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Cerebral palsy research news

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Interventions and Management

1. Dexterity of the Less Affected Hand in Children With Hemiplegic Cerebral Palsy
Matthew B Burn, Gloria R Gogola

Hand (N Y). 2021 Feb 19;1558944721990803. doi: 10.1177/1558944721990803. Online ahead of print.

Background: To determine if the "unaffected" hand in children with hemiplegic cerebral palsy (CP) is truly unaffected. Methods: We performed a retrospective review of manual dexterity as measured by the Functional Dexterity Test (FDT) in 66 children (39 boys, 27 girls, mean age: 11 years 4 months) with hemiplegic CP. Data were stratified by Manual Ability Classification System (MACS) level, birth weight, and gestational age at birth, and compared with previously published normative values. Results: The FDT speed of the less affected hand is significantly lower than typically developing (TD) children ($P < .001$). The development of dexterity is significantly lower than TD children (0.009 vs. 0.036 pegs/s/year, $P < .001$), with a deficit that increases with age. MACS score, birth weight, and age at gestation are not predictors of dexterity. The dexterity of the less affected hand is poorly correlated with that of the more affected hand. Conclusions: Both dexterity and rate of fine motor skill acquisition in the less affected hand of children with hemiplegic CP is significantly less than that of TD children. The less affected hand should be evaluated and included in comprehensive treatment plans for these children.

PMID: 33605176

2. The effect of therapeutic instrumental music performance method on upper extremity functions in adolescent cerebral palsy
Bilinc Dogruoz Karatekin, Afitap Icagasioglu

Acta Neurol Belg. 2021 Feb 15;1-11. doi: 10.1007/s13760-021-01618-0. Online ahead of print.

The aim of the study is to investigate the improvement of upper extremity functions with piano training of adolescent cerebral palsy. Nine adolescent cerebral palsy patients admitted to the Pediatric Disability Clinic between 2018 and 2020 and 9 healthy adolescent volunteers as control group were included. Therapeutic Instrumental Music Performance method was applied 2 days a week, 3 months in 40-min sessions. Before/after intervention, MACS, Box Block Test, Nine-Hole Peg Test, Jamar hand dynamometer and key pressing force of fingers were evaluated with Cubase MIDI program. Five of our patients included in the study were spastic hemiplegic and 4 were spastic diplegic cerebral palsy. All measurements made after intervention were found to be statistically significant compared to the measurements made before piano training ($p < 0.05$). The fingers that improved the most in the key pressing force of the fingers were found as the right hand 4th, left hand the 4th and 5th fingers ($p < 0.01$). A significant strong negative relationship was detected between the Box Block Test and the Nine-Hole Peg Test ($p < 0.001$). With therapeutic instrumental music performance method, functional gains can be achieved in the grip strength, strengths of the fingers, gross and fine motor skills of adolescent cerebral palsy patients. Further studies are needed to establish a piano training protocol in neurological music therapy.

PMID: 33590470

3. The value-added benefit of utilizing two attending surgeons for patients with scoliosis secondary to cerebral palsy
Tyler C McDonald, Ashley L Gnam, Jaysson T Brooks, Hamdi Sukkarieh, William H Replogle, Patrick B Wright

Spine Deform. 2021 Feb 15. doi: 10.1007/s43390-021-00301-x. Online ahead of print.

Purpose: The use of two attending surgeons during posterior spinal fusion (PSF) for cerebral palsy (CP) patients has been shown to improve perioperative outcomes. This study aims to determine if the use of two surgeons is associated with an increase in the number of subsequent surgeries that can be performed in the same operating room (OR) during business hours. Methods: Patients with scoliosis and CP treated with PSF with minimum 90-day follow-up were included. Patients were grouped based on whether one or two attending surgeons performed the case. The primary outcome was the number of surgeries that followed in the same OR before 5 PM. Secondary outcomes included operative time, estimated blood loss (EBL), length of stay, rate of surgical site infection, and rate of unplanned return to the operating room. Results: Thirty-six patients were included (10 with 1 surgeon and 26 with 2 surgeons). The two surgeon group had a significant increase in the average number of surgeries subsequently performed in the same OR during business hours (1.1 vs. 0.3, $p = 0.01$), as well as shorter mean operative time (159 vs. 307 min, $p = 0.007$) and EBL (554 vs. 840 cc, $p = 0.01$; 26 vs. 39%EBV, $p = 0.03$). Conclusion: The use of two attending surgeons was associated with a significant increase in the number of cases subsequently performed in the same OR during business hours, and significant decreases in operative time and EBL. Hospitals should consider the patient care and potential system-level improvements when considering implementation of two surgeon teams for PSF in CP patients. Level of evidence: Therapeutic Level III.

PMID: 33587269

4. The effect of GMFCS level, age, sex, and dystonia on multi-dimensional outcomes after selective dorsal rhizotomy: prospective observational study
Conor Scott Gillespie, Alan Matthew George, Benjamin Hall, Steven Toh, Abdurrahman Ismail Islim, Dawn Hennigan, Alder Hey Physiotherapy Group; Ram Kumar, Benedetta Pettorini

Childs Nerv Syst. 2021 Feb 18. doi: 10.1007/s00381-021-05076-0. Online ahead of print.

Purpose: Investigate the effect of age category (1-9 years vs 10-18 years), sex, Gross Motor Function Classification System (GMFCS) level, and presence of dystonia on changes in eight function test parameters 24 months after selective dorsal rhizotomy (SDR). Methods: Prospective, single-center study of all children aged 3-18 years with bilateral cerebral palsy with spasticity who underwent SDR at a tertiary pediatric neurosurgery center between 2012 and 2019. A linear mixed effects model was used to assess longitudinal changes. Results: From 2012 to 2019, 42 children had follow-up available at 24 months. Mean GMFM-66 scores increased after SDR (mean difference 5.1 units: 95% CI 3.05-7.13, $p < 0.001$). Statistically significant improvements were observed in CPQoL, PEDI Self-care and Mobility, 6MWT, Gillette, and MAS scores. There was no significant difference in the improvements seen for age category, sex, GMFCS level, and presence of dystonia for most of the parameters tested (5/8, 6/8, 5/8, and 6/8 respectively). Conclusion: SDR may improve gross and fine motor function, mobility and self-care, quality of life, and overall outcome based on extensive scoring parameter testing at 24 months. Atypical patient populations may benefit from SDR if appropriately selected. Multi-center, prospective registries investigating the effect of SDR are required.

PMID: 33599808

5. Neurophysiological validation of simultaneous intrinsic and reflexive joint impedance estimates
Ronald C van 't Veld, Alfred C Schouten, Herman van der Kooij, Edwin H F van Asseldonk

J Neuroeng Rehabil. 2021 Feb 17;18(1):36. doi: 10.1186/s12984-021-00809-3.

Background: People with brain or neural injuries, such as cerebral palsy or spinal cord injury, commonly have joint hyper-

resistance. Diagnosis and treatment of joint hyper-resistance is challenging due to a mix of tonic and phasic contributions. The parallel-cascade (PC) system identification technique offers a potential solution to disentangle the intrinsic (tonic) and reflexive (phasic) contributions to joint impedance, i.e. resistance. However, a simultaneous neurophysiological validation of both intrinsic and reflexive joint impedances is lacking. This simultaneous validation is important given the mix of tonic and phasic contributions to joint hyper-resistance. Therefore, the main goal of this paper is to perform a group-level neurophysiological validation of the PC system identification technique using electromyography (EMG) measurements. Methods: Ten healthy people participated in the study. Perturbations were applied to the ankle joint to elicit reflexes and allow for system identification. Participants completed 20 hold periods of 60 seconds, assumed to have constant joint impedance, with varying magnitudes of intrinsic and reflexive joint impedances across periods. Each hold period provided a paired data point between the PC-based estimates and neurophysiological measures, i.e. between intrinsic stiffness and background EMG, and between reflexive gain and reflex EMG. Results: The intrinsic paired data points, with all subjects combined, were strongly correlated, with a range of [Formula: see text] in both ankle plantarflexors and dorsiflexors. The reflexive paired data points were moderately correlated, with [Formula: see text] in the ankle plantarflexors only. Conclusion: An agreement with the neurophysiological basis on which PC algorithms are built is necessary to support its clinical application in people with joint hyper-resistance. Our results show this agreement for the PC system identification technique on group-level. Consequently, these results show the validity of the use of the technique for the integrated assessment and training of people with joint hyper-resistance in clinical practice.

PMID: 33596944

6. Short walking exercise leads to gait changes and muscle fatigue in children with cerebral palsy who walk with jump gait
Audrey Parent, Fabien Dal Maso, Annie Pouliot-Laforte, Yosra Cherni, Pierre Marois, Laurent Ballaz

Am J Phys Med Rehabil. 2021 Feb 10. doi: 10.1097/PHM.0000000000001713. Online ahead of print.

Objective: To evaluate kinematic changes and muscle fatigue in jump gait during a walking exercise, and the relationship between kinematic changes and muscle fatigue and strength. Design: This preliminary study included ten children with cerebral palsy (CP) who walk with jump gait. Hip and knee maximal isometric muscle strength were measured using a dynamometer. Then, lower-limb kinematics and electromyography were collected while children walked continuously for 6-min at their self-selected speed. Electromyography median frequency and lower-limb joint angles were compared between the first and the sixth minute of the walking exercise using T-test and Wilcoxon rank test. Relationship between kinematic changes and muscle strength and changes in electromyography median frequency were assessed using correlation analyses. Results: During stance, maximal knee flexion significantly increased at the sixth minute (P=0.01) and was associated with knee extensor muscle weakness (rho=-0.504, P=0.03). Muscle fatigue was only observed in gluteus medius muscle (P=0.01). Conclusions: Children with CP who walked with jump gait and who had knee extensor weakness were more prone to an increase in knee flexion during a continuous walk. The fatigue in the gluteus medius muscle suggests that physical intervention should target the endurance of this muscle to improve jump gait.

PMID: 33587452

7. Highly Selective Partial Neurectomy for Lower-Extremity Spasticity: 2-Dimensional Operative Video
Hussam Abou-Al-Shaar, Mark A Mahan

Oper Neurosurg (Hagerstown). 2021 Feb 13;opab020. doi: 10.1093/ons/opab020. Online ahead of print.

Spasticity is a common debilitating condition after central nervous system injury. The principal therapies-sedating antispasticity medications and focal therapies (eg, botulinum toxin)-may not provide sufficient reduction in tone, have intolerable side effects, and lose efficacy over time. Selective neurectomy is a surgical option for durable reduction in tone.1-6 Although commonly performed internationally, neurectomies are used less often within the USA. We present the surgical case of a 23-yr-old woman with cerebral palsy and severe spastic diplegia. Medications, injections, and tendon surgeries had failed to relieve her spastic lower extremities. She presented with crouch gait, adductor scissoring, and bilateral equinovarus. She had previously benefitted significantly from bilateral hamstring and obturator neurectomies, with improvement in mobility. She desired tibial neurectomies for her bilateral equinovarus, which impacted her gait substantially. To reduce unwanted plantarflexion and internal rotation tone, selective neurectomies of the motor nerves to the medial and lateral gastrocnemius, soleus, and posterior tibialis muscles were performed. The surgical video details a technique for longitudinally opening the

epineurium, separating small nerves into their individual fascicles, and subdividing submillimeter fascicles by approximately 50% to 60% of the fascicle cross-sectional area. She reported significant improvement in gait, her modified Ashworth score dropped from 3 to 0, and her motor power remained unchanged, which is equivalent or better than most published results.2,7 Neurectomies are a highly effective procedure for focal extremity spasticity. Additional clinical series or trials would help establish the appropriate indications and durability and quantify the risks and benefits. The patient consented to treatment and publication.

PMID: 33582808

8. Accelerometric Gait Analysis Devices in Children-Will They Accept Them? Results From the AVAPed Study
Isabella Wiedmann, Marcello Grassi, Ibrahim Duran, Ricardo Lavrador, Evelyn Alberg, Martin Daumer, Eckhard Schoenau, Jörn Rittweger

Front Pediatr. 2021 Jan 28;8:574443. doi: 10.3389/fped.2020.574443. eCollection 2020.

Aims: To assess children's acceptance to wear a 3D-accelerometer which is attached to the waist under real-world conditions, and also to compare gait speed during supervised testing with the non-supervised gait speed in every-day life. Methods: In a controlled observational, cross sectional study thirty subjects with cerebral palsy (CP), with level I&II of the Gross Motor Function Classification System (GMFCS) and 30 healthy control children (Ctrl), aged 3-12 years, were asked to perform a 1-min-walking test (1 mwt) under laboratory conditions, and to wear an accelerometric device for a 1-week wearing home measurement (1 WHM). Acceptance was measured via wearing time, and by a questionnaire in which subjects rated restrictions in their daily living and wearing comfort. In addition, validity of 3D-accelerometric gait speed was checked through gold standard assessment of gait speed with a mobile perambulator. Results: Wearing time amounted to 10.3 (SD 3.4) hours per day, which was comparable between groups ($T = 1.10$, $P = 0.3$). Mode for wearing comfort [CP 1, Range (1,4), Ctrl 1, Range (1,6)] and restriction of daily living [CP 1, Range (1,3), Ctrl 1, Range (1,4)] was comparable between groups. Under laboratory conditions, Ctrl walked faster in the 1 mwt than CP (Ctrl 1.72 ± 0.29 m/s, CP 1.48 ± 0.41 m/s, $P = 0.018$). Similarly, a statistically significant difference was found when comparing real-world walking speed and laboratory walking speed (CP: 1 mwt 1.48 ± 0.41 m/s, 1 WHM 0.89 ± 0.09 m/s, $P = 0.012$; Ctrl: 1mwt 1.72 ± 0.29, 1 WHM 0.97 ± 0.06, $P < 0.001$). Conclusion: 3D-accelerometry is well-enough accepted in a pediatric population of patients with CP and a Ctrl group to allow valid assessments. Assessment outside the laboratory environment yields information about real world activity that was not captured by routine clinical tests. This suggests that assessment of habitual activities by wearable devices reflects the functioning of children in their home environment. This novel information constitutes an important goal for rehabilitation medicine. The study is registered at the German Register of Clinical Trials with the title "Acceptance and Validity of 3D Accelerometric Gait Analysis in Pediatric Patients" (AVAPed; DRKS00011919).

PMID: 33585360

9. Dynamic and Static Stability in Para-Athletes with Cerebral Palsy Considering their Impairment Profile
Raul Reina, David Barbado, Héctor Hernández-Davó, Alba Roldan

PM R. 2021 Feb 18. doi: 10.1002/pmrj.12579. Online ahead of print.

Background: Balance impairment is a common feature in people with cerebral palsy (CP), impacting the performance of daily-life and physical activities. Objectives: This study aimed to (a) explore the absolute and relative intra-session reliability of two balance tests to assess dynamic and static balance in ambulant para-athletes with CP; (b) explore the relationships between the two balance tests to determine its potential application in sport classification; (c) assess the differences between CP profiles (i.e. spastic diplegia, athetosis/ataxia, and spastic hemiplegia) in comparison to those with a minimum impairment; and (d) compare the outcomes of the static and dynamic balance of ambulant para-athletes with CP regarding controls. Methods: A group of 129 male well-trained para-footballers with CP, classified as level I according to the Gross Motor Function Classification System, participated in the present study. Static balance was assessed using the One-Leg Stance test (OLS), performed bilaterally on a force platform, while the dynamic balance was assessed in two conditions of the Tandem Walk test (TW): walking heel-toe contact over a 5m straight line and performing 10 steps. Results: Moderate-to-excellent intra-session reliability (ICC = 0.60-0.98) was obtained for all the measurements and groups. However, only small-to-moderate correlations were found between the dynamic and the static measurements of balance for the CP group when performing the OLS test with the unimpaired or dominant leg ($0.23 < r < 0.30$; $p < 0.01$). The TW performed over 10 steps revealed more sensitivity to discriminate between CP profiles. Those para-athletes with ataxia/athetosis performed worse in all the tests while all the CP

profiles performed worse than the control group ($p < 0.01$). Conclusions: Balance performance and postural control are constrained to a higher extent in those with impaired voluntary control due to ataxia or with involuntary contractions of the muscles due to athetosis. This article is protected by copyright. All rights reserved.

PMID: 33599066

10. Time-Motion Characteristics and Physiological Responses of Para-Footballers With Cerebral Palsy in Two Small-Sided Games and a Simulated Game
Matías Henríquez, Aitor Iturricastillo, Arturo González-Olguín, Felipe Herrera, Sonny Riquelme, Raul Reina

Adapt Phys Activ Q. 2021 Feb 17;1-16. doi: 10.1123/apaq.2020-0077. Online ahead of print.

This study compared physical performance in a group of international cerebral palsy football players during two formats of small-sided games (SSGs) and performance in a simulated game (SG) according to players' sport classes (FT1, FT2, and FT3). Internal load (heart rate and rating of perceived exertion) and external load (total distance, distance covered at different velocities, maximum speed reached, acceleration, and deceleration) were obtained with global positioning system devices during two formats of SSGs (2-a-side/SSG2 and 4-a-side/SSG4) and an SG (7-a-side). SSG2 demands faster actions compared with SSG4/SG, and significant differences and large effect sizes were found in the distance covered in Speed Zones 5 (16.0-17.9 km/hr) and 6 (>18.0 km/hr; $p < .05$; $.35<\eta p2<.50$, large). Lower moderate accelerations and decelerations per minute in SSG4/SG compared with SSG2 were also found ($p < .01$; $.77<\eta p2<.81$, large). In the SSG2 task, the FT3 players reached maximum speeds, covered more distance at the highest intensities, and performed more moderate/high accelerations/decelerations and more sprints compared with FT1 and FT2 players ($p < .05$; $-0.85 < dg < -4.64$, large). The SSG2 task could be the best option for discriminating physical demands in important variables for cerebral palsy football performance between classes FT3 versus FT1/FT2.

PMID: 33596537

11. Comparative external workload analysis based on the new functional classification in cerebral palsy football 7-a-side. A full-season study
J M Gamonales, J Muñoz-Jiménez, Carlos D Gómez-Carmona, S J Ibáñez

Res Sports Med. 2021 Feb 12;1-13. doi: 10.1080/15438627.2021.1888105. Online ahead of print.

The evolution of functional classification (FT) is important for promoting competitive balance. Technological advances allow the objective monitoring of competitive demands that is required to manage and individualize workloads. Therefore, this study aimed to characterize external workload in all matches from the 2018/2019 season of the CPF7 Spanish National League and to compare demands based on the new FT (FT1, FT2 yFT3) in time-motion (locomotion and speed changes) and accelerometer-based workload (impacts). Statistical analysis was composed of one-way ANOVA with Bonferroni post-hoc and omega partial squared effect size. Differences were found among all FT in total distance, running, high-intensity, sprinting, very high accelerations and decelerations (FT3> FT2> FT1; $p < .01$; $\omega p 2 = 0.29$-to-0.43); and with respect to the highest functional limitation (FT3 = FT2> FT1) in maximum sprinting, moderate-high accelerations and decelerations, total impacts and at very-low intensity ($\omega p 2 = 0.13$-to-0.29). In conclusion, FT3 players presented a physical advantage with respect to FT2-FT1 players in competition, especially in high-intensity actions that are crucial in team-sports performance. The present results facilitate designing specific training workloads according to FT, players' disability and competition demands, being the first approach to characterize match demands with inertial devices based on the new FT.

PMID: 33579162

12. Validation of new measures of arm coordination impairment in Wheelchair Rugby
Viola C Altmann, Brenda E Groen, Sascha Groeneweg, Gonnie van der Weijde, Noël L W Keijsers

J Sports Sci. 2021 Feb 17;1-8. doi: 10.1080/02640414.2021.1882731. Online ahead of print.

This study aims were twofold: (1) to evaluate the construct validity of the Repetitive Movement Test (RMT) a novel test developed for Wheelchair Rugby classification which evaluates arm coordination impairment at five joints - shoulder, elbow, forearm, wrist and fingers - and (2), pending sufficiently positive results, propose objective minimum impairment criteria (MIC). Forty-two WR athletes with an eligible coordination impairment, and 20 volunteers without impairment completed the RMT and two clinically established coordination tests: the finger-nose test (FNT) and the spiral test (ST). Coordination deduction (CD), an ordinal observational coordination scale, currently used in WR classification, was obtained. Spearman-rank correlation coefficients (SCC) between RMT and ST (0.40 to 0.67) and between RMT and CD (0.31 to 0.53) generally supported RMT construct validity, SCC between RMT and FNT were lower (0.12-0.31). When the scores on ST, FNT and RMT from the sample of WR players were compared with the scores from volunteers without impairment, 93.5% to 100% of WR players had scores > 2SD below the mean of volunteers without impairment on the same test. In conclusion, RMT at the elbow, forearm, wrist and fingers have sufficient construct validity for use in WR. MIC were recommended with ST and RMT.

PMID: 33593245

13. Predictors of mental health among parents of children with cerebral palsy during the COVID-19 pandemic in Iran: A web-based cross-sectional study
Ata Farajzadeh, Moslem Dehghanizadeh, Saman Maroufizadeh, Malek Amini, Aryan Shamili

Res Dev Disabil. 2021 Feb 16;112:103890. doi: 10.1016/j.ridd.2021.103890. Online ahead of print.

Background: Caring for children with cerebral palsy (CP) for many aspects of their lives may affect caregiver's psychological health. Emergence of COVID-19 put added pressure on caregivers. Aims: The aim of this study was to investigate the psychological health of Iranian caregivers of children with CP and associated risks during a lockdown period. Methods: Using online snowball sampling, 160 caregivers of children with CP participated in this web-based cross-sectional study. The Hospital Anxiety and Depression Scale (HADS), Perceived Stress Scale (PSS-4), Caregiver Difficulties Scale (CDS), and a demographic questionnaire were administered. Hierarchical multiple linear regression analysis was applied to identify risk factors related to caregiver psychological health. Outcomes and results: Mental health problems were prevalent; (depression = 45.0% and anxiety = 40.6%). Significant correlations were found between CDS and HADS-Anxiety ($r = 0.472$, $P < 0.001$), HADS-depression ($r = 0.513$, $P < 0.001$), and perceived stress (PSS) related to COVID-19 ($r = 0.425$, $P < 0.001$). After controlling for demographic and clinical variables, burden (CDS) was found to significantly predict caregiver anxiety, depression and stress. Furthermore, several demographic characteristics (being married, low educational level and low income) were significantly related to high HADS Anxiety scores. For depression, only having a physical problem was significantly related to HADS among demographic variables. No significant correlations were found between PSS-4 and demographic variables. Conclusions and implications: During COVID-19 outbreak, the mental health of caregivers of children with CP is affected by multiple factors such as burden of care and demographic characteristics. Due to the importance of well-being among caregivers of disabled children, a comprehensive plan including psychological consultation, remote education, or in-person handouts for the self-care or handling of the children and adequate distance support may enable better mental health for these caregivers.

PMID: 33607484

14. The Effect of Osteoporosis Medication on Risk Attenuation of Non-Trauma Fracture Among Adults with Cerebral Palsy: A Propensity Score-Matched Observational Study
Daniel G Whitney, Edward A Hurvitz, Michelle S Caird

Clin Epidemiol. 2021 Feb 12;13:91-102. doi: 10.2147/CLEP.S294202. eCollection 2021.

Purpose: The efficacy of osteoporosis medication on reducing the risk of non-trauma fracture (NTFx) among adults with cerebral palsy (CP) has not been comprehensively investigated. There are many logistical and biological factors that may reduce this efficacy, and therefore requires attention. The purpose of this propensity score-matched, observational cohort study was to determine if osteoporosis medication was associated with NTFx risk attenuation among adults with CP and compared to adults without CP. Materials and methods: Data from 07/01/2011 to 09/30/2015 were extracted from Optum Clinformatics® Data Mart. Claims identified adults (≥18 years), CP, osteoporosis medication, pre-index NTFx (6-months), and post-index NTFx (12-months). CP without osteoporosis medication (CPMeds-) and without CP with Meds (non-CPMeds+; reflects

"background" population) served as controls and were matched (6:1 ratio) to adults with CP with Meds (CPMeds+; n=306). The Meds groups were further stratified by the initiation of their medication as new users or consistent users. Changes in the prevalence of NTFx from pre- to post-index periods were examined with risk ratios (RR) and the change was compared among groups using the ratio of the RR (RRR) via difference-in-difference analysis. Results: New users with CP had: a larger risk attenuation of any NTFx compared to CPMeds- (RRR=0.39; 95% CI=0.22-0.71), which was consistent for vertebral column/ hip and lower extremities; a larger risk attenuation for NTFx of the lower extremities compared to consistent users with CP (RRR=0.22; 95% CI=0.05-0.93); and a similar risk attenuation of any NTFx compared to new users without CP (RRR=0.81; 95% CI=0.45-1.43), which was consistent for vertebral column/hip and lower extremities. Conclusion: The findings suggest that osteoporosis medication is associated with clinically meaningful risk attenuation of NTFx, especially for new users with CP.

PMID: 33603490

15. A multicenter, randomized controlled trial of massage in children with pediatric cerebral palsy: Efficacy of pediatric massage for children with spastic cerebral palsy
Can Zhang, Guangyi Xiong, Jian Wang, Xinan Shi, Taipin Guo, Yaju Jin, Yan Zhao, Xiantao Tai

Medicine (Baltimore). 2021 Feb 5;100(5):e23469. doi: 10.1097/MD.0000000000023469.

Background: Cerebral palsy is 1 of the diseases critically affecting the health of children. The spasmodic type is the most common, characterized by the increased muscular tension. It often leads to lifelong disability, bringing a heavy economic burden to families and society. As a key treatment in traditional Chinese medicine, pediatric massage has a significant clinical effect on cerebral palsy in children; however, high-quality randomized controlled studies are lacking. The main objective of this study was to evaluate the efficacy of pediatric massage for children with spastic cerebral palsy. Methods/design: The study will be a multicenter, single-blinded, randomized-controlled pilot trial. During the period from June 2019 to December 2020, 182 children with spastic cerebral palsy will be randomly divided into experimental and control groups in a 1:1 ratio. The experimental group will undergo the modified selective spinal massage method combined with the basic rehabilitation treatment, while only the basic rehabilitation treatment would be performed for the control group. The intervention period of the study will last 12 weeks, 5 days weekly on weekdays. The primary outcomes include a modified Ashworth scale assessment and gross motor function test. The secondary outcomes include the 4-diagnostic scale of Chinese medicine and children's intelligence. The observation index will be measured during the complete 12 weeks duration after the treatment of the child, that is, before treatment, after 4 weeks of treatment, after 8 weeks, and after 12 weeks of treatment. Discussion: This study aims to evaluate the efficacy of pediatric massage on children with spastic cerebral palsy; if the outcome is positive, it can provide a reference for the further promotion and application of pediatric massage in the treatment of spastic cerebral palsy. Trial registration: Chinese ClinicalTrials.gov, ID: ChiCTR1900021666. Acupuncture-Moxibustion Clinical Trial Registry, AMCTR: (AMCTR-IPR-19000260) Registered on 04 March 2019.

PMID: 33592825

16. Reliability of Shear Wave Elastography and Ultrasound Measurement in Children with Unilateral Spastic Cerebral Palsy
Clément Boulard, Laure Mathevon, Louis Florian Arnaudeau, Vincent Gautheron, Paul Calmels

Ultrasound Med Biol. 2021 Feb 9;S0301-5629(21)00038-7. doi: 10.1016/j.ultrasmedbio.2021.01.013. Online ahead of print.

In clinical practice, few data exist on the feasibility of performing reliable shear wave elastography (SWE) and ultrasonography (US) measurements in spastic muscles of children with cerebral palsy (CP). Ten children with unilateral CP took part in SWE and US assessment of the tibialis anterior and medialis gastrocnemius muscles during two sessions separated by a 1-wk interval. Intra- and inter-investigator reliability of shear modulus (μ) and muscle thickness (MT) measurements, at neutral and maximal dorsiflexion angles on both legs, was assessed by two investigators with different levels of experience. Reliability was assessed with the coefficient of variation (CV), standard error of measurement and intra-class correlation coefficient (ICC). Reliability of the μ measurement was insufficient, regardless of angle position (CV >10% and >20% for neutral and maximal dorsiflexion angles, respectively). The intra- and inter-investigator reliability of MT measurements was good (CV >10%, ICC >0.74) for both muscles in both legs. SWE measurements must be performed using a rigorous standardized protocol while MT should be considered an important parameter to monitor change in muscle morphology.

PMID: 33579563

17. EEG measures of sensorimotor processing and their development are abnormal in children with isolated dystonia and dystonic cerebral palsy
Verity M McClelland, Petra Fischer, Eleonora Foddai, Sofia Dall'Orso, Etienne Burdet, Peter Brown, Jean-Pierre Lin

Neuroimage Clin. 2021 Jan 19;102569. doi: 10.1016/j.nicl.2021.102569. Online ahead of print.

Dystonia is a disorder of sensorimotor integration associated with abnormal oscillatory activity within the basal ganglia-thalamo-cortical networks. Event-related changes in spectral EEG activity reflect cortical processing but are sparsely investigated in relation to sensorimotor processing in dystonia. This study investigates modulation of sensorimotor cortex EEG activity in response to a proprioceptive stimulus in children with dystonia and dystonic cerebral palsy (CP). Proprioceptive stimuli, comprising brief stretches of the wrist flexors, were delivered via a robotic wrist interface to 30 young people with dystonia (20 isolated genetic/idiopathic and 10 dystonic CP) and 22 controls (mean age 12.7 years). Scalp EEG was recorded using the 10-20 international system and the relative change in post-stimulus power with respect to baseline was calculated for the alpha (8-12 Hz) and beta (14-30 Hz) frequency bands. A clear developmental profile in event-related spectral changes was seen in controls. Controls showed a prominent early alpha/mu band event-related desynchronisation (ERD) followed by an event-related synchronisation (ERS) over the contralateral sensorimotor cortex following movement of either hand. The alpha ERD was significantly smaller in the dystonia groups for both dominant and non-dominant hand movement (ANCOVA across the 3 groups with age as covariate: dominant hand $F(2,47) = 4.45$ $p = 0.017$; non-dominant hand $F(2,42) = 9.397$ $p < 0.001$. Alpha ERS was significantly smaller in dystonia for the dominant hand (ANCOVA $F(2,47) = 7.786$ $p = 0.001$). There was no significant difference in ERD or ERS between genetic/idiopathic dystonia and dystonic CP. CONCLUSION: Modulation of alpha/mu activity by a proprioceptive stimulus is reduced in dystonia, demonstrating a developmental abnormality of sensorimotor processing which is common to isolated genetic/idiopathic and acquired dystonia/dystonic CP.

PMID: 33583764

18. [The impact of disease and sociodemographic background on children suffering from cerebral palsy] [Article in Hu]
Melinda Fejes, Beatrix Varga, Katalin Hollódy

Orv Hetil. 2021 Feb 14;162(7):269-279. doi: 10.1556/650.2021.31990.

Introduction: Self-reported health-related quality of life (HRQoL) of 99 children (8-18 years) with cerebral palsy (CP) was assessed and compared with 237, age-matched healthy control children from the general population. Objective: The aim was to find out the opinions of children with CP about their health status and social condition. Method: Assessment of quality of life questionnaire was carried out. Measurements of disease-specific and sociodemographic variables were done. Results: Children with CP and their parents rated HRQoL poorer than their counterparts. Our results show that female sex, worse gross motor function and comorbidities (epilepsy, incontinence and intellectual impairment) had negative impact. The parental opinion was suitable as proxy report because of the measured strength of the correlation. Among the types of CP, interestingly, children with unilateral spastic CP had the poorest HRQoL. They were likely to feel a functional difference between the two sides of the body. Intellectual disability occurred in more than half of our patient population. Among their siblings, mental illness is 5.7 times more common. The family environment was much more disadvantageous than in the case of healthy children. As our study shows, lower education, inactive status in the labour market and single-parent family occurred at a much higher rate and worsened the quality of life. Conclusion: Quality of life of children with disability was influenced by both the sociodemographic background and the disease. Orv Hetil. 2021; 162(7): 269-279.

PMID: 33582650

19. The Challenge of Identifying Causal Pathways Leading to Cerebral Palsy
Sandra Julsen Hollung, Torstein Vik, Guro L Andersen

Pediatrics. 2021 Feb 18;e2020033720. doi: 10.1542/peds.2020-033720. Online ahead of print.

PMID: 33602801

20. Fifteen years of human research using stem cells for cerebral palsy: A review of the research landscape
Madison C B Paton, Megan Finch-Edmondson, Michael C Fahey, Jessica London, Nadia Badawi, Iona Novak

J Paediatr Child Health. 2021 Feb;57(2):295-296. doi: 10.1111/jpc.15329.

PMID: 33600635

21. Maternal Chronic Conditions and Risk of Cerebral Palsy in Offspring: A National Cohort Study
Marianne S Strøm, Mette C Tollånes, Allen J Wilcox, Rolv Terje Lie, Ingeborg Forthun, Dag Moster

Pediatrics. 2021 Feb 18;e20201137. doi: 10.1542/peds.2020-1137. Online ahead of print.

Background and objectives: Previous studies suggest that children of mothers with certain chronic conditions may be at increased risk of cerebral palsy (CP). We explored possible associations between 17 maternal chronic conditions and CP in offspring. Methods: We conducted a prospective cohort study of Norwegian children born in 1990-2012 and surviving to 2 years of age. Information on maternal chronic conditions during pregnancy were extracted from the Medical Birth Registry of Norway (1990-2012). Information on chronic conditions in mothers and fathers recorded in the Norwegian Patient Registry (2008-2014) was available for a subset of children. CP diagnoses were extracted from the National Insurance Scheme (1990-2014) and the Norwegian Patient Registry (2008-2014). We estimated relative risks (RRs) and 95% confidence intervals (CIs) of CP in offspring of parents with chronic conditions compared with the general population using log binominal regression models. Results: A total of 1 360 149 Norwegian children, including 3575 children with CP (2.6 per 1000 live births), fulfilled the inclusion criteria. The highest risk of CP was among offspring of mothers with type 2 diabetes (RR 3.2; 95% CI 1.8-5.4), lupus erythematosus (RR 2.7; 95% CI 0.9-8.3), type 1 diabetes (RR 2.2; 95% CI 1.4-3.4), and Crohn disease (RR 2.1; 95% CI 1.0-4.1) during pregnancy. No increased risks were seen for offspring of fathers with chronic conditions. Conclusions: Several maternal chronic conditions were associated with increased risk of CP in offspring. Maternal autoimmune disorders carried a particular risk.

PMID: 33602799

22. Polyglucosan bodies in medullary catecholaminergic neurones in SUDEP
Smriti Patodia, Alyma Somani, Maria Thom

Case Reports Epilepsy Behav Rep. 2021 Jan 28;15:100430. doi: 10.1016/j.ebr.2021.100430. eCollection 2021.

Polyglucosan bodies have been reported in the context of hypoxic-ischaemic perinatal brain injury, mainly in the pallidum but with rare reports in brainstem neurons. We report a case of a five-year-old boy with cerebral palsy and complex neurological features including epilepsy who experienced sudden nocturnal death. At post-mortem long-standing bilateral necrosis of basal ganglia and hippocampal atrophy was identified in keeping with hypoxic-ischaemic perinatal injury. In addition numerous polyglucosan bodies, which were PAS, p62 and ubiquitin positive, were noted in brainstem neurones and dendrites, primarily involving the ventrolateral and dorsomedial medulla. Immunohistochemistry confirmed relative preservation of medullary neuronal populations in the reticular formation, including catecholaminergic (tyrosine hydroxylase, TH), serotonergic (tryptophan hydroxylase) and neurokinin1 receptor/somatostatin positive neurones. The polyglucosan bodies predominated in catecholaminergic neurones which could indicate their selective vulnerability and a functional deficiency, which during a critical peri-ictal period contributed to the sudden unexpected death in epilepsy.

PMID: 33604535

23. Sustained low-dose prophylactic early erythropoietin for improvement of neurological outcomes in preterm infants:A systematic review and meta-analysis
Liang Liang, Jia Yu, Ling Xiao, Gaohua Wang

J Affect Disord. 2021 Mar 1;282:1187-1192. doi: 10.1016/j.jad.2021.01.018. Epub 2021 Jan 12.

The aim of this meta-analysis was conducted to assess the effects of different doses of prophylactic rhEPO on neurodevelopmental outcomes and provide reference for rational drug use. The primary outcome was the number of infants with a Mental Developmental Index (MDI) <70 on the Bayley Scales of Infant Development. Five RCTs, comprising 2282 infants, were included in this meta-analysis. Overall, prophylactic rhEPO administration reduced the incidence of infants with an MDI <70, with an odds ratio (95% confidence interval) of 0.55 (0.38-0.79), P <0.05. The low-dose rhEPO subgroup was superior to the placebo subgroup, with an OR (95% CI) of 0.47 (0.25-0.87), P <0.05. However, high-dose rhEPO subgroup had no significant impact on MDI <70 in infants <28 weeks' gestational age. The definitions of the secondary outcome showed that there was no significant effect of rhEPO on cerebral palsy. For neonatal complications, although four studies showed that there were no differences in the pooled results of BPD and ICH events between rhEPO treatment and placebo, the ICH events were significantly lower in the low-dose rhEPO (OR 0.36; 95% CI 0.23-0.59). In addition, in the pooled results of NEC and ROP events, there were significant differences between the two groups (OR 0.63; 95% CI 0.43-0.93) (OR 0.80; 95% CI 0.65-0.98). And the NEC events were significantly lower in the low-dose rhEPO (OR 0.45; 95% CI 0.27-0.73). Sustained low-dose prophylactic early erythropoietin might be more superior than high-dose for improvement of neurological outcomes and several neonatal complications in preterm infants.

PMID: 33601694

24. Outcomes of Preterm Infants With Congenital Heart Defects After Early Surgery: Defining Risk Factors at Different Time Points During Hospitalization
Po-Yin Cheung, Morteza Hajihosseini, Irina A Dinu, Heather Switzer, Ari R Joffe, Gwen Y Bond, Charlene M T Robertson

Front Pediatr. 2021 Jan 28;8:616659. doi: 10.3389/fped.2020.616659. eCollection 2020.

Background: Compared with those born at term gestation, infants with complex congenital heart defects (CCHD) who were delivered before 37 weeks gestational age and received neonatal open-heart surgery (OHS) have poorer neurodevelopmental outcomes in early childhood. We aimed to describe the growth, disability, functional, and neurodevelopmental outcomes in early childhood of preterm infants with CCHD after neonatal OHS. Prediction models were evaluated at various timepoints during hospitalization which could be useful in the management of these infants. Study Design: We studied all preterm infants with CCHD who received OHS within 6 weeks of corrected age between 1996 and 2016. The Western Canadian Complex Pediatric Therapies Follow-up Program completed multidisciplinary comprehensive neurodevelopmental assessments at 2-year corrected age at the referral-site follow-up clinics. We collected demographic and acute-care clinical data, standardized age-appropriate outcome measures including physical growth with calculated z-scores; disabilities including cerebral palsy, visual impairment, permanent hearing loss; adaptive function (Adaptive Behavior Assessment System-II); and cognitive, language, and motor skills (Bayley Scales of Infant and Toddler Development-III). Multiple variable logistic or linear regressions determined predictors displayed as Odds Ratio (OR) or Effect Size (ES) with 95% confidence intervals. Results: Of 115 preterm infants (34 ± 2 weeks gestation, 2,339 ± 637 g, 64% males) with CCHD and OHS, there were 11(10%) deaths before first discharge and 21(18%) deaths by 2-years. Seven (6%) neonates had cerebral injuries, 7 had necrotizing enterocolitis; none had retinopathy of prematurity. Among 94 survivors, 9% had cerebral palsy and 6% had permanent hearing loss, with worse outcomes in those with syndromic diagnoses. Significant predictors of mortality included birth weight z-score [OR 0.28 (0.11,0.72), P = 0.008], single-ventricle anatomy [OR 5.92(1.31,26.80), P = 0.021], post-operative ventilation days [OR 1.06 (1.02,1.09), P = 0.007], and cardiopulmonary resuscitation [OR 11.58 (1.97,68.24), P = 0.007]; for adverse functional outcome in those without syndromic diagnoses, birth weight 2,000-2,499 g [ES -11.60(-18.67, -4.53), P = 0.002], post-conceptual age [ES -0.11(-0.22,0.00), P = 0.044], post-operative lowest pH [ES 6.75(1.25,12.25), P = 0.017], and sepsis [ES -9.70(-17.74, -1.66), P = 0.050]. Conclusions: Our findings suggest preterm neonates with CCHD and early OHS had significant mortality and morbidity at 2-years and were at risk for cerebral palsy and adverse neurodevelopment. This information may be important for management, parental counseling and the decision-making process.

PMID: 33585367

25. Automation of training and testing motor and related tasks in pre-clinical behavioural and rehabilitative neuroscience
Kar Men Mah, Abel Torres-Espín, Ben W Hallworth, John L Bixby, Vance P Lemmon, Karim Fouad, Keith K Fenrich

Review Exp Neurol. 2021 Feb 15;113647. doi: 10.1016/j.expneurol.2021.113647. Online ahead of print.

Testing and training animals in motor and related tasks is a cornerstone of pre-clinical behavioural and rehabilitative neuroscience. Yet manually testing and training animals in these tasks is time consuming and analyses are often subjective. Consequently, there have been many recent advances in automating both the administration and analyses of animal behavioural training and testing. This review is an in-depth appraisal of the history of, and recent developments in, the automation of animal behavioural assays used in neuroscience. We describe the use of common locomotor and non-locomotor tasks used for motor training and testing before and after nervous system injury. This includes a discussion of how these tasks help us to understand the underlying mechanisms of neurological repair and the utility of some tasks for the delivery of rehabilitative training to enhance recovery. We propose two general approaches to automation: automating the physical administration of behavioural tasks (i.e., devices used to facilitate task training, rehabilitative training, and motor testing) and leveraging the use of machine learning in behavior analysis to generate large volumes of unbiased and comprehensive data. The advantages and disadvantages of automating various motor tasks as well as the limitations of machine learning analyses are examined. In closing, we provide a critical appraisal of the current state of automation in animal behavioural neuroscience and a prospective on some of the advances in machine learning we believe will dramatically enhance the usefulness of these approaches for behavioural neuroscientists.

PMID: 33600814

Prevention and Cure

26. Neuroprotective effect of apigenin against hypoxic-ischemic brain injury in neonatal rats via activation of the PI3K/Akt/Nrf2 signaling pathway
Changchang Fu, Yihui Zheng, Kun Lin, Hongzeng Wang, Tingting Chen, Luyao Li, Jiali Huang, Wei Lin, Jianghu Zhu, Peijun Li, Xiaoqin Fu, Zhenlang Lin

Food Funct. 2021 Feb 18. doi: 10.1039/d0fo02555k. Online ahead of print.

Neonatal hypoxic-ischemic (HI) brain injury can lead to mortality and severe long-term disabilities including cerebral palsy and brain injury. However, the treatment options for neonatal hypoxic-ischemic (HI) brain injury are limited. Apigenin is abundantly present in vegetables, celery, and chamomile tea with diverse biological functions, such as anti-inflammatory, anti-apoptotic, antioxidant, and anticancer effects. However, it has not yet been reported whether apigenin exerts a neuroprotective effect against neonatal hypoxic-ischemic (HI) brain injury. In this study, we investigated whether apigenin could ameliorate HI brain injury and explored the associated mechanism using in vivo experiments. We found that apigenin remarkably reduced the infarct volume and ameliorated cerebral edema, decreased inflammatory response, inhibited apoptosis, promoted the recovery of tissue structure, and improved prognosis following HI brain injury. Mechanistically, we found that apigenin exerted a neuroprotective effect against HI brain injury by activating the PI3K/Akt/Nrf2 pathway. In summary, all these results demonstrate that apigenin could be a potential therapeutic approach for neonatal hypoxic-ischemic (HI) brain injury.

PMID: 33599218

27. Melatonin for the prevention of fetal injury associated with intrauterine inflammation
Jang Mee Kim, Seung-Yun Lee, Ji Yeon Lee

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Intrauterine inflammation is shown to be associated with preterm birth, fetal inflammatory response syndrome, and other pregnancy-related comorbidities such as central nervous system diseases including cerebral palsy and periventricular leukomalacia, pulmonary diseases such as bronchopulmonary dysplasia and respiratory distress syndrome, and necrotizing

enterocolitis, to name a few. Many animal studies on intrauterine inflammation demonstrate that ascending infection of reproductive organs or the production of proinflammatory cytokines by some stimuli in utero results in such manifestations. Melatonin, known for its primary function in maintaining circadian rhythm, is now recognized as one of the most potent antioxidant and anti-inflammatory drugs. In some studies, melatonin injection in pregnant animals with intrauterine inflammation significantly reduced the number of preterm births, the severity of structural disintegration of the fetal lungs observed in bronchopulmonary dysplasia, and perinatal brain injuries with improvement in neuromotor function. These implicated benefits of melatonin in pregnant women with intrauterine inflammation seems promising in many research studies, strongly supporting the hypothesis that melatonin has antioxidative and anti-inflammatory properties that can potentially be taken by pregnant women who are at risk of having intrauterine inflammation. In this review, the potential of melatonin for improving outcomes of the pregnancies with intrauterine inflammation will be discussed.

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