebral body, the passage under the sternocleidomastoid muscle, the posterior pharyngeal space and the anterior vertebral fascia passage, the modified posterior esophageal anterior vertebral passage, the anterior vertebral passage that cuts off the bilateral anterior scalene, and Huashan anterior pathway, etc. Among them, how to establish the shortest, safe, and effective way of anterior vertebral canal has been paid more attention and discussed by peripheral nerve repair doctors. Conclusion: It is a safe and effective surgical method to repair unilateral total brachial plexus injury, cerebral palsy, stroke, and traumatic brain injury patients with contralateral C 7 nerve root transfer via prevertebral pathway.

PMID: 33624485

23. Predictive value of electroencephalogram, event-related potential, and general movements quality assessment in neurodevelopmental outcome of high-risk infants
Qinfen Zhang, Yongsu Hu, Xuan Dong, Wenjuan Tu

Appl Neuropsychol Child. 2021 Feb 22;1-6. doi: 10.1080/21622965.2021.1879085. Online ahead of print.

Objective: The objective of the study is to investigate the predictive value of electroencephalogram (EEG), event-related potential (ERP), and general movements (GMs) quality assessment in the neurodevelopmental outcome of high-risk infants at one year old. Methods: EEG and ERP were performed in high-risk infants at four weeks old, and GMs quality was evaluated once at 4 weeks and once at 12 weeks. The Gesell score was used to assess neurodevelopment outcome at one year old. A comparative analysis of the effects of EEG, GMs, EEG + ERP, and EEG + ERP + GMs was used to predict high-risk neonatal neurodevelopmental outcome. Results: Of 71 high-risk infants at the age of one year, 3 (4.23%) had cerebral palsy, 14 (19.72%) had psychomotor retardation, and 54 (76.05%) were normal. The sensitivity, specificity, positive predictive value, and negative predictive value of EEG + ERP + GMs method were 90.00%, 95.08%, 75.00%, and 98.31%, respectively, and these indexes were the highest among the four methods (EEG, GMs, EEG + ERP, and EEG + ERP + GMs). The kappa statistic for the reliability of predicting neurodevelopmental outcome of high risk newborns by the EEG + ERP + GMs method was substantial at 0.785, while the other three methods obtained relatively low Kappa values (0.599, 0.586, and 0.712, respectively). Conclusions: The combination of EEG, ERP, and GMs quality assessment can greatly improve the prediction of neurodevelopmental outcome of high-risk newborns.

PMID: 33617357

24. Neuroimaging Patterns and Function in Cerebral Palsy-Application of an MRI Classification
Kate Himmelmann, Veronka Horber, Elodie Sellier, Javier De la Cruz, Antigone Papavasiliou, Ingeborg Krägeloh-Mann, Surveillance of Cerebral Palsy in Europe (SCPE) Collaboration

Front Neurol. 2021 Feb 3;11:617740. doi: 10.3389/fneur.2020.617740. eCollection 2020.

Background: Cerebral palsy (CP) is a disorder of movement and posture and every child with CP has a unique composition of neurological symptoms, motor severity, and associated impairments, constituting the functional profile. Although not part of the CP definition, magnetic resonance imaging (MRI) sheds light on the localization, nature, and severity of brain compromise. The MRI classification system (MRICS), developed by the Surveillance of Cerebral Palsy in Europe (SCPE), describes typical MRI patterns associated with specific timing of vulnerability in different areas of the brain. The classification has proven to be reliable and easy to use. Aims: The aim of this study is to apply the MRICS on a large dataset and describe the functional profile associated with the different MRI patterns of the MRICS. Materials and Methods: Data on children with CP born in 1999-2009 with a post-neonatal MRI from 20 European registers in the JRC-SCPE Central Registry was included. The CP classification and the MRICS was applied, and The Gross Motor Function Classification (GMFCS) and the Bimanual Fine Motor Function (BFMF) classification were used. The following associated impairments were documented: intellectual impairment, active epilepsy, visual impairment, and hearing impairment. An impairment index was used to characterize severity of impairment load. Results: The study included 3,818 children with post-neonatal MRI. Distribution of CP type, motor, and associated impairments differed by neuroimaging patterns. Functional profiles associated with neuroimaging patterns were described, and the impairment index showed that bilateral findings were associated with a more severe outcome both regarding motor impairment and associated impairments than unilateral compromise. The results from this study, particularly the differences in functional severity regarding uni- and bilateral brain compromise, may support counseling and service planning of support of children with CP.

PMID: 33613420

25. Early clinical and MRI biomarkers of cognitive and motor outcomes in very preterm born infants
Joanne M George, Paul B Colditz, Mark D Chatfield, Simona Fiori, Kerstin Pannek, Jurgen Fripp, Andrea Guzzetta, Stephen E Rose, Robert S Ware, Roslyn N Boyd

Pediatr Res. 2021 Feb 24. doi: 10.1038/s41390-021-01399-5. Online ahead of print.

Background: This study aimed to identify which MRI and clinical assessments, alone or in combination, from (i) early (32 weeks postmenstrual age, PMA), (ii) term equivalent age (TEA) and (iii) 3 months corrected age (CA) are associated with motor or cognitive outcomes at 2 years CA in infants born <31 weeks gestation. Methods: Prospective cohort study of 98 infants who underwent early and TEA MRI (n = 59 males; median birth gestational age 28 + 5 weeks). Hammersmith Neonatal Neurological Examination (HNNE), NICU Neonatal Neurobehavioural Scale and General Movements Assessment (GMs) were performed early and at TEA. Premie-Neuro was performed early and GMs, Test of Infant Motor Performance and visual assessment were performed at TEA and 3 months CA. Neurodevelopmental outcomes were determined using Bayley Scales of Infant and Toddler Development 3rd edition. Results: The best combined motor outcome model included 3-month GMs (β = -11.41; 95% CI = -17.34, -5.49), TEA MRI deep grey matter score (β = -6.23; 95% CI = -9.47, -2.99) and early HNNE reflexes (β = 3.51; 95% CI = 0.86, 6.16). Combined cognitive model included 3-month GMs (β = -10.01; 95% CI = -15.90, -4.12) and TEA HNNE score (β = 1.33; 95% CI = 0.57, 2.08). Conclusion: Early neonatal neurological assessment improves associations with motor outcomes when combined with term MRI and 3-month GMs. Term neurological assessment combined with 3-month GMs improves associations with cognitive outcomes. Impact: We present associations between 32- and 40-week MRI, comprehensive clinical assessments and later 2-year motor and cognitive outcomes for children born <31 weeks gestation. MRI and clinical assessment of motor, neurological and neurobehavioural function earlier than term equivalent age in very preterm infants is safe and becoming more available in clinical settings. Most of these children are discharged from hospital before term age and so completing assessments prior to discharge can assist with follow up. MRI and neurological assessment prior to term equivalent age while the child is still in hospital can provide earlier identification of children at highest risk of adverse outcomes and guide follow-up screening and intervention services.

PMID: 33627820

26. Magnetic resonance imaging pattern recognition in childhood bilateral basal ganglia disorders
Shekeeb S Mohammad, Rajeshwar Reddy Angiti, Andrew Biggin, Hugo Morales-Briceño, Robert Goetti, Belen Perez-Dueñas, Allison Gregory, Penelope Hogarth, Joanne Ng, Apostolos Papandreou, Kaustuv Bhattacharya, Shamima Rahman, Kristina Prelog, Richard I Webster, Evangeline Wassmer, Susan Hayflick, John Livingston, Manju Kurian, W Kling Chong, Russell C Dale, Basal Ganglia MRI Study Group

Brain Commun. 2020 Oct 26;2(2):fcaa178. doi: 10.1093/braincomms/fcaa178. eCollection 2020.

Bilateral basal ganglia abnormalities on MRI are observed in a wide variety of childhood disorders. MRI pattern recognition can enable rationalization of investigations and also complement clinical and molecular findings, particularly confirming genomic findings and also enabling new gene discovery. A pattern recognition approach in children with bilateral basal ganglia abnormalities on brain MRI was undertaken in this international multicentre cohort study. Three hundred and five MRI scans belonging to 201 children with 34 different disorders were rated using a standard radiological scoring proforma. In addition, literature review on MRI patterns was undertaken in these 34 disorders and 59 additional disorders reported with bilateral basal ganglia MRI abnormalities. Cluster analysis on first MRI findings from the study cohort grouped them into four clusters: Cluster 1-T2-weighted hyperintensities in the putamen; Cluster 2-T2-weighted hyperintensities or increased MRI susceptibility in the globus pallidus; Cluster 3-T2-weighted hyperintensities in the globus pallidus, brainstem and cerebellum with diffusion restriction; Cluster 4-T1-weighted hyperintensities in the basal ganglia. The 34 diagnostic categories included in this study showed dominant clustering in one of the above four clusters. Inflammatory disorders grouped together in Cluster 1. Mitochondrial and other neurometabolic disorders were distributed across clusters 1, 2 and 3, according to lesions dominantly affecting the striatum (Cluster 1: glutaric aciduria type 1, propionic acidaemia, 3-methylglutaconic aciduria with deafness, encephalopathy and Leigh-like syndrome and thiamine responsive basal ganglia disease associated with SLC19A3), pallidum (Cluster 2: methylmalonic acidaemia, Kearns Sayre syndrome, pyruvate dehydrogenase complex deficiency and succinic semialdehyde dehydrogenase deficiency) or pallidum, brainstem and cerebellum (Cluster 3: vigabatrin toxicity, Krabbe disease). The Cluster 4 pattern was exemplified by distinct T1-weighted hyperintensities in the basal ganglia and other brain regions in genetically determined hypermanganesemia due to SLC39A14 and SLC30A10. Within the clusters, distinctive basal ganglia MRI patterns were noted in acquired disorders such as cerebral palsy due to hypoxic ischaemic encephalopathy in full-term babies, kernicterus and vigabatrin toxicity and in rare genetic disorders such as 3-methylglutaconic aciduria with deafness, encephalopathy and Leigh-like syndrome, thiamine responsive basal ganglia disease, pantothenate kinase-associated neurodegeneration, TUBB4A and hypermanganesemia. Integrated findings from the study cohort and literature review were used to propose a diagnostic algorithm to approach bilateral basal ganglia abnormalities on MRI. After integrating clinical summaries and MRI findings from the literature review, we developed a prototypic decision-making electronic tool to be tested using further cohorts and clinical practice.

PMID: 33629063

27. Infant Head Lag
Ihianle E. Osagie, Donald N. Givler

Review In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan.

Infants generally have a large head compared to the rest of their habitus, and the cervical group of paraspinal muscles is relatively weak at birth. Hence the reason for the notable head lag, especially during the first few weeks of life. During this stage, caregivers routinely support the infant's head until neck control is achieved. The gross motor skill development in infants typically follows a cephalocaudal sequence, and the gain of postural control heralds it. Postural control is an infant's ability to stabilize the center of their body mass/trunk with a dynamic or static base. This innate maturational process of the neck and trunk muscles is expected to evolve rapidly during the infancy stage. When an infant is pulled by the hand from a lying to sitting position, the expected response is to activate the head righting reflex and maintain the head position in line with his/her shoulders. Conversely, infant head lag is observed when the head seems to flop around or lags posteriorly behind the trunk during the pull-to-sit maneuver. Several articles have maintained that head lag should be absent by age 3 to 4 months when infants typically experience an increased ability to control their neck muscles. Once neck control is attained, infants participate actively in a normal pick-up routine by stiffening their neck muscles while tensing up their trunk to decrease the lag between the chin and chest. Persistent head lag beyond age 4 months has been associated with poor neurodevelopmental outcomes. There is a higher incidence of head lag amongst preterm neonates and infants with cerebral palsy, and it is a likely predictor of developmental outcome. It may, however, not be accurate in predicting neurobehavioral effects when used as an isolated metric. A possible explanation could be that assessing one isolated response is not enough to predict neurodevelopmental outcomes accurately. Many studies have suggested that a combination of neonatal responses, like reflex responses, postural reactions, and tone, may hold the potential to predict alteration in brain development correctly. Studies have also shown that head lag combined with other early childhood developmental alterations may be intricately linked with a higher risk of autism in specific populations. Head lag was more commonly observed in siblings of children with autism spectrum disorder (ASD) than low-risk infants. Similarly, developmental problems relating to postural instability and axial hypotonicity have been described in infants with ASD.

PMID: 33620859

28. Bevacizumab and neurodevelopmental outcomes of preterm infants with retinopathy of prematurity: should we still

worry?
Pelin Celik, Iclal Ayranci Sucakli, Caner Kara, Ikbal Seza Petricli, Sumru Kavurt, Istemi Han Celik, Ahmet Yagmur Bas, Nihal Demirel

J Matern Fetal Neonatal Med. 2021 Feb 22;1-8. doi: 10.1080/14767058.2021.1888913. Online ahead of print.

Aim: Bevacizumab may affect preterm infants' ongoing organogenesis with its antiangiogenic effects. We aimed to compare neurodevelopmental outcomes (NDO) of preterm infants treated for retinopathy of prematurity (ROP) with laser photocoagulation (LP), intravitreal bevacizumab (IVB) or both treatments, and to find out the effects of IVB on NDO. Methods: Medical records of preterm infants with ROP treatment and evaluation for NDO were retrospectively collected between 1 January 2017 and 31 June 2019. Primary outcome was Bayley Scales of Infant and Toddler Development 3rd Edition (Bayley-III) scores including cognitive, language, and motor scores. Secondary outcomes were neurodevelopmental impairments (NDIs) classified as the presence of any of cerebral palsy (CP), sensorineural/mixed hearing loss, visual impairment, and developmental delay with any Bayley-III score <85. Severe NDI (sNDI) was defined as presence of any of CP with a Gross Motor Function Classification Scale of 3, 4, or 5, requirement for hearing aids or cochlear implants, bilateral visual impairment or severe developmental delay with any Bayley-III score <70. Results: LP, IVB, and IVB + LP groups included 32, 12, and 10 patients, respectively. Patent ductus arteriosus treatment rates were as 68.7, 75, and 90% in groups, respectively ($p<.05$ between LP and IVB + LP groups). Grades 3 and 4 intraventricular hemorrhage (IVH) was lower in LP group than IVB group (9.4% vs. 33.4%, $p<.05$) while IVB + LP group had no grades 3 and 4 IVH. Other neonatal characteristics were similar ($p > .05$). CP was in 50%, 28%, and 0% of LP, IVB, and IVB + LP groups ($p<.05$). There was no difference in median Bayley-III cognitive, language, and motor scores between groups ($p > .05$). Moderate and severe developmental delays were similar between groups ($p > .05$) whereas IVB group had more moderate cognitive delay; and more severe cognitive, language, and motor delay. NDI rate was not different (59.3%, 50%, and 40% in groups, $p > .05$). sNDI was highest in IVB group but not statistically significant (31.2, 41.7, and 10% in groups, $p > .05$). Multiple logistic regression analysis showed that ROP treatment type and grades 3 and 4 IVH did not have any significant effect on NDO ($p > .05$). Odds of NDI was not effected by ROP treatment type ($p > .05$). Conclusions: Patients treated with bevacizumab should be carefully monitored for neurodevelopmental problems, although the frequency of grades 3 and 4 IVH in the bevacizumab group is thought to contribute to higher rates of sNDI and Bayley-III score <70.

PMID: 33618591

29. Commentary: Muscle Microbiopsy to Delineate Stem Cell Involvement in Young Patients: A Novel Approach for Children With Cerebral Palsy
Richard L Lieber, Andrea A Domenighetti

Comment Front Physiol. 2021 Feb 5;12:642366. doi: 10.3389/fphys.2021.642366. eCollection 2021.

PMID: 33633592

30. Comment on Muscle Microbiopsy to Delineate Stem Cell Involvement in Young Patients: A Novel Approach for Children With Cerebral Palsy.
Corvelyn M, De Beukelaer N, Duelen R, Deschrevel J, Van Campenhout A, Prinsen S, Gayan-Ramirez G, Maes K, Weide G, Desloovere K, Sampaolesi M, Costamagna D.

Front Physiol. 2020 Aug 6;11:945. doi: 10.3389/fphys.2020.00945. eCollection 2020.

PMID: 32848872

31. A systematic review of neurogenesis in animal models of early brain damage: Implications for cerebral palsy
Diego Bulcão Visco, Ana Elisa Toscano, Pedro Alberto Romero Juárez, Henrique José Cavalcanti Bezerra Gouveia, Omar Guzman-Quevedo, Luz Torner, Raul Manhães-de-Castro

Review Exp Neurol. 2021 Feb 22;113643. doi: 10.1016/j.expneurol.2021.113643. Online ahead of print.

Brain damage during early life is the main factor in the development of cerebral palsy (CP), which is one of the leading neurodevelopmental disorders in childhood. Few studies, however, have focused on the mechanisms of cell proliferation, migration, and differentiation in the brain of individuals with CP. We thus conducted a systematic review of preclinical evidence of structural neurogenesis in early brain damage and the underlying mechanisms involved in the pathogenesis of CP. Studies were obtained from Embase, Pubmed, Scopus, and Web of Science. After screening 2329 studies, 29 studies, covering a total of 751 animals, were included. Prenatal models based on oxygen deprivation, inflammatory response and infection, postnatal models based on oxygen deprivation or hypoxic-ischemia, and intraventricular hemorrhage models showed varying neurogenesis responses according to the nature of the brain damage, the time period during which the brain injury occurred, proliferative capacity, pattern of migration, and differentiation profile in neurogenic niches. Results mainly from rodent studies suggest that prenatal brain damage impacts neurogenesis and curbs generation of neural stem cells, while postnatal models show increased proliferation of neural precursor cells, improper migration, and reduced survival of new neurons.

PMID: 33631199

32. Disrupted brain connectivity in children treated with therapeutic hypothermia for neonatal encephalopathy

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Neuroimage Clin. 2021 Feb 10;30:102582. doi: 10.1016/j.nicl.2021.102582. Online ahead of print.

Therapeutic hypothermia following neonatal encephalopathy due to birth asphyxia reduces death and cerebral palsy. However, school-age children without cerebral palsy treated with therapeutic hypothermia for neonatal encephalopathy still have reduced performance on cognitive and motor tests, attention difficulties, slower reaction times and reduced visuo-spatial processing abilities compared to typically developing controls. We acquired diffusion-weighted imaging data from school-age children without cerebral palsy treated with therapeutic hypothermia for neonatal encephalopathy at birth, and a matched control group. Voxelwise analysis (33 cases, 36 controls) confirmed reduced fractional anisotropy in widespread areas of white matter in cases, particularly in the fornix, corpus callosum, anterior and posterior limbs of the internal capsule bilaterally and cingulum bilaterally. In structural brain networks constructed using probabilistic tractography (22 cases, 32 controls), graph-theoretic measures of strength, local and global efficiency, clustering coefficient and characteristic path length were found to correlate with IQ in cases but not controls. Network-based statistic analysis implicated brain regions involved in visuo-spatial processing and attention, aligning with previous behavioural findings. These included the precuneus, thalamus, left superior parietal gyrus and left inferior temporal gyrus. Our findings demonstrate that, despite the manifest successes of therapeutic hypothermia, brain development is impaired in these children.

PMID: 33636541

33. Evidence that autosomal recessive spastic cerebral palsy-1 (CPSQ1) is caused by a missense variant in HPDL

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Brain Commun. 2021 Jan 28;3(1):fcab002. doi: 10.1093/braincomms/fcab002. eCollection 2021.

A subset of individuals diagnosed with cerebral palsy will have an underlying genetic diagnosis. Previously, a missense variant in GAD1 was described as a candidate mutation in a single family diagnosed with autosomal recessive spastic cerebral palsy-1 (CPSQ1; OMIM 603513). Following the ascertainment of a further branch of the CPSQ1 kindred, we found that the previously reported GAD1 variant did not segregate with the neurological disease phenotype in the recently ascertained branch of the kindred. Following genetic linkage studies to map autozygous regions and whole-exome sequencing, a missense variant (c.527 T > C; p. Leu176Pro, rs773333490) in the HPDL gene was detected and found to segregate with disease status in both branches of the kindred. HPDL encodes a 371-amino acid protein (4-Hydroxyphenylpyruvate Dioxygenase Like) that localizes to mitochondria but whose function is uncertain. Recently, biallelic loss of function variants and missense substitution-causing variants in HPDL were reported to cause a childhood onset progressive spastic movement disorder with a variable presentation. These findings suggest that HPDL-related neurological disease may mimic spastic cerebral palsy and that GAD1 should not be included in diagnostic gene panels for inherited cerebral palsy.

PMID: 33634263

34. The Role of Neuroimaging and Genetic Analysis in the Diagnosis of Children With Cerebral Palsy
Veronka Horber, Ute Grasshoff, Elodie Sellier, Catherine Arnaud, Ingeborg Krägeloh-Mann, Kate Himmelmann

Front Neurol. 2021 Feb 9;11:628075. doi: 10.3389/fneur.2020.628075. eCollection 2020.

Cerebral magnetic resonance imaging (MRI) is considered an important tool in the assessment of a child with cerebral palsy (CP), as it is abnormal in more than 80% of children with CP, disclosing the pathogenic pattern responsible for the neurological condition. MRI, therefore, is recommended as the first diagnostic step after medical history taking and neurological examination. With the advances in genetic diagnostics, the genetic contribution to CP is increasingly discussed, and the question arises about the role of genetic testing in the diagnosis of cerebral palsy. The paper gives an overview on genetic findings reported in CP, which are discussed with respect to the underlying brain pathology according to neuroimaging findings. Surveillance of Cerebral Palsy in Europe (SCPE) classifies neuroimaging findings in CP into five categories, which help to stratify decisions concerning genetic testing. Predominant white and gray matter injuries are by far predominant (accounting for around 50 and 20% of the findings). They are considered to be acquired. Here, predisposing genetic factors may play a role to increase vulnerability (and should especially be considered, when family history is positive and/or causative external factors are missing). In maldevelopments and normal findings (around 11% each), monogenic causes are more likely, and thus, genetic testing is clearly recommended. In the miscellaneous category, the precise nature of the MRI finding has to be considered as it could indicate a genetic origin.

PMID: 33633660

35. The role of G-CSF neuroprotective effects in neonatal hypoxic-ischemic encephalopathy (HIE): current status
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Hypoxic-ischemic encephalopathy (HIE) is an important cause of permanent damage to central nervous system (CNS) that may result in neonatal death or manifest later as mental retardation, epilepsy, cerebral palsy, or developmental delay. The primary cause of this condition is systemic hypoxemia and/or reduced cerebral blood flow with long-lasting neurological disabilities and neurodevelopmental impairment in neonates. About 20 to 25% of infants with HIE die in the neonatal period, and 25-30% of survivors are left with permanent neurodevelopmental abnormalities. The mechanisms of hypoxia-ischemia (HI) include activation and/or stimulation of myriad of cascades such as increased excitotoxicity, oxidative stress, N-methyl-D-aspartic acid (NMDA) receptor hyperexcitability, mitochondrial collapse, inflammation, cell swelling, impaired maturation, and loss of trophic support. Different therapeutic modalities have been implicated in managing neonatal HIE, though translation of most of these regimens into clinical practices is still limited. Therapeutic hypothermia, for instance, is the most widely used standard treatment in neonates with HIE as studies have shown that it can inhibit many steps in the excito-oxidative cascade including secondary energy failure, increases in brain lactic acid, glutamate, and nitric oxide concentration. Granulocyte-colony stimulating factor (G-CSF) is a glycoprotein that has been implicated in stimulation of cell survival, proliferation, and function of neutrophil precursors and mature neutrophils. Extensive studies both in vivo and ex vivo have shown the neuroprotective effect of G-CSF in neurodegenerative diseases and neonatal brain damage via inhibition of apoptosis and inflammation. Yet, there are still few experimentation models of neonatal HIE and G-CSF's effectiveness, and extrapolation of adult stroke models is challenging because of the evolving brain. Here, we review current studies and/or researches of G-CSF's crucial role in regulating these cytokines and apoptotic mediators triggered following neonatal brain injury, as well as driving neurogenesis and angiogenesis post-HI insults.

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