

# Cerebral palsy research news

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## **Interventions and Management**

#### 1. Longitudinal development of hand use in children with unilateral spastic cerebral palsy from 18 months to 18 years

No authors listed

Dev Med Child Neurol. 2023 Aug 16. doi: 10.1111/dmcn.15735. Online ahead of print.

No abstract available

#### PMID: 37587730

## 2. Study protocol for a randomised controlled trial to determine the efficacy of an intensive seated postural intervention delivered with robotic and rigid trunk support systems

Victor Santamaria, Xupeng Ai, Karen Chin, Joseph P Dutkowsky, Andrew M Gordon, Sunil K Agrawal

BMJ Open. 2023 Aug 17;13(8):e073166. doi: 10.1136/bmjopen-2023-073166.

Introduction: Children with cerebral palsy (CP) classified as gross motor function classification system (GMFCS) levels III-IV demonstrate impaired sitting and reaching control abilities that hamper their overall functional performance. Yet, efficacious interventions for improving sitting-related activities are scarce. We recently designed a motor learning-based intervention delivered with a robotic Trunk-Support-Trainer (TruST-intervention), in which we apply force field technology to individualise sitting balance support. We propose a randomised controlled trial to test the efficacy of the motor intervention delivered with robotic TruST compared with a static trunk support system. Methods and analysis: We will recruit 82 participants with CP, GMFCS III-IV, and aged 6-17 years. Randomisation using concealed allocation to either the TruSTsupport or static trunk-support intervention will be conducted using opaque-sealed envelopes prepared by someone unrelated to the study. We will apply an intention-to-treat protocol. The interventions will consist of 2 hours/sessions, 3/week, for 4 weeks. Participants will start both interventions with pelvic strapping. In the TruST-intervention, postural task progression will be implemented by a progressive increase of the force field boundaries and then by removing the pelvic straps. In the static trunk support-intervention, we will progressively lower the trunk support and remove pelvic strapping. Outcomes will be assessed at baseline, training midpoint, 1-week postintervention, and 3-month follow-up. Primary outcomes will include the modified functional reach test, a kinematic evaluation of sitting workspace, and the Box and Block test. Secondary outcomes will include The Segmental Assessment of Trunk Control test, Seated Postural & Reaching Control test, Gross Motor Function Measure-Item Set, Canadian Occupational Performance Outcome, The Participation and Environment Measure and Youth, and postural and reaching kinematics. Ethics and dissemination: The study was approved by the Columbia University Institutional Review Board (AAAS7804). This study is funded by the National Institutes of Health (1R01HD101903-01) and is registered at clinicaltrials.gov. Trial registration number: NCT04897347; clinicaltrials.gov.

PMID: <u>37591642</u>

## **3.** Postural control telerehabilitation with a low-cost virtual reality protocol for children with cerebral palsy: Protocol for a clinical trial

Valeska Gatica-Rojas, Ricardo Cartes-Velásquez, Alex Soto-Poblete, Luis Eduardo Cofré Lizama

PLoS One. 2023 Aug 17;18(8):e0268163. doi: 10.1371/journal.pone.0268163. eCollection 2023.

Objective: To establish the feasibility and effectiveness of a rehabilitation programme using low-cost virtual reality aimed at improving postural control in children with cerebral palsy-spastic hemiplegia. It also aims to compare the effectiveness of this programme under two delivery modalities, telerehabilitation (TR) and face-to-face (FtF). Methods: This is a registered randomized controlled clinical trial protocol (ACTRN12621000117819). Eighteen sessions of low-cost virtual reality therapy will be provided through both, FtF and TR modalities using a Nintendo Wii balance board. Each programme will last for 6 weeks and will consist of 3 sessions per week of 25 minutes each. Twenty patients diagnosed with cerebral palsy-spastic hemiplegia will be recruited for each group: FtF or TR (n = 40). Participants will be assessed at baseline, by the end of weeks 2, 4, and 6, and at weeks 8 and 10 (post-intervention follow-ups). The primary outcome will be the Center of Pressure sway area (CoParea); secondary outcomes will be standard deviation and velocity of the CoP in the mediolateral and anteriorposterior directions; tertiary outcomes will include the Modified-Modified Ashworth Scale for lower limbs, Modified Ashworth Scale for upper limbs, timed up-and-go tests, the timed one-leg standing and 6-minute walk test. Results: This study provides an assessment of the feasibility and effectiveness of an affordable rehabilitation programme using low-cost virtual reality aimed at improving postural control in children with cerebral palsy. Conclusion: The designed rehabilitation programme using low-cost virtual reality may improve postural control in children with cerebral palsy-spastic hemiplegia. The TR modality is likely to be as effective as the FtF modality. The TR programme has been designed to overcome access barriers to physiotherapy services for children with cerebral palsy in low-resource settings, remote areas, and in restricted mobility contexts.

#### PMID: 37590295

#### 4. Spinal motoneurons respond aberrantly to serotonin in a rabbit model of cerebral palsy

Emily J Reedich, Landon T Genry, Preston R Steele, Elvia Mena Avila, Lisa Dowaliby, Alexander Drobyshevsky, Marin Manuel, Katharina A Quinlan

J Physiol. 2023 Aug 16. doi: 10.1113/JP284803. Online ahead of print.

Cerebral palsy (CP) is caused by a variety of factors that damage the developing central nervous system. Impaired motor control, including muscle stiffness and spasticity, is the hallmark of spastic CP. Rabbits that experience hypoxic-ischaemic (HI) injury in utero (at 70%-83% gestation) are born with muscle stiffness, hyperreflexia and, as recently discovered, increased 5-HT in the spinal cord. To determine whether serotonergic modulation of spinal motoneurons (MNs) contributes to motor deficits, we performed ex vivo whole cell patch clamp in neonatal rabbit spinal cord slices at postnatal day (P) 0-5. HI MNs responded to the application of  $\alpha$ -methyl 5-HT (a 5-HT1 /5-HT2 receptor agonist) and citalopram (a selective 5-HT reuptake inhibitor) with increased amplitude and hyperpolarization of persistent inward currents and hyperpolarized threshold voltage for action potentials, whereas control MNs did not exhibit any of these responses. Although 5-HT similarly modulated MN properties of HI motor-unaffected and motor-affected kits, it affected sag/hyperpolarization-activated cation current (Ih) and spike frequency adaptation only in HI motor-affected MNs. To further explore the differential sensitivity of MNs to 5-HT, we performed immunostaining for inhibitory 5-HT1A receptors in lumbar spinal MNs at P5. Fewer HI MNs expressed the 5-HT1A receptor compared to age-matched control MNs. This suggests that HI MNs may lack a normal mechanism of central fatigue, mediated by 5-HT1A receptors. Altered expression of other 5-HT receptors (including 5-HT2) likely also contributes to the robust increase in HI MN excitability. In summary, by directly exciting MNs, the increased concentration of spinal 5-HT in HI-affected rabbits can cause MN hyperexcitability, muscle stiffness and spasticity characteristic of CP. Therapeutic strategies that target serotonergic neuromodulation may be beneficial to individuals with CP. KEY POINTS: We used whole cell patch clamp electrophysiology to test the responsivity of spinal motoneurons (MNs) from neonatal control and hypoxiaischaemia (HI) rabbits to 5-HT, which is elevated in the spinal cord after prenatal HI injury. HI rabbit MNs showed a more robust excitatory response to 5-HT than control rabbit MNs, including hyperpolarization of the persistent inward current and threshold voltage for action potentials. Although most MN properties of HI motor-unaffected and motor-affected kits responded similarly to 5-HT, 5-HT caused larger sag/hyperpolarization-activated cation current (Ih) and altered repetitive firing patterns only in HI motor-affected MNs. Immunostaining revealed that fewer lumbar MNs expressed inhibitory 5-HT1A receptors in HI rabbits compared to controls, which could account for the more robust excitatory response of HI MNs to 5-HT. These results suggest that elevated 5-HT after prenatal HI injury could trigger a cascade of events that lead to muscle stiffness and altered motor unit development.

#### PMID: 37584461

#### 5. Current Concept and Management of Spastic Hip in Children: A Narrative Review

Mohammed H Al-Rumaih, Mark W Camp, Unni G Narayanan

Review Cureus. 2023 Aug 11;15(8):e43347. doi: 10.7759/cureus.43347. eCollection 2023 Aug.

Cerebral palsy (CP) is a non-progressive motor condition that hinders the development of movement and posture. One of the common problems faced in CP is spastic hips, which can cause discomfort, deformity, and functional restrictions. This review article seeks to offer a thorough summary of the most recent methods for treating spastic hips in cerebral palsy patients. Additionally, it describes the success and potential risks of various conservative and surgical procedures. It also looks at new treatments and potential avenues for managing this complicated ailment.

#### PMID: <u>37577278</u>

## 6. Addition of backward walking training to forward walking training improves walking speed in children with cerebral palsy: a systematic review with meta-analysis

Kênia K P Menezes, Patrick R Avelino, Lucas R Nascimento

Int J Rehabil Res. 2023 Aug 15. doi: 10.1097/MRR.00000000000598. Online ahead of print.

The objective was to examine the effects of backward walking training for improving walking speed and balance in children with cerebral palsy. A systematic review of randomized trials was conducted. Trials had to include children with cerebral palsy, with a Gross Motor Function Classification System, between I and III, that delivered backward walking training as a solo intervention or in combination with forward walking training. The outcomes of interest were walking speed and balance. The methodological quality of included trials was assessed by the PEDro scale, and the quality of evidence was assessed according to Grading of Recommendations Assessment, Development and Evaluation. Eight papers, involving 156 participants, were included. Using random-effects meta-analysis, we estimated that backward walking training improved walking speed by 0.10 m/s [95% confidence interval (CI) 0.05-0.16] and by 2 points on the Pediatric Balance Scale (0-56) (95% CI 1.5-2.2) more than forward walking training. We also estimated that the addition of backward walking training increased walking speed by 0.20 m/s (95% CI 0.07-0.34) and reduced the angular excursion of the center of gravity by 0.5 degrees (95% CI -0.7 to -0.3). The quality of the evidence was classified as low to moderate. In conclusion, overall, backward walking training appears to be as effective or slightly superior to forward walking training for improving walking speed in children with CP. The addition of backward walking training speed.

#### PMID: 37581293

## 7. Is peak hamstrings muscle-tendon length criterion a sufficient indicator to recommend against surgical lengthening of hamstrings?

Prabhav Saraswat, Bruce A MacWilliams, Mark L McMulkin, Ashley M Carpenter, Emily R Shull, Kristen L Carroll, Alan K Stotts, Ted Sousa, Lauren C Hyer, David E Westberry

Gait Posture. 2023 Aug 10;105:149-157. doi: 10.1016/j.gaitpost.2023.08.004. Online ahead of print.

Background: Excessive knee flexion during stance in children with cerebral palsy is often treated by surgical hamstrings lengthening. Pre-operative hamstrings muscle-tendon length can be estimated from kinematics and often used for decision making to rule out surgical lengthening if peak hamstrings muscle-tendon length is 'Not Short'. Research question: If peak hamstrings muscle-tendon length is within two standard deviations of typical, is that a sufficient indicator to rule out surgical hamstrings lengthening? Methods: Three motion analysis centers retrospectively identified children with cerebral palsy, age 6-17 years, who had consecutive gait analyses with knee flexion at initial contact  $> 20^{\circ}$  and popliteal angle  $> 35^{\circ}$  at initial study. Three groups were considered: Medial Hamstrings Lengthening (MHL), Medial and Lateral Hamstrings Lengthening (MLHL), no surgical intervention (Control). Peak hamstrings muscle-tendon length at initial gait study was computed and categorized as 'Short' or 'Not Short'. Two outcomes variables were considered: change in peak knee extension (PKE) and change in pelvic tilt. Univariate comparisons of all variables were assessed along with a multivariate stepwise regression analysis to identify preoperative characteristics that may predict post-operative improvement. Results: 440 individuals met inclusion criteria. Percentage of individuals with improved PKE by grouping were- MHL-'Short': 60%, MHL-'Not Short': 65%, MLHL-'Short': 74%, MLHL-'Not Short': 74%, Control 'Short': 20%, Control 'Not Short': 19%. Percentage of individuals with worsened pelvic tilt were- MHL-'Short': 25%, MHL-'Not Short': 11%, MLHL-'Short': 42%, MLHL-'Not Short': 21% with significantly more individuals in MHL-'Short' subgroup compared to MHL-'Not Short'. Multivariate analysis suggested that pre-operative pelvic tilt and weak hip extensor strength have the largest effect on predicting post-operative increase in APT. Peak muscle-tendon length was not a significant predictor of post-operative knee kinematics or increase in APT. Significance: This study suggests that hamstrings muscle-tendon length criteria by itself is not a sufficient indicator to recommend against hamstrings lengthening.

#### PMID: <u>37573759</u>

## 8. Effect of low-level laser therapy on quadriceps and foot muscle fatigue in children with spastic diplegia: a randomized controlled study

Sarah Mohamed Abdelhalim, Kamal Elsayed Shoukry, Jehan Alsharnoubi

Randomized Controlled Trial Lasers Med Sci. 2023 Aug 12;38(1):182. doi: 10.1007/s10103-023-03841-y.

Spastic diplegia is the most common form of cerebral palsy; children with spastic diplegia are suffering from muscle fatigue and spasticity which lead to decreasing power of muscles, impaired motor control, and many functional abilities. The effect of low-level laser (LLL) has a good result as it improves muscles pain and spasticity and in decreasing lactate levels. Forty children were selected with spastic diplegia and were divided into two groups: A and B. Group A received low-level laser treatment (LLLT) with physiotherapy treatment. Group B got physiotherapy sessions. Pain intensity was assessed by the visual analog scale (VAS) of pain which is reliable from age 5, before treatment and after 1-month follow-up. Muscle fatigue and power were assessed by maximum voluntary isometric contraction (MVIC) before treatment and after 1-month follow-up. Also, we tested blood lactate level in both groups; all evaluations were done before treatment and after 1-month follow-up. We found a significant difference between the two groups in VAS and MVIC and blood lactate level test regarding low-level therapy after 1-month follow-up. There is a good effect of low-level laser in increasing muscle power, decreasing blood lactate level, and improving pain.

PMID: <u>37572215</u>

## 9. Task-specific training for bicycle-riding goals in ambulant children with cerebral palsy: A randomized controlled trial

No authors listed

Dev Med Child Neurol. 2023 Aug 18. doi: 10.1111/dmcn.15737. Online ahead of print.

No abstract available

#### PMID: 37593906

## 10. The Experience of Dancing Among Individuals with Cerebral Palsy at an Inclusive Dance Group: A Qualitative Study

Lydia Lentzari, Evdokia Misouridou, Vicky Karkou, Marianthe Paraskeva, Chrysoula Tsiou, Ourania Govina, Antonia Kalogianni, Stelios Parissopoulos

Adv Exp Med Biol. 2023;1425:443-456. doi: 10.1007/978-3-031-31986-0\_43.

Background: Art practices such as dance have the potential to support people with disabilities. It is possible that through dancing, bodies that may be regarded as "deficient" can be strengthened while enhancing their personal and cultural identities. It is also possible that inclusive group dance classes can enable the integration of people with disabilities in their social context. However, there is limited research on how these potential benefits are experienced by participants. Aim: The purpose of this research is to describe the experience of people with cerebral palsy participating in regular dance classes. Methods: Semi-structured interviews were conducted with six participants with cerebral palsy who participated in an inclusive dance group that was informed by the creative approach of Laban. The interviews were transcribed, coded, and analyzed according to the thematic analysis of Braun and Clarke. The qualitative analysis software program ATLAS.TI version 8 was used for organizing and data analysis. Findings: The six interviews were analyzed and codified in four main categories: (1) the experience of cerebral palsy (the body does not help); (2) dance as a form of relationship with myself and the other; (3) the value of dancing and; (4) the dancer. These categories led to the creation of two subthemes: (a) the "unlocking" concerning the therapeutic effect of dance and (b) the "acquisition of a dancer's identity" by engaging with dance as an artform. An overall theme also emerged, "the passage from darkness to light." Conclusions: Individuals with cerebral palsy, while taking the risk of being physically "exposed" in dance classes and dance group performances, managed to unlock their bodies, develop connections with others, acquire the identity of a dancer, and move from "darkness" to "light."

#### PMID: 37581818

## 11. Barriers to and facilitators of a just-in-time adaptive intervention for respiratory illness in cerebral palsy: a qualitative study

Kristina Devi Singh-Verdeflor, Heidi M Kloster, Carlos Lerner, Thomas S Klitzner, Christopher C Cushing, Danielle M Gerber, Barbara J Katz, Paul J Chung, Roxana Delgado-Martinez, Lorena Porras-Javier, Siem Ia, Teresa Wagner, Mary L Ehlenbach, Gemma Warner, Ryan J Coller

#### BMJ Open. 2023 Aug 17;13(8):e074147. doi: 10.1136/bmjopen-2023-074147.

Objective: To understand caregiver, healthcare professional and national expert perspectives on implementation of a just-intime adaptive intervention, RE-PACT (Respiratory Exacerbation-Plans for Action and Care Transitions) to prevent respiratory crises in severe cerebral palsy. Design: Qualitative research study. Setting: Paediatric complex care programmes at two academic medical institutions. Participants: A total of n=4 focus groups were conducted with caregivers of children with severe cerebral palsy and chronic respiratory illness, n=4 with healthcare professionals, and n=1 with national experts. Methods: Participants viewed a video summarising RE-PACT, which includes action planning, mobile health surveillance of parent confidence to avoid hospitalisation and rapid clinical response at times of low confidence. Moderated discussion elicited challenges and benefits of RE-PACT's design, and inductive thematic analysis elicited implementation barriers and facilitators. Results: Of the 19 caregivers recruited, nearly half reported at least one hospitalisation for their child in the prior year. Healthcare professionals and national experts (n=26) included physicians, nurses, respiratory therapists, social workers and researchers. Four overarching themes and their barriers/facilitators emphasised the importance of design and interpersonal relationships balanced against health system infrastructure constraints. Intervention usefulness in crisis scenarios relies on designing action plans for intuitiveness and accuracy, and mobile health surveillance tools for integration into daily life. Trust, knowledge, empathy and adequate clinician capacity are essential components of clinical responder-caregiver relationships. Conclusions: RE-PACT's identified barriers are addressable. Just-in-time adaptive interventions for cerebral palsy appear wellsuited to address families' need to tailor intervention content to levels of experience, preference and competing demands.

#### PMID: 37591653

#### 12. Rate of paediatric gastrostomy insertion in England and relationship to epidemiology of cerebral palsy

#### Mara Popescu, Mohamed Mutalib

Frontline Gastroenterol. 2023 May 8;14(5):399-406. doi: 10.1136/flgastro-2022-102356. eCollection 2023.

Background and objectives: Gastrostomy tubes are commonly used to provide an alternative route for enteral nutrition. Most of the gastrostomies are inserted in children with cerebral palsy. Previous studies have shown an increase in insertion rate, however, epidemiological studies reveal a stasis in prevalence of cerebral palsy. We aimed to provide an up-to-date rate of gastrostomy insertion in children in England over a 20-year period and systematically review the prevalence of cerebral palsy to ascertain an epidemiological explanation for insertion trends. Methods: Retrospective search of Hospital Episode Statistic, a database held diagnosis and procedural code from all England National Health Service hospitals from 2000 to 2021 using International Classification of Disease-10 and Office of Population Censuses and Survey's Classification-4. England Office for National Statistics data were used for population census. MEDLINE and EMBASE were systematically searched for epidemiology of cerebral palsy. Results: There were 23 079 gastrostomies inserted in children <15 years in England (2000-2021) leading to a frequency of 12.4 insertions per 100 000 children per year and 1383 gastrostomy insertions in 15-18 years age group (6 per 100 000). The overall gastrostomy insertion rate in children <15 years has increased from 3.7 procedures per 100 000 in 2000 to 18.3 per 100 000 in 2017. Prevalence of cerebral palsy remained stable (1.5-3.3 per 1000 birth) since 1985. Conclusions: There was a significant increase in the rate of gastrostomy insertion in children in England during most of the last 20 years not explained by a stable prevalence of cerebral palsy.

#### PMID: 37581183

#### 13. Limb-specific thalamocortical tracts are impaired differently in hemiplegic and diplegic subtypes of cerebral palsy

Julia Jaatela, Dogu Baran Aydogan, Timo Nurmi, Jaakko Vallinoja, Helena Mäenpää, Harri Piitulainen

Cereb Cortex. 2023 Aug 18; bhad279. doi: 10.1093/cercor/bhad279. Online ahead of print.

Thalamocortical pathways are considered crucial in the sensorimotor functioning of children with cerebral palsy (CP). However, previous research has been limited by non-specific tractography seeding and the lack of comparison between different CP subtypes. We compared limb-specific thalamocortical tracts between children with hemiplegic (HP, N = 15) or diplegic (DP, N = 10) CP and typically developed peers (N = 19). The cortical seed-points for the upper and lower extremities were selected (i) manually based on anatomical landmarks or (ii) using functional magnetic resonance imaging (fMRI) activations following proprioceptive-limb stimulation. Correlations were investigated between tract structure (mean diffusivity, MD; fractional anisotropy, FA; apparent fiber density, AFD) and sensorimotor performance (hand skill and postural stability). Compared to controls, our results revealed increased MD in both upper and lower limb thalamocortical tracts in the nondominant hemisphere in HP and bilaterally in DP subgroup. MD was strongly lateralized in participants with hemiplegia, while AFD seemed lateralized only in controls. fMRI-based tractography results were comparable. The correlation analysis indicated an association between the white matter structure and sensorimotor performance. These findings suggest distinct impairment of functionally relevant thalamocortical pathways in HP and DP subtypes. Thus, the organization of thalamocortical white matter tracts may offer valuable guidance for targeted, life-long rehabilitation in children with CP.

#### PMID: <u>37595205</u>

#### 14. Abnormal changes of bone metabolism markers with age in children with cerebral palsy

Wen Xing, Lin Liang, Na Dong, Liang Chen, Zhizhong Liu

Front Pediatr. 2023 Aug 1;11:1214608. doi: 10.3389/fped.2023.1214608. eCollection 2023.

Cerebral palsy (CP) is a broad range of diseases with permanent and nonprogressive motor impairments, carrying a high cost for both the individual and the society. The characteristics of low bone mineral density and high risk of fractures suggest that bone metabolism disorders are present in CP. This study aims to investigate the association between indicators of bone metabolism and children with CP. A total of 139 children (75 children with CP and 64 healthy controls) were included in this cross-sectional study. Participants were divided into three age groups (0-2 years, 2.1-4 years, and 4.1-7 years). All children with CP were diagnosed according to clinical criteria and furtherly divided into clinical subtypes. The levels of total procollagen type I N-terminal propeptide (TPINP), N-MID osteocalcin (OC), beta-crosslaps ( $\beta$ -CTX), 25-hydroxyvitamin D (25-OHD) and parathyroid hormone (PTH) in the serum were measured with corresponding detection kits according to the manufacturer's instructions. Serum levels of TPINP and 25-OHD were lower with older age, whereas  $\beta$ -CTX and PTH were higher with older age. In the CP group, TPINP (age 0-2 years and 2.1-4 years) and OC (age 2.1-4 years) levels were higher, while  $\beta$ -CTX (age 2.1-4 years and 4.1-7 years) and PTH (age 2.1-4 years) values were lower than the control group. In addition, there were no statistically significant differences in the levels of these indicators among the CP subgroups with different clinical characteristics. Our study shows that bone turnover markers, indicators of bone metabolism, in children with CP differ significantly from healthy controls. The indicators we studied changed with age, and they did not correlate with disease severity.

#### PMID: <u>37593441</u>

## 15. Association of Acute Infarct Topography With Development of Cerebral Palsy and Neurological Impairment in Neonates With Stroke

Mark T Mackay, Jian Chen, Jesse Shapiro, Manuela Pastore-Wapp, Nedelina Slavova, Sebastian Grunt, Belinda Stojanovski, Maja Steinlin, Richard J Beare, Joseph Yuan-Mou Yang

Neurology. 2023 Aug 17;10.1212/WNL.000000000207705. doi: 10.1212/WNL.000000000207705. Online ahead of print.

Objectives: Research investigating neonatal arterial ischemic stroke (NAIS) outcomes have shown that combined cortical and basal ganglia infarction or involvement of the corticospinal tract predict cerebral palsy (CP). The research question was whether voxel-based lesion-symptom mapping (VLSM) on acute MRI can identify brain regions associated with CP and neurodevelopmental impairments in neonatal arterial ischemic stroke (NAIS). Methods: Newborns were recruited from prospective Australian and Swiss pediatric stroke registries. CP diagnosis was based on clinical examination. Language and cognitive-behavioral impairments were assessed using the Pediatric Stroke Outcome Measure, dichotomized to good (0-0.5) or poor  $(\geq 1)$ , at  $\geq 18$  months of age. Infarcts were manually segmented using diffusion-weighted imaging, registered to a neonatalspecific brain template. VLSM was conducted using MATLAB SPM12 toolbox. A general linear model was used to correlate lesion masks with motor, language and cognitive-behavioral outcomes. Voxel-wise t-test statistics were calculated, correcting for multiple comparisons using family-wise error rate (FWE). Results: Eighty-five newborns met inclusion criteria. Infarct lateralization was left hemisphere (62%), right (8%) and bilateral (30%). At median age 2.1 years (IQR 1.9-2.6), 33% developed CP and 42% had neurological impairments. 54 grey and white matter regions correlated with CP (t>4.33; FWE <0.05), including primary motor pathway regions, such as the precentral gyrus, and cerebral peduncle, and regions functionally connected to the primary motor pathway, such as the pallidum, and corpus callosum motor segment. No significant correlations were found for language or cognitive-behavioral outcomes. Conclusions: CP following NAIS correlates with infarct regions directly involved in motor control and, or in functionally connected regions. Areas associated with language or cognitivebehavioral impairment are less clear.

#### PMID: 37591776

#### 16. The impact of ageing on adults with cerebral palsy

Brian Bell, Sonali Shah, Neil Coulson, Janice McLaughlin, Philipa Logan, Richard Luke, Anthony J Avery

BJGP Open. 2023 Aug 17;BJGPO.2023.0028. doi: 10.3399/BJGPO.2023.0028. Online ahead of print.

Background: Cerebral palsy (CP) is one of the most common neurological disorders in children and results in lifelong physical impairments. Adults with CP have approximately the same life expectancy as their non-disabled peers, so helping them to stay healthy throughout the life course will have long-term cost benefits via reductions in hospital admissions, long term care and unemployment rates. Aim: This paper reports on a national online survey that explores how adults with CP experience ageing. Design & setting: Online survey given to adults with CP in the UK. Method: The participants were adults with CP. Items for the online survey were taken from existing self-report measures, with additional items developed for the survey. Several domains of functioning were assessed including mobility, dexterity, fatigue, pain, speech, mental health, swallowing and health

maintenance/self-care as well as healthcare usage. Data were analysed using chi-square to examine the relationships between the demographic variables and the survey responses. Results: The survey was completed by 395 participants, of which 72.2% were female and approximately 60% under the age of 45. Respondents reported having problems with mobility, pain and fatigue with older participants reporting higher levels of pain and more mobility problems, although the correlations were fairly small. Healthcare usage was surprisingly low. Conclusion: We found that age was associated with a decline in mobility and a higher level of pain, although the relationships were weak. It is possible that the low healthcare usage among our respondents is due to services not being available to respond to their needs.

#### PMID: 37591553

#### 17. Abdominal Massage to Improve Motor Dysfunction in Rats with Cerebral Palsy

Rui Qiao, Ayipaxiaguli Kasimu, Danmei Chen, Chao Gao, Bing Li

J Vis Exp. 2023 Aug 11;(198). doi: 10.3791/65625.

Cerebral palsy (CP) is a disease with a high disability rate and morbidity. The clinical symptoms of cerebral palsy are motor dysfunction and abnormal posture development, often accompanied by cognitive impairment. Massage, a traditional Chinese Medicine therapy, can coordinate Zang and Fu, regulate Qi and blood, make the viscera work more smoothly, and calm Yin and Yang. Furthermore, it has been an effective method for CP in clinical. This paper summarizes a set of simple and standardized manipulations of massage for young rats with CP, which is easy to follow. The procedure follows: first, massage of four limb acupoints, including Quchi (L111) and Zusanli (ST36); second, massage of the abdomen acupoints Zhongwan (RN12), Tianshu (ST25), Guanyuan (CV4), and Qihai (CV6); and finally, massage of the abdomen of the rats. This set of massage methods considerably improved the motor function of young rats with CP and is simple, standardized, and easy to follow. We adapted this set of manipulation methods in animal models to promote the internationalization and standardization of massage.

#### PMID: 37590501

#### 18. Infant movement classification through pressure distribution analysis

Tomas Kulvicius, Dajie Zhang, Karin Nielsen-Saines, Sven Bölte, Marc Kraft, Christa Einspieler, Luise Poustka, Florentin Wörgötter, Peter B Marschik

Commun Med (Lond). 2023 Aug 16;3(1):112. doi: 10.1038/s43856-023-00342-5.

Background: Aiming at objective early detection of neuromotor disorders such as cerebral palsy, we propose an innovative non -intrusive approach using a pressure sensing device to classify infant general movements. Here we differentiate typical general movement patterns of the "fidgety period" (fidgety movements) vs. the "pre-fidgety period" (writhing movements). Methods: Participants (N = 45) were sampled from a typically-developing infant cohort. Multi-modal sensor data, including pressure data from a pressure sensing mat with 1024 sensors, were prospectively recorded for each infant in seven succeeding laboratory sessions in biweekly intervals from 4 to 16 weeks of post-term age. 1776 pressure data snippets, each 5 s long, from the two targeted age periods were taken for movement classification. Each snippet was pre-annotated based on corresponding synchronised video data by human assessors as either fidgety present or absent. Multiple neural network architectures were tested to distinguish the fidgety present vs. fidgety absent classes, including support vector machines, feed-forward networks, convolutional neural networks, and long short-term memory networks. Results: Here we show that the convolution neural network achieved the highest average classification accuracy (81.4%). By comparing the pros and cons of other methods aiming at automated general movement assessment to the pressure sensing approach, we infer that the proposed approach has a high potential for clinical applications. Conclusions: We conclude that the pressure sensing approach has great potential for efficient large-scale motion data acquisition and sharing. This will in return enable improvement of the approach that may prove scalable for daily clinical application for evaluating infant neuromotor functions.

#### PMID: 37587165

#### 19. Multiple motor disorders in cerebral palsy

Hayim Dar, Kirsty Stewart, Sarah McIntyre, Simon Paget

Dev Med Child Neurol. 2023 Aug 14. doi: 10.1111/dmcn.15730. Online ahead of print.

Aim: To characterize motor disorders in children and young people with cerebral palsy (CP). Method: This was a crosssectional study of 582 children and young people with CP (mean age 9 years 7 months; range 11 months-19 years 9 months; standard deviation 4 years 11 months; 340 males) attending a rehabilitation clinic at a specialized children's hospital (May 2018 -March 2020). Data on motor disorders, topography, functional classifications, and non-motor features, such as epilepsy, intellectual disability, and sensory impairments, were collected using the Australian Cerebral Palsy Register CP Description Form. Results: Fifty-five per cent (n = 321) of children and young people with CP presented with multiple motor disorders, often affecting the same limb(s). The most common motor disorders were spasticity and dystonia (50%), spasticity only (36%), and dystonia only (6%), but 18 different combinations were identified, including choreoathetosis, ataxia, and generalized hypotonia with increased reflexes. Children with spasticity only had less severe functional deficits (p < 0.001) and lower rates of associated intellectual disability (p < 0.01) and epilepsy (p < 0.001) than those with both spasticity and dystonia. Interpretation: Multiple motor disorders in children and young people with CP are common and associated with more severe functional impairment. Accurate assessment of motor disorders is essential to guide prognosis and ensure personalized evidence-based interventions.

#### PMID: 37579020

## 20. Prevalence and related factors of epilepsy in children and adolescents with cerebral palsy: a systematic review and meta-analysis

Chao Gong, Annan Liu, Beibei Lian, Xixi Wu, Pei Zeng, Chaoli Hao, Bobo Wang, Zhimei Jiang, Wei Pang, Jin Guo, Shaobo Zhou

Review Front Pediatr. 2023 Jul 28;11:1189648. doi: 10.3389/fped.2023.1189648. eCollection 2023.

Objective: To study the worldwide prevalence and associated factors of epilepsy in children and adolescents with Cerebral Palsy (CP) and to analyze the differences between various subgroups. Method: We identified all potential studies on the prevalence of epilepsy in children and adolescents with CP from PubMed, Web of Science, and Embase. The search time was from the establishment of the database to November 2022. Randomized effects meta-analysis models were used to calculate the prevalence of epilepsy in CP. Subgroup analysis and meta-regression were utilized to further explore heterogeneity between articles and prevalence disparities between subgroups. The funnel plot and Egger's test were used to investigate potential publication bias. Results: Seventy-two articles, comprising 53,969 children and adolescents with CP, were included in this study. The results indicated a total epilepsy prevalence of 38.0% (95% CI: 34.8%-41.2%) in CP. The prevalence of epilepsy was 46.4% (95% CI: 41.4%-51.5%) in clinical sample-based studies and 31.6% (95% CI: 28.7%-34.5%) in population-based studies. Meta-regression demonstrated that the sample source, neonatal seizure, family history of epilepsy, EEG or cranial imaging abnormalities, intellectual/cognitive impairment, and topographical types of CP were heterogeneous contributors to the epilepsy prevalence in CP. Conclusion: Approximately one-third of children and adolescents with CP have epilepsy, and the sample source can significantly impact the total prevalence of epilepsy. Neonatal seizures, family history of epilepsy, EEG abnormalities, cranial imaging abnormalities, severe intellectual disability, and quadriplegia may be contributing factors to epilepsy comorbid in CP. Further study is required to verify the strength of these associations with epilepsy. This study aids in identifying the clinical characteristics of young people with CP at risk of developing epilepsy, which may assist clinicians in the early prevention and diagnosis of epilepsy within this population.

#### PMID: 37576141

#### 21. Icono: a universal language that shows what it says

Peter Kramer

Front Psychol. 2023 Jul 28;14:1149381. doi: 10.3389/fpsyg.2023.1149381. eCollection 2023.

This article lays out the foundation of a new language for easier written communication that is inherently reader-friendly and inherently international. Words usually consist of strings of sounds or squiggles whose meanings are merely a convention. In Icono, instead, they typically are strings of icons that illustrate what they stand for. "Train," for example, is expressed with the icon of a train, "future" with the icon of a clock surrounded by a clockwise arrow, and "mammal" with the icons of a cow and a mouse-their combination's meaning given by what they have in common. Moreover, Icono reveals sentence structure graphically before, rather than linguistically after, one begins reading. On smartphones and computers, writing icons can now be faster than writing alphabetic words. And using simple pictures as words helps those who struggle with conditions like dyslexia, aphasia, cerebral palsy, and autism with speech impairment. Because learning its pronunciation or phonetic spelling is optional rather than a prerequisite, and because it shows what it says, Icono is bound to be easier to learn to read-and then easier to read-than any other language, including our own.

#### PMID: 37575437

#### 22. Safety of botulinum toxin injections in children less than one year old: A retrospective chart review

Nikhil Deshpande, Mark E Gormley, Supreet Deshpande

J Pediatr Rehabil Med. 2023 Aug 10. doi: 10.3233/PRM-220003. Online ahead of print.

Purpose: Infants can have muscle hypertonia due to cerebral palsy, muscle strength imbalances due to brachial plexus palsy, refractory clubfoot, and torticollis. These muscle problems can cause significant development impairments. A child with severe sialorrhea and dysphagia from leukodystrophy can aspirate, causing respiratory problems. Botulinum toxin (BoNT) injections can improve these conditions but may lead to adverse effects from the toxin spreading to non-targeted muscles, potentially impacting breathing, swallowing, and overall strength. This is particularly concerning in infants. This study assessed the safety of BoNT injections in children less than one year of age. Methods: This was a retrospective cohort study. Results: Forty-seven patients (22 male, 25 female) received BoNT injections before one year of age (three to 12 months). Thirty-seven received one round of injections and 10 were injected on multiple occasions. Forty-five received onabotulinumtoxinA (15-100 units [U], 1.9 -15.2 U/kg), one received abobotulinumtoxinA (70 U, 9.0 U/kg), and one received incobotulinumtoxinA (25 U, 3.5 U/kg). Lower extremities were treated in 15 patients, upper extremities in 38, the sternocleidomastoid in two, and the salivary glands in one. Forty-five patients had no reported complications. One experienced transient fever, vomiting, and diarrhea. The parent of another reported subjective weakness in one muscle. Conclusion: BoNT injections in children less than one year of age appear to be safe.

#### PMID: <u>37574745</u>

## 23. Neonatal encephalopathy and hypoxic-ischemic encephalopathy: moving from controversy to consensus definitions and subclassification

Eleanor J Molloy, Aoife Branagan, Tim Hurley, Fiona Quirke, Declan Devane, Petek E Taneri, Mohamed El-Dib, Frank H Bloomfield, Beccy Maeso, Betsy Pilon, Sonia L Bonifacio, Courtney J Wusthoff, Lina Chalak, Cynthia Bearer, Deirdre M Murray, Nadia Badawi, Suzann Campbell, Sarah Mulkey, Pierre Gressens, Donna M Ferriero, Linda S de Vries, Karen Walker, Sarah Kay, Geraldine Boylan, Chris Gale, Nicola J Robertson, Mary D'Alton, Alistair Gunn, Karin B Nelson; Steering Group for DEFiNE (Definition of Neonatal Encephalopathy)

Editorial Pediatr Res. 2023 Aug 12. doi: 10.1038/s41390-023-02775-z. Online ahead of print.

No abstract available

#### PMID: 37573378

## 24. The long-term effects of aggressive spasticity reducing treatment, including selective dorsal rhizotomy, on joint kinematic outcomes of persons with cerebral palsy

Mark L McMulkin, Bruce A MacWilliams, Elizabeth A Nelson, Meghan E Munger, Brian Po-Jung Chen, Tom F Novacheck, Kristen L Carroll, Alan K Stotts, Lisa H Carter, Shelley L Mader, Brianna Hayes, Glen O Baird, Michael H Schwartz

Gait Posture. 2023 Aug 2;105:139-148. doi: 10.1016/j.gaitpost.2023.07.348. Online ahead of print.

Background: Selective dorsal rhizotomy (SDR) creates a large and permanent reduction of spasticity for children with cerebral palsy (CP). Previous SDR outcomes studies have generally lacked appropriate control groups, had limited sample sizes, or reported short-term follow-up, limiting evidence for improvement in long-term gait function. Research question: Does aggressive spasticity management for individuals with CP improve long-term gait kinematics (discrete joint kinematics) compared to a control group of individuals with CP with minimal spasticity management? Methods: This study was a secondary analysis - focused on joint-level kinematics - of a previous study evaluating the long-term outcomes of SDR. Two groups of participants were recruited based on a retrospectively completed baseline clinical gait study. One group received aggressive spasticity treatment including a selective dorsal rhizotomy (Yes-SDR group), while the other group had minimal spasticity management (No-SDR group). Both groups had orthopedic surgery treatment. Groups were matched on baseline spasticity. All participants prospectively returned for a follow-up gait study in young adulthood (greater than 21 years of age and at least 10 years after baseline). Change scores in discrete kinematic variables from baseline to follow-up were assessed using a linear model that included treatment arm (Yes-SDR, No-SDR), baseline age, and baseline kinematic value. For treatment arm, 5° and 5 Gait Deviation Index points were selected as thresholds to be considered a meaningful difference between treatment groups.Results: At follow-up, there were no meaningful differences in pelvis, hip, knee, or ankle kinematic variable changes between treatment arms. Max knee flexion - swing showed a moderate treatment effect for Yes-SDR, although it did not reach the defined threshold.Significance: Aggressive spasticity treatment does not result in meaningful differences in gait kinematics for persons with cerebral palsy in young adulthood compared to minimal spasticity management with both groups having orthopedic surgery.

PMID: 37572544

### **Prevention and Cure**

## 25. Prenatal Intravenous Magnesium at 30-34 Weeks' Gestation and Neurodevelopmental Outcomes in Offspring: The MAGENTA Randomized Clinical Trial

Caroline A Crowther, Pat Ashwood, Philippa F Middleton, Andrew McPhee, Thach Tran, Jane E Harding; MAGENTA Study Group

Randomized Controlled Trial JAMA. 2023 Aug 15;330(7):603-614. doi: 10.1001/jama.2023.12357.

Importance: Intravenous magnesium sulfate administered to pregnant individuals before birth at less than 30 weeks' gestation reduces the risk of death and cerebral palsy in their children. The effects at later gestational ages are unclear. Objective: To determine whether administration of magnesium sulfate at 30 to 34 weeks' gestation reduces death or cerebral palsy at 2 years. Design, setting, and participants: This randomized clinical trial enrolled pregnant individuals expected to deliver at 30 to 34 weeks' gestation and was conducted at 24 Australian and New Zealand hospitals between January 2012 and April 2018. Intervention: Intravenous magnesium sulfate (4 g) was compared with placebo. Main outcomes and measures: The primary outcome was death (stillbirth, death of a live-born infant before hospital discharge, or death after hospital discharge before 2 years' corrected age) or cerebral palsy (loss of motor function and abnormalities of muscle tone and power assessed by a pediatrician) at 2 years' corrected age. There were 36 secondary outcomes that assessed the health of the pregnant individual, infant, and child. Results: Of the 1433 pregnant individuals enrolled (mean age, 30.6 [SD, 6.6] years; 46 [3.2%] self-identified as Aboriginal or Torres Strait Islander, 237 [16.5%] as Asian, 82 [5.7%] as Māori, 61 [4.3%] as Pacific, and 966 [67.4%] as White) and their 1679 infants, 1365 (81%) offspring (691 in the magnesium group and 674 in the placebo group) were included in the primary outcome analysis. Death or cerebral palsy at 2 years' corrected age was not significantly different between the magnesium and placebo groups (3.3% [23 of 691 children] vs 2.7% [18 of 674 children], respectively; risk difference, 0.61% [95% CI, -1.27% to 2.50%]; adjusted relative risk [RR], 1.19 [95% CI, 0.65 to 2.18]). Components of the primary outcome did not differ between groups. Neonates in the magnesium group were less likely to have respiratory distress syndrome vs the placebo group (34% [294 of 858] vs 41% [334 of 821], respectively; adjusted RR, 0.85 [95% CI, 0.76 to 0.95]) and chronic lung disease (5.6% [48 of 858] vs 8.2% [67 of 821]; adjusted RR, 0.69 [95% CI, 0.48 to 0.99]) during the birth hospitalization. No serious adverse events occurred; however, adverse events were more likely in pregnant individuals who received magnesium vs placebo (77% [531 of 690] vs 20% [136 of 667], respectively; adjusted RR, 3.76 [95% CI, 3.22 to 4.39]). Fewer pregnant individuals in the magnesium group had a cesarean delivery vs the placebo group (56% [406 of 729] vs 61% [427 of 704], respectively; adjusted RR, 0.91 [95% CI, 0.84 to 0.99]), although more in the magnesium group had a major postpartum hemorrhage (3.4% [25 of 729] vs 1.7% [12 of 704] in the placebo group; adjusted RR, 1.98 [95% CI, 1.01 to 3.91)).Conclusions and relevance: Administration of intravenous magnesium sulfate prior to preterm birth at 30 to 34 weeks' gestation did not improve child survival free of cerebral palsy at 2 years, although the study had limited power to detect small between-group differences. Trial registration: anzctr.org.au Identifier: ACTRN12611000491965.

PMID: 37581672