

# **Cerebral palsy** research news

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### Interventions and Management

1. Wrist Arthrodesis in Athetoid Type Cerebral Palsy: A Case Study of 2 Patients Hyun Sik Seok, Young Ju Chae, Hyun Sik Gong

J Hand Surg Asian Pac Vol. 2021 Jun;26(2):297-300. doi: 10.1142/S2424835521720115.

Wrist arthrodesis has been used successfully for the management of severe wrist flexion deformity when soft tissue procedures would not provide adequate correction. However, in athetoid type cerebral palsy which has a component of involuntary movement, the outcome of wrist arthrodesis has not been discussed much. We present our experience in 2 athetoid type cerebral palsy patients who underwent wrist arthrodesis due to severe involuntary movement of the wrist. One patient had a nonunion and both patients had unexpected aggravation of involuntary movement in the adjacent joints. Secure fixation using a pre-contoured plate is necessary and preparation for iliac bone grafting should be considered as proximal row carpectomy is usually not necessary in these patients. In addition, although single-event, multi-level surgery is advocated for patients with cerebral palsy, potential additional procedures for the adjacent joints should be discussed preoperatively because unexpected aggravation of involuntary movement of adjacent joints can occur after stabilization of the wrist.

PMID: <u>33928861</u>

### 2. Systematic review on use and efficacy of selective dorsal rhizotomy (SDR) for the management of spasticity in nonpediatric patients

Pramath Kakodkar, Aria Fallah, Albert Tu

Review Childs Nerv Syst. 2021 Apr 29. doi: 10.1007/s00381-021-05167-y. Online ahead of print.

Purpose: Selective dorsal rhizotomy (SDR) has been used to improve mobility and reduce lower extremity spasticity in patients with a various CNS conditions. Incidentally, literature on SDR has been performed in the pediatric population as such there is a paucity of research on the use in adult patients. Methods: Studies describing SDR in adults were identified from Medline and Embase databases. Combinations of search terms "Selective Dorsal Rhizotomy," "Selective Posterior Rhizotomy," and "Adult" were used. Only literature in English language on patients over the age of 18 years and that included measures for lower extremity outcome (i.e., spasticity, mobility) were included. Case reports, reviews without primary data, or inaccessible publications were excluded. Results: One hundred twenty-nine publications between 1970 and 2019 were identified. Twelve of these publications fit the inclusion criteria (n = 141 patients). In series where it was reported, SDR resulted in ambulatory improvement (54%, n = 44 out of 81), reduced spasticity (75.2%, n = 106 out of 141), and minimized muscle and joint pain (74.5%, n = 64 out of 86). SDR also showed improvement in parameters of the activities of daily life. 92.3% (n = 48 out of 52) of patients post-SDR developed new lower limb paresthesia. Conclusion: The success and efficacy

appear durable in the short-term, but further follow-up is necessary to validate these findings. The goal of the intervention dictates the ideal adult patient for SDR. Patients seeking ambulatory improvement, any etiology of spasticity besides MS, seem favorable. Positive locomotive predictors include the ability to isolate lower extremity function, lack of contractures, lower limb strength, and post-SDR physiotherapy.

PMID: 33928427

### 3. Engaging Spinal Networks to Mitigate Supraspinal Dysfunction After CP

V Reggie Edgerton, Susan Hastings, Parag N Gad

Front Neurosci. 2021 Apr 12;15:643463. doi: 10.3389/fnins.2021.643463. eCollection 2021.

Although children with cerebral palsy seem to have the neural networks necessary to generate most movements, they are markedly dysfunctional, largely attributable to abnormal patterns of muscle activation, often characterized as spasticity, largely reflecting a functionally abnormal spinal-supraspinal connectivity. While it is generally assumed that the etiologies of the disruptive functions associated with cerebral palsy can be attributed primarily to supraspinal networks, we propose that the more normal connectivity that persists between peripheral proprioception-cutaneous input to the spinal networks can be used to guide the reorganization of a more normal spinal-supraspinal connectivity. The level of plasticity necessary to achieve the required reorganization within and among different neural networks can be achieved with a combination of spinal neuromodulation and specific activity-dependent mechanisms. By engaging these two concepts, we hypothesize that bidirectional reorganization of proprioception-spinal cord-brain connectivity to higher levels of functionality can be achieved without invasive surgery.

PMID: <u>33912005</u>

### 4. Neurogenic Bowel Dysfunction in Children and Adolescents

Giovanni Mosiello, Shaista Safder, David Marshall, Udo Rolle, Marc A Benninga

Review J Clin Med. 2021 Apr 13;10(8):1669. doi: 10.3390/jcm10081669.

Neurogenic/neuropathic bowel dysfunction (NBD) is common in children who are affected by congenital and acquired neurological disease, and negatively impacts quality of life. In the past, NBD received less attention than neurogenic bladder, generally being considered only in spina bifida (the most common cause of pediatric NBD). Many methods of conservative and medical management of NBD are reported, including relatively recently Transanal Irrigation (TAI). Based on the literature and personal experience, an expert group (pediatric urologists/surgeons/gastroenterologists with specific experience in NBD) focused on NBD in children and adolescents. A statement document was created using a modified Delphi method. The range of causes of pediatric NBD are discussed in this paper. The various therapeutic approaches are presented to improve clinical management. The population of children and adolescents with NBD is increasing, due both to the higher survival rate and better diagnosis. While NBD is relatively predictable in producing either constipation or fecal incontinence, or both, its various effects on each patient will depend on a wide range of underlying causes and accompanying comorbidities. For this reason, management of NBD should be tailored individually with a combined multidisciplinary therapy appropriate for the status of the affected child and caregivers.

PMID: <u>33924675</u>

**5. Neuromuscular Control before and after Independent Walking Onset in Children with Cerebral Palsy** Annike Bekius, Coen S Zandvoort, Jennifer N Kerkman, Laura A van de Pol, R Jeroen Vermeulen, Jaap Harlaar, Andreas Daffertshofer, Annemieke I Buizer, Nadia Dominici

Sensors (Basel). 2021 Apr 12;21(8):2714. doi: 10.3390/s21082714.

Early brain lesions which produce cerebral palsy (CP) may affect the development of walking. It is unclear whether or how neuromuscular control, as evaluated by muscle synergy analysis, differs in young children with CP compared to typically developing (TD) children with the same walking ability, before and after the onset of independent walking. Here we grouped twenty children with (high risk of) CP and twenty TD children (age 6.5-52.4 months) based on their walking ability, supported or independent walking. Muscle synergies were extracted from electromyography data of bilateral leg muscles using non-negative matrix factorization. Number, synergies' structure and variability accounted for when extracting one (VAF1) or two (VAF2) synergies were compared between CP and TD. Children in the CP group recruited fewer synergies with higher VAF1 and VAF2 compared to TD children in the supported and independent walking group. The most affected side in children with asymmetric CP walking independently recruited fewer synergies with higher VAF1 compared to the least affected side. Our findings suggest that early brain lesions result in early alterations of neuromuscular control, specific for the most affected side in asymmetric CP.

PMID: <u>33921544</u>

6. Children with Cerebral Palsy Have Similar Walking and Running Quality Assessed by an Overall Kinematic Index Devin K Kelly, Mark L McMulkin, Corinna Franklin, Kevin M Cooney

Int J Environ Res Public Health. 2021 Apr 28;18(9):4683. doi: 10.3390/ijerph18094683.

Running ability is critical to maintaining activity participation with peers. Children and adolescents with cerebral palsy (CP) are often stated to run better than they walk, but running is not often quantitatively measured. The purpose of this study was to utilize overall gait deviation indices to determine if children with diplegic CP run closer to typically developing children than they walk. This retrospective comparative study utilized 3D running kinematics that were collected after walking data at two clinical motion analysis centers for children with diplegic cerebral palsy. Separate walking and running Gait Deviation Indices (GDI Walk and GDI\* Run), overall indices of multiple plane/joint motions, were calculated and scaled for each participant so that a typically developing mean was 100 with standard deviation of 10. An analysis of variance was used to compare the variables Activity (walking vs running) and Center (data collected at two different motion analysis laboratories). Fifty participants were included in the study. The main effect of Activity was not significant, mean GDI Walk = 76.4 while mean GDI\* Run = 77.1, p = 0.84. Mean GDI scores for walking and running were equivalent, suggesting children with diplegic cerebral palsy as a group have similar walking and running quality. However, individual differences varied between activities, emphasizing the need for individual assessment considering specific goals related to running.

PMID: 33924873

# 7. Validity of Hololens Augmented Reality Head Mounted Display for Measuring Gait Parameters in Healthy Adults and Children with Cerebral Palsy

Anne-Laure Guinet, Guillaume Bouyer, Samir Otmane, Eric Desailly

Sensors (Basel). 2021 Apr 11;21(8):2697. doi: 10.3390/s21082697.

Serious games are a promising approach to improve gait rehabilitation for people with gait disorders. Combined with wearable augmented reality headset, serious games for gait rehabilitation in a clinical setting can be envisaged, allowing to evolve in a real environment and provide fun and feedback to enhance patient's motivation. This requires a method to obtain accurate information on the spatiotemporal gait parameters of the playing patient. To this end, we propose a new algorithm called HoloStep that computes spatiotemporal gait parameters using only the head pose provided by an augmented reality headset (Hololens). It is based on the detection of peaks associated to initial contact event, and uses a combination of locking distance, locking time, peak amplitude detection with custom thresholds for children with CP. The performance of HoloStep was compared during a walking session at comfortable speed to Zeni's reference algorithm, which is based on kinematics and a full 3D motion capture system. Our study included 62 children with cerebral palsy (CP), classified according to Gross Motor Function Classification System (GMFCS) between levels I and III, and 13 healthy participants (HP). Metrics such as sensitivity, specificity, accuracy and precision for step detection with HoloStep were above 96%. The Intra-Class Coefficient between steps length calculated with HoloStep and the reference was 0.92 (GMFCS I), 0.86 (GMFCS II/III) and 0.78 (HP). HoloStep demonstrated good performance when applied to a wide range of gait patterns, including children with CP using walking aids. Findings provide important insights for future gait intervention using augmented reality games for children with CP.

### PMID: <u>33920452</u>

# 8. The association between gait analysis measures associated with crouch gait, functional health status and daily activity levels in cerebral palsy

Rory O'Sullivan, Helen P French, Sam Van Rossom, Ilse Jonkers, Frances Horgan

J Pediatr Rehabil Med. 2021 Apr 23. doi: 10.3233/PRM-200676. Online ahead of print.

Purpose: The aim of this study was to examine the relationship between gait analysis measures associated with crouch gait, functional health status and daily activity in ambulant cerebral palsy (CP). Methods: Three-dimensional gait analysis was carried out on 35 ambulant participants with bilateral CP crouch gait (knee flexion at mid-stance (KFMS)  $\ge$  190). KFMS, knee -flexion at initial contact, gait speed and step-lengths were extracted for analysis. Steps/day and sedentary time/day were assessed using an ActivPAL accelerometer. Functional health status was assessed using the five relevant domains of the Pediatric Outcomes Data Collection Instrument (PODCI) questionnaire. Associations between variables were assessed with correlation coefficients and multivariable linear regression. Results: There were no significant correlations between KFMS and PODCI domains  $\rho$ =-0.008-0.110) or daily activity  $\rho$ =-0.297-0.237) variables. In contrast, multivariable analysis found that step -length was independently associated with the Sports and Physical Function (p= 0.030), Transfers and Basic Mobility (p= 0.041) and Global Function (< 0.001) domains of the PODCI assessment. Gait speed was independently associated with mean steps/day (p< 0.001). Conclusions: Step length and gait speed are more strongly associated with functional health status and daily activity than knee flexion during stance in children and adolescents with CP crouch gait.

### PMID: 33896854

**9.** Changes in Muscle Mass after Botulinum Toxin Injection in Children with Spastic Hemiplegic Cerebral Palsy Dongwoo Lee, Jaewon Kim, Ja-Young Oh, Mi-Hyang Han, Da-Ye Kim, Ji-Hye Kang, Dae-Hyun Jang

Toxins (Basel). 2021 Apr 14;13(4):278. doi: 10.3390/toxins13040278.

We aimed to evaluate muscle mass changes after injection of botulinum toxin (BoNT) in children with spastic hemiplegic cerebral palsy (CP). Children aged between 2 and 12 years who were diagnosed with hemiplegic CP with spastic equinus foot were prospectively recruited and administered BoNT in the affected leg. Lean body mass (LBM) of both legs and total limbs was measured by dual-energy X-ray absorptiometry (DXA) preinjection and 4 and 12 weeks after injection. A total of 15 children were enrolled into the study. LBM of both legs and total limbs increased significantly over 12 weeks of growth. The ratio of LBM of the affected leg to total limbs and to the unaffected leg significantly reduced at 4 weeks after injection compared with preinjection but significantly increased at 12 weeks after injection compared with 4 weeks after injection. In conclusion, the muscle mass of the affected leg after BoNT injection in children with hemiplegic spastic CP decreased at 4 weeks after BoNT injection but significantly recovered after 12 weeks after injection.

PMID: 33919735

**10. Machine-learning-based Prediction of Gait Events from EMG in Cerebral Palsy Children** Christian Morbidoni, Alessandro Cucchiarelli, Valentina Agostini, Marco Knaflitz, Sandro Fioretti, Francesco Di Nardo

IEEE Trans Neural Syst Rehabil Eng. 2021 Apr 28; PP. doi: 10.1109/TNSRE.2021.3076366. Online ahead of print.

Machine-learning techniques are suitably employed for gait-event prediction from only surface electromyographic (sEMG) signals in control subjects during walking. Nevertheless, a reference approach is not available in cerebral-palsy hemiplegic children, likely due to the large variability of foot-floor contacts. This study is designed to investigate a machine-learning-based approach, specifically developed to binary classify gait events and to predict heel-strike (HS) and toe-off (TO) timing

from sEMG signals in hemiplegic-child walking. To this objective, sEMG signals are acquired from five hemiplegic-leg muscles in nearly 2500 strides from 20 hemiplegic children, acknowledged as Winters' group 1 and 2. sEMG signals, segmented in overlapping windows of 600 samples (pace = 5 samples), are used to train a multi-layer perceptron model. Intrasubject and inter-subject experimental settings are tested. The best-performing intra-subject approach is able to provide in the hemiplegic population a mean classification accuracy () of  $0.97\pm0.01$  and a suitable prediction of HS and TO events, in terms of average mean absolute error (MAE,  $14.8\pm3.2$  ms for HS and  $17.6\pm4.2$  ms for TO) and F1-score ( $0.95\pm0.03$  for HS and  $0.92\pm0.07$  for TO). These results outperform previous sEMG-based attempts in cerebral-palsy populations and are comparable with outcomes achieved by reference approaches in control populations. In conclusion, the findings of the study prove the feasibility of neural networks in predicting the two main gait events using surface EMG signals, also in condition of high variability of the signal to predict as in hemiplegic cerebral palsy.

PMID: 33909568

## **11. Impact of scaling errors of the thigh and shank segments on musculoskeletal simulation results** Willi Koller, Arnold Baca, Hans Kainz

Gait Posture. 2021 Feb 18;87:65-74. doi: 10.1016/j.gaitpost.2021.02.016. Online ahead of print.

Background: Musculoskeletal simulations are widely used in the research community. The locations of surface markers are mostly used to scale a generic model to the participant's anthropometry. Marker-based scaling approaches include errors due to inaccuracies in marker placements. Research question: How do scaling errors of the thigh and shank segments influence simulation results? Methods: Motion capture data and magnetic resonance images from a child with cerebral palsy and a typically developing child were used to create a subject-specific reference model for each child. These reference models were modified to mimic scaling errors due to inaccurately placed lateral epicondyle markers, which are frequently used to scale the thigh and shank segments. The thigh length was altered in 1 % steps from the original length and the shank length was accordingly adjusted to keep the total leg length constant. Thirty additional models were created, which included models with an altered thigh length of  $\pm 15$  %. Subsequently, musculoskeletal simulations with OpenSim were performed with all models. Joint kinematics, joint kinetics, muscle forces and joint contact forces (JCF) were compared between the reference and altered models. Results: The investigated scaling error influenced joint kinematics and joint kinetics by up to 9.4° (hip flexion angle) and 0.15 Nm/kg (knee flexion moment), respectively. Maximum muscle and JCF differences of 46 % (medial gastrocnemius) and 72 % (hip JCF) bodyweight, respectively, were observed between the reference and altered models. Scaling errors mainly changed the magnitude but not the shape of most analyzed parameters. The influence of scaling errors on simulation results were similar in both participants. Significance: Scaling errors of the thigh segment influence simulation results at all joints due to the global optimization approach used in musculoskeletal simulations. Our findings can be used to estimate potential errors due to marker-based scaling approaches in previous and future studies.

PMID: 33894464

**12.** Foot and ankle somatosensory deficits in children with cerebral palsy: A pilot study Anastasia Zarkou, Samuel C K Lee, Laura Prosser, Sungjae Hwan, Corinna Franklin, John Jeka

J Pediatr Rehabil Med. 2021 Apr 23. doi: 10.3233/PRM-190643. Online ahead of print.

Purpose: To investigate foot and ankle somatosensory function in children with cerebral palsy (CP). Methods: Ten children with spastic diplegia (age  $15 \pm 5$  y; GMFCS I-III) and 11 typically developing (TD) peers (age  $15 \pm 10$  y) participated in the study. Light touch pressure and two-point discrimination were assessed on the plantar side of the foot by using a monofilament kit and an aesthesiometer, respectively. The duration of vibration sensation at the first metatarsal head and medial malleolus was tested by a 128 Hz tuning fork. Joint position sense and kinesthesia in the ankle joint were also assessed. Results: Children with CP demonstrated significantly higher light touch pressure and two-point discrimination thresholds compared to their TD peers. Individuals with CP perceived the vibration stimulus for a longer period compared to the TD participants. Finally, the CP group demonstrated significant impairments in joint position sense but not in kinesthesia of the ankle joints. Conclusions: These findings suggest that children with CP have foot and ankle tactile and proprioceptive deficits. Assessment of lower extremity somatosensory function should be included in clinical practice as it can guide clinicians in designing more effective treatment protocols to improve functional performance in CP.

### PMID: 33896853

### 13. Hearing Loss Diagnosis and Early Hearing-Related Interventions in Infants With or at High Risk for Cerebral Palsy: A Systematic Review

Céline Richard, Caitlin Kjeldsen, Ursula Findlen, Alison Gehred, Nathalie L Maitre

J Child Neurol. 2021 Apr 29;8830738211004519. doi: 10.1177/08830738211004519. Online ahead of print.

Aim: To synthesize published evidence regarding hearing impairment diagnosis and interventions in infants with or at high risk for cerebral palsy in the first year after birth. Method: Nine databases were searched for MeSH terms up to February 2020. Included studies were published in English, enrolled infants with or at high risk for cerebral palsy, and addressed hearing evaluation/rehabilitation within the first year after birth. Quality of evidence was evaluated using RTI Item Bank and QUADAS-2. Results: Eighteen articles met inclusion criteria. Quality of the evidence ranged from low to high, revealing variability in diagnostic assessment methodologies and adherence to diagnostic schedules. Concerns for bias included lack of recognition of cerebral palsy effects and etiologies on functional hearing assessment methods and results. Two interventions (hearing aid and cochlear implantation) were identified; however, reported use was inconsistent. Interpretation: Hearing screening in infants with or at high risk for cerebral palsy requires evaluation of the entire auditory pathway preferentially using comprehensive electrophysiological panels of assessments. For infants with perinatal neural insults, pediatric neurologists are uniquely positioned to recommend adherence to systematic surveillance and comprehensive audiology assessments, regardless of comorbidities and motor impairments.

### PMID: 33913778

14. Effect of Social Support in Pain Sensitivity in Children with Cerebral Palsy and Typically Developing Children Inmaculada Riquelme, Isabel Escobio-Prieto, Ángel Oliva-Pascual-Vaca, Alberto Marcos Heredia-Rizo, Pedro Montoya

Int J Environ Res Public Health. 2021 Apr 27;18(9):4661. doi: 10.3390/ijerph18094661.

Pain and abnormal somatosensory processing are important associated conditions in children and adolescents with cerebral palsy (CP). Perceived social support is highly relevant for pain perception and coping. Aim: The aim of the present study was to assess the influence of social support on pain sensitivity in children and adolescents with cerebral palsy and healthy peers. Design: Cross-sectional study. Methods: Pressure pain thresholds were assessed in 42 children and adolescents with CP and 190 healthy peers during three different conditions: alone, with their mother and with a stranger. Results: Children with CP reported lower pain sensitivity related to the social condition. Sex or clinical characteristics did not affect the relationship between pain perception and social support. Conclusion: The present study shows how children with CP are highly affected by social and contextual influences for regulating pain sensitivity. Solicitous parental support may enhance pain perception in children with CP. Further research on the topic is warranted in order to attain well-founded conclusions for clinical practice.

PMID: <u>33925690</u>

# 15. Pain, health-related quality of life, and mental health of adolescents and adults with cerebral palsy in urban South Africa

Roshaan Salie, Maaike Maria Eken, Kirsten Ann Donald, Anthony Graham Fieggen, Nelleke Gertrude Langerak

Disabil Rehabil. 2021 Apr 28;1-9. doi: 10.1080/09638288.2021.1916101. Online ahead of print.

Purpose: The aim of this study was to investigate the prevalence and level of disability due to pain, health-related quality of life (HRQoL) and mental health in adolescents and adults with cerebral palsy (CP), living in a low-to-middle income country (LMIC), compared to matched typically developing (TD) peers, and to explore associations with individual characteristics.

Materials and methods: This case-control study included 31 adolescents and 30 adults with CP (gross motor function classification system [GMFCS] Level I-V) and matched TD peers. Assessment tools used were a pain questionnaire, the Oswestry Disability Index (ODI), Short-Form Health Survey (SF-36v2), Hospital Anxiety and Depression Scale (HADS), and General Self Efficacy (GSE) scale. Results: Both CP cohorts reported more frequent pain in their lower limbs, higher level of disability due to pain (total ODI score) and lower perceived physical HRQoL compared to TD peers, while their mental health (mental HRQoL, HADS, and GSE) was not different. Conclusions: Despite the physical challenges faced by adolescents and adults with CP living in urban South Africa, the mental health scores showed no difference compared to TD peers. Care should be taken to maintain this positive mental state during ageing across their lifespan. IMPLICATIONS FOR REHABILITATION The prognosis of individuals with cerebral palsy (CP) has improved over the last three decades and CP should therefore be considered as a lifelong condition. Adolescents and adults with CP living in urban South Africa reported a higher level of disability due to pain and lower physical health-related quality of life compared to typically developing peers, while their level of depression, anxiety, and self-esteem was not different. These results were similar to findings of studies conducted in high-income countries, though it cannot be generalised to other low to middle-income countries with different cultural and government systems. In order to promote healthy ageing across their lifespan, intervention programmes should be considered to improve physical well-being, and care should be taken to maintain their positive mental health.

PMID: 33909514

### **16. Evaluation of Anxiety, Depression and Burden on Caregivers of Children with Cerebral Palsy** Adnan Barutcu, Saliha Barutcu, Safi Kolkiran, Fatih Ozdener

Dev Neurorehabil. 2021 Apr 24;1-6. doi: 10.1080/17518423.2021.1917718. Online ahead of print.

In this study, we investigated the relationship of demographic variables with mental disorders generally encountered by the caregivers. The cohort includes 109 caregivers ( $38.53 \pm 9.62$  year-old) of pediatric cerebral palsy patients (1-18 year-old) taken more than 3 months of caregiving. Data were obtained via face-to-face interviews and a 13-questioned survey followed by a statistical correlation with Zarit-Caregiver-Burden-Scale (Zarit-CBS), Beck Anxiety Inventory (BAI), and Beck Depression Inventory-II scores (BDI-II). BAI scores were lower in the case of collaborative caregiving (p = .034) and a better financial status (p = .045) but higher in families having more than 1 disabled child (p = .019). Zarit-CBS scores were significantly higher in caregiving mothers with older age (p = .027) and lower in families having only 1 disabled child (p = .025). Mental disorders related to caregiving are dependent on the burden directed on the caregivers and having collaboration decreases anxiety. Medical assistance should be provided to caregivers showing signs of a mental disorder.

PMID: 33896338

# 17. The Effects of Virtual Reality Based Rehabilitation on Upper Extremity Function in a Child with Cerebral Palsy: A Case Report

Rachael Mirich, Anastasia Kyvelidou, Bobbi S Greiner

Phys Occup Ther Pediatr. 2021 Apr 29;1-17. doi: 10.1080/01942638.2021.1909688. Online ahead of print.

Aim: This case report was designed to assess the efficacy of virtual reality (VR) rehabilitation on improving upper extremity function for a child with spastic hemiplegic cerebral palsy. Methods: In addition to conventional therapies completed three times per week, the participant engaged in virtual reality rehabilitation with the Neofect Smart Kids five to seven days per week for six weeks totaling just over twelve hours of intervention time. Outcome measures were administered pre-intervention, post-intervention, and 6-weeks post-intervention. Results: Varying levels of improvement in motor function, quality of movement, and functional use were observed during intervention evidenced by improved scores on the following standardized assessments: Peabody Developmental Motor Scales, Second Edition; the Quality of Upper Extremity Skills Test; and the Pediatric Evaluation and Disability Inventory-Computer Adaptive Test. The participant maintained improvements in motor skills at 6-weeks post intervention, however, the quality of his movements and overall frequency of use with his affected upper extremity decreased in the 6-weeks following termination of intervention. Conclusions: Even though the results are not generalizable, the VR intervention for this child allowed for greater movement repetition and improved functional upper extremity use.

#### PMID: 33926350

**18. Virtual Reality in Neurorehabilitation: An Umbrella Review of Meta-Analyses** Alexandra Voinescu, Jie Sui, Danaë Stanton Fraser

Review J Clin Med. 2021 Apr 2;10(7):1478. doi: 10.3390/jcm10071478.

Neurological disorders are a leading cause of death and disability worldwide. Can virtual reality (VR) based intervention, a novel technology-driven change of paradigm in rehabilitation, reduce impairments, activity limitations, and participation restrictions? This question is directly addressed here for the first time using an umbrella review that assessed the effectiveness and quality of evidence of VR interventions in the physical and cognitive rehabilitation of patients with stroke, traumatic brain injury and cerebral palsy, identified factors that can enhance rehabilitation outcomes and addressed safety concerns. Forty-one meta-analyses were included. The data synthesis found mostly low- or very low-quality evidence that supports the effectiveness of VR interventions. Only a limited number of comparisons were rated as having moderate and high quality of evidence, but overall, results highlight potential benefits of VR for improving the ambulation function of children with cerebral palsy, mobility, balance, upper limb function, and body structure/function and activity of people with stroke, and upper limb function of vR systems is one important factor linked with improved outcomes. Most studies do not address safety concerns, as only nine reviews reported adverse effects. The results provide critical recommendations for the design and implementation of future VR programs, trials and systematic reviews, including the need for high quality randomized controlled trials to test principles and mechanisms, in primary studies and in meta-analyses, in order to formulate evidence-based guidelines for designing VR-based rehabilitation interventions.

### PMID: 33918365

19. Potential Value of Customized Video Self-Modelling for Motor Skill Learning in Individuals with Cerebral Palsy: A Case-Study Approach

Kylie A Steel, David I Anderson, Caroline A Smith, Eathan Ellem, Karen P Y Liu, Andrew Morrison-Gurza, Tinashe Dune, Lauren H Fairley

Percept Mot Skills. 2021 Apr 23;315125211012810. doi: 10.1177/00315125211012810. Online ahead of print.

Cerebral Palsy (CP) is a common physical disability that is managed with a variety of strategies. One non-invasive intervention for people living with CP is a type of video self-modelling (VSM) referred to as positive self-review (PSR). PSR involves watching a video of oneself performing only the best examples of a desired task; this technique has been associated with improved performance and learning for people without disabilities and for those in various clinical populations, including children with spina bifida and stroke patients. PSR may have similar benefits for people living with CP. In this study we examined the effectiveness of PSR for improving a self-selected movement task among individuals living with CP. In this case study approach, eight participants completed a pre-, post-, and second post-test measuring and recording well-being, movement self-consciousness and tendency to consciously monitor movements. Results were mixed, with some participants improving their movement time, well-being ratings and tendency toward self-consciousness and conscious monitoring of movements and others showing no changes or regressions. The effectiveness of VSM appears to depend upon the match between type of task and disability and/or the length of practice. More study is needed.

PMID: 33892615

# **20.** The functional health status of children with cerebral palsy during the COVID-19 pandemic stay-at-home period: a parental perspective Kübra Seyhan Bıyık, Cemil Özal, Merve Tunçdemir, Sefa Üneş, Kıvanç Delioğlu, Mintaze Kerem Günel

Rubia Seynan Biyik, Cenin Ozai, Merve Tunçdenin, Seta Oneş, Rivanç Denogiu, Mintaze Refeni O

Turk J Pediatr. 2021;63(2):223-236. doi: 10.24953/turkjped.2021.02.006.

Background: Coronavirus disease 2019 (COVID-19) pandemic was effective all over the world. The stay-at-home period was proposed to protect against the pandemic. The aim of this study was to investigate the effects of the COVID-19 pandemic stayat-home period on body structures and functions, activity and participation levels, and environmental factors of children with cerebral palsy (CP) from the parental perspective in Turkey. Methods: A twenty-question survey, using the International Classification of Functioning, Disability and Health for Children and Youth set to understand the functional changes of children with CP during the stay-athome period, was sent to parents in this prospective study. Motor function levels of children were determined by the Gross Motor Function Classification System parent report. The structural equation model was used for statistical analysis. Results: One hundred and three parents of children with CP participated. At least one of four children with CP had increased levels of anxiety (41.8%), and increased level of a sensation of pain (34%) and sleep problems (25.2%). More than half of the children had increased tonus (67%), decreased range of motion (60.2%), decreased physical activity level (55.3%), and decreased support level of rehabilitation services (82.6%). During the stayat- home period activity and participation levels and environmental factors of children explained the changes of body functions as 70% and 33% (RMSEA=0.077, p < 0.05). Conclusions: This study is the first study to examine the functional health of children with CP biopsychosocially during the COVID-19 stay-at-home period. According to the parents, the functional health of children with CP was affected at different levels during the COVID-19 pandemic. Body functions may also be affected positively if physical activity level, home program and environmental supports increase.

PMID: 33929112

### **21. Weight and alternative measures for nutrition assessment in children with cerebral palsy** Richard D Stevenson

Dev Med Child Neurol. 2021 Apr 30. doi: 10.1111/dmcn.14909. Online ahead of print.

PMID: 33929049

### 22. Neurodevelopmental outcomes at age 5 among children born preterm: EPIPAGE-2 cohort study

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BMJ. 2021 Apr 28;373:n741. doi: 10.1136/bmj.n741.

Objectives: To describe neurodevelopment at age 5 among children born preterm. Design: Population based cohort study, EPIPAGE-2. Setting: France, 2011. Participants: 4441 children aged 5<sup>1/2</sup> born at 24-26, 27-31, and 32-34 weeks MAIN OUTCOME MEASURES: Severe/moderate neurodevelopmental disabilities, defined as severe/moderate cerebral palsy (Gross Motor Function Classification System (GMFCS)  $\geq 2$ ), or unilateral or bilateral blindness or deafness, or full scale intelligence quotient less than minus two standard deviations (Wechsler Preschool and Primary Scale of Intelligence, 4th edition). Mild neurodevelopmental disabilities, defined as mild cerebral palsy (GMFCS-1), or visual disability  $\geq 3.2/10$  and <5/10, or hearing loss <40 dB, or full scale intelligence quotient (minus two to minus one standard deviation) or developmental coordination disorders (Movement Assessment Battery for Children, 2nd edition, total score less than or equal to the fifth centile), or behavioural difficulties (strengths and difficulties questionnaire, total score greater than or equal to the 90th centile), school assistance (mainstream class with support or special school), complex developmental interventions, and parents' concerns about development. The distributions of the scores in contemporary term born children were used as reference. Results are given after multiple imputation as percentages of outcome measures with exact binomial 95% confidence intervals. Results: Among 4441 participants, 3083 (69.4%) children were assessed. Rates of severe/moderate neurodevelopmental disabilities were 28% (95% confidence interval 23.4% to 32.2%), 19% (16.8% to 20.7%), and 12% (9.2% to 14.0%) and of mild disabilities were 38.5% (33.7% to 43.4%), 36% (33.4% to 38.1%), and 34% (30.2% to 37.4%) at 24-26, 27-31, and 32-34 weeks, respectively. Assistance at school was used by 27% (22.9% to 31.7%), 14% (12.1% to 15.9%), and 7% (4.4% to 9.0%) of children at 24-26, 27-31, and 32-34 weeks, respectively. About half of the children born at 24-26 weeks (52% (46.4% to 57.3%)) received at least one developmental intervention which decreased to 26% (21.8% to 29.4%) for those born at 32-34 weeks. Behaviour was the concern most commonly reported by parents. Rates of neurodevelopment disabilities increased as gestational age decreased and were higher in families with low socioeconomic status. Conclusions: In this large cohort of children born preterm, rates of severe/moderate neurodevelopmental disabilities remained high in each gestational age group. Proportions of children receiving school assistance or complex developmental interventions might have a significant impact on educational and health organisations. Parental concerns about behaviour warrant attention.

### PMID: 33910920

# 23. Survey of clinical staff knowledge on the long-term outcomes of very preterm infants delivered in a tertiary referral hospital

Safiyyah Abdul Aziz, Gayatri Athalye-Jape, Sachin Agrawal, Mary Sharp

J Paediatr Child Health. 2021 Apr 26. doi: 10.1111/jpc.15512. Online ahead of print.

Aim: To assess knowledge of our neonatal intensive care unit clinical staff regarding preterm neurodevelopmental outcomes using the 33-item Preterm Birth Knowledge Scale (PB-KS). Methods: An anonymous convenience sampling survey of clinical staff in the Neonatal Directorate was conducted between July and December 2019. PB-KS, demographic information and prior staff education on long-term outcomes in very preterm infants were collected. Results: There were 56 responses (five neonatologists, eight paediatric trainees, 41 neonatal nurses and two allied health staff). Responses were scored as correct or incorrect. The mean score on the PB-KS was 19.5 (range: 4-29 out of 40) with 50% correct answers. Accuracy was highest (96%) for rates of cerebral palsy and lowest (11%) for estimation of quality of life among preterm survivors. Staff reported training in long-term outcomes of preterm infants through attending a conference/seminar (20%) or a combination of formal training and seminars (41.1%). Over half of our clinical staff reported a lack of formal training. Formally trained clinical staff scored significantly better in this survey. Didactic seminars were indicated as preferred choice for staff education. Conclusions: Results of our survey will assist in developing a customised educational programme to address identified gaps in the knowledge of clinical staff as our survey also showed significantly better scores among staff who were formally trained about long-term outcomes in very preterm infants. Staff responses indicated that knowledge on long-term outcomes was variable but more accurate with regard to more severe disabilities and shorter-term developmental outcomes.

### PMID: <u>33900665</u>

24. Multiple Cellular Therapies Along with Neurorehabilitation in Spastic Diplegic Cerebral Palsy: A Case Report Alok Sharma, Nandini Gokulchandran, Pooja Kulkarni, Sandhya Kiran Mullangi, Khushboo Bhagawanani, Vishal Ganar, Hemangi Sane, Prerna Badhe

Case Reports Innov Clin Neurosci. 2020 Oct 1;17(10-12):31-34. eCollection Oct-Dec 2020.

Cerebral palsy (CP) is a chronic childhood disorder that is characterized by a group of motor and cognitive impairments, resulting in abnormal movement patterns, loss of motor control, incoordination, and unbalanced posture. It can also have an impact on fine motor skills, gross motor skills, and oral motor functioning. Currently, the treatment of CP is palliative and does not cure the disease pathology. Hence, there is a need for an intervention that might be able to alter the core pathology. Autologous bone marrow mononuclear cells (BMMNC) transplantation is one of the novel treatment strategies in recent years. In this study, we presented the case of a 4-year-old male child with spastic diplegic CP who underwent two intrathecal transplantations at interval of seven months with autologous BMMNC along with neurorehabilitation program. During an overall 16-month follow-up, significant improvements were observed in motor control, coordination, balance, sitting tolerance, and memory. The abnormal 'W' sitting posture and scissoring gait pattern of the patient resolved. Started sitting with good head, trunk, and pelvic alignment and attained regular gait pattern; the patient started to walk independently without support as well. On objective scale, Gross Motor Functional Measure score improved from 60.67 to 81.78. The patient's Gross Motor Functional Classification System grade improved from Level 3 to Level 2, and Functional Independent Measure score improved from 97 to 99. A comparative positron emission tomography-computed tomography (PET CT) brain scan was performed before and seven months after the first intervention, which revealed improvement in the metabolism of the anterior cingulate lobe, parietal cortex, medial temporal cortex, thalamus, basal ganglia, and cerebellum. No adverse events were recorded throughout the study. Thus, multiple cellular therapies, along with neurorehabilitation, might be a novel safe, feasible option to enhance recovery in CP.

PMID: 33898099

### 25. Optimization of behavioral testing in a long-term rat model of hypoxic ischemic brain injury

Tayla R Penny, Yen Pham, Amy E Sutherland, Madeleine J Smith, Joohyung Lee, Graham Jenkin, Michael C Fahey, Suzanne L Miller, Courtney A McDonald

Behav Brain Res. 2021 Apr 23;113322. doi: 10.1016/j.bbr.2021.113322. Online ahead of print.

Background: Hypoxic ischemic (HI) brain injury is a significant cause of childhood neurological deficits. Preclinical rodent models are often used to study these deficits; however, no preclinical study has determined which behavioral tests are most appropriate for long-term follow up after neonatal HI. Methods: HI brain injury was induced in postnatal day (PND) 10 rat pups using the Rice-Vannucci method of unilateral carotid artery ligation. Rats underwent long-term behavioral testing to assess motor and cognitive outcomes between PND11-50. Behavioral scores were transformed into Z-scores and combined to create composite behavioral scores. Results: HI rats showed a significant deficit in three out of eight behavioral tests: negative geotaxis analysis, the cylinder test and the novel object recognition test. These individual test outcomes were transformed into Z-scores and combined to create a composite Z-score. This composite z-score showed that HI rats had a significantly increased behavioral burden over the course of the experiment. Conclusion: In this study we have identified tests that highlight specific cognitive and motor deficits in a rat model of neonatal HI. Due to the high variability in this model of neonatal HI brain injury, significant impairment is not always observed in individual behavioral tests, but by combining outcomes from these individual tests, long-term behavioral burden can be measured.

PMID: <u>33901432</u>

**26.** Recessive COL4A2 Mutation Leads to Intellectual Disability, Epilepsy, and Spastic Cerebral Palsy Somayeh Bakhtiari, Abbas Tafakhori, Sheng Chih Jin, Brandon S Guida, Elham Alehabib, Saghar Firouzbadi, Kaya Bilguvar, Michael C Fahey, Hossein Darvish, Michael C Kruer

Neurol Genet. 2021 Apr 22;7(3):e583. doi: 10.1212/NXG.00000000000583. eCollection 2021 Jun.

PMID: <u>33912663</u>

### **27. Forensic Analysis of Umbilical and Newborn Blood Gas Values for Infants at Risk of Cerebral Palsy** Michael G Ross

J Clin Med. 2021 Apr 14;10(8):1676. doi: 10.3390/jcm10081676.

Cerebral palsy litigation cases account for the highest claims involving obstetricians/gynecologists, a specialty that ranks among the highest liability medical professions. Although epidemiologic studies indicate that only a small proportion of cerebral palsy (10-20%) is due to birth asphyxia, negligent obstetrical care is often alleged to be the etiologic factor, resulting in contentious medical-legal conflicts. Defense and plaintiff expert opinions regarding the etiology and timing of injury are often polarized, as there is a lack of established methodology for analysis. The objective results provided by umbilical cord and newborn acid/base and blood gas values and the established association with the incidence of cerebral palsy provide a basis for the forensic assessment of both the mechanism and timing of fetal neurologic injury. Using established physiologic and biochemical principles, a series of case examples demonstrates how an unbiased expert assessment can aid in both conflict resolution and opportunities for clinical education.

PMID: <u>33919691</u>

### **28.** Fathers of children with a disability: health, work, and family life issues Helen M Bourke-Taylor, Claire Cotter, Kahli S Joyce, Dinah S Reddihough, Ted Brown

Disabil Rehabil. 2021 Apr 25;1-11. doi: 10.1080/09638288.2021.1910739. Online ahead of print.

Purpose: Fathers in families raising children with disabilities are under-researched. Fathers' perspectives can be better accommodated in childhood disability services that operate on a family-centred paradigm if their perspectives are understood. This study aimed to investigate the perspectives of fathers on caring and family life, work, and health. Methods: A mixedmethods design with an online questionnaire included open-ended questions and three instruments: Depression Anxiety Stress Scales (DASS); Health Promoting Activities Scale (HPAS-M); Fathers of Children with Developmental Challenges (FCDC) Scale. Results: Fathers (n = 33) reported high depressive (58%), anxiety (37%), and stress symptoms (61%). Fathers reported low participation in health-promoting activity with less than weekly: planning health activities (58%); solo physical activity (26%); social activity (3%); time relaxing (16%). Sixty-four percent worked full-time, although work was reported to be challenged by family responsibilities. Fathers described directly caring for their children although service interactions were low and delegated to mothers. Conclusions: Fathers in this study reported stress, mental health issues, and low participation in healthy activity. Fathers experienced challenges related to career progression and job choices due to family responsibilities. Providing individualised and responsive support to fathers of a child with a disability would better support the family unit. IMPLICATIONS FOR REHABILITATION Fathers of children with a disability in this study experienced high mental health symptoms. Fathers were involved with their child's care at home but had low service interactions suggesting that service providers need to discover new ways to better engage fathers. Fathers experienced challenges to participation in paid work secondary to care responsibilities for their child with a disability and resulting needs of their family. Services that better support fathers are important to promote better health and wellbeing and support families.

PMID: 33896319

# 29. Using Decision Trees to Support Classifiers' Decision-Making about Activity Limitation of Cerebral Palsy Footballers

José M Sarabia, Alba Roldan, Matías Henríquez, Raul Reina

Int J Environ Res Public Health. 2021 Apr 19;18(8):4320. doi: 10.3390/ijerph18084320.

This study aimed (1) to determine the appropriateness of using decision trees as a classification tool for determining the allocation of sport classes of para-footballers with "moderate vs. mild" cerebral palsy (CP) profiles of spastic diplegia/ hemiplegia and ataxia/athetosis based on observational outcomes by international classifiers, and (2) to identify what key observational features were relevant to discriminating among different impairment levels. A sample of 16 experienced international classifiers from five world regions participated in this study, observing activity limitation of a final sample of 21 international CP footballers when performing 16 gross-motor and sports-specific tests for balance (n = 3), coordination (n = 5), running, accelerations and decelerations (n = 3), jumping (n = 4), and change of direction ability (n = 1). For the overall sample (336 observations), the model included eight decision nodes and 24 branches with 17 leaves, including side-step, side-stepping, and triple hop as the tests with the best sensitivity (precision = 67.0%). For those with spastic diplegia (64 observations: Two nodes, six branches with five leaves), the range of motion in the side-step test and the balance in the tandem walk tests correctly classified 89.1% of the observations. In those with athetosis and ataxia (96 observations), the model included five nodes, 15 branches, and 11 leaves (176 observations, precision = 86.5%). For those with spastic hemiplegia, a model containing two nodes, six branches, and five leaves had 90.9% accuracy, including observational features of balance in the side -step test and symmetry in the side-stepping test. The observational tool used in this study, based on the impact of specific impairment measurements of hypertonia, athetosis, and ataxia, can be used to determine which assessments are more appropriate for discriminating between functional profiles in para-footballers with CP.

PMID: <u>33921841</u>

### **Prevention and Cure**

**30.** Human Cord Blood Derived Unrestricted Somatic Stem Cells Restore Aquaporin Channel Expression, Reduce Inflammation and Inhibit the Development of Hydrocephalus After Experimentally Induced Perinatal Intraventricular Hemorrhage

Deepti Purohit, Dina A Finkel, Ana Malfa, Yanling Liao, Larisa Ivanova, George M Kleinman, Furong Hu, Shetal Shah, Carl Thompson, Etlinger Joseph, Michael S Wolin, Mitchell S Cairo, Edmund F La Gamma, Govindaiah Vinukonda Front Cell Neurosci. 2021 Apr 9;15:633185. doi: 10.3389/fncel.2021.633185. eCollection 2021.

Intraventricular hemorrhage (IVH) is a severe complication of preterm birth associated with cerebral palsy, intellectual disability, and commonly, accumulation of cerebrospinal fluid (CSF). Histologically, IVH leads to subependymal gliosis, fibrosis, and disruption of the ependymal wall. Importantly, expression of aquaporin channels 1 and 4 (AQP1 and AQP4) regulating respectively, secretion and absorption of cerebrospinal fluids is altered with IVH and are associated with development of post hemorrhagic hydrocephalus. Human cord blood derived unrestricted somatic stem cells (USSCs), which we previously demonstrated to reduce the magnitude of hydrocephalus, as having anti-inflammatory, and beneficial behavioral effects, were injected into the cerebral ventricles of rabbit pups 18 h after glycerol-induced IVH. USSC treated IVH pups showed a reduction in ventricular size when compared to control pups at 7 and 14 days (both, P < 0.05). Histologically, USSC treatment reduced cellular infiltration and ependymal wall disruption. In the region of the choroid plexus, immuno-reactivity for AOP1 and ependymal wall AOP4 expression were suppressed after IVH but were restored following USSC administration. Effects were confirmed by analysis of mRNA from dissected choroid plexus and ependymal tissue. Transforming growth factor beta (TGF-β) isoforms, connective tissue growth factor (CTGF) and matrix metalloprotease-9 (MMP-9) mRNA, as well as protein levels, were significantly increased following IVH and restored towards normal with USSC treatment (P < 0.05). The anti-inflammatory cytokine Interleukin-10 (IL-10) mRNA was reduced in IVH, but significantly recovered after USSC injection (P < 0.05). In conclusion, USSCs exerted anti-inflammatory effects by suppressing both TGF- $\beta$  specific isoforms, CTGF and MMP-9, recovered IL-10, restored aquaporins expression towards baseline, and reduced hydrocephalus. These results support the possibility of the use of USSCs to reduce IVH consequences in prematurity.

PMID: 33897371