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Interventions and Management

1. Content of upper limb therapy for children with cerebral palsy

Brian J Hoare

Dev Med Child Neurol. 2020 Aug 5. doi: 10.1111/dmcn.14645. Online ahead of print.

PMID: [32757274](#)

2. Kinematic and Somatosensory Gains in Infants with Cerebral Palsy After a Multi-Component Upper-Extremity Intervention: A Randomized Controlled Trial

Nathalie L Maitre, Arnaud Jeanvoine, Paul J Yoder, Alexandra P Key, James C Slaughter, Helen Carey, Amy Needham, Micah M Murray, Jill Heathcock, BBOP group

Brain Topogr. 2020 Aug 3. doi: 10.1007/s10548-020-00790-5. Online ahead of print.

Upper extremity (UE) impairments in infants with cerebral palsy (CP) result from reduced quality of motor experiences and "noisy" sensory inputs. We hypothesized that a neuroscience-based multi-component intervention would improve somatosensory processing and motor measures of more-affected (UEs) in infants with CP and asymmetric UE neurologic impairments, while remaining safe for less-affected UEs. Our randomized controlled trial compared infants (6-24 months) with CP receiving intervention (N = 37) versus a waitlisted group (N = 36). Treatment effects tested a direct measurement of reach smoothness (3D-kinematics), a measure of unimanual fine motor function (Bayley unimanual fine motor raw scores), and EEG measures of cortical somatosensory processing. The four-week therapist-directed, parent-administered intervention included daily (1) bimanual play; (2) less-affected UE wearing soft-constraint (6 h/day, electronically-monitored); (3) reach training on more-affected UE; (4) graduated motor-sensory training; and (5) parent education. Waitlist infants received only bimanual play. Effectiveness and safety were tested; z-scores from 54 posttest-matched typically-developing infants provided benchmarks for treatment effects. Intervention and waitlist infants had no pretest differences. Median weekly constraint wear was 38 h; parent-treatment fidelity averaged > 92%. On the more affected side, the intervention significantly increased smoothness of reach (Cohen's $d = -0.90$; $p < .001$) and unimanual fine motor skill ($d = 0.35$; $p = .004$). Using unadjusted p values, intervention improved somatosensory processing ($d = 0.53$; $p = .04$). All intervention effects referenced well to typically developing children. Safety of the intervention was demonstrated through positive- or non-effects on measurements involving the constrained, less-affected UE and gross motor function; unexpected treatment effects on reach smoothness occurred in less-affected UEs ($d = -0.85$; $p = .01$). This large clinical trial demonstrated intervention effectiveness and safety for developing sensory and motor systems with improvements in reach smoothness, and developmental abilities. Clinical Trial Registration: ClinicalTrials.gov NCT02567630, registered October 5, 2015.

PMID: [32748303](#)

3. Identifying mechanisms of change in a magic-themed hand-arm bimanual intensive therapy programme for children with unilateral spastic cerebral palsy: a qualitative study using behaviour change theory

Daisy Fancourt, Jaeyoung Wee, Fabianna Lorencatto

BMC Pediatr. 2020 Jul 31;20(1):363. doi: 10.1186/s12887-020-02246-y.

Background: There has been much research into how to promote upper-limb skills to achieve functional independence in children with unilateral spastic cerebral palsy (USCP). One researched intervention is the Breathe Magic programme, which follows the protocol of hand-arm bimanual intensive therapy (HABIT) whilst, incorporating magic tricks to develop children's motor skills and bimanual skills. However, whilst research has found the programme to be effective, there has been little consideration of how the intervention leads to a positive outcome: what the psychological, social and physical mechanisms of action are. **Methods:** Qualitative semi-structured interviews with 21 children with USCP who participated in the Breathe Magic HABIT intervention, and focus groups with 17 parents and/or carers were undertaken. Analysis was conducted through the lens of the COM-B behaviour change model using a combined deductive framework and inductive thematic analysis. Reliability of coding was confirmed through random extraction and double coding of a portion of responses and the calculation of inter-rater reliability. **Results:** Breathe Magic brings about change and positive outcomes by increasing children's psychological and physical capabilities, providing social opportunities, and enhancing reflective and automatic motivation. Additionally, a number of enablers to engaging in the intervention were identified, particularly under psychological capabilities, social opportunities and both reflective and automatic motivation. Very few barriers were raised; those that were raised were of relatively low frequency of reporting. **Conclusions:** By conducting a theory-based qualitative process evaluation, this study demonstrated the mechanisms of change behind the Breathe Magic HABIT intervention for children with USCP. Breathe Magic was found to be a well-structured combination of intended and unintended mechanisms of change. Overall, the success of Breathe Magic was observed through not only its intended mechanisms to enhance hand skills, but also through unintended psychological improvements in children's hand function, as well as social and motivational benefits resulting from interaction between children and parents.

PMID: [32736618](https://pubmed.ncbi.nlm.nih.gov/32736618/)

4. Powering strategies for implanted multi-function neuroprostheses for spinal cord injury

Kevin L Kilgore, Brian Smith, Alex Campean, Ronald L Hart, Joris M Lambrecht, James R Buckett, Paul Hunter Peckham

Healthc Technol Lett. 2020 Jun 24;7(3):81-86. doi: 10.1049/htl.2019.0113. eCollection 2020 Jun.

Implantable motor neuroprosthetic systems can restore function to individuals with significant disabilities, such as spinal cord injury, stroke, cerebral palsy, and multiple sclerosis. Neuroprostheses provide restored functionality by electrically activating paralysed muscles in coordinated patterns that replicate (enable) controlled movement that was lost through injury or disease. It is important to consider the general topology of the implanted system itself. The authors demonstrate that the wired multipoint implant technology is practical and feasible as a basis for the development of implanted multi-function neuroprosthetic systems. The advantages of a centralised power supply are significant. Heating due to recharge can be mitigated by using an actively cooled external recharge coil. Using this approach, the time required to perform a full recharge was significantly reduced. This approach has been demonstrated as a practical option for regular clinical use of implanted neuroprostheses.

PMID: [32754342](https://pubmed.ncbi.nlm.nih.gov/32754342/)

5. Anatomical and dynamic rotational alignment in spastic unilateral cerebral palsy

Jacques Riad, Thröstur Finnbogason, Eva Broström

Gait Posture. 2020 Jul 13;81:153-158. doi: 10.1016/j.gaitpost.2020.07.010. Online ahead of print.

Background: Even in mild unilateral cerebral palsy increased internal hip rotation can be noted on physical- and gait examination. The influence of spasticity on femoral growth in the transverse plane is not clear. These deviations and asymmetry in movement pattern may negatively affect efficiency of gait and cause psychological concerns about appearance. **Research question:** Is increased internal hip rotation on the involved side in mild unilateral CP common and is there compensatory external pelvic rotation to keep foot progression symmetrical? **Methods:** This prospective study included 45

individuals with unilateral cerebral palsy, mean age 17.7 (13.0-24.0) years. All were Gross Motor Function Classification Level I. Physical examination, three-dimensional gait analysis and magnetic resonance imaging for assessment of rotational alignment was performed. Results: On physical examination internal hip rotation was mean 50.6 (SD 10.4) degrees on the involved side and 44.3 (SD 10.3) on the non-involved side, $p = 0.001$. In gait analysis calculating the whole gait cycle, internal hip rotation was mean 2.3 (6.2) degrees on the involved side, and on the non-involved side external 1.8 (7.6) degrees, $p = 0.004$. Increased external pelvic rotation was noted on the involved side, mean 2.0 (4.3) degrees with corresponding internal rotation on the non-involved side, mean 3.6 (4.4), $p = 0.001$. There was no difference in foot progression, $p = 0.067$, with mean 5.1 (8.6) and 3.9 (6.4) external respectively. Magnetic resonance imaging revealed femoral torsion on the involved side mean 17.3 (11.3) degrees compared to 11.4 (10.8) on the non-involved side, $p = 0.001$. Significance: Transverse plane asymmetry in the femur was noted in mild unilateral cerebral palsy. Increased anatomical and dynamic internal rotation was compensated for by external pelvic rotation. Rotational malalignment may contribute to gait deviations in this mild group and should be part of the overall assessment.

PMID: [32738739](#)

6. Translation, reliability and validity of the Greek functional mobility scale (FMS) for children with cerebral palsy

Vasileios C Skoutelis, Zacharias Dimitriadis, Efstratia Kalamvoki, Stamatis Vrettos, Vasileios Kontogeorgakos, Argirios Dinopoulos, Panayiotis Papageopoulos, Anastasios Kanellopoulos

Disabil Rehabil. 2020 Aug 3;1-7. doi: 10.1080/09638288.2020.1799439. Online ahead of print.

Purpose: To translate and investigate the reliability and validity of the Greek version of the Functional Mobility Scale (FMS). Methods: FMS was translated into Greek. Test-retest reliability (Cohen's weighted kappa coefficient, κ_w) and concurrent validity (Spearman's rank correlation coefficient, r_s) of the Greek version of FMS were assessed in children with Cerebral Palsy (CP). Sixty children (mean age 7.82 ± 3.20 years) were recruited. Physical therapists administered the FMS by interviewing parents about their children's mobility status. The Gross Motor Function Classification System (GMFCS) was additionally used for testing concurrent validity. Results: The translation of the FMS was deemed easy to understand and administer. The Greek FMS was demonstrated to have almost perfect test-retest reliability ($\kappa_w = 0.98-1.00$), and very strong correlation with the GMFCS ($-0.85 \leq r_s \leq -0.89$, $p < 0.001$). Conclusions: The Greek version of the FMS was shown to be a reliable and valid classification system for CP and can be used with confidence by Greek physical therapists. Implications for rehabilitation The FMS provides a very simple and practical outcome measure of functional mobility in children with CP. The use of the reliable and valid Greek FMS will enhance the physical therapy assessment process in the Greek population, by offering the feasibility to detect the motor performance changes in children with CP as they grow or following interventions. The current study renders the Greek FMS available for utilization by physical therapists in order to quantify the independent mobility in children with CP.

PMID: [32744923](#)

7. Effect of Functional Progressive Resistance Exercise on Lower Extremity Structure, Muscle Tone, Dynamic Balance and Functional Ability in Children with Spastic Cerebral Palsy

Hye-Jin Cho, Byoung-Hee Lee

Children (Basel). 2020 Jul 31;7(8):E85. doi: 10.3390/children7080085.

The purpose of this study was to investigate the effects of functional progressive resistance exercise (FPRE) on muscle tone, dynamic balance and functional ability in children with spastic cerebral palsy. Twenty-five subjects were randomized into two groups: the FPRE group ($n = 13$) and the control group ($n = 12$). The experimental group participated in an FPRE program for 30 min per day, three times per week for six weeks. Knee extensor strength, rehabilitative ultrasound imaging (RUSI), muscle tone, dynamic balance, and functional ability was evaluated. The results showed statistically significant time \times group interaction effects on the dominant side for knee extensor strength and cross-sectional area (CSA) in RUSI ($p < 0.05$). On both sides for thickness of the quadriceps (TQ) in RUSI, muscle tone and dynamic balance were statistically significant time \times group interaction effects ($p < 0.05$). Additionally, knee extensor strength, CSA, TQ in RUSI, muscle tone, dynamic balance and gross motor function measure (GMFM) in functional ability were significantly increased between pre- and post-intervention within the FPRE group ($p < 0.05$). The results suggest that FPRE is both feasible and beneficial for improving muscle tone, dynamic balance and functional ability in children with spastic cerebral palsy.

PMID: [32751813](#)

8. Oromotor dysfunction in minimally verbal children with cerebral palsy: characteristics and associated factors

Cristina Mei, Madeleine Hodgson, Sheena Reilly, Bethany Fern, Dinah Reddihough, Fiona Mensah, Lindsay Pennington, Annabel Losche, Angela Morgan

Disabil Rehabil. 2020 Aug 3;1-9. doi: 10.1080/09638288.2020.1788179. Online ahead of print.

To explore the characteristics and associated factors of oromotor dysfunction in minimally verbal children with cerebral palsy (CP) aged five to six years, recruited from a population-based registry. Methods: Twenty children with CP who were minimally verbal completed a standardised, observational oromotor assessment. Linear regression analyses examined the relationship between oromotor dysfunction and potential associated factors (e.g., fine and gross motor function, communication, and feeding). Results: Oromotor dysfunction affected every participant and was identified in all structures examined (i.e., face, jaw, lips, and tongue). Oromotor movements showed little dissociation among jaw, lip, and tongue movements. Oromotor dysfunction was univariately associated with the Manual Ability Classification System levels IV-V ($p = 0.001$), reduced communication skills ($p = 0.002$), and a prolonged eating duration (>45 min) ($p = 0.006$), even when non-verbal cognition served as a covariate. Interpretation: Oromotor dysfunction was highly prevalent in our sample of minimally verbal children with CP, having significant functional impacts on feeding and communication. Findings suggest that fine motor function (i.e., Manual Ability Classification System levels IV-V) is a stronger predictor than gross motor function for identifying children with CP who are minimally verbal and at risk of oromotor dysfunction. IMPLICATIONS FOR REHABILITATION Oromotor dysfunction was highly prevalent in our sample of minimally verbal children with cerebral palsy. Severe fine motor impairment strongly predicted oromotor dysfunction, indicating that fine motor function may provide an early indicator of impaired oromotor function for this clinical population. Robust, standardised measures of motor speech-related oromotor development suitable for children with cerebral palsy who are minimally verbal are lacking. Until such a measure is developed, formal evaluation may be achieved via oral motor assessments standardised for typically developing children, with the caveat one must interpret the results with caution.

PMID: [32744922](#)

9. 'Flower of the body': menstrual experiences and needs of young adolescent women with cerebral palsy in Bangladesh, and their mothers providing menstrual support

R Power, K Wiley, M Muhit, E Heanoy, T Karim, N Badawi, G Khandaker

BMC Womens Health. 2020 Aug 1;20(1):160. doi: 10.1186/s12905-020-01032-3.

Background: This study offers voice to young adolescent women with cerebral palsy (CP) in Bangladesh as they describe their menstrual experiences and needs, and their mothers providing menstrual support. Method: Semi-structured focus groups with adolescents with CP, and separately their mother. Data was analysed using a material discursive framework and drawing on feminist disability theory. Participants were recruited from the Bangladesh CP Register (BCPR); a population-based surveillance of children and adolescents with CP in rural Bangladesh. Results: Participants were 45 women including 12 female adolescents with CP and 33 female caregivers. Participants reported a wide range of experiences and needs; menarche acted as a gateway to menstrual information although for some a discourse of silence prevailed due to exclusion from peer and familial networks. Menstruation was discursively constructed as a sign of 'female maturation' marked by an expectation of 'independence', required for acceptance into socially valued adult roles, and was positioned alongside increased vulnerability to sexual abuse. Young adolescent women with CP were expected to 'quietly endure' the material aspects of menstruation although unmanaged pain and distress were described. Mothers reported an imperative for meeting their adolescent's menstrual needs however this role was discursively positioned as 'painful', 'irritating' and 'shameful', in part due to an absence of affordable, functional menstrual resources. Conclusion: The findings of the present study provide motivation for disability services in Bangladesh to account for the menstrual needs of young adolescent women with CP within service delivery through strategies such as providing menstrual education and by embedding value in constructs such as 'interdependence'. Moreover, interventions focused on alleviating menstrual pain among young adolescent women with CP as well as those targeted to alleviate distress among mothers providing menstrual care are required. Finally, policy responses are required to ensure that 'inclusive development' considers the needs of menstruating women with disability.

PMID: [32738885](#)

10. Ambient Exposure to Agricultural Pesticides during Pregnancy and Risk of Cerebral Palsy: A Population-Based Study in California

Zeyan Liew, Ondine S von Ehrenstein, Chenxiao Ling, Yuying Yuan, Qi Meng, Xin Cui, Andrew S Park, Peter Uldall, Jørn Olsen, Myles Cockburn, Beate Ritz

Toxics. 2020 Jul 31;8(3):E52. doi: 10.3390/toxics8030052.

Cerebral palsy (CP) is the most common neuro-motor disability in young children. Disruptions of maternal hormone function during pregnancy have been linked to CP risk. We investigated whether prenatal exposure to pesticide compounds with endocrine-disrupting action affect CP risk. We conducted a case-control study of 3905 CP cases and 39,377 controls born between 1998 and 2010 in California to mothers who lived in proximity (within 2 km) to any agricultural pesticide application recorded in the California Pesticide Use Reporting (PUR) system. We focused on 23 pesticides considered endocrine disruptors that are frequently used, and we found that exposure to any of the 23 pesticides in the first trimester was associated with elevated CP risks in female offspring (OR = 1.19; 95% CI: 1.05-1.35) but not males (OR = 0.99; 95% CI: 0.89-1.09) compared to the unexposed offspring. Positive associations were estimated for 15 pesticides suspected to affect the estrogen and 7 pesticides suspected to affect the thyroid hormone system. Our study suggests that first trimester exposure to pesticides that are suspected endocrine disruptors are associated with CP risk in female offspring. Pesticide exposures in early pregnancy may have sex-specific influences on the neuro-motor development of the fetus by interfering with endocrine systems.

PMID: [32751992](#)

11. Determinants of Time to Care for Children and Adolescents With Disabilities

Leticia Rocha Dutra, Wendy J Coster, Jorge A B Neves, Marina de Brito Brandão, Rosana Ferreira Sampaio, Marisa Cotta Mancini

OTJR (Thorofare N J). 2020 Aug 1;1539449220944600. doi: 10.1177/1539449220944600. Online ahead of print.

Time use studies uncover the organization of daily routine of families of children with disabilities. The objective of this study is to identify determinants of time spent caring for children/adolescents with cerebral palsy (CP), autism spectrum disorder (ASD), and typical development (TD). Participants were caregivers of children/adolescents with/without disability. Structural equation modeling tested a proposed model of time spent in child care. The variables in the model were as follows: questionnaire (families' socioeconomic status [SES]), children's functioning (The Pediatric Evaluation of Disability Inventory-Computer Adaptive Test [PEDI-CAT]); hours of care (daily diaries), number of adaptations used, and help with child care (parents' report). Distinct variable combinations explained 78% of the variation in the time to care (TD model), followed by 42% (ASD) and 29% (CP). Adaptations indirectly affected time to care through its effect on functioning (CP); family's SES affected functioning through its effect on adaptation use (ASD). In conclusion, knowledge of factors affecting caregivers' time spent on children's care help occupational therapists implement family-centered strategies.

PMID: [32741244](#)

12. Prenatal cranial MR findings in fetuses with suspected CMV infection: Correlation with postnatal outcome and differential diagnostic considerations

Stacy Goergen, Zhengjie Lim, Jenni Clark, Mark Teoh, Kedar Humnabadkar, Michael Fahey, Michelle Giles

J Med Imaging Radiat Oncol. 2020 Jul 27. doi: 10.1111/1754-9485.13083. Online ahead of print.

Purpose: To: (1) Evaluate intrauterine MRI (iuMRI) findings in fetuses with suspected cCMV and correlate these with final diagnosis(es). (2) Correlate iuMRI in cases of confirmed cCMV with clinical outcomes. Methods: Retrospective cohort of iuMRI referrals for suspected cCMV between 2010 and 2018. Confirmed cCMV defined as positive amniotic fluid or postnatal CMV polymerase chain reaction (PCR) test and excluded cCMV defined by negative postnatal PCR. Results: Twenty-nine singleton fetuses had iuMRI for suspected cCMV (median gestation 28 weeks (IQR 24-32)). No postnatal outcome (n = 6) and no cCMV ascertainment (n = 5) provided 18 cases for analysis. cCMV positive (n = 11): three fetal deaths occurred, one spontaneous and two terminations of pregnancy (TOP), one for microcephaly and one for extensive polymicrogyria; 4/ 8

survivors had normal US and iuMRI with normal newborn hearing screen (AABR)/ neurological examination; two had polymicrogyria and cerebral palsy (CP) GMFCS II and V; 1 had isolated ventriculomegaly and failed newborn AABR; 1 had ventriculomegaly with germinolytic cysts, normal AABR and development at 3/12. cCMV negative (n = 7): Germinolytic cysts were present in 4 cases with 2/4 also having callosal hypogenesis and postnatal genetic and clinical diagnosis of mitochondrial disorder. The third and fourth had a normal newborn metabolic screen and neurological examination. Three deaths were due to toxoplasmosis (n = 1), TOP for severe ventriculomegaly (n = 1) and bilateral schizencephaly (n = 1). Conclusions: Polymicrogyria in fetuses with cCMV, undetected with prenatal US, was associated with CP. Germinolytic cysts were non-specific for cCMV and due to mitochondrial disorders when callosal hypogenesis was present.

PMID: [32741149](#)

13. From singular to holistic: approaches in pediatric rehabilitation medicine for children with cerebral palsy

Carole Vuillerot, Mickael Dinomais, Vincent Gautheron, Sylvain Brochard

Editorial Ann Phys Rehabil Med. 2020 Aug 2;S1877-0657(20)30144-5. doi: 10.1016/j.rehab.2020.07.002. Online ahead of print.

PMID: [32755641](#)

14. Outcomes Following Post-Hemorrhagic Ventricular Dilatation among Extremely Low Gestational Age Infants

Seetha Shankaran, Monika Bajaj, Girija Natarajan, Shampa Saha, Athina Pappas, Alexis S Davis, Susan R Hintz, Ira Adams-Chapman, Abhik Das, Edward F Bell, Barbara J Stoll, Michele C Walsh, Abbot R Laptook, Waldemar A Carlo, Krisa P Van Meurs, Pablo J Sánchez, M Bethany Ball, Ellen C Hale, Ruth Seabrook, Rosemary D Higgins, Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network

J Pediatr. 2020 Jul 30;S0022-3476(20)30979-3. doi: 10.1016/j.jpeds.2020.07.080. Online ahead of print.

Objective: To assess outcomes following post-hemorrhagic ventricular dilatation (PHVD) among infants born at ≤ 26 weeks of gestation. Study design: Observational study of infants born 4/1/11-12/31/15 in the NICHD Neonatal Research Network and categorized into three groups: PHVD, intracranial hemorrhage without ventricular dilatation, or normal head ultrasound. PHVD was treated per center practice. Neurodevelopmental impairment at 18-26 months was defined by cerebral palsy, Bayley III cognitive or motor score < 70 , blindness or deafness. Multivariable logistic regression examined the association of death or impairment, adjusting for neonatal course, center, maternal education and parenchymal hemorrhage. Results: Of 4216 infants, 815 had PHVD, 769 had hemorrhage without ventricular dilatation, and 2632 had normal head ultrasounds. Progressive dilatation occurred among 119/815 infants; the initial intervention in 66 infants was reservoir placement and 53 had ventriculoperitoneal shunt placement. Death or impairment occurred among 68%, 39%, and 28% of infants with PHVD, hemorrhage without dilatation and normal head ultrasound, respectively; adjusted odds ratios (aOR) 95% CI were 4.6 (3.8-5.7) PHVD vs. normal head ultrasound and 2.98 (2.3-3.8) for PHVD vs hemorrhage without dilatation. Death or impairment was more frequent with intervention for progressive dilatation vs. no intervention [80% vs. 65%; aOR 2.2 (1.38-3.8)]. Death or impairment increased with parenchymal hemorrhage, intervention for PHVD, male sex and surgery for retinopathy; odds decreased with each additional gestational week. Conclusions: PHVD was associated with high rates of death or impairment among infants with gestational ages ≤ 26 weeks; risk was further increased among those with progressive ventricular dilatation requiring intervention.

PMID: [32739261](#)

15. A genetic mimic of cerebral palsy: Homozygous NFU1 mutation with marked intrafamilial phenotypic variation

Tuğçe Aksu Uzunhan, Nafiye Emel Çakar, Serhat Seyhan, Kürşad Aydın

Case Reports Brain Dev. 2020 Jul 31;S0387-7604(20)30191-1. doi: 10.1016/j.braindev.2020.07.009. Online ahead of print.

Background: Genetic defects in the NFU1, an iron-sulfur cluster scaffold protein coding gene, which is vital in the final stage

of assembly for iron sulfur proteins, have been defined as multiple mitochondrial dysfunctions syndrome I. This disorder is a severe autosomal recessive disease with onset in early infancy. It is characterized by disruption of the energy metabolism, resulting in weakness, neurological regression, hyperglycinemia, lactic acidosis, and early death. Patient description: This report documents the case of a 27-month-old girl, who showed clinical signs and symptoms of spastic paraparesis with a relapsing-remitting course. The patient had a sister with a severe phenotype who died at the age of 16 months. Results: Magnetic resonance imaging revealed hyperintensity of the cerebral white matter that was more prominent in the frontal regions, with milder involvement in the posterior periventricular regions. There was also evidence of partial cystic degeneration and cavitation in the frontal regions. In addition, she had hyperglycinemia. Homozygous NM_001002755.4:c.565G>A (p.Gly189Arg) mutation was identified in the NFU1 gene; this had not previously been reported as homozygous. Conclusion: Hyperglycinemia and cavitating leukodystrophy are suggestive of an NFU1 mutation diagnosis. An intrafamilial phenotypic variation has not been published in NFU1-associated disorders before. Presenting with spasticity as a rare phenotype, NFU1 mutations could be considered a genetic mimic of cerebral palsy.

PMID: [32747156](#)

Prevention and Cure

16. Transient receptor potential vanilloid 4 agonist GSK1016790A improves neurological outcomes after intracerebral hemorrhage in mice

Yasunori Asao, Shota Tabori, Masashi Kakae, Kazuki Nagayasu, Koji Shibasaki, Hisashi Shirakawa, Shuji Kaneko

Biochem Biophys Res Commun. 2020 Aug 27;529(3):590-595. doi: 10.1016/j.bbrc.2020.06.103. Epub 2020 Jul 16.

Intracerebral hemorrhage (ICH) is one of the most severe subtypes of stroke with high morbidity and mortality. Although a lot of drug discovery studies have been conducted, the drugs with satisfactory therapeutic effects for motor paralysis after ICH have yet to reach clinical application. Transient receptor potential vanilloid 4 (TRPV4), a Ca²⁺-permeable cation channel and activated by hypoosmolarity and warm temperature, is expressed in various cell types. The present study investigated whether TRPV4 would participate in the brain damage in a mouse model of ICH. ICH was induced by intrastriatal treatment of collagenase. Administration of GSK1016790A, a selective TRPV4 agonist, attenuated neurological and motor deficits. The inhibitory effects of the TRPV4 agonist in collagenase-injected WT mice were completely disappeared in TRPV4-KO mice. The TRPV4 agonist did not alter brain injury volume and brain edema at 1 and 3 days after ICH induction. The TRPV4 agonist did not show any differences with respect to the increased number of Iba1-positive microglia/macrophages, GFAP-positive astrocytes, and Gr1-positive neutrophils at 1 and 3 days after ICH induction. Quantitative RT-PCR experiments revealed that the TRPV4 agonist significantly upregulated the expression level of c-fos, a marker of neuronal activity, while the agonist gave no effects on the expression level of cytokines/chemokines at 1 day after ICH induction. These results suggest that stimulation of TRPV4 would ameliorate ICH-induced brain injury, presumably by increased neuronal activity and TRPV4 provides a novel therapeutic target for the treatment for ICH.

PMID: [32736678](#)