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Interventions and Management

1. J Child Neurol. 2014 May 7. [Epub ahead of print]

Relevant Areas of Functioning in Children With Cerebral Palsy Based on the International Classification of Functioning, Disability and Health Coding System: A Clinical Perspective.

Schiariti V1, Mâsse LC.

In the context of the development of the International Classification of Functioning, Disability and Health Core Sets for children and youth with cerebral palsy, an evidence-based methodology was implemented to select the most relevant categories out of the entire classification. The aim of this study was to describe the contribution of the clinical perspective to select categories of functioning in children and youth with cerebral palsy. We conducted a chart review of clinical assessments of children and youth with cerebral palsy aged 0 to 18 years in a tertiary level center. In total, 129 International Classification of Functioning categories were covered in clinical encounters: representing 19% body structures, 33% body functions, 37% activity and participation, and 11% environmental factors. Our findings can guide clinical assessments and goal-setting of this population. This important perspective will inform the development of the International Classification of Functioning, Disability and Health Core Sets for children and youth with cerebral palsy.

[PMID: 24810085](https://pubmed.ncbi.nlm.nih.gov/24810085/) [PubMed - as supplied by publisher]

2. J Child Neurol. 2014 May 7. [Epub ahead of print]

Emerging Therapy Approaches: An Emphasis on Function.

Law M1, Darrah J.

Children and youth with cerebral palsy receive ongoing physical and occupational therapy services to improve their functional performance and participation in activities at home, school, and in the community. Over the past 2 decades, rehabilitation interventions have become more functional and goal oriented. In this article, we discuss factors that have influenced emerging intervention approaches. These factors include greater involvement of families in decision making, changing conceptual frameworks and theories underlying skill development and improved outcome measures. New research findings indicate that rehabilitation interventions embracing family-centered services and focusing on functional improvement can be more effective in promoting participation. This knowledge can serve as the platform for further examination of the most effective rehabilitation interventions for

children and youth with cerebral palsy.

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3. J Child Neurol. 2014 May 7. [Epub ahead of print]

Classification in Childhood Disability: Focusing on Function in the 21st Century.

Rosenbaum P1, Eliasson AC, Hidecker MJ, Palisano RJ.

Classification systems in health care are usually based on current understanding of the condition. They are often derived empirically and adopted applying sound principles of measurement science to assess whether they are reliable (consistent) and valid (true) for the purposes to which they are applied. In the past 15 years, the authors have developed and validated classification systems for specific aspects of everyday function in people with cerebral palsy-gross motor function, manual abilities, and communicative function. This article describes the approaches used to conceptualize each aspect of function, develop the tools, and assess their reliability and validity. We report on the utility of each system with respect to clinical applicability, use of these tools for research, and the uptake and impact that they have had around the world. We hope that readers will find these accounts interesting, relevant, and applicable to their daily work with children and youth with disabilities.

[PMID: 24810083](#) [PubMed - as supplied by publisher]

4. Assist Technol. 2014 Spring;26(1):33-44.

Assessing mouse alternatives to access to computer: a case study of a user with cerebral palsy.

Pousada T, Pareira J, Groba B, Nieto L, Pazos A.

The purpose of this study is to describe the process of assessment of three assistive devices to meet the needs of a woman with cerebral palsy (CP) in order to provide her with computer access and use. The user has quadriplegic CP, with anarthria, using a syllabic keyboard. Devices were evaluated through a three-step approach: (a) use of a questionnaire to preselect potential assistive technologies, (b) use of an eTAO tool to determine the effectiveness of each device, and (c) a conducting semi-structured interview to obtain qualitative data. Touch screen, joystick, and trackball were the preselected devices. The best device that met the user's needs and priorities was joystick. The finding was corroborated by both the eTAO tool and the semi-structured interview. Computers are a basic form of social participation. It is important to consider the special needs and priorities of users and to try different devices when undertaking a device-selection process. Environmental and personal factors have to be considered, as well. This leads to a need to evaluate new tools in order to provide the appropriate support. The eTAO could be a suitable instrument for this purpose. Additional research is also needed to understand how to better match devices with different user populations and how to comprehensively evaluate emerging technologies relative to users with disabilities.

[PMID: 24800452](#) [PubMed - in process]

5. Arch Phys Med Rehabil. 2014 Apr 30. pii: S0003-9993(14)00329-3. doi: 10.1016/j.apmr.2014.04.013. [Epub ahead of print]

How do changes in motor capacity, motor capability and motor performance relate in children and adolescents with cerebral palsy?

Smits DW1, Gorter JW2, van Schie PE3, Dallmeijer AJ3, Ketelaar M4; PERRIN+ study group.

OBJECTIVE: To investigate the relationships between changes in motor capacity (can do, in standardized environment), in motor capability (can do, in daily environment), and in motor performance (does do, in daily environment) among children with cerebral palsy (CP). **DESIGN:** Prospective longitudinal study. After baseline measurements (at the age of 18 months, 30 months, 5 years, 7 years, 9 years, 11 years, or 13 years), 2-year follow-up measurements were performed. Change-scores were calculated and Pearson correlations were used for

change-score-relationships. SETTING: A clinic-based population of children with CP. PARTICIPANTS: Toddlers, school-age children, and adolescents with CP (N=321; 200 boys and 121 girls). Levels of severity according to the GMFCS: Level I 42%, Level II 15%, Level III 17%, Level IV 13%, and Level V 13%. INTERVENTIONS: Not applicable MAIN OUTCOME MEASURES: Change in motor capacity was assessed with the Gross Motor Function Measure-66. Change in motor capability and motor performance were assessed with the Pediatric Evaluation of Disability Inventory, using the Functional-Skills-Scale and Caregiver-Assistance-Scale, respectively. RESULTS: Within the total group, change-score-correlations were moderate (between 0.52 and 0.67) and significant ($p < 0.001$). For age groups, correlations were significantly higher in toddlers compared with school-age children and with adolescents. For severity levels, correlations were significantly higher in children at level III compared with level I, IV, and V. CONCLUSIONS: Results imply that change in motor capacity does not automatically translate to change in motor capability, nor that change in motor capability automatically translates in change in motor performance. Results also show different relationships for clinically relevant subgroups. These are important insights for clinical practice as it can guide evidence-based interventions with a focus on activities.

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6. Arch Phys Med Rehabil. 2014 Apr 30. pii: S0003-9993(14)00311-6. doi: 10.1016/j.apmr.2014.04.010. [Epub ahead of print]

Clinical application of a robotic ankle training program for cerebral palsy compared to the research laboratory application: Does it translate to practice?

Sukal-Moulton T1, Clancy T2, Zhang LQ3, Gaebler-Spira D4.

OBJECTIVE: To determine the clinical efficacy of an ankle robotic rehabilitation protocol for patients with cerebral palsy. DESIGN: The clinic cohort was identified from a retrospective chart review in a before-after intervention trial design and compared to a previously published prospective research cohort. SETTING: Urban rehabilitation hospital outpatient clinic. PARTICIPANTS: Children ($n=28$, 8.2 ± 3.62 years) with Gross Motor Function Classification System level I, II or III who were referred for ankle stretching and strengthening used a robotic ankle device in the clinic setting. Clinic results were compared to a previously published cohort of 12 participants (7.8 ± 2.91 years) seen in a research laboratory-based intervention protocol. INTERVENTIONS: Patients in the clinic cohort were seen 2 times per week for 75 minute sessions for a total of 6 weeks. The first 30 minutes of the session was spent using the robotic ankle device for ankle stretching and strengthening and the remaining 45 minutes were spent on functional movement activities. There was no control group. MAIN OUTCOME MEASURES: We compared pre- and post-intervention measures of plantarflexor and dorsiflexor range of motion, strength, spasticity, mobility (timed up and go, 6-minute walk, 10-meter walk), balance (Pediatric Balance Scale), Selective Motor Control Assessment of the Lower Extremity (SCALE), and the Gross Motor Function Measure (GMFM). RESULTS: Significant improvements were found for the clinic cohort in all main outcome measures except for the GMFM. These improvements were equivalent to those reported in the research cohort, except for larger SCALE test changes in the research cohort. CONCLUSION: These findings suggest that translation of repetitive, goal directed biofeedback training into the clinic setting is both feasible and beneficial for patients with cerebral palsy.

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[PMID: 24792141](#) [PubMed - as supplied by publisher]

7. Gait Posture. 2014 Apr 18. pii: S0966-6362(14)00478-0. doi: 10.1016/j.gaitpost.2014.04.187. [Epub ahead of print]

Observational gait assessment tools in paediatrics - A systematic review.

Rathinam C1, Bateman A2, Peirson J3, Skinner J4.

Instrumented gait analysis (IGA) is an expensive technique used to objectively detect gait abnormalities in children. Observational gait assessment is considered as a cost effective alternate for IGA in regular clinical practice. This article is aimed at systematically reviewing the available paediatric gait analysis tools and examines their reliability

and validity compared to IGA. This review also examines the structure of these tools, their clinical use and limitations. Articles were searched from PubMed, CINHL, AMED, BNI, EMBASE, PEDro and Cochrane library from the earliest record on the database to December 2012. Hand searches were carried out in a few journals. Studies that examined children's gait using a structured assessment tool were included and analysed for their quality, reliability and validity. Pre-established criteria were used to judge the quality of methodology and reliability and validity. Five observational gait tools for children with Cerebral Palsy (CP) and one for children with Downs Syndrome were identified. Nine studies related to children with CP were enrolled for this review. None of the tools have accomplished the level of IGA's consistency. Edinburgh Visual Gait Score (EVGS) was found to have better reliability and validity than the other tools. Very limited studies were available for most of the gait assessment tools therefore their clinical use cannot be judged based on the existing evidence. EVGS was found to have better concurrent validity and reliability and it should be considered to assess CP gait in regular practice. Future work to investigate the use of low cost technology to improve observers' accuracy of EVGS is suggested.

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8. J Child Orthop. 2014 May 6. [Epub ahead of print]

One-stage hip reconstruction in children with cerebral palsy: long-term results at skeletal maturity.

Mallet C1, Ilharreborde B, Presedo A, Khairouni A, Mazda K, Penneçot GF.

PURPOSE: Hip subluxation is common in children with cerebral palsy (CP). Surgery is indicated in case of pain or progressive increase of Reimers index on radiographs. Peri-iliac osteotomy combined with femoral osteotomy is one of the numerous operative techniques available, but results at skeletal maturity remain unclear. The purpose of this radiological study was to report the long-term results of this procedure. **MATERIALS AND METHODS:** Twenty hips in 20 children were retrospectively evaluated at skeletal maturity. Mean age at surgery was 8.1 years and follow-up averaged 9.1 years. All patients underwent Dega acetabuloplasty, soft-tissue release and femoral-shortening varus derotation osteotomy without open reduction. Reimers index, acetabular angle (AA) and neck-shaft angle (NSA) were compared on preoperative, postoperative and latest follow-up radiographs. **RESULTS:** Dega osteotomy significantly improved the AA and the correction remained stable at maturity. The NSA significantly decreased postoperatively (153° - 115°), but recurrence of the valgus deformity (130°) of the proximal femur was observed at maturity. Consequently, Reimers index followed the same evolution. No case of osteonecrosis was reported but one hip dislocated and one subluxated during follow-up. **CONCLUSION:** Progressive recurrence of the valgus deformity of the proximal femur, attributable to adductors spasticity and gluteus medius weakness, led to a significant increase in the Reimers index. However, hip coverage remained $>70\%$ at maturity in 90% of the hips. This one-stage procedure without hip dislocation efficaciously corrected acetabulum dysplasia and successfully treated neurological hips in CP patients.

LEVEL OF EVIDENCE: IV: reospective study.

[PMID: 24796563](#) [PubMed - as supplied by publisher]

9. Autoimmune Dis. 2014;2014:237107. doi: 10.1155/2014/237107. Epub 2014 Apr 2.

Anti-transglutaminase 6 antibodies in children and young adults with cerebral palsy.

Stenberg R1, Hadjivassiliou M2, Aeschlimann P3, Hoggard N2, Aeschlimann D3.

Author information

Objectives. We have previously reported a high prevalence of gluten-related serological markers (GRSM) in children and young adults with cerebral palsy (CP). The majority had no enteropathy to suggest coeliac disease (CD). Antibodies against transglutaminase 6 (anti-TG6) represent a new marker associated with gluten-related neurological dysfunction. The aim of this study was to investigate the prevalence of anti-TG6 antibodies in this group of individuals with an early neurological injury resulting in CP. **Materials and Methods.** Sera from 96 patients with CP and 36 controls were analysed for IgA/IgG class anti-TG6 by ELISA. **Results.** Anti-TG6 antibodies were found in 12/96 (13%) of patients with CP compared to 2/36 (6%) in controls. The tetraplegic subgroup of CP had a

significantly higher prevalence of anti-TG6 antibodies 6/17 (35%) compared to the other subgroups and controls. There was no correlation of anti-TG6 autoantibodies with seropositivity to food proteins including gliadin. Conclusions. An early brain insult and associated inflammation may predispose to future development of TG6 autoimmunity.

[PMID: 24804082](#) [PubMed] PMID: PMC3996887 Free PMC Article

10. Int J Urol. 2014 Apr;21(4):431. Epub 2014 Feb 19.

Editorial Comment to Sacral neuromodulation is an effective option for non-obstructive urinary retention in men with cerebral palsy.

Yamamoto T, Gotoh M.

Comment on: Sacral neuromodulation is an effective option for non-obstructive urinary retention in men with cerebral palsy. [Int J Urol. 2014]

[PMID: 24812688](#) [PubMed - in process]

11. Klin Padiatr. 2014 May 8. [Epub ahead of print]

Perianal Streptococcal Dermatitis is not a Major Cause of Constipation in Pediatric Patients with Cerebral Palsy.

Nava E, Heininger U, Weber P.

[PMID: 24810751](#) [PubMed - as supplied by publisher]

12. Res Dev Disabil. 2014 Apr 30. pii: S0891-4222(14)00165-6. doi: 10.1016/j.ridd.2014.04.016. [Epub ahead of print]

Can serious games be incorporated with conventional treatment of children with cerebral palsy? A review.

Bonnechère B1, Jansen B2, Omelina L3, Degelaen M4, Wermenbol V5, Rooze M6, Van Sint Jan S6.

The use of video games in rehabilitation is becoming more popular to clinicians. These games are embedded in off-the-shelf commercial entertainment applications or especially-developed for clinical purposes. Treatment of cerebral palsy (CP) children is a challenging task for clinicians. Lack of motivation and progress monitoring are two important factors clinicians need to deal with. The use of serious games (SG), sometimes referred to as Virtual Rehabilitation (VR), could therefore be an interesting adjuvant to conventional treatment for these patients. This is however a new discipline and many scientific issues remain to be solved. The aim of this paper is to describe available conventional treatment for CP children together with the level of evidence of each approach. A systematic review of the use of SG in rehabilitation is then conducted. 31 papers (7 randomized clinical trials, 16 cohort studies and 8 single-cases studies) were selected and analyzed, and their level of evidence compared to the conventional treatment. These studies reported outcomes for 352 patients. In summary, this review shows that it is difficult to compare those studies despite the large amount of patients. This is due to the lack of standardization in patient rehabilitation strategy and to the use of various clinical scales and scores. This non-standardization in patient follow-up between previously-published works make evidence-based conclusions difficult to obtain in order to support these techniques objectively. The use of SG for rehabilitation purposes currently meets similar issues. This paper proposes standardization strategies in order to improve treatment comparison and SG use in rehabilitation.

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13. J Child Neurol. 2014 May 5. [Epub ahead of print]**Role of Virtual Reality for Cerebral Palsy Management.**

Weiss PL1, Tirosh E, Fehlings D.

Virtual reality is the use of interactive simulations to present users with opportunities to perform in virtual environments that appear, sound, and less frequently, feel similar to real-world objects and events. Interactive computer play refers to the use of a game where a child interacts and plays with virtual objects in a computer-generated environment. Because of their distinctive attributes that provide ecologically realistic and motivating opportunities for active learning, these technologies have been used in pediatric rehabilitation over the past 15 years. The ability of virtual reality to create opportunities for active repetitive motor/sensory practice adds to their potential for neuroplasticity and learning in individuals with neurologic disorders. The objectives of this article is to provide an overview of how virtual reality and gaming are used clinically, to present the results of several example studies that demonstrate their use in research, and to briefly remark on future developments.

[PMID: 24799367](#) [PubMed - as supplied by publisher]

14. J Child Neurol. 2014 May 7. [Epub ahead of print]**Family-Centered Care for Children With Cerebral Palsy: Conceptual and Practical Considerations to Advance Care and Practice.**

King G1, Chiarello L.

This article focuses on conceptual and practical considerations in family-centered care for children with cerebral palsy and their families. In the last 5 years, there have been important advances in our understanding of the components of family-centered care, and initial attempts to understand the client change processes at play. Recent research elaborates on family-centered care by delving into aspects of family-provider partnership, and applying family-centered principles to organizational service delivery to bring about organizational cultures of family-centered care. Recent research has also begun to consider mediators of client change, and new practice models have been proposed that embrace family-centered principles and illustrate the "art" of practice. Future research directions are discussed, including explorations of causal relationships between family-centered care principles, elements of caregiving practice, client change processes, and child and family outcomes. The meaning of the recent literature for pediatric neurology practice is considered.

[PMID: 24810084](#) [PubMed - as supplied by publisher]

15. Acta Paediatr. 2014 May 6. doi: 10.1111/apa.12675. [Epub ahead of print]**The Nordic Five to Fifteen questionnaire could provide the basis for a common neurological disability variable.**

Illum NO1, Gradel KO.

AIMS: Assessing disabilities in children is essential and Danish parents provide increasingly important feedback on how their child's disability affects daily living. The Nordic Five to Fifteen (FTF) parent questionnaire is widely used in Nordic countries to detect atypical or delayed development in children. Our study evaluated its internal validity and whether it could be used to generate a common disability variable across childhood neurological disorders and severities. **METHODS:** The 28-statement FTF questionnaire was completed by the parents of children with spina bifida, muscular disorders, spinal atrophy, cerebral palsy, blindness, deafness, mental retardation and disability, who received treatment for brain tumours. Psychometric analysis and Rasch analysis of the five FTF code qualifier level data were carried out. **RESULTS:** A total of 227 out of 332 (68.4%) parents participated. The mean qualifier score was 3.06 (standard deviation 0.89, range 2.31-4.26) and the variances mean was 1.57 (range 0.87-2.38). The corrected code-total correlation was 0.65 and reliability was 0.96. The Rasch analysis demonstrated good fit alignment of codes. **CONCLUSION:** The FTF questionnaire can be used with children with neurological disabilities and the Rasch scale analysis results indicate that it could form the analytical basis for developing a common disability variable.

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16. Child Care Health Dev. 2014 May 6. doi: 10.1111/cch.12151. [Epub ahead of print]

Living in transition - experiences of health and well-being and the needs of adolescents with cerebral palsy.

Björquist E1, Nordmark E, Hallström I.

BACKGROUND: Transition to adulthood for adolescents in general is a multifaceted process, and for adolescents with cerebral palsy (CP) it also involves transition from child- to adult-oriented support. CP entails a variety and combination of disabilities, which in association with external factors may make the transition to adult health services difficult. The aim of this study was to gain a deeper understanding of how adolescents with CP experience their own health, well-being and need of support during their transition to adulthood. **METHODS:** An inductive qualitative approach was used based on interviews with 12 adolescents with CP aged 17-18 years and living in Sweden. Manifest and latent content analysis was used for the analysis of data. **RESULTS:** The results are described in the main theme 'Living in transition and looking forward to being an adult, but not feeling ready yet and being in need of further support'. Five subthemes highlight the adolescents' experiences of belonging to a family, of the importance of friends and love, of managing daily activities, being surrounded by support and having hopes for the future. **CONCLUSIONS:** Interviews with adolescents with CP provide valuable information for the planning of transition programmes and for the support of adolescents with disabilities who are in the transition to adult living. According to the adolescents in this study, the support should be flexible and not be fixed to biological age. Personal, individualized information and support was desired by the adolescents in order to be able to manage their own transition. One option to facilitate transition is the stepping-stone of being close to parents or staff members during the first phase, after leaving the parental home.

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17. J Law Med. 2014 Mar;21(3):516-27.

The Australian National Disability Insurance Scheme for cerebral palsy: an end to the "forensic lottery"?

O'Connor M.

The new Australian National Disability Insurance Scheme is set to revolutionise disability support for an estimated 440,000 disabled persons and in particular for over 35,000 victims of cerebral palsy. The current support for sufferers of cerebral palsy is fragmented and their families and carers expend great time and effort accessing a range of different support agencies. The present "forensic lottery" means that only a small percentage of cerebral palsy victims whose injuries have been caused by medical negligence can secure large settlements under civil tort litigation. The NDIS promises a much more equitable scheme where severely disabled children can receive the necessary early intervention, which is so important to their long-term outcome. Such support will be provided irrespective of "fault", although recouping the costs of lifelong care through civil litigation in medical negligence remains an option. Debate continues about the affordability of such an ambitious Scheme. This is no doubt fuelled by the perceived New Zealand experience of its no-fault Accident Compensation Scheme. The NDIS advantage over almost all "no fault" schemes internationally is that it provides unified comprehensive care and support to cerebral palsy sufferers irrespective of a "treatment injury". Determinations for eligibility will no doubt involve extensive medical documentation. Uncertainty remains about the preparedness of the Chief Executive Officer of the NDIS to pursue health providers in civil negligence where treatment injuries may have been causative.

[PMID: 24804524](#) [PubMed - in process]

Prevention and Cure

18. *Am J Obstet Gynecol.* 2014 May;210(5):426.e1-9. doi: 10.1016/j.ajog.2014.01.046.

Correlation between initial neonatal and early childhood outcomes following preterm birth.

Manuck TA1, Sheng X2, Yoder BA3, Varner MW1.

OBJECTIVE: Neonatal diagnoses are often used as surrogate endpoints for longer-term outcomes. We sought to characterize the correlation between neonatal diagnoses and early childhood neurodevelopment. **STUDY DESIGN:** We conducted secondary analysis of a multicenter randomized controlled trial of antenatal magnesium sulfate vs placebo administered to women at imminent risk for delivery <32.0 weeks to prevent death and cerebral palsy in their offspring. Singletons and twins delivering 23.0-33.9 weeks who survived to hospital discharge and had 2-year-old outcome data were included. Those surviving to age 2 years were assessed by trained physicians and the Bayley II Scales of Infant Development Mental Development and Psychomotor Development Indices. Neonatal diagnoses at the time of each baby's initial hospital discharge were examined singly and in combination to determine those most predictive of childhood neurodevelopmental impairment, defined as a childhood diagnosis of moderate/severe cerebral palsy and/or Bayley scores >2 SD below the mean. Data were analyzed by multiple regression models and area under receiver operating characteristic curves. **RESULTS:** A total of 1771 children met criteria. Children were delivered at a mean of 29.4 weeks' gestation. In all, 459 (25.9%) had neurodevelopmental impairment. In models controlling for gestational age at delivery, maternal education, maternal race, tobacco/alcohol/drug use during pregnancy, randomization to magnesium, fetal sex, and chorioamnionitis, individual neonatal morbidities were moderately predictive of childhood neurodevelopmental impairment (best model area under receiver operating characteristic curve, 0.68; 95% confidence interval, 0.65-0.71). Combinations of 2, 3, and 4 morbidities did not improve the prediction of neurodevelopmental impairment. **CONCLUSION:** Approximately 1 in 4 previously preterm children had neurodevelopmental impairment at age 2 years. Prediction of childhood outcomes from neonatal diagnoses remains imperfect.

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19. *Cell Death Dis.* 2014 May 8;5:e1207. doi: 10.1038/cddis.2014.165.

EphrinB3 blocks EphB3 dependence receptor functions to prevent cell death following traumatic brain injury.

Theus MH1, Ricard J2, Glass SJ2, Travieso LG2, Liebl DJ2.

Eph receptor tyrosine kinases and their membrane-bound ligands, ephrins, have a variety of roles in the developing and adult central nervous system that require direct cell-cell interactions; including regulating axon path finding, cell proliferation, migration and synaptic plasticity. Recently, we identified a novel pro-survival role for ephrins in the adult subventricular zone, where ephrinB3 blocks Eph-mediated cell death during adult neurogenesis. Here, we examined whether EphB3 mediates cell death in the adult forebrain following traumatic brain injury and whether ephrinB3 infusion could limit this effect. We show that EphB3 co-labels with microtubule-associated protein 2-positive neurons in the adult cortex and is closely associated with ephrinB3 ligand, which is reduced following controlled cortical impact (CCI) injury. In the complete absence of EphB3 (EphB3(-/-)), we observed reduced terminal deoxynucleotidyl transferase-dUTP nick end labeling (TUNEL), and functional improvements in motor deficits after CCI injury as compared with wild-type and ephrinB3(-/-) mice. We also demonstrated that EphB3 exhibits dependence receptor characteristics as it is cleaved by caspases and induces cell death, which is not observed in the presence of ephrinB3. Following trauma, infusion of pre-clustered ephrinB3-Fc molecules (eB3-Fc) into the contralateral ventricle reduced cortical infarct volume and TUNEL staining in the cortex, dentate gyrus and CA3 hippocampus of wild-type and ephrinB3(-/-) mice, but not EphB3(-/-) mice. Similarly, application of eB3-Fc improved motor functions after CCI injury. We conclude that EphB3 mediates cell death in the adult cortex through a novel dependence receptor-mediated cell death mechanism in the injured adult cortex and is attenuated following ephrinB3 stimulation.

[PMID: 24810043](#) [PubMed - in process]

20. Front Cell Neurosci. 2014 Apr 28;5:115. eCollection 2014.

CXCL12 chemokine and GABA neurotransmitter systems crosstalk and their putative roles.

Guyon A.

Since CXCL12 and its receptors, CXCR4 and CXCR7, have been found in the brain, the role of this chemokine has been expanded from chemoattractant in the immune system to neuromodulatory in the brain. Several pieces of evidence suggest that this chemokine system could crosstalk with the GABAergic system, known to be the main inhibitory neurotransmitter system in the brain. Indeed, GABA and CXCL12 as well as their receptors are colocalized in many cell types including neurons and there are several examples in which these two systems interact. Several mechanisms can be proposed to explain how these systems interact, including receptor-receptor interactions, crosstalk at the level of second messenger cascades, or direct pharmacological interactions, as GABA and GABAB receptor agonists/antagonists have been shown to be allosteric modulators of CXCR4. The interplay between CXCL12/CXCR4-CXCR7 and GABA/GABAA-GABAB receptors systems could have many physiological implications in neurotransmission, cancer and inflammation. In addition, the GABAB agonist baclofen is currently used in medicine to treat spasticity in patients with spinal cord injury, cerebral palsy, traumatic brain injury, multiple sclerosis, and other disorders. More recently it has also been used in the treatment of alcohol dependence and withdrawal. The allosteric effects of this agent on CXCR4 could contribute to these beneficial effects or at the opposite, to its side effects.

[PMID: 24808825](#) [PubMed - as supplied by publisher]

21. JAMA. 2014 May 7;311(17):1742-9. doi: 10.1001/jama.2014.2624.

Effect of fluconazole prophylaxis on candidiasis and mortality in premature infants: a randomized clinical trial.

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IMPORTANCE: Invasive candidiasis in premature infants causes death and neurodevelopmental impairment. Fluconazole prophylaxis reduces candidiasis, but its effect on mortality and the safety of fluconazole are unknown. **OBJECTIVE:** To evaluate the efficacy and safety of fluconazole in preventing death or invasive candidiasis in extremely low-birth-weight infants. **DESIGN, SETTING, AND PATIENTS:** This study was a randomized, blinded, placebo-controlled trial of fluconazole in premature infants. Infants weighing less than 750 g at birth (N=361) from 32 neonatal intensive care units (NICUs) in the United States were randomly assigned to receive either fluconazole or placebo twice weekly for 42 days. Surviving infants were evaluated at 18 to 22 months corrected age for neurodevelopmental outcomes. The study was conducted between November 2008 and February 2013. **INTERVENTIONS:** Fluconazole (6 mg/kg of body weight) or placebo. **MAIN OUTCOMES AND MEASURES:** The primary end point was a composite of death or definite or probable invasive candidiasis prior to study day 49 (1 week after completion of study drug). Secondary and safety outcomes included invasive candidiasis, liver function, bacterial infection, length of stay, intracranial hemorrhage, periventricular leukomalacia, chronic lung disease, patent ductus arteriosus requiring surgery, retinopathy of prematurity requiring surgery, necrotizing enterocolitis, spontaneous intestinal perforation, and neurodevelopmental outcomes-defined as a Bayley-III cognition composite score of less than 70, blindness, deafness, or cerebral palsy at 18 to 22 months corrected age. **RESULTS:** Among infants receiving fluconazole, the composite primary end point of death or invasive candidiasis was 16% (95% CI, 11%-22%) vs 21% in the placebo group (95% CI, 15%-28%; odds ratio, 0.73 [95% CI, 0.43-1.23]; P=.24; treatment difference, -5% [95% CI, -13% to 3%]). Invasive candidiasis occurred less frequently in the fluconazole group (3% [95% CI, 1%-6%]) vs the placebo group (9% [95% CI, 5%-14%]; P=.02; treatment difference, -6% [95% CI, -11% to -1%]). The cumulative incidences of other secondary outcomes were not statistically different between groups. Neurodevelopmental impairment did not differ between the groups (fluconazole, 31% [95% CI, 21%-41%] vs placebo, 27% [95% CI, 18%-37%]; P=.60; treatment difference, 4% [95% CI, -10% to 17%]). **CONCLUSIONS AND RELEVANCE:** Among infants with a birth weight of less than 750 g, 42 days of fluconazole prophylaxis compared

with placebo did not result in a lower incidence of the composite of death or invasive candidiasis. These findings do not support the universal use of prophylactic fluconazole in extremely low-birth-weight infants.

TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00734539.

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Prediction of Fetal Compromise in Labor.

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OBJECTIVE: The majority of intrapartum fetal hypoxia occurs in uncomplicated pregnancies. Current intrapartum monitoring techniques have not resulted in a reduction in the incidence of cerebral palsy in term neonates. We report the development of a composite risk score to allow risk stratification of normal pregnancies before labor. **METHODS:** Six hundred one women were recruited to this prospective observational study. All women underwent an ultrasound examination before active labor, during which fetal biometry and fetal Doppler flow resistance indices were measured. A composite risk score, amalgamating data from the umbilical artery, middle cerebral artery, and umbilical vein, was then developed and correlated with intrapartum outcomes. **RESULTS:** In cases with the highest composite risk scores, the incidence of fetal compromise (the primary outcome) was 80.0% compared with just 15.3% in cases with the lowest risk scores (relative risk 5.2, 95% confidence interval 2.7-10.1). These cases were also at increased risk of cesarean delivery (53.3% compared with 3.4%, $P < .001$) and of developing a fetal heart rate pattern considered pathologic by National Institute for Health and Clinical Excellence criteria ($P = .003$). No significant variation in Apgar scores or umbilical artery pH was observed. **CONCLUSION:** Intrapartum fetal compromise remains a significant global health issue. The composite risk score reported here can identify fetuses at both high risk and low risk of a subsequent diagnosis of intrapartum fetal compromise. This may enable more judicious use of current intrapartum fetal monitoring techniques, which are hampered by low specificity.

LEVEL OF EVIDENCE: II.

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Risk of neurodisability and other long-term outcomes for infants born following assisted reproductive technologies.

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Children born after assisted reproductive technologies (ART) have an increased morbidity. The risk of developing cerebral palsy is nearly doubled and the risk of developing epilepsy is also higher. Behavioural problems including attention deficit/hyperactivity disorder may be more common in children born following ART than among naturally conceived children but the finding is uncertain. Data on autism are difficult to interpret. There may exist a small increase in the incidence of childhood cancer and there is greater evidence of an elevated risk of asthma. To some extent, these risks are mediated by neonatal complications including prematurity and low birth weight but some effects such as cerebral palsy are likely to be linked to the increased rate of multiple births after ART. Many of the neonatal complications after ART are most likely linked to parental subfertility and are less an effect of the ART technology. The possibility exists that imprinting errors, associated with subfertility and/or ART, may result in long-term morbidity.

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