Cerebral Palsy Alliance is delighted to bring you this free weekly bulletin of the latest published research into cerebral palsy. Our organisation is committed to supporting cerebral palsy research worldwide - through information, education, collaboration and funding. Find out more at research.cerebralpalsy.org.au

Professor Nadia Badawi AM
Macquarie Group Foundation Chair of Cerebral Palsy

Australian Cerebral Palsy Register Report

The Australian Cerebral Palsy Register (ACPR) Group released their fourth report this year, highlighting trends in cerebral palsy from children born in 1995-2012.

A full copy of the report can be found at Australian Cerebral Palsy Register Report 2018. A community summary can be found on the following pages of this edition of Cerebral Palsy Research News.

This report doesn’t fall within our regular search criteria, but we are releasing it in case it is of interest and helpful for clinicians, researchers and the community.
Main findings, children born 1995-2012:

For 94% of the group, the injury that caused their CP occurred during pregnancy and/or around the time of birth. Amongst this group rates of CP declined by one-third:
- CP declined mostly amongst children born extremely early (20-27 weeks) and those born at term (37+ weeks)
- CP amongst twin born children declined
- more children with CP were able to walk

In a smaller group of children (6%) their CP was caused by a brain injury that happened more than 28 days after birth and before 2 years of age (for example, due to stroke, infection, or an accident). Amongst this group the rate of CP declined. There were proportionally more Aboriginal and Torres Strait Islander children in this group. These children had more severe disability than other children with CP.

The decline in rates of CP reported here likely reflects advances in research and practice in all areas including:
- the health and care of pregnant women and their babies, particularly high risk pregnancies
- neonatal intensive care and
- the impact of public health initiatives for healthy pregnancies and to prevent accidents.

Amidst this good news, it was also noted that at least a quarter of children with CP included in this report still had severe motor difficulties and used a wheelchair for mobility.

“This report tells us that we are on track, but there is still much to do and we must continue to invest in research”
Professor Nadia Badawi AM

Currently in Australia it is estimated that there are more than 37,000 people living with CP.
The Australian Cerebral Palsy Register exists as the result of collaborative partnerships between all Australian state and territory CP registers and the organisations which support each register. The contributing registers and their organisations are as follows:

<table>
<thead>
<tr>
<th>Cerebral Palsy Register</th>
<th>Custodian Organisation</th>
<th>Year the register commenced</th>
<th>Contact details</th>
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<td>2005</td>
<td><a href="mailto:cpregister@cerebralpalsy.org.au">cpregister@cerebralpalsy.org.au</a></td>
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<tr>
<td>Northern Territory CP Register</td>
<td>Centre for Disease Control</td>
<td>2008</td>
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<td>Queensland CP Register</td>
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<td>Tasmanian CP Register</td>
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<td>Victorian CP Register</td>
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<td>1986</td>
<td><a href="mailto:vic.cpregister@rch.org.au">vic.cpregister@rch.org.au</a></td>
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<td>Western Australian Register of Developmental Anomalies - CP</td>
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<td>1977</td>
<td><a href="mailto:linda.watson@health.wa.gov.au">linda.watson@health.wa.gov.au</a></td>
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A full copy of the Australian Cerebral Palsy Register Report is available at: [https://www.cpregister.com](https://www.cpregister.com)
Interventions and Management

1. Encouraging trends in the prevalence of cerebral palsy: available to all?
Durkin MS.


PMID: 30536791

2. Time Course of Upper Limb Function in Children with Unilateral Cerebral Palsy: A Five-Year Follow-Up Study.


Knowledge on long-term evolution of upper limb function in children with unilateral cerebral palsy (CP) is scarce. The objective was to report the five-year evolution in upper limb function and identify factors influencing time trends. Eighty-one children (mean age 9 y and 11 mo, SD 3 y and 3 mo) were assessed at baseline with follow-up after 6 months, 1, and 5 years. Passive range of motion (PROM), tone, muscle, and grip strength were assessed. Activity measurements included Melbourne Assessment, Jebsen-Taylor test, Assisting Hand Assessment (AHA), and ABILHAND-Kids. At 5-year follow-up, PROM (p < 0.001) and AHA scores (p < 0.001) decreased, whereas an improvement was seen for grip strength (p < 0.001), Melbourne Assessment (p = 0.003), Jebsen-Taylor test (p < 0.001), and ABILHAND-Kids (p < 0.001). Age influenced the evolution of AHA scores (p = 0.003), with younger children being stable over time, but from 9 years onward, children experienced a decrease in bimanual performance. Manual Ability Classification System (MACS) levels also affected the evolution of AHA scores (p = 0.02), with stable scores in MACS I and deterioration in MACS II and III. In conclusion, over 5 years, children with unilateral CP develop more limitations in PROM, and although capacity measures improve, the spontaneous use of the impaired limb in bimanual tasks becomes less effective after the age of 9 years.

PMID: 30538737

3. Somatosensory Plasticity in Pediatric Cerebral Palsy following Constraint-Induced Movement Therapy.
Matusz PJ, Key AP, Gogliotti S, Pearson J, Auld ML, Murray MM, Maitre NL.


Cerebral palsy (CP) is predominantly a disorder of movement, with evidence of sensory-motor dysfunction. CIMT1 is a widely used treatment for hemiplegic CP. However, effects of CIMT on somatosensory processing remain unclear. To examine potential CIMT-induced changes in cortical tactile processing, we designed a prospective study, during which 10 children with hemiplegic CP (5 to 8 years old) underwent an intensive one-week-long nonremovable hard-constraint CIMT. Before and directly after the treatment, we recorded their cortical event-related potential (ERP) responses to calibrated light touch (versus a control stimulus) at the more and less affected hand. To provide insights into the core neurophysiological deficits in light touch processing in CP as well as into the plasticity of this function following CIMT, we analyzed the ERPs within an electrical neuroimaging framework. After CIMT, brain areas governing the more affected hand responded to touch in configurations similar to those activated by the hemisphere controlling the less affected hand before CIMT. This was in contrast to the affected hand where configurations resembled those of the more affected hand before CIMT. Furthermore, dysfunctional patterns of brain activity, identified using hierarchical ERP cluster analyses, appeared reduced after CIMT in proportion with changes in sensory-motor measures (grip or pinch movements). These novel results suggest recovery of functional sensory activation as one possible mechanism underlying the effectiveness of intensive constraint-based therapy on motor functions in the more affected upper extremity in CP. However, maladaptive effects on the less affected constrained extremity may also have occurred. Our findings also highlight the use of electrical neuroimaging as feasible methodology to measure changes in tactile function after treatment even in young children, as it does not require active participation.

PMID: 30532772
4. Concept and treatment outcomes of dynamic spinal brace for scoliosis in cerebral palsy.


We developed a novel device, dynamic spinal brace (DSB), with the basic concept of automatic correction by maximizing posture control. Herein, we report the structure of the DSB and preliminary treatment outcomes for scoliosis in patients with cerebral palsy. The study cohort comprised 219 patients with cerebral palsy treated for scoliosis with Cobb angle of at least 20° and follow-up of more than 3 years under the DSB. Cobb angle, trunk shift, and pelvic obliquity were assessed by semi-sitting radiography, and a questionnaire on daily lifestyle was collected. The immediate correction of these parameters by wearing DSB was demonstrated. In those who aged older than 15 years, the annual progression was 1.0°, and trunk shift was not deteriorated statistically. The questionnaire survey indicated that the DSB led to improvements in QOL and caregiving, and only 3.5% of the patients discontinued DSB because of intolerance. However, we could not find clear evidence that DSB affects the natural history of scoliosis in children with cerebral palsy.

PMID: 30543558

Zarkou A, Lee SCK, Prosser LA, Hwang S, Jeka J.


BACKGROUND: Stochastic Resonance (SR) Stimulation has been used to enhance balance in populations with sensory deficits by improving the detection and transmission of afferent information. Despite the potential promise of SR in improving postural control, its use in individuals with cerebral palsy (CP) is novel. The objective of this study was to investigate the immediate effects of electrical SR stimulation when applied in the ankle muscles and ligaments on postural stability in children with CP and their typically developing (TD) peers. METHODS: Ten children with spastic diplegia (GMFCS level I-III) and ten age-matched TD children participated in this study. For each participant the SR sensory threshold was determined. Then, five different SR intensity levels (no stimulation, 25, 50, 75, and 90% of sensory threshold) were used to identify the optimal SR intensity for each subject. The optimal SR and no stimulation condition were tested while children stood on top of 2 force plates with their eyes open and closed. To assess balance, the center of pressure velocity (COPV) in anteroposterior (A/P) and medial-lateral (M/L) direction, 95% COP confidence ellipse area (COPA), and A/P and M/L root mean square (RMS) measures were computed and compared. RESULTS: For the CP group, SR significantly decreased COPV in A/P direction, and COPA measures compared to the no stimulation condition for the eyes open condition. In the eyes closed condition, SR significantly decreased COPV only in M/L direction. Children with CP demonstrated greater reduction in all the COP measures but the RMS in M/L direction during the eyes open condition compared to their TD peers. The only significant difference between groups in the eyes closed condition was in the COPV in M/L direction. CONCLUSIONS: SR electrical stimulation may be an effective stimulation approach for decreasing postural sway and has the potential to be used as a therapeutic tool to improve balance. Applying subject-specific SR stimulation intensities is recommended to maximize balance improvements. Overall, balance rehabilitation interventions in CP might be more effective if sensory facilitation methods, like SR, are utilized by the clinicians. TRIAL REGISTRATION: ClinicalTrials.gov identifier NCT02456376; 28 May 2015 (Retrospectively registered); https://clinicaltrials.gov/ct2/show/NCT02456376.

PMID: 30526617

6. Radiation Prophylaxis for Hip Salvage Surgery in Cerebral Palsy: Can We Reduce the Incidence of Heterotopic Ossification?
Davis E, Williams K, Matheney TH, Snyder B, Marcus KJ, Shore BJ.


BACKGROUND: Heterotopic ossification (HO) is a well-recognized complication of proximal femoral resection (PFR) surgery in children with cerebral palsy (CP). Although single-dose radiation prophylaxis (SDRP) has been shown to be effective at lowering the rates of HO following adult total hip arthroplasty; there has been limited study examining the efficacy of SDRP for HO prevention in children with CP undergoing PFR. The purpose of this study was to assess the efficacy of SDRP in children with CP undergoing PFR. METHODS: This retrospective case control series identified all patients from one tertiary children's hospital undergoing PFHR. Patients were dichotomized into (1) SDRP and (2) non-SDRP groups. In SDRP, radiation
was delivered preoperatively at a dose of 7.5 Gy utilizing a 6 MV photon beam. The incidence of HO in the SDRP cohort was compared to historic data using binomial testing. The size of HO lesions was compared using Wilcoxon signed-rank test. McCarthy, Brooker, and Anatomic Classifications of HO were compared using repeated measures logistic regression.

RESULTS: Twenty-three patients (mean age, 15.5) and 35 hips (17 SDRP, 18 Non-SDRP) were included in the analysis. There were 17 females and 6 males in the cohort with the majority classified as GMFCS V, 21/23 (91%). HO was seen in 6 of the SDRP cohort (6/17, 35%) and 15 of the non-SDRP cohort (15/18, 83%) (P=0.015). The average size of HO at maturity was 282.7 mm in the SDRP cohort compared with 1221.5 mm in the Non-SDRP cohort (P=0.026). Radiation treatment was associated with a 938.9 mm decrease in HO size at maturity (P= 0.026). Multivariate repeated measures logistic regression analysis found that non-SDRP hips had 13 times higher odds of developing HO (P=0.015). There were no significant differences in infection rates between the 2 cohorts and there were no radiation-associated complications. CONCLUSIONS: Short-term follow up demonstrates that SDRP is a safe and efficacious intervention in decreasing the incidence and size of HO in children with CP undergoing PFR. LEVELS OF EVIDENCE: Level III-Case control cohort study.

PMID: 30543561

7. The popliteal angle tests in patients with cerebral palsy.
Manikowska F, Chen BP, Jóźwiak M, Lebiedowska MK.


The aims were to determine during the popliteal angle (PA) tests whether particular knee muscles are activated and whether the position of pelvis affects the level of muscles activation. Twenty-two patients with cerebral palsy were recruited (age: 14±4.94 years). Knee muscle activities and range of motion were measured during PA. Knee flexors were active during tests, with fivefold increase of activation of ipsilateral hamstring. Higher and more frequent activation of muscles only in the contralateral limb was seen. Muscles activation should be considered as a confounding factor during tests. PA should not be relied upon as a major criterion for the treatment selection in cerebral palsy.

PMID: 30550510

8. Validity and reliability of a freehand 3D ultrasound system for the determination of triceps surae muscle volume in children with cerebral palsy.
Barber L, Alexander C, Shipman P, Boyd R, Reid S, Elliott C.


This study assessed the validity, intra-rater and inter-rater reliability of segmentation of in vivo medial gastrocnemius (MG), lateral gastrocnemius (LG) and soleus (SOL) muscle volume measurement using a single sweep freehand 3D ultrasound (3DUS) in children with cerebral palsy (CP). The MG, LG and SOL of both limbs of 18 children with CP (age 8 years 4 months ± 1 year 10 months, 11 males, unilateral CP = 9, bilateral CP = 9, Gross Motor Functional Classification System I = 11, II = 7) were scanned using freehand 3DUS and magnetic resonance imaging (MRI). All freehand 3DUS and MRI images were segmented and volumes rendered by two raters. Validity was assessed using limits of agreement method. Intra-rater and inter-rater reliability was assessed using intra-class correlation (ICC), coefficient of variance (CV) and minimal detectable change (MDC). Freehand 3DUS overestimated muscle volume of the MG and LG by < 0.3 mL (1%) and underestimated SOL by < 1.3 mL (1.5%) compared with MRI. ICCs for intra-rater reliability of the segmentation process for the freehand 3DUS system and MRI for muscle volume were > 0.98 and 0.99, respectively, for all muscles. ICCs for inter-rater reliability of the segmentation process for freehand 3DUS and MRI volumes were > 0.96 and 0.98, respectively, for all muscles. MDCs for single rater freehand 3DUS and MRI were < 4.0 mL (14%) and 3.2 mL (11%), respectively, in all muscles. Freehand 3DUS is a valid and reliable method for the measurement of lower leg muscle volume that can be measured with a single sweep in children with CP in vivo. It can be used as an alternative to MRI for the detection of clinically relevant changes in calf muscle volume as the result of growth and interventions.

PMID: 30525186
9. Children with cerebral palsy have larger Achilles tendon moment arms than typically developing children.

Alexander CF, Reid S, Stannage K, Dwyer B, Elliott C, Valentine J, Donnelly CJ.


The effectiveness of the plantarflexor muscle group to generate desired plantarflexion moments is modulated by the geometry of the Achilles tendon moment arm (ATMA). Children with cerebral palsy (CP) frequently have reduced plantarflexion function, which is commonly attributed to impaired muscle structure and function, however little attention has been paid to the potential contribution of ATMA geometry. The use of musculoskeletal modelling for the simulation of gait and understanding of gait mechanics, rely on accuracy of ATMA estimates. This study aimed to compare 3D in-vivo estimates of ATMA of adults, children with CP and typically developing (TD) children, as well as compare 3D in-vivo estimates to linearly scaled musculoskeletal model estimates. MRI scans for eight children with CP, 11 TD children and nine healthy adults were used to estimate in-vivo 3D ATMA using a validated method. A lower limb musculoskeletal model was linearly scaled to individual tibia length to provide a scaled ATMA estimate. Normalised in-vivo 3D ATMA for children with CP was 17.2% ± 2.0 tibia length, which was significantly larger than for TD children (15.2% ± 1.2, p = 0.013) and adults (12.5% ± 0.8, p < 0.001). Scaled ATMA estimates from musculoskeletal models significantly underestimated in-vivo estimates for all groups, by up to 34.7%.

The results of this study show children with CP have larger normalised 3D ATMA compared to their TD counterparts, which may have implications in understanding reduced plantarflexor function and the efficacy of surgical interventions whose aim is to modify the musculoskeletal geometry of this muscle group.

PMID: 30527388


Hegarty AK, Hubert TV, Kurz MJ, Stuber W, Silverman AK.


Cerebral palsy (CP) is a neurological disorder that results in life-long mobility impairments. Musculoskeletal models used to investigate mobility deficits for children with CP often lack subject-specific characteristics such as altered muscle strength, despite a high prevalence of muscle weakness in this population. We hypothesized that incorporating subject-specific strength scaling within musculoskeletal models of children with CP would improve accuracy of muscle excitation predictions in walking simulations. Ten children (13.5 ± 3.3 years; GMFCS level II) with spastic CP participated in a gait analysis session where lower-limb kinematics, ground reaction forces, and bilateral electromyography (EMG) of five lower-limb muscles were collected. Isometric strength was measured for each child using handheld dynamometry. Three musculoskeletal models were generated for each child including a 'Default' model with the generic musculoskeletal model's muscle strength, a 'Uniform' model with muscle strength scaled allometrically, and a 'Custom' model with muscle strength scaled based on handheld dynamometry strength measures. Muscle-driven gait simulations were generated using each model for each child. Simulation accuracy was evaluated by comparing predicted muscle excitation and measured EMG signals, both in the duration of muscle activity and the root-mean-square difference (RMSD) between signals. Improved agreement with EMG were found in both the 'Custom' and 'Uniform' models compared to the 'Default' model indicated by improvement in RMSD summed across all muscles, as well as RMSD and duration of activity for individual muscles. Incorporating strength scaling into musculoskeletal models can improve the accuracy of walking simulations for children with CP.

PMID: 30545605

11. A spasticity model based on feedback from muscle force explains muscle activity during passive stretches and gait in children with cerebral palsy.

Falisse A, Bar-On L, Desloovere K, Jonkers I, De Groote F.


Muscle spasticity is characterized by exaggerated stretch reflexes and affects about 85% of the children with cerebral palsy. However, the mechanisms underlying spasticity and its influence on gait are not well understood. Here, we first aimed to model the response of spastic hamstrings and gastrocnemii in children with cerebral palsy to fast passive stretches. Then, we evaluated how the model applied to gait. We developed three models based on exaggerated proprioceptive feedback. The first model relied on feedback from muscle fiber length and velocity (velocity-related model), the second model relied on feedback from muscle fiber length, velocity, and acceleration (acceleration-related model), and the third model relied on feedback from...
muscle force and its first time derivative (force-related model). The force-related model better reproduced measured hamstrings and gastrocnemii activity during fast passive stretches (coefficients of determination (R²): 0.73 ± 0.10 and 0.60 ± 0.13, respectively, and root mean square errors (RMSE): 0.034 ± 0.031 and 0.009 ± 0.007, respectively) than the velocity-related model (R²: 0.46 ± 0.15 and 0.07 ± 0.13, and RMSE: 0.053 ± 0.051 and 0.015 ± 0.009), and the acceleration-related model (R²: 0.47 ± 0.15 and 0.09 ± 0.14, and RMSE: 0.052 ± 0.050 and 0.015 ± 0.008). Additionally, the force-related model predicted hamstrings and gastrocnemii activity that better correlated with measured activity during gait (cross correlations: 0.82 ± 0.09 and 0.85 ± 0.06, respectively) than the activity predicted by the velocity-related model (cross correlations: 0.49 ± 0.17 and 0.71 ± 0.22) and the acceleration-related model (cross correlations: 0.51 ± 0.16 and 0.67 ± 0.20). Our results therefore suggest that force encoding in muscle spindles and gastrocnemii activity during passive stretches and gait. Our model of spasticity opens new perspectives for studying movement impairments due to spasticity through simulation.

PMID: 30532154

12. Efficacy of participation-focused therapy on performance of physical activity participation goals and habitual physical activity in children with cerebral palsy: a randomized controlled trial.
Reedman SE, Boyd RN, Trost SG, Elliott C, Sakzewski L.


OBJECTIVE: To determine the efficacy of a participation-focused therapy (ParticiPAte CP) on leisure-time physical activity goal performance and habitual physical activity (HPA) in children with cerebral palsy (CP). DESIGN: Randomized waitlist-controlled trial. SETTING: Home and community. PARTICIPANTS: Thirty-seven children Gross Motor Function Classification System (GMFCS) I-III were recruited (18 males, mean age 10y 0mo [SD 1y 5mo]) from a population-based register. INTERVENTIONS: Participants were randomized to Participate CP (an 8-week goal-directed, individualized, participation-focused therapy delivered by a physical therapist) or waitlist usual care. MAIN OUTCOME MEASURES: The primary outcome was Canadian Occupational Performance Measure (COPM). Accelerometers were worn for objective measurement of HPA (min day-1 moderate to vigorous physical activity, MVPA, and sedentary time). Barriers to participation, community participation, and quality of life outcomes were also collected. Data were analysed by intention-to-treat using generalized estimating equations. RESULTS: Participate CP led to significant improvements in goal performance (MD=3.58, 95% CI=2.19 to 4.97, p<0.001), satisfaction (MD=1.87, 95% CI=0.37 to 3.36, p=0.014), and barriers to participation (MD=26.39, 95% CI=6.13 to 46.67, p=0.011) compared with usual care at eight weeks. There were no between group differences on min day-1 MVPA at eight weeks (MD=1.17, 95% CI=13.27 to 15.61, p=0.874). There was a significant difference in response to intervention between participants who were versus were not meeting HPA guidelines at baseline (MD=15.85, 95% CI=3.80 to 27.89, p=0.0061). Following Participate CP, low active participants had increased average MVPA by 5.98 (SD=12.16) min day-1. CONCLUSION: Participate CP was effective at increasing perceived performance of leisure-time physical activity goals in children with CP GMFCS I-III by reducing modifiable barriers to participation. This did not translate into change in HPA on average, however low active children may have a clinically meaningful response.

PMID: 30543803


BACKGROUND AND PURPOSE: Periventricular white matter injury is the common cause of spastic cerebral palsy. However, the early diagnosis of spastic cerebral palsy still remains a challenge. Our aim was to investigate whether infants with periventricular white matter injury with bilateral spastic cerebral palsy have unique lesions different from those in infants without cerebral palsy and to evaluate the efficiency of DTI in the early diagnosis of spastic cerebral palsy. MATERIALS AND METHODS: Infants with periventricular white matter injury and controls underwent MR imaging at 6-18 months of age. Fractional anisotropy was calculated from DTI. Cerebral palsy was diagnosed by 24-30 months of age. Subjects were divided into 3 groups: infants with periventricular white matter injury with bilateral spastic cerebral palsy, infants with periventricular white matter injury without cerebral palsy, and controls. Tract-Based Spatial Statistics and Automated Fiber Quantification were used to investigate intergroup differences. Receiver operating characteristic curves were used to assess the diagnostic accuracy of spastic cerebral palsy. Correlations between motor function scores and fractional anisotropy were evaluated along white matter tracts. RESULTS: There were 20, 19, and 33 subjects in periventricular white matter injury with spastic cerebral palsy, periventricular white matter injury without cerebral palsy, and control groups, respectively. Decreased fractional
anisotropy in the corticospinal tract was only observed in infants with periventricular white matter injury with spastic cerebral palsy, whereas decreased fractional anisotropy in the posterior thalamic radiation and genu and splenium of the corpus callosum was seen in both periventricular white matter injury subgroups. Fractional anisotropy in the corticospinal tract at the internal capsule level was effective in differentiating infants with periventricular white matter injury with spastic cerebral palsy from those without cerebral palsy by a threshold of 0.53, and it had strong correlations with motor function scores. CONCLUSIONS: Corticospinal tract lesions play a crucial role in motor impairment related to spastic cerebral palsy in infants with periventricular white matter injury. Fractional anisotropy in the corticospinal tract at the internal capsule level could aid in the early diagnosis of spastic cerebral palsy with high diagnostic accuracy.

PMID: 30545838


BACKGROUND: Despite advances in antenatal and neonatal care, preterm birth remains a leading cause of neurological disabilities in children. Infants born prematurely, particularly those delivered at the earliest gestational ages, commonly demonstrate increased rates of impairment across multiple neurodevelopmental domains. Indeed, the current literature establishes that preterm birth is a leading risk factor for cerebral palsy, is associated with executive function deficits, increases risk for impaired receptive and expressive language skills, and is linked with higher rates of co-occurring attention deficit hyperactivity disorder, anxiety, and autism spectrum disorders. These same infants also demonstrate elevated rates of aberrant cerebral structural and functional connectivity, with persistent changes evident across advanced magnetic resonance imaging modalities as early as the neonatal period. Emerging findings from cross-sectional and longitudinal investigations increasingly suggest that aberrant connectivity within key functional networks and white matter tracts may underlie the neurodevelopmental impairments common in this population. MAIN BODY: This review begins by highlighting the elevated rates of neurodevelopmental disorders across domains in this clinical population, describes the patterns of aberrant structural and functional connectivity common in prematurely-born infants and children, and then reviews the increasingly established body of literature delineating the relationship between these brain abnormalities and adverse neurodevelopmental outcomes. We also detail important, typically understudied, clinical, and social variables that may influence these relationships among preterm children, including heritability and psychosocial risks. CONCLUSION: Future work in this domain should continue to leverage longitudinal evaluations of preterm infants which include both neuroimaging and detailed serial neurodevelopmental assessments to further characterize relationships between imaging measures and impairment, information necessary for advancing our understanding of modifiable risk factors underlying these disorders and best practices for improving neurodevelopmental trajectories in this high-risk clinical population.

PMID: 30541449


AIM: To investigate the impact of auditory stimulation on motor function in children with cerebral palsy (CP) and disabling hypertonia. METHOD: 9 matched pairs (age: 7y5m, SD 4y1m; 13 boys; gross-motor-functional-classification-scale: median 4; manual-ability-classification-system: median 4) were randomized to receive either auditory stimulation embedded in music (study, n = 9) or music alone (sham, control, n = 9) for at least 10 minutes 4 times a week for 4 weeks. Goal-Attainment-Scale, Care-and-Comfort-Hypertonicity-Questionnaire, Gross-Motor-Function-Measure and Quality-of-Upper-Extremity-Skills-Test (QUEST) were assessed before and 5 months following intervention. RESULT: Children receiving auditory stimulation attained more goals than children who listened to music alone (p = 0.002). Parents reported improved care and comfort in children in the study group compared to a slight deterioration in controls (p = 0.002). Upper extremity skills improved in the study group compared to controls (p = 0.006). Similar gross motor function changes were documented in both groups (p = 0.41). One participant reported increased seizure frequency; no other participants with epilepsy reported increased seizure frequency (n = 6/18) and no other adverse events were reported. INTERPRETATION: Auditory stimulation alleviated hypertonia and improved fine and gross motor functions.

PMID: 30543665
Eunson P.


PMID: 30536998

17. Visceral and Neural Manipulation in Children with Cerebral Palsy and Chronic Constipation: Five Case Reports.
Zollars JA, Armstrong M, Whisler S, Williamson S.


The purpose of this case study series was to assess improvement in the quality of life, function, and colonic motility before and after visceral and neural manipulation in five children with cerebral palsy and chronic constipation who had Gross Motor Function Classification System (GMFCS) levels of IV and V. Quality of life and function were assessed using the CPCHILD and the WeeFIM respectively. The CPCHILD and WeeFIM were administered at baseline before the intervention, after the intervention, and again at least three months post intervention. Colonic motility was assessed radiographically at baseline and post-intervention utilizing ingested radiopaque markers (Sitz markers). Bowel movement number and quality were assessed through family diaries. All subjects showed some degree of improved quality of life and function on the CPCHILD and WeeFIM at the end of the intervention. Colonic motility assessed radiographically before and after treatment was not statistically significant due to the small number of participants; however, the number of bowel movements increased during the study for 100% of the participants. Visceral and neural manipulation modalities may provide clinicians and families with an alternative to medications and/or other more invasive interventions.

PMID: 30528865

18. Closed-loop cortical control of virtual reach and posture using cartesian and joint velocity commands.
Young D, Willett F, Memberg WD, Murphy BA, Rezaii P, Walter B, Sweet JA, Miller J, Shenoy KV, Hochberg L, Kirsch RF, Ajiboye AB.


Brain-computer interfaces (BCIs) are a promising technology for the restoration of function to people with paralysis, especially for controlling coordinated reaching. Typical BCI studies decode Cartesian endpoint velocities as commands, but human arm movements might be better controlled in a joint-based coordinate frame, which may match underlying movement encoding in the motor cortex. A better understanding of BCI controlled reaching by people with paralysis may lead to performance improvements in brain-controlled assistive devices. Approach. Two intracortical BCI participants in the BrainGate2 pilot clinical trial performed a 3D endpoint virtual reaching task using two decoders: Cartesian and joint velocity. Task performance metrics (i.e. success rate and path efficiency) and single feature and population tuning were compared across the two decoder conditions. The participants also demonstrated the first BCI control of a fourth dimension of reaching, the arm's swivel angle, in a 4D posture matching task. Main Results. Both users achieved significantly higher success rates using Cartesian control, and joint controlled trajectories were more variable and significantly more curved. Neural tuning analyses showed that most single feature activity was best described by a Cartesian kinematic encoding model, and population analyses revealed only slight differences in aggregate activity between the decoder conditions. Simulations of a BCI user reproduced trajectory features seen during closed-loop joint control when assuming only Cartesian-tuned features passed through a joint decoder. With minimal training, both participants controlled the virtual arm's swivel angle to complete a 4D posture matching task, and achieved significantly higher success using a Cartesian+swivel decoder compared to a joint velocity decoder. Significance. These results suggest that Cartesian command interfaces may provide better BCI control of arm movements than other kinematic variables, even in 4D posture tasks with swivel angle targets.

PMID: 30523839
Gupta M, Bhatia D.

INTRODUCTION: Transcranial magnetic stimulation is a new tool that has been employed to modulate the neuronal activity of brain by its excitatory and inhibitory property. In cerebral palsy (CP) learning of any new task is an extremely slow process due to damage in sensory and motor areas of brain affecting the cognitive ability of the child and putting constraints in achieving timely developmental milestones. For such patients the electroencephalogram (EEG) is one of the most cost effective diagnostic tools used that minimizes hospital stay. Its analysis helps to identify various neurological disorders determining the role of brain waves outlining the present status of mind. MATERIALS AND METHODS: This study evaluated the EEG power spectrum density (PSD) of CP children both pre and post rTMS intervention to identify significance changes in signal patterns arising from different brain regions. thirty CP children participated in this study. Fifteen individuals underwent repetitive TMS (rTMS) therapy for 20 session comprising of 10 Hz frequency for 5 days a week for 4 weeks and another fifteen individual participated in activities of daily living for 20 sessions where they were administered mandatory standard therapy only. pre-EEG versus post EEG data recorded and analyzed employing the standard montage configuration. PSD was extracted employing fast fourier transform post acquisition of artifact free signal to undermine changes in signal pattern. DISCUSSION AND CONCLUSION: The results revealed that rTMS improves learning ability in CP children and it shows higher power peak at frequency of 50 Hz and lower power peak frequency at 100 Hz. The power intensity in gamma wave region shows significant reduction post-rTMS therapy between 38-24 power peak frequency and 7-4 range in 100 Hz power peak frequency. In future, it will be used as effective tool as memory enhancers, especially for children with neurological disorders.

PMID: 30532357

20. Opportunities and challenges for developing closed-loop bioelectronic medicines.
Ganzer PD, Sharma G.

The peripheral nervous system plays a major role in the maintenance of our physiology. Several peripheral nerves intimately regulate the state of the brain, spinal cord, and visceral systems. A new class of therapeutics, called bioelectronic medicines, are being developed to precisely regulate physiology and treat dysfunction using peripheral nerve stimulation. In this review, we first discuss new work using closed-loop bioelectronic medicine to treat upper limb paralysis. In contrast to open-loop bioelectronic medicines, closed-loop approaches trigger 'on demand' peripheral nerve stimulation due to a change in function (e.g., during an upper limb movement or a change in cardiopulmonary state). We also outline our perspective on timing rules for closed-loop bioelectronic stimulation, interface features for non-invasively stimulating peripheral nerves, and machine learning algorithms to recognize disease events for closed-loop stimulation control. Although there will be several challenges for this emerging field, we look forward to future bioelectronic medicines that can autonomously sense changes in the body, to provide closed-loop peripheral nerve stimulation and treat disease.

PMID: 30531069


PURPOSE: The presentation and etiology of cerebral palsy (CP) are heterogeneous. Diagnostic evaluation can be a prolonged and expensive process that might remain inconclusive. This study aimed to determine the diagnostic yield and impact on management of next-generation sequencing (NGS) in 50 individuals with atypical CP (ACP). METHODS: Patient eligibility criteria included impaired motor function with onset at birth or within the first year of life, and one or more of the following: severe intellectual disability, progressive neurological deterioration, other abnormalities on neurological examination, multiorgan disease, congenital anomalies outside of the central nervous system, an abnormal neurotransmitter profile, family
history, brain imaging findings not typical for cerebral palsy. Previous assessment by a neurologist and/or clinical geneticist, including biochemical testing, neuroradiography, and chromosomal microarray, did not yield an etiologic diagnosis. RESULTS: A precise molecular diagnosis was established in 65% of the 50 patients. We also identified candidate disease genes without a current OMIM disease designation. Targeted intervention was enabled in eight families (~15%). CONCLUSION: NGS enabled a molecular diagnosis in ACP cases, ending the diagnostic odyssey, improving genetic counseling and personalized management, all in all enhancing precision medicine practices.

PMID: 30542205

22. Threshold of Metabolic Acidosis Associated with Newborn Cerebral Palsy: Medical Legal Implications.
Ross MG.

Obstetricians and gynecologists belong to one of the medical specialties with the highest rate of litigation claims. Among birth injury cases, those with cerebral palsy outcomes account for litigation settlements or judgements often in the millions of dollars. In cases of potential perinatal asphyxia, a threshold level of metabolic acidosis (base deficit (BD) >12 mmol/l) is necessary to attribute neonatal encephalopathy to an intrapartum hypoxic event. With increasing duration or severity of a hypoxic stress resulting in metabolic acidosis, newborn umbilical artery BD increases. It may be alleged that as BD levels increase beyond 12 mmol/l, there is an increased likelihood and severity of cerebral palsy. As a corollary, it may be claimed that an earlier delivery (by minutes) would reduce the BD and prevent or reduce the severity of cerebral palsy. This issue is of relevance to obstetricians as defendants, as retrospective "expert" analysis of cases may suggest that optimal management decisions would have resulted in an earlier delivery. In addressing the association of metabolic acidosis and cerebral palsy, BD should be measured as the extracellular component (Base Deficitextracellular fluid) rather than the commonly used BD,blood. Studies suggest that beyond the BD threshold of 12 mmol/l, the incidence and severity of cerebral palsy does not significantly increase (until > 20 mmol/l), although the risk of neonatal death rises markedly. Thus, among most infants with hypoxia-associated neonatal encephalopathy, the occurrence of cerebral palsy is unlikely to be impacted by delivery time variation of few minutes, and this argument should not serve as the basis for medical legal claims.

PMID: 30529344

23. Mesenchymal stromal cells as a potential therapeutic for neurological disorders.
Mukai T, Tojo A, Nagamura-Inoue T.

Several studies have reported that mesenchymal stromal/stem cells (MSCs) restore neurological damage through their secretion of paracrine factors or their differentiation to neuronal cells. Based on these studies, many clinical trials have been conducted using MSCs for neurological disorders, and their safety and efficacy have been reported. In this review, we provide a brief introduction to MSCs, especially umbilical cord derived-MSCs (UC-MSCs), in terms of characteristics, isolation, and cryopreservation, and discuss the recent progress in regenerative therapies using MSCs for various neurological disorders.

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