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**Professor Nadia Badawi AM**  
Macquarie Group Foundation Chair of Cerebral Palsy

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## Interventions and Management

### **1. Relationship Between Integrity of the Corpus Callosum and Bimanual Coordination in Children With Unilateral Spastic Cerebral Palsy.**

Hung YC, Robert MT, Friel KM, Gordon AM.

Front Hum Neurosci. 2019 Sep 24;13:334. doi: 10.3389/fnhum.2019.00334. eCollection 2019.

Children with unilateral spastic cerebral palsy (USCP) have shown impaired bimanual coordination. The corpus callosum (CC) connects the two hemispheres and is critical for tasks that require inter-hemisphere communication. The relationship between the functional bimanual coordination impairments and structural integrity of the CC is unclear. We hypothesized that better integrity of the CC would relate to better bimanual coordination performance during a kinematic bimanual drawer-opening task. Thirty-nine children with USCP (Age: 6-17 years old; MACS levels: I-III) participated in the study. Measurement of the CC integrity was performed using diffusion tensor imaging. The CC was measured as a whole and was also divided into three regions: genu, midbody, and splenium. Fractional anisotropy, axial diffusivity (AD), radial diffusivity, mean diffusivity, number of voxels, and number of streamlines were evaluated in whole and within each region of the CC. 3-D kinematic analyses of bimanual coordination were also assessed while children performed the bimanual task. There were negative correlations between bimanual coordination measures of total movement time and AD of whole CC ( $p = 0.037$ ), number of streamlines and voxels of splenium ( $p = 0.038, 0.032$ , respectively); goal synchronization and AD of whole CC ( $p = 0.04$ ), and number of streamlines and voxels of splenium ( $p = 0.001, 0.01$ , respectively). The current results highlight the possible connection between the integrity of the CC, especially between the splenium region and temporal bimanual coordination performance for children with USCP.

PMID: [31607881](#)

### **2. Frequency of mirror movements and comparison of hand function in spastic cerebral palsy children with and without mirror movements.**

Shahid J, Khan S, Marryam M, Amjad I.

J Pak Med Assoc. 2019 Oct;69(10):1459-1463.

**OBJECTIVE:** To assess the frequency of mirror movements in spastic cerebral palsy children and to compare hand function and functional independence of such children with and without mirror movements. **METHODS:** The comparative cross-sectional study was conducted in special education schools of Lahore and Islamabad from August 2017 to January 2018, and comprised children of either gender aged 5-18 years diagnosed with spastic cerebral palsy who were able to make a gross grip. Wood and Teuber criteria for the assessment of mirror movements and Jebsen-Taylor hand function test for hand function assessment were used, while manual ability classification system was used for the assessment of functional independence. Data was analysed using SPSS 21. **RESULTS:** Of the 140 subjects, 113(80.7%) were boys and 27(19.3%) were girls. The

overall mean age was 11.17±3.69 years. Of the total, 51(36.4%) subjects had diplegic cerebral palsy, while 50(35.7%) were suffering from mirror movements. There was no difference in the unimanual hand function of children with and without mirror movements ( $p>0.05$ ). However, children without mirror movements had more functional independence ( $p<0.001$ ).

**CONCLUSIONS:** Mirror movement was found in one third of the sample, and there was no difference in hand function in children with and without mirror movements.

PMID: [31622297](#)

### **3. Selective Dorsal Root Rhizotomy for Spastic Cerebral Palsy: A Longitudinal Case-Control Analysis of Functional Outcome.**

Iorio-Morin C, Yap R, Dudley RWR, Poulin C, Cantin MA, Benaroch TE, Farmer JP.

Neurosurgery. 2019 Oct 17. pii: nyz422. doi: 10.1093/neuros/nyz422. [Epub ahead of print]

**BACKGROUND:** The benefit of selective dorsal rhizotomies (SDR) on motor function relative to the cerebral palsy (CP) natural history remains unknown. **OBJECTIVE:** To determine the functional benefit of SDR over the longitudinal CP natural history. **METHODS:** Retrospective, single-center, case-control study of patients post-SDR after 1990. Inclusion criteria were the following: diagnosis of spastic CP, at least 1 preoperative and 1 postoperative Gross Motor Function Measure (GMFM-88), at least 1 yr of postoperative follow-up. GMFM-88 assessments were performed at 1, 2, 3, 5, 10, and 15 yr postoperatively and converted to GMFM-66. Cases were stratified by preoperative Gross Motor Function Classification System (GMFCS) and matched against their expected natural history using published reference centiles. After age 12, our cohort and matched controls were also fitted to published nonlinear mixed models of GMFM-66 evolution over time. **RESULTS:** Analysis included 190 patients. Median follow-up, 5.3 yr (range: 1-16.9), median age at surgery, 4.6 yr, and 81.6% of patients grouped as GMFCS II or III pre-op. SDR patients performed statistically significantly better than their expected natural history ( $P < .0005$ ). At 21 yr old, a modeled benefit of 8.435 was observed for GMFCS I ( $P = .0051$ ), 0.05 for GMFCS II ( $P = .9647$ ), 6.31 for GMFCS III ( $P < .0001$ ), and 1.191 for GMFCS IV patients ( $P = .0207$ ). **CONCLUSION:** These results support the use of SDR in carefully selected spastic CP children.

PMID: [31620799](#)

### **4. [Clinical observation of selective posterior rhizotomy for improving spasticity and gross movement in patients with cerebral palsy].**

Xu J, Xu L, Zeng J, Yang XK, Li ZH, Shao GK, Li XY, Deng BW, Mu XH.

Zhongguo Gu Shang. 2019 Sep 25;32(9):815-819. doi: 10.3969/j.issn.1003-0034.2019.09.008. [Article in Chinese]

**OBJECTIVE:** To explore the effect of selective lumbosacral posterior rhizotomy (SPR) on lower limb spasticity and gross motor function in patients with cerebral palsy. **METHODS:** From January 2018 to October 2018, 47 patients with cerebral palsy were treated with rehabilitation alone and SPR combined with rehabilitation. According to whether SPR was performed, the patients were divided into group A and group B. Group A was treated with rehabilitation combined with SPR at lumbosacral level, and group B was treated with rehabilitation alone. There were 23 cases in group A, including 15 males and 8 females, with an average age of  $(7.30\pm 3.25)$  years old; 24 cases in group B, 13 males and 11 females, with an average age of  $(7.00\pm 3.09)$  years old. Forty-seven patients were assessed with modified Ashworth (MAS) and Gross Motor Function Scale (GMFM-88 items) before and after treatment. The changes of MAS and GMFM-88 scores before and after treatment were compared to evaluate the degree of spasm and the improvement of gross motor function in the two groups. **RESULTS:** All 47 patients were followed up. At 6 months after treatment, the MAS classification of the two groups was significantly improved ( $P<0.05$ ), and the improvement of group A was more obvious than that of group B ( $P<0.05$ ). Six months after treatment, the D, E and total scores of GMFM-88 between two groups were significantly improved compared with those before operation ( $P<0.05$ ). The improvement of D and total scores in group A was more obvious than that in group B. There was no significant difference in the improvement of area E between two groups. **CONCLUSIONS:** Selective posterior rhizotomy combined with rehabilitation can significantly improve the spastic state and gross motor function of lower limbs in children with cerebral palsy, and can effectively promote the reconstruction and recovery of motor function of lower limbs in children with cerebral palsy.

PMID: [31615177](#)

## 5. Role of positioning between trunk and pelvis in locomotor function of ambulant children with and without cerebral palsy.

Sanz-Mengibar JM, Santonja-Medina F.

Ideggyogy Sz. 2019 Sep 30;72(9-10):343-351. doi: 10.18071/isz.72.0343.

**BACKGROUND AND PURPOSE:** To understand if children with and without cerebral palsy share the same lumbar postural control threshold on the sagittal plane for the transition between each walking locomotor stage. **METHODS:** Observational analysis of sagittal trunk-pelvis kinematics of 97 children with cerebral palsy and 73 with typical development, according to their locomotor stage. **RESULTS:** Among children with typical development, all average and minimum measurements of the sagittal lumbar curve during the gait events were correlated with age and the locomotor stages of development. Among children with cerebral palsy, there were significant correlations between all average and minimum values of the sagittal lumbar curve and locomotor stages of development but not age. **CONCLUSION:** We conclude that, for the same locomotor level, there are no common postural patterns between children with typical development and those with spastic bilateral cerebral palsy for the position between trunk and pelvis in the sagittal plane. Maximal lordosis reduction between trunk and pelvis may change with age or even training, but does not make a positive effect on the locomotor level, while basal and maintenance capacities could explain locomotor function. Trials that failed to assess quality of movement may now have a better understanding of how different interventions improve posture towards the next functional level.

PMID: [31625701](#)

## 6. Gait Classification in Unilateral Cerebral Palsy.

Tsitlakidis S, Horsch A, Schaefer F, Westhauser F, Goetze M, Hagmann S, Klotz MCM.

J Clin Med. 2019 Oct 11;8(10). pii: E1652. doi: 10.3390/jcm8101652.

As unilateral cerebral palsy represents a complex disorder, gait classification is difficult. Knowledge of the most frequent gait patterns and functional impairment is crucial for proper decision-making. This study analyzes the prevalence of gait patterns as well as the relation of different gait patterns and the Gross Motor Function Classification System (GMFCS). Eighty-nine patients were classified retrospectively using the GMFCS, the classification of Winters, Gage, and Hicks (WGH), and Sutherland et al. The distribution of GMFCS levels among the different gait patterns was analyzed using Chi-squared test. The most common subtypes were GMFCS level I, WGH type I, and recurvatum knee. Seventeen percent (WGH) and 59% (Sutherland) of the patients did not match any criteria. Applying both classifications complementarily reduced the number of unclassified patients significantly. There was no significant difference concerning the distribution of GMFCS levels or age among the different gait patterns. A combined use of various classification systems is beneficial for proper decision-making. Unclassified patients seem to be a heterogeneous subgroup concerning functional impairment. There is a need of further characterization of the unclassifiable gait patterns and the caused functional impairment. Instrumented gait analysis remains the gold standard and should be broadly used for future studies and in clinical practice.

PMID: [31614496](#)

## 7. Muscle Synergies in Response to Biofeedback-Driven Gait Adaptations in Children With Cerebral Palsy.

Booth ATC, van der Krogt MM, Harlaar J, Dominici N, Buizer AI.

Front Physiol. 2019 Sep 27;10:1208. doi: 10.3389/fphys.2019.01208. eCollection 2019.

**BACKGROUND:** Children with cerebral palsy (CP) often show impaired selective motor control (SMC) that induces limitations in motor function. Children with CP can improve aspects of pathological gait in an immediate response to visual biofeedback. It is not known, however, how these gait adaptations are achieved at the neural level, nor do we know the extent of SMC plasticity in CP. **AIM:** Investigate the underlying SMC and changes that may occur when gait is adapted with biofeedback. **METHODS:** Twenty-three ambulatory children with CP and related (hereditary) forms of spastic paresis (Aged:  $10.4 \pm 3.1$ , 6-16 years, M: 16/F: 9) were challenged with real-time biofeedback to improve step length, knee extension, and ankle power while walking on an instrumented treadmill in a virtual reality environment. The electromyograms of eight superficial muscles of the leg were analyzed and synergies were further decomposed using non-negative matrix factorization (NNMF) using 1 to 5 synergies, to quantify SMC. Total variance accounted for (tVAF) was used as a measure of synergy complexity. An imposed four synergy solution was investigated further to compare similarity in weightings and timing patterns of matched paired synergies between baseline and biofeedback trials. **RESULTS:** Despite changes in walking pattern, changes

in synergies were limited. The number of synergies required to explain at least 90% of muscle activation increased significantly, however, the change in measures of tVAF1 from baseline ( $0.75 \pm 0.08$ ) were less than  $\pm 2\%$  between trials. In addition, within-subject similarity of synergies to baseline walking was high ( $>0.8$ ) across all biofeedback trials. CONCLUSION: These results suggest that while gait may be adapted in an immediate response, SMC as quantified by synergy analysis is perhaps more rigidly impaired in CP. Subtle changes in synergies were identified; however, it is questionable if these are clinically meaningful at the level of an individual. Adaptations may be limited in the short term, and further investigation is essential to establish if long term training using biofeedback leads to adapted SMC.

PMID: [31611807](#)

### **8. Management of Spastic Paresis and Cervical Dystonia: access to Therapeutic Innovations Through an International Program of Practical Courses.**

Colosimo C, Bhidayasiri R, Fheodoroff K, Bhatia K, Chung TM, Landreau T, Jacinto LJ.

Clin Ther. 2019 Oct 10. pii: S0149-2918(19)30484-9. doi: 10.1016/j.clinthera.2019.09.007. [Epub ahead of print]

PURPOSE: Our purpose was to determine satisfaction and confidence of the Ixcellence Network training program on health care practitioners using botulinum toxin A (BoNT-A) for neurologic disorders, including spastic paresis and cervical dystonia. METHODS: The Ixcellence Network training program was designed by a scientific committee of 6 experts and then tested at centers in Europe, and Latin America. The training, provided by 16 experienced neurologists and rehabilitation specialists, consisted of theoretic and practical sessions that covered the different stages of the patient's journey from diagnosis to tailored treatment and rehabilitation. Trainees' feedback and the impact on participants' practice were evaluated by 2 individual questionnaires, at the end of the session (T0) and at 6 months (T6). Trainers' feedback was also collected through an individual questionnaire. FINDINGS: Between September 2012 and December 2017, 728 trained physicians participated in training programs with 48%, 23%, and 29% of attendees participating in training sessions dedicated to adult spastic paresis, child spastic paresis, and cervical dystonia, respectively. At T0, 93% of attendees thought that they had been given new information and 90% thought that the training would change their daily practice. This was confirmed at T6 by 93% of respondents. Trainees were highly satisfied with the program, in particular with the practical sessions. Trainers expectations were met for attendees' level of expertise, motivation, language, and participation. IMPLICATIONS: In this descriptive study, we show that the Ixcellence Network program represents a new educational approach to promote consistency in care practices and dissemination of expertise on the use of BoNT-A for neurologic disorders. (Clin Ther. 2019; 41:XXX-XXX). © 2019 Elsevier HS Journals, Inc.

PMID: [31607560](#)

### **9. Demystifying spasticity in primary care.**

Milligan J, Ryan K, Lee J.

Can Fam Physician. 2019 Oct;65(10):697-703.

OBJECTIVE: To raise awareness of spasticity in primary care and clarify how to identify, diagnose, and manage it effectively and efficiently in patients with pre-existing neurologic conditions. SOURCES OF INFORMATION: PubMed was searched for articles published from 1970 to May 2018 using the terms spasticity, spasticity in physical disability, spasticity in mobility impairment, and spasticity with family medicine or primary care. Other relevant guidelines and resources were reviewed and used. MAIN MESSAGE: Spasticity is a common secondary complication in conditions such as spinal cord injury, multiple sclerosis, stroke, cerebral palsy, and other neuromuscular physical disabilities and can have a negative effect on health and quality of life. Factors such as inconsistent definition, poorly understood mechanism, and relatively low prevalence make spasticity seem like a daunting condition to manage. Furthermore, its variable presentation and effect on a patient's quality of life, and its range of treatments with varying levels of evidence, can make treatment challenging in primary care and in other clinical settings. Family physicians play an important role in recognizing and inquiring about spasticity and its changes, triggers, and effects on function. Ruling out reversible causes is important. Many management strategies can be instituted by family physicians. CONCLUSION: Managing spasticity might be unfamiliar to many practitioners. It is important for physicians to understand spasticity and the potential treatment options available to improve quality of life. The current review provides concise information on the clinical relevance of spasticity in primary care and how to assess and manage it effectively and efficiently in those with chronic neurologic conditions.

PMID: [31604736](#)

## 10. Effect of extracorporeal shock wave therapy on muscle spasticity in patients with cerebral palsy: meta-analysis and systematic review.

Kim HJ, Park JW, Nam K.

Eur J Phys Rehabil Med. 2019 Oct 15. doi: 10.23736/S1973-9087.19.05888-X. [Epub ahead of print]

**INTRODUCTION:** Recently, clinical trials have been performed to evaluate the efficacy of extracorporeal shock wave therapy (ESWT) in patients with cerebral palsy (CP). However, various studies adopted different clinical scales, making it insufficient to draw a definite conclusion about the efficacy of ESWT in reducing spasticity after cerebral palsy. The purpose of this meta-analysis was to assess the effects of ESWT on reducing spasticity after applying ESWT in patients with CP. **EVIDENCE ACQUISITION:** In accordance with the PRISMA statement, authors searched MEDLINE, EMBASE, Web of Science, Cochrane Central Register of Controlled Trials and Scopus from their inception dates through December 11th 2018. We included randomised controlled trials in any language that using ESWT for the purpose of ameliorating spasticity in patients with CP. We assessed spasticity measured by modified Ashworth Scale (MAS), range of motion (ROM) and baropodometric values as outcomes. **EVIDENCE SYNTHESIS:** Two authors independently extracted and verified data. Meta-analysis was completed where possible, otherwise data were synthesised narratively. From a total of 206 articles, 16 manuscripts were selected and 5 of them were ultimately included in this meta-analysis. **CONCLUSIONS:** MAS grade as primary outcome was significantly improved after ESWT compared to that in the control group (mean difference [MD]: -0.62; 95% confidence interval [CI]: -1.52 to -0.18). ROM after ESWT was also significantly improved compared to that in the control groups (MD: 18.01; 95% CI: 6.11 to 29.91). Baropodometric measures showed significantly increases in foot contact area during gait (SMD: 29.00; 95% CI: 11.08 to 46.92), but not significantly in peak pressure under the heel (MD: 15.12; 95% CI: -1.85 to 32.10) immediately after ESWT. No serious side effects were observed in any patient after ESWT. ESWT may be a valid alternative to existing treatment options targeting spasticity diminishment and ROM improvement in CP patients to maintain healthy lifestyles and normalize spastic gait pattern. Further standardization of treatment protocols including treatment intervals and intensities needs to be established and long-term follow up studies are needed to verify our results.

PMID: [31615195](#)

## 11. Potential of Vibroacoustic Therapy in Persons with Cerebral Palsy: An Advanced Narrative Review.

Kantor J, Kantorová L, Marečková J, Peng D, Vilímek Z.

Int J Environ Res Public Health. 2019 Oct 16;16(20). pii: E3940. doi: 10.3390/ijerph16203940.

Vibroacoustic therapy (VAT) is a treatment method that uses sinusoidal low-frequency sound and music. The purpose of this narrative review is to describe the effects of VAT on motor function in people with spastic cerebral palsy (CP) according to study design as well as providing information about the age of the participants, measurement tools, and sound frequencies that were used. The systematic search strategy based on the first two steps of a standard evidence-based approach were used: (1) formulation of a search question and (2) structured documented search including assessment of the relevance of abstracts and full texts to the search question and inclusion criteria. Out of 823 results of the search in 13 scholarly databases and 2 grey literature sources, 7 papers were relevant. Most of the relevant studies in children and adults presented significant improvement of motor function. According to the study design, only five experimental studies and two randomized controlled trial (RCT) studies were available. In the discussion, findings of this review are compared to other related methods that use mechanical vibrations without music. The authors recommend continuing to research the effects of VAT on motor function and spasticity in adolescents and young adults with spastic CP.

PMID: [31623221](#)

## 12. MRI evaluation of motor function recovery by rTMS and intensive occupational therapy and changes in the activity of motor cortex.

Ueda R, Yamada N, Abo M, Ruwan WAP, Senoo A.

Int J Neurosci. 2019 Oct 14:1-10. doi: 10.1080/00207454.2019.1680553. [Epub ahead of print]

**Purpose/aim:** An intervention that combines low-frequency repetitive transcranial magnetic stimulation and intensive occupational therapy can improve brain function in post-stroke patients with motor paralysis. The purpose of the present study is examined motor function recovery by repetitive transcranial magnetic stimulation and intensive occupational therapy and changes in the activity of motor cortex based on magnetic resonance imaging data. **MATERIALS AND METHODS:** In total, we assessed 30 patients with post-stroke upper extremity paralysis who were hospitalized for 12 sessions of low-frequency

repetitive transcranial magnetic stimulation over the lesion-free hemisphere plus daily occupational therapy for 15 days. Imaging analysis was performed using 3-dimensional T1-weighted image and functional magnetic resonance imaging. Hemispheric dominance was assessed by functional magnetic resonance imaging using the laterality index. In addition, Seed-based functional connectivity analysis was used to evaluate functional connectivity between the precentral gyrus of the affected side and other areas. **RESULTS:** A positive correlation was found between laterality index before intervention and the Brunnstrom recovery stage for hand/fingers ( $p < 0.05$ ). The intervention resulted in significantly higher functional connectivity between the precentral gyrus of the affected side and that of the healthy side (false discovery rate corrected  $p < 0.05$ ). **CONCLUSIONS:** We clarified that the recovery of motor function by intervention with low-frequency repetitive transcranial magnetic stimulation and occupational therapy and the increase of functional connectivity between the precentral gyrus on the affected side and the healthy side are related. These results facilitate prognostic predictions and evidence-based medical care.

PMID: [31607202](#)

### **13. The Effect of Virtual Reality Games on the Gross Motor Skills of Children with Cerebral Palsy: A Meta-Analysis of Randomized Controlled Trials.**

Ren Z, Wu J.

Int J Environ Res Public Health. 2019 Oct 14;16(20). pii: E3885. doi: 10.3390/ijerph16203885.

This review aimed to systematically evaluate the rehabilitative effect of Virtual Reality Games (VRGs) for gross motor skills of children with cerebral palsy (CP), and to give scientific grounds for the formulation of rehabilitation therapy for these children. To this end, the literature in Chinese databases (CNKI and Wanfang Data) as well as the databases of other countries (Web of Science, PubMed, EBSCOhost, Informat, Scopus, Science Direct and ProQuest) from the establishment dates of these databases to June 3rd 2019 was retrieved in order to collect randomized controlled trials with regard to the intervention effect of VRGs and traditional therapy on gross motor skills of children with CP, and the literature was screened as per inclusion and exclusion criteria. The PEDro scale was then used to evaluate the methodological quality of the included literature, and the software Review Manager 5.3 was employed to analyze the combined effect size. As a result, 7 randomized controlled trials and 234 children with CP were included. Meta-analysis showed that VRGs could improve gross motor skills of children with CP. Combined effect size of gross motor skills  $SMD = 0.37$  [95% CI = (0.06, 0.68),  $p = 0.02$ ]. In conclusion, the VRG intervention program can enhance gross motor skills of children with CP to some extent. In view of the limitations regarding methodologies and the quality and quantity of the literature in this research, more quality randomized controlled trials are needed so as to draw convincing conclusions of effect of VRG intervention on gross motor skill development of children with CP in future studies.

PMID: [31614990](#)

### **14. Intellectual Disability.**

Lee K, Cascella M, Marwaha R.

SourceStatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019-. 2019 Oct 3.

Individuals with an intellectual disability have neurodevelopmental deficits characterized by limitations in intellectual functioning and adaptive behavior. These disabilities originate and manifest before the age of 18 and can be associated with a considerable number of related and co-occurring problems including mental health (e.g., depression, and anxiety), neurodevelopmental (e.g., autism spectrum disorders, and attention deficit hyperactivity disorder), as well as neurological (e.g., infantile cerebral palsy) and medical conditions (e.g., meningitis). Intellectual functioning is generally called intelligence and includes a wide range of mental activities such as the ability of logical reasoning and practical intelligence (problem-solving), ability in learning, verbal skills, and so on. It manifests and expresses itself through a numerous set of capabilities, behaviors, thoughts, and emotions. In other words, intellectual functioning is definable as the global ability that allows the individual to understand reality and interact with it. Intellectual functioning is commonly measured by the intelligence quotient (IQ), which represents a total score obtained from standardized tests (IQ tests) developed for evaluating human intelligence. IQ test score has a median of 100 and a standard deviation of 15. A score of 70 or below (two standard deviations below the median) indicates intellectual limitations. Adaptive behavior These disabilities express as lacking competence in social, conceptual, and practical skills. Social skills include interpersonal skills, social responsibility, self-esteem, gullibility, naivety, resolution of social problems, and the ability to follow the rules of the society and to obey the laws. Conceptual skills include the ability to understand time, finance, and language. Practical skills include the ability to use tools, carry out activities of daily living, and interact with other people. All these skills are learned throughout development and performed in response to common problems and simple/complex tasks as well as expectations from our community and society. Obviously, these behavioral responses become progressively more complex with age. Several validated tools are useful

for assessing limitations in adaptive behavior.

PMID: [31613434](#)

### **15. Toilet Training: Common Questions and Answers.**

Baird DC, Bybel M, Kowalski AW.

Am Fam Physician. 2019 Oct 15;100(8):468-474.

Toilet training is a significant developmental milestone in early childhood. Most U.S. children achieve the physiologic, cognitive, and emotional development necessary for toilet training by 18 to 30 months of age. Markers of readiness for toilet training include being able to walk, put on and remove clothing, and follow parental instruction; expressive language; awareness of a full bladder or rectum; and demonstrated dissatisfaction with a soiled diaper. Other readiness cues include imitating toileting behavior, expressing desire to toilet, and demonstrating bladder or bowel control (staying dry through a nap or through the night). Physicians should provide anticipatory guidance to parents beginning at about 18 to 24 months of age, noting the signs of toilet training readiness, and setting realistic expectations for parents. Parents should be counseled that no training method is superior to another. Parents should choose a method that is best suited to them and their child, and the method should use positive reinforcement. Complications of toilet training include stool toileting refusal, stool withholding, encopresis, hiding to defecate, and enuresis. These problems typically resolve with time, although some may require further investigation and treatment. Medical comorbidities such as Down syndrome, autism spectrum disorder, and cerebral palsy reduce the likelihood of successfully attaining full toilet training and often require early consultation with occupational therapists, developmental pediatricians, or other subspecialists to aid in toilet training.

PMID: [31613577](#)

### **16. Early Diagnosis and Classification of Cerebral Palsy: An Historical Perspective and Barriers to an Early Diagnosis.**

Te Velde A, Morgan C, Novak I, Tantsis E, Badawi N.

J Clin Med. 2019 Oct 3;8(10). pii: E1599. doi: 10.3390/jcm8101599.

Since the 1800s, there have been calls in the literature for the early diagnosis of cerebral palsy (CP). However, diagnosis still often occurs late, from 12 to 24 months in high income countries and as late as 5 years in low resource settings. This is after the optimal timeframe for applying interventions which could harness neuroplastic potential in the developing brain. Multiple barriers exist which affect clinicians' confidence in diagnosing CP early. These range from the lack of definitive biomarkers to a lack of curative treatments for CP. Further barriers to diagnosis are proposed including; (a) difficulty finding a congruent fit with the definition of CP in an infant, where expected activity limitations might not yet be apparent; and (b) differences in the presentation of motor type and topography classifications between infants and children. These barriers may affect a clinicians' confidence using "pattern recognition" in the differential diagnosis process. One of the central tenets of this paper is that diagnosis and classification are different, involving different instruments, and are more accurately conducted separately in infants, whereas they are fundamentally interconnected in older children and inform therapeutic decisions. Furthermore, we need to be careful not to delay early diagnosis because of the low reliability of early classification, but instead uncouple these two processes. Ongoing implementation of best practice for early detection requires creative solutions which might include universal screening for CP. Implementation and accompanying knowledge translation studies are underway to decrease the average age of diagnosis in CP.

PMID: [31623303](#)

### **17. Stroke in the artery of percheron territory: the two edges of one diagnosis.**

Payenok AV, Shevaha VM, Kulyk AR, Netliukh AM, Kulmatytskyi AV.

Wiad Lek. 2019;72(9 cz 2):1851-1853.

Occlusion of artery of Percheron is a rare condition caused by a peculiar anatomic variation in cerebral blood supply, leading to a bilateral thalamic infarction. Strokes in artery of Percheron account for 0.1% to 2% of all cerebral infarctions. Thalamic area is supplied by the arteries arising directly from the P1 segment of the posterior cerebral artery. However, in 1/3 of cases the

supply is provided by a single trunk referred to as artery of Percheron (AOP). Early diagnosis of stroke in AOP can be very challenging due to an ambiguous clinical presentation and the absence of neurovisualization findings. This article presents two clinical cases of stroke in artery of Percheron observed at Lviv Emergency Hospital. Different clinical progression of a cerebrovascular accident contrasted with a similar neurovisualization pattern was a distinctive feature in these patients. Taking into consideration the rarity of this condition and a characteristic clinical presentation, these clinical cases were retrospectively analyzed and compared. A stroke in AOP should be suspected in all patients with symptoms of interrupted blood supply in the vertebrobasilar territory. The diagnosis primarily depends on clinical features; patients with paramedian bilateral thalamic lesions may develop sudden problems with consciousness, vertical gaze palsy and memory disorders. Early diagnosis of this condition allows for more effective therapeutic interventions and improves patient prognosis.

PMID: [31622278](#)

### **18. Prescription opioid dispensing in Australian children and adolescents: a national population-based study.**

Bell J, Paget SP, Nielsen TC, Buckley NA, Collins J, Pearson SA, Nassar N.

Lancet Child Adolesc Health. 2019 Oct 7. pii: S2352-4642(19)30329-3. doi: 10.1016/S2352-4642(19)30329-3. [Epub ahead of print]

**BACKGROUND:** There are few population-based studies of paediatric opioid use. We aimed to investigate the prevalence of opioid dispensing in Australian children and adolescents. **METHODS:** In this population-based study, we used data from a random sample of 15% of the children and adolescents who had received any medicines between Feb 1, 2013, and Dec 31, 2017, through the Australian Pharmaceutical Benefits Scheme (PBS). We identified children younger than 18 years who had been dispensed at least one PBS-listed opioid in the study period. We calculated the annual prevalence of children being dispensed one or more opioid prescriptions, by age group and by opioid characteristics (such as strength and mode of action), and we assessed trends over time with negative binomial regression. We also identified new treatment episodes and quantified the number of opioid prescriptions dispensed in the ensuing year. **FINDINGS:** During the study period, 78 320 opioid prescriptions were dispensed to 50 730 Australian children, aged 0-17 years, in our sample. In 2017, 135.4 children per 10 000 were dispensed opioids, representing a slight decrease equal to a change of -2.2% (95% CI -3.5 to -0.8) per annum since 2013. The prevalence of opioid dispensing was greater at older ages: in 2017, 5.7 infants per 10 000 younger than 1 year were dispensed opioids, versus 404.8 adolescents per 10 000 aged 13-17 years, meaning that roughly one in 25 adolescents were dispensed opioids. Weak opioids (ie, codeine and tramadol) accounted for 60.7% of the opioids dispensed, and codeine was the most commonly dispensed opioid, accounting for 39 531 (50.5%) prescriptions dispensed. The prevalence of weak opioid dispensing significantly decreased in all age groups (other than infants younger than 1 year), particularly in those younger than 12 years, for whom weak opioids are not recommended. Dispensing of strong opioids, particularly oxycodone, increased in every age group. Of the 29 073 children who received a new course of treatment, 23 318 (80.2%) children were dispensed only one prescription of opioids in that year. Those dispensed two or more opioids were more likely to be adolescents (vs children younger than 13 years), female, and to have been dispensed several unique medicine types in the 3 previous months (vs those receiving one or fewer types). **INTERPRETATION:** In 2017, one in 74 Australian children, including one in 25 adolescents, were dispensed an opioid. Dispensing of weak opioids decreased between 2013 and 2017, but codeine is still commonly dispensed in younger children and education to reduce this practice is required. Dispensing of strong opioids increased in all age groups. Children and adolescents must receive appropriate pain management, but further evidence on the risks and benefits of opioid use in this young population is needed. **FUNDING:** Financial Markets Foundation for Children, National Health and Medical Research Council Centre of Research Excellence in Medicines and Ageing, Australian Government Department of Industry, Innovation and Science, Research Foundation of the Cerebral Palsy Alliance (Australia).

PMID: [31604614](#)

### **19. Mid-sagittal plane detection for advanced physiological measurements in brain scans.**

Bertacchini F, Rizzo R, Bilotta E, Pantano P, Luca A, Mazzuca A, Lopez A.

Physiol Meas. 2019 Oct 18. doi: 10.1088/1361-6579/ab4f2e. [Epub ahead of print]

The diagnostic process of many neurodegenerative diseases, such as Parkinson, Progressive Supranuclear Palsy, etc., involves the study of brain MRI scans in order to individuate morphological markers that can highlight on the healthy status of the subject. A fundamental step in the pre-processing and analysis of MRI is the identification of the Mid-Sagittal Plane, which corresponds to the mid-brain and allows a coordinate reference system for the whole MRI scans set. To improve the identification of the Mid-Sagittal, we have developed an algorithm in Matlab®, based on the k-means clustering function. The results have been compared with the evaluation of four experts that manually identified the mid-sagittal and whose performances have been crossed with a cognitive decisional algorithm in order to define a gold standard. The comparison

provided a mean percentage error of 0.96%. To further refine the automatic procedure, we trained a machine learning considering the results coming from the proposed algorithm and the gold standard. Therefore, we tested the machine learning and obtained results comparable to medical raters with a mean percentage error of 0.65%. Even if the sample of data analyzed needs to be increased, the system is promising and it could be directly incorporated into broader diagnostic support systems.

PMID: [31627198](#)

## **20. Types of intrapartum hypoxia on the cardiocotograph (CTG): do they have any relationship with the type of brain injury in the MRI scan in term babies?**

Yatham SS, Whelehan V, Archer A, Chandraharan E.

J Obstet Gynaecol. 2019 Oct 15:1-6. doi: 10.1080/01443615.2019.1652576. [Epub ahead of print]

Electronic foetal monitoring using cardiocotography is aimed at the timely recognition and management of foetal hypoxia. The primary objective of this study was to examine whether a relationship exists between the types of foetal hypoxia (acute, subacute, evolving, chronic), as identified on cardiocotography and the nature of hypoxic ischaemic encephalopathy, as observed on MRI scans after birth. We conducted a retrospective study of 16 babies born (out of 52,187 births) at St George's Hospital in London during 2006-2017 with a postnatal diagnosis of HIE. Of the 16 babies, only 11 had both MRI scans and CTG traces available. Of those, 9 showed evidence of intrapartum hypoxia on CTG, but only 6 demonstrated evidence of HIE on MRI. Those with acute hypoxia showed abnormalities in the basal ganglia and thalami. A gradually evolving hypoxia or subacute hypoxia was associated with lesions in myelination and cerebral cortex. Impact Statement What is already known on this subject? It has been reported that inter-observer agreement for CTG interpretation is low (30%) when pattern recognition based guidelines are used (Rhöse et al. 2014 ; Reif et al. 2016 ), even amongst 'experts' (Hruban et al. 2015 ). Furthermore, it has been shown that CTG traces do not reliably predict neonatal encephalopathy (Spencer et al. 1997 ). What do the results of this study add? Our study indicates that if 'types of intrapartum hypoxia' are used for interpretation, then inter-observer agreement increases to 81%, from the reported 30% when traces are classified into 'normal, suspicious and pathological' using guidelines based on 'pattern recognition'. Furthermore, our study shows a good correlation between the type of intrapartum hypoxia observed on CTG trace and the nature of injury observed on the MRI. What are the implications of these findings for clinical practise and/or further research? Improving inter-observer agreement of CTGs with the use of pattern recognition in combination with the good correlation to MRI scan findings ultimately leads to better management and post-natal outcomes. This is evidenced by the fact that after the introduction of physiology-based CTG interpretation and mandatory competency testing on CTG interpretation for all staff in 2010, St. George's Maternity Unit has half the nationally reported rate of cerebral palsy.

PMID: [31612740](#)

## **21. Best practice guidelines for communicating to parents the diagnosis of disability.**

Novak I, Morgan C, McNamara L, Te Velde A.

Early Hum Dev. 2019 Oct 10:104841. doi: 10.1016/j.earlhumdev.2019.104841. [Epub ahead of print]

Conveying a diagnosis of a disability to the parents of young children is difficult both for the parent and the clinician, however there is an ethical and medical imperative to do so. However, the process and manner of disclosure needs to be done well. When communication between parent and clinicians fails, parental mental health can be adversely affected. This paper adapts and explains how to use the SPIKES protocol to deliver "bad news" about a developmental disability diagnosis with families of infants <12-months old, using cerebral palsy as an example. Next, the range of responses parents experience to the delivery of bad news from "watchful waiting" to "acceptance" are outlined and explained. The knowledge needs of parents range from causes and prognosis to treatments and outcomes. Using clinical scenarios of recently diagnosed infants, commonly asked questions and suggested answers are tabled.

PMID: [31607402](#)

## **22. Experiences of primary caregivers of children with cerebral palsy across the trajectory of diagnoses in Ghana.**

Kyeremateng JDA, Édusei A, Dogbe JA, Opoku MP, Nketsia W, Hammond C, Afriyie SA.

BACKGROUND: Cerebral palsy (CP) is a non-progressive disorder of posture or movement caused by a lesion to the

developing brain that results in functional limitations. The diagnosis of CP can vary from one child to another, causing family stress because of vague and unknown outcomes of the disorder. Although there are negative attitudes in Ghanaian societies towards primary caregivers and children with disabilities, fewer attempts have been made to understand their experiences. **OBJECTIVES:** The main aim of this study was to explore the experiences of primary caregivers across the trajectory of the diagnosis (before, during and after) of CP in the setting of a tertiary hospital. **METHOD:** Using Social Capital Theory as framework, 40 primary caregivers of children with CP, who were receiving treatment at a major referral hospital in Ghana, were interviewed about their experiences before, during and after diagnosis. **RESULTS:** The results that emerged from the thematic analysis were discussed as follows: experiences before diagnosis, experiences during the diagnosis and experiences after the diagnosis. Particularly, participants discussed their inability to access essential services such as education for their children with CP. **CONCLUSION:** In light of systemic challenges faced by participants and their children with CP, the need for health policymakers to prioritise the public education about CP, promoting the well-being of caregivers and other implications of the study have been discussed.

PMID: [31616620](#)

### **23. The New West Japan Twins and Higher Order Multiple Births Registry.** Yokoyama Y.

Twin Res Hum Genet. 2019 Oct 14:1-4. doi: 10.1017/thg.2019.88. [Epub ahead of print]

The new West Japan Twins and Higher Order Multiple Births Registry was established by recruiting young twins and multiple births and by referrals from public health centers in the 1990s. The participants included in the survey comprised over 7800 twins and 4241 higher order multiples, and their families. Specifically, the present registry contains one of the largest triplet samples in the world. For these twins and multiples, data on year of delivery, mode of delivery, gestational age, intrapartum complications, longitudinal physical measures, motor milestones, cerebral palsy and feeding methods were obtained from records in the Maternal and Child Health Handbooks and schools. Participating mothers were asked to indicate family structure, parental educational history, maternal sleeping time, maternal health condition, maternal and paternal age at multiple delivery, complications during pregnancy, handedness of multiples and age at menarche of multiples. However, the zygosity differed among the various collaborating public health centers according to factors such as the time of investigation. Follow-up questionnaires have been mailed out every 3-4 years for longitudinal studies. This article describes the goals of this registry, recruitment of multiples and the focus of the study. The goals of this registry are not only to conduct research on human genetics and maternal and child health, but also to contribute to providing appropriate information for families with multiples.

PMID: [31608848](#)

## **Prevention and Cure**

### **24. Human Neural stem cell (hNSC) Transplant Location dependent neuroprotection and motor deficit amelioration in rats with penetrating TBI (PTBI).**

Hu Z, Gajavelli S, Spurlock MS, Mahavadi A, Quesada LS, Gajavelli GR, Andreoni CB, Di L, Janecki J, Lee SW, Rivera KN, Shear DA, Bullock RM.

J Trauma Acute Care Surg. 2019 Oct 15. doi: 10.1097/TA.0000000000002510. [Epub ahead of print]

**BACKGROUND:** Penetrating traumatic brain injury (PTBI) induced chronic inflammation that drives persistent tissue loss long after injury. Absence of endogenous reparative neurogenesis and effective neuroprotective therapies render injury-induced disability an unmet need. Cell replacement via neural stem cell transplantation could potentially rebuild the tissue and alleviate PTBI disability. The optimal transplant location remains to be determined. **METHODS:** To test if subacute human neural stem cells (hNSCs) transplant location influences engraftment, lesion expansion, and motor deficits, rats (n=10/group) were randomized to following four groups (uninjured and three injured). Gr1: uninjured rats with cell transplants (sham+hNSCs), one-week post-unilateral pTBI, after establishing motor deficit, Gr2 was treated with vehicle (media, no cells), Gr3 hNSCs were transplanted into lesion core (intra), or in Gr4, tissue surrounding the lesion (peri). All animals were immunosuppressed for twelve weeks and euthanized following motor assessment. **RESULTS:** In Gr2, pTBI injury effect manifest as porencephalic cyst, 22.53±2.87 (% of intact hemisphere), with p-value <0.0001 compared to uninjured Gr1. Gr3 lesion volume at 17.44±2.11 did not differ significantly from Gr2 (p=0.36) while Gr4 value, 9.17±1.53 differed significantly (p=0.0001). Engraftment and neuronal differentiation were significantly lower in the uninjured Gr1 (p<0.05), compared to injured groups. However, there

were no differences between Gr3 and G4. Significant increase in cortical tissue sparing ( $p=0.03$ ), including motor cortex ( $p=0.005$ ) was observed in Gr4 but not Gr3. Presence of transplant within lesion or in penumbra attenuated motor deficit development ( $p<0.05$ ) compared to Gr2. CONCLUSIONS: In aggregate, injury milieu supports transplanted cell proliferation and differentiation independent of location. Unexpectedly, cortical sparing is transplant location dependent. Thus, apart from cell replacement and transplant mediated deficit amelioration, transplant location dependent neuroprotection may be key to delaying onset or preventing development of injury-induced disability. LEVEL OF EVIDENCE: Preclinical study evaluation of therapeutic intervention, Level VI.

PMID: [31626023](#)

## 25. Microglia in developing white matter and perinatal brain injury.

McNamara NB, Miron VE.

Neurosci Lett. 2019 Oct 12:134539. doi: 10.1016/j.neulet.2019.134539. [Epub ahead of print]

Perinatal brain injury (PBI) to the developing white matter results in hypomyelination of axons and can cause long-term motor and cognitive deficits e.g. cerebral palsy. There are currently no approved therapies aimed at repairing the white matter following insult, underscoring the need to investigate the mechanisms underlying the pathogenesis of PBI. Microglia have been strongly implicated, but their function and heterogeneity in this context remain poorly understood, posing a barrier to the development of microglia-targeted therapies for white matter repair following PBI. In this review, we discuss the roles of microglia in normal white matter development and in PBI, and potential drug strategies to influence microglial responses in this setting.

PMID: [31614181](#)

## 26. Cannabidiol Administration Prevents Hypoxia-Ischemia-Induced Hypomyelination in Newborn Rats.

Ceprián M, Vargas C, García-Toscano L, Penna F, Jiménez-Sánchez L, Achicallende S, Elezgarai I, Grandes P, Hind W, Pazos MR, Martínez-Orgado J.

Front Pharmacol. 2019 Sep 26;10:1131. doi: 10.3389/fphar.2019.01131. eCollection 2019.

Neonatal hypoxia-ischemia (HI) is a risk factor for myelination disturbances, a key factor for cerebral palsy. Cannabidiol (CBD) protects neurons and glial cells after HI insult in newborn animals. We hereby aimed to study CBD's effects on long-lasting HI-induced myelination deficits in newborn rats. Thus, P7 Wistar rats received s.c. vehicle (HV) or cannabidiol (HC) after HI brain damage (left carotid artery electrocoagulation plus 10% O<sub>2</sub> for 112 min). Controls were non-HI pups. At P37, neurobehavioral tests were performed and immunohistochemistry [quantifying mature oligodendrocyte (mOL) populations and myelin basic protein (MBP) density] and electron microscopy (determining axon number, size, and myelin thickness) studies were conducted in cortex (CX) and white matter (WM). Expression of brain-derived neurotrophic factor (BDNF) and glial-derived neurotrophic factor (GDNF) were analyzed by western blot at P14. HI reduced mOL or MBP in CX but not in WM. In both CX and WM, axon density and myelin thickness were reduced. MBP impairment correlated with functional deficits. CBD administration resulted in normal function associated with normal mOL and MBP, as well as normal axon density and myelin thickness in all areas. CBD's effects were not associated with increased BDNF or GDNF expression. In conclusion, HI injury in newborn rats resulted in long-lasting myelination disturbance, associated with functional impairment. CBD treatment preserved function and myelination, likely as a part of a general neuroprotective effect.

PMID: [31611802](#)