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NEWS
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Macquarie Group Foundation Chair of Cerebral Palsy

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Interventions and Management

1. Eur J Paediatr Neurol. 2015 Jan 26. pii: S1090-3798(15)00011-2. doi: 10.1016/j.ejpn.2015.01.004. [Epub ahead of print]

Effects of botulinum toxin A and/or bimanual task-oriented therapy on upper extremity impairments in unilateral Cerebral Palsy: An explorative study.

Speth L1, Janssen-Potten Y2, Leffers P3, Rameckers E2, Defesche A4, Winkens B5, Becher J6, Smeets R7, Vles JS8.

OBJECTIVE: This study reports on the effects of botulinum toxin A (BoNT-A) injections in the upper extremity (UE) of children with unilateral Cerebral Palsy (uCP) combined with bimanual task oriented therapy (BITT) or either treatment modality performed separately on UE range of motion (ROM), spasticity and (functional) strength. METHODS:Thirty-five children, mean age 7.14 years (SD 2.63) of whom 11 had a Manual Ability Classification Score (MACS) I, 15 MACS II and 9 MACS III, participated. The trial started with four study groups: BoNT-A-only (n = 5), BITT-only (n = 11), BoNT-A + BITT (n = 13), and control (n = 6). Twenty-two children were randomized and, due to recruitment problems 13 children received their parents' preferred treatment: BoNT-A + BITT or BITT-only. Three comparisons were analysed: BITT (BoNT-A + BITT and BITT-only; n = 24) versus no BITT (BoNT-A-only and control; n = 11), BoNT-A (BoNT-A-only and BoNT-A + BITT; n = 18) versus no BoNT-A (BITT-only and control; n = 17), and the additional effect of BoNT-A (BoNT-A + BITT versus BITT-only). RESULTS: BoNT-A significantly decreased key grip strength and finger flexion tone, had a clinically relevant (additional) positive effect on active thumb abduction and supination and a significantly negative effect on unilateral functional strength. BITT + BoNT-A significantly increased active supination. BITT reduced elbow flexor tone and BITT-only resulted in more improvement than BoNT-A + BITT in functional unimanual and, to a lesser extent, in bimanual grip strength. CONCLUSIONS: In comparison with BoNT-A + BITT, BITT-only gives more improvement on functional grip strength and, therefore, could possibly increase bimanual performance. In this case, the (additional) role of BoNT-A may be an increase in active supination and thumb abduction.

PMID: 25661064 [PubMed - as supplied by publisher]

2. Res Dev Disabil. 2015 Feb 9;39C:67-75. doi: 10.1016/j.ridd.2015.01.001. [Epub ahead of print]

Postural stability in children with hemiplegia estimated for three postural conditions: Standing, sitting and kneeling.

Szopa A1, Domagalska-Szopa M2.

Postural control deficit is one of the most important problems in children with cerebral palsy (CP). The purpose of the presented study was to compare the effects of body posture asymmetry alone (i.e., in children with mild scoliosis) with the effects of body posture impairment (i.e., in children with hemiplegia) on postural stability. Forty-five outpatients with hemiplegia and 51 children with mild scoliosis were assessed using a posturography device. The examination comprised two parts: (1) analysis of the static load distribution; and (2) a posturographic test (CoP measurements) conducted in three postural conditions: standing, sitting and kneeling. Based on the asymmetry index of the unaffected/affected body sides while standing, the children with hemiplegia were divided into two different postural patterns: a pro-gravitational postural pattern (PGPP) and an anti-gravitational postural pattern (AGPP) (Domagalska-Szopa & Szopa (2013). BioMed Research International, 2013, 462094; (2014). Therapeutics and Clinical Risk Management, 10, 113). The group of children with mild scoliosis, considered as a standard for static body weight distribution, was used as the reference group. The results of present study only partially confirmed that children with hemiplegia have increased postural instability. Strong weight distribution asymmetry was found in children with an AGPP, which induced larger lateral-medial CoP displacements compared with children with scoliosis. In children with hemiplegia, distinguishing between their postural patterns may be useful to improve the guidelines for early therapy children with an AGPP before abnormal patterns of weight-bearing asymmetry are fully established.

PMID: 25677032 [PubMed - as supplied by publisher]

3. Arch Dis Child. 2015 Feb 10. pii: archdischild-2014-306874. doi: 10.1136/archdischild-2014-306874. [Epub ahead of print]

Selective dorsal rhizotomy: an old treatment re-emerging.

Aquilina K1, Graham D2, Wimalasundera N3.

Selective dorsal rhizotomy (SDR) is a neurosurgical technique developed to reduce spasticity and improve mobility in children with cerebral palsy (CP) and lower extremity spasticity. It involves the selective division of lumbosacral afferent (sensory) rootlets at the conus or at the intervertebral foramina under intraoperative neurophysiological guidance. First described in 1908, early procedures were effective at reducing spasticity but were associated with significant morbidity. Technical advancements over the last two decades have reduced the invasiveness of the procedure, typically from a five-level laminoplasty to a single-level laminotomy at the conus. As practised today, SDR is an effective treatment for young patients with bilateral spastic CP who are rigorously selected for surgery and for whom realistic objectives are set. SDR has therefore re-emerged as a valuable management option for spastic CP. In this article, the authors review the single-level SDR technique and its role in the management of bilateral spastic CP, with particular emphasis on patient selection and outcomes.

PMID: 25670404 [PubMed - as supplied by publisher]

4. J Pediatr Orthop. 2015 Mar;35(2):167-71. doi: 10.1097/BPO.0000000000000209.

Three-dimensional Computed Tomography for Determination of Femoral Anteversion in a Cerebral Palsy Model.

Riccio AI1, Carney CJ, Hammel LN, Stanley M, Cassidy J, Davids JR.

BACKGROUND: Previous investigation has proven 3-dimensional (3D) computed tomography (CT) to be a poor method of assessing femoral anteversion in patients with cerebral palsy. However, new advancements in CT software yield the potential to improve upon those dated results. METHODS: CT was performed on 9 femoral models with varying amounts of anteversion (20 to 60 degrees) and varying neck-shaft angles (120 to 160 degrees). Each model was scanned in 2 holding devices. One holder placed the femur in an ideal position relative to the gantry. The other placed the femur in flexion, adduction, and internal rotation simulating a common lower extremity posture in cerebral palsy. Femoral anteversion was measured on 3D reconstructions by 4 observers on 2 separate occasions. Interobserver and intraobserver reliability, accuracy, and the effect of increasing neck-shaft angle of the measurements were examined and compared with previously published data using the same models. RESULTS: Pearson correlation coefficients between first and second measurements by the same examiner were all above 0.96 regardless of positioning of the femur in the gantry. The correlation coefficients among all examiners were 0.97 regardless of positioning of the femur in the gantry. Accuracy in measurements was comparable using 3D CT techniques with mean differences between the normal and cerebral palsy-positioned models of <3.6 degrees (SD, 3.1 to 3.3 degrees). Accuracy of the study's 3D CT technique in measuring femoral anteversion in cerebral palsy-positioned femurs was significantly more accurate than that of 2D CT (P<0.0001). CONCLUSIONS: Recent improvements in processing software and 3D reconstruction have made assessment of femoral anteversion with 3D CT accurate through the studied range of anteversion and neck-shaft angles. Using this technique, high intraobserver and interobserver reliability in the determination of femoral anteversion can be expected regardless of neck-shaft angle or postural deformity.

LEVEL OF EVIDENCE: Level II.

PMID: 25668788 [PubMed - in process]

5. J Rehabil Med. 2015 Feb 12. doi: 10.2340/16501977-1929. [Epub ahead of print]

Cost-utility of a lifestyle intervention in adolescents and young adults with spastic cerebral palsy.

Slaman J1, van den Berg-Emons R, Tan SS, Russchen H, van Meeteren J, Stam H, Roebroeck M.

Objective: To evaluate the cost-utility of a lifestyle intervention among adolescents and young adults with cerebral palsy. Design: Single-blind, randomized controlled trial. Setting: Six university hospital/clinics in the Netherlands. Participants: Fifty-seven adolescents and young adults with spastic cerebral palsy classified as Gross Motor Functioning Classification System (GMFCS) level I-IV. Intervention: A 6-month lifestyle intervention consisting of physical fitness training combined with counselling sessions focusing on physical behaviour and sports participation. Main outcome measures: Data on quality of life, direct medical costs and productivity costs were collected using stan-dardized questionnaires. Quality adjusted life years (QALYs) were derived from the Short-Form 36 questionnaire using the Short-Form 6D. Results: Quality of life remained stable over time for both groups. No significant differences between groups were found for direct medical costs or productivity costs. A cost-utility ratio of -€23,664 per QALY was found for the lifestyle intervention compared with no treatment. Conclusion: The results of this study are exploratory, but indicate that implementing a lifestyle intervention for the cere-bral palsy population might be cost-effective or cost-saving compared with offering no intervention to improve physical behaviour and fitness. However, the large range of uncertainty for the cost-utility ratio should be taken into account and the results interpreted with caution.

PMID: 25678311 [PubMed - as supplied by publisher]

6. Epilepsy Behav Case Rep. 2014 Oct 10;2:179-83. doi: 10.1016/j.ebcr.2014.09.006. eCollection 2014.

Slow pseudoperiodic lateralized epileptiform discharges in nonconvulsive status epilepticus in a patient with cerebral palsy and a large central meningioma.

Imam YZ1, Deleu D2, Mesraoua B1, D'souza A1, Al Hail H1, Kaplan PW3.

The presence of cerebral palsy and that of slow growing brain tumors are risk factors for convulsive and nonconvulsive status epilepticus. Nonconvulsive status epilepticus (NCSE) needs electroencephalographic (EEG) monitoring to be confirmed as it may be clinically subtle. Furthermore, it may present with a variety of ictal EEG morphologies. We report a case of a patient with cerebral palsy and a large central meningioma.

Electroencephalogram showed a slow pattern of periodic lateralized epileptiform discharges (PLEDs) (a pattern considered as being situated in the ictal-interictal continuum) on an alpha background. The patient was treated for NCSE successfully with benzodiazepines followed by up-titration of his antiepileptic drug doses.

PMID: 25667901 [PubMed] PMCID: PMC4308029 Free PMC Article

7. Eur J Neurol. 2015 Mar;22(3):423-5. doi: 10.1111/ene.12656.

Deep brain stimulation in dystonic cerebral palsy: for whom and for what?

Cif L1.

PMID: 25677456 [PubMed - in process]

8. Science. 2015 Jan 9;347(6218):159-63. doi: 10.1126/science.1260318.

Biomaterials. Electronic dura mater for long-term multimodal neural interfaces.

Minev IR1, Musienko P2, Hirsch A1, Barraud Q3, Wenger N3, Moraud EM4, Gandar J3, Capogrosso M4, Milekovic T3, Asboth L3, Torres RF3, Vachicouras N5, Liu Q6, Pavlova N2, Duis S3, Larmagnac A7, Vörös J7, Micera S8, Suo Z6, Courtine G9, Lacour SP10.

The mechanical mismatch between soft neural tissues and stiff neural implants hinders the long-term performance of implantable neuroprostheses. Here, we designed and fabricated soft neural implants with the shape and elasticity of dura mater, the protective membrane of the brain and spinal cord. The electronic dura mater, which we call e-dura, embeds interconnects, electrodes, and chemotrodes that sustain millions of mechanical stretch cycles, electrical stimulation pulses, and chemical injections. These integrated modalities enable multiple neuroprosthetic applications. The soft implants extracted cortical states in freely behaving animals for brain-machine interface and delivered electrochemical spinal neuromodulation that restored locomotion after paralyzing spinal cord injury.

PMID: 25574019 [PubMed - indexed for MEDLINE]

9. Spec Care Dentist. 2015 Feb 11. doi: 10.1111/scd.12106. [Epub ahead of print]

Teeth grinding, oral motor performance and maximal bite force in cerebral palsy children.

Botti Rodrigues Santos MT1, Cristina Duarte Ferreira M, de Oliveira Guaré R, Sergio Guimarães A, Lira Ortega A.

AIM: Identify whether the degree of oral motor performance is related to the presence of teeth grinding and maximal bite force values in children with spastic cerebral palsy. METHODS: Ninety-five spastic cerebral palsy children with and without teeth grinding, according to caregivers' reports, were submitted to a comprehensive oral motor performance evaluation during the feeding process using the Oral Motor Assessment Scale. Maximal bite force was measured using an electronic gnathodynamometer. RESULTS: The teeth grinding group (n = 42) was younger, used anticonvulsant drugs, and was more frequently classified within the subfunctional oral motor performance category. Teeth grinding subfunctional spastic cerebral palsy children presented lower values of maximal bite force. The functional groups showing the presence or absence of teeth grinding presented higher values of maximal bite force compared with the subfunctional groups. CONCLUSION: In spastic cerebral palsy children, teeth grinding is associated with the worse oral motor performance.

PMID: 25676552 [PubMed - as supplied by publisher]

10. Eur J Paediatr Neurol. 2015 Jan 26. pii: S1090-3798(15)00026-4. doi: 10.1016/j.ejpn.2015.01.007. [Epub ahead of print]

Evaluation of the efficacy of cervical perivascular sympathectomy on drooling in children with athetoid cerebral palsy.

Duan Y1, Gao X2, Luo X2, Sun C3.

OBJECTIVE: To evaluate the efficacy of cervical perivascular sympathectomy (CPVS) for drooling in children with athetoid cerebral palsy (ACP). METHODS: The severity and frequency of drooling and the amount of salivation of 32 ACP children with drooling were evaluated before CPVS and at 4th, 12th and 24 weeks postoperatively by the teacher drooling scale (TDS) and salivary flow rate (SFR). RESULTS: Fifteen children exhibited improvements on drooling according to the TDS score at 4th week after surgery ($P < 0.05$). Later, the number of children decreased to 10 at 12th week ($P < 0.05$) and to 8 at 24 week after surgery ($P < 0.05$). SFR was 0.67 mg/min at baseline, which decreased to 0.58 mg/min ($P < 0.05$) at 4th week after surgery. However, SFR showed a gradual increase at 12th week and 24 week with no significant difference. CONCLUSIONS: Although CPVS was effective in improving drooling in some children with ACP, the results were not satisfactory. Thus, CPVS still needs to be cautiously used. Furthermore, more rigorous clinical studies should be performed to detect the effectiveness and safety of this procedure.

PMID: 25662757 [PubMed - as supplied by publisher]

11. Folia Phoniatr Logop. 2014;66(6):258-264. Epub 2015 Feb 7.

Familiarization Effects on Word Intelligibility in Dysarthric Speech.

Kim H1, Nanney S.

Background/Aims: This study investigated the effects of familiarization on naïve listeners' ability to perceive dysarthric speech produced by speakers with cerebral palsy and evaluated the degree of intelligibility improvement, both in the short and long term, as a function of (1) familiarization paradigms and (2) the number of familiarization phases. Methods: A total of 120 listeners (30 listeners/speaker) were recruited to complete word transcription tasks over a 6-week period. The listeners were assigned to one of the following familiarization paradigms: passive familiarization with audio signal only, active familiarization with both audio and orthography, and no explicit familiarization. Intelligibility scores were measured as the percentage of words correctly transcribed. Results: The active familiarization paradigm that provided listeners with both audio and orthography resulted in higher intelligibility scores compared to the passive familiarization and no explicit familiarization conditions. The degree of intelligibility improvement as a function of passive familiarization varied depending on the speaker. Last, the advantage of active familiarization was also found as a long-term effect. Conclusion: Our findings provide evidence for the benefits of familiarization in enhancing the intelligibility of dysarthric speech and support the efficacy of familiarization paradigms as an intervention technique in the management of dysarthria.

PMID: 25676630 [PubMed - as supplied by publisher]

12. Ann Phys Rehabil Med. 2015 Jan 9. pii: S1877-0657(14)01843-0. doi: 10.1016/j.rehab.2014.11.005. [Epub ahead of print]

Thought-based row-column scanning communication board for individuals with cerebral palsy.

Scherer R1, Billinger M2, Wagner J2, Schwarz A2, Hettich DT3, Bolinger E3, Lloria Garcia M4, Navarro J4, Müller-Putz G2.

Impairment of an individual's ability to communicate is a major hurdle for active participation in education and social life. A lot of individuals with cerebral palsy (CP) have normal intelligence, however, due to their inability to communicate, they fall behind. Non-invasive electroencephalogram (EEG) based brain-computer interfaces (BCIs)

have been proposed as potential assistive devices for individuals with CP. BCIs translate brain signals directly into action. Motor activity is no longer required. However, translation of EEG signals may be unreliable and requires months of training. Moreover, individuals with CP may exhibit high levels of spontaneous and uncontrolled movement, which has a large impact on EEG signal quality and results in incorrect translations. We introduce a novel thought-based row-column scanning communication board that was developed following user-centered design principles. Key features include an automatic online artifact reduction method and an evidence accumulation procedure for decision making. The latter allows robust decision making with unreliable BCI input. Fourteen users with CP participated in a supporting online study and helped to evaluate the performance of the developed system. Users were asked to select target items with the row-column scanning communication board. The results suggest that seven among eleven remaining users performed better than chance and were consequently able to communicate by using the developed system. Three users were excluded because of insufficient EEG signal quality. These results are very encouraging and represent a good foundation for the development of real-world BCI-based communication devices for users with CP.

PMID: 25661447 [PubMed - as supplied by publisher]

13. PLoS One. 2015 Feb 11;10(2):e0115643. doi: 10.1371/journal.pone.0115643. eCollection 2015.

Psychometric Properties of the Autoquestionnaire Qualité De Vie Enfant Imagé (AUQEI) Applied to Children with Cerebral Palsy.

Barbosa-Resende W1, Rangel Vde O2, Frontarolli AC3, Araújo RR4, da Silva CH5, Pinto Rde M6, Morales Nde M5.

BACKGROUND: Quality of life (QL) assessments of children with incapacitating diseases, such as cerebral palsy (CP), have often been conducted with the help of the representatives of a child, making QL assessment more subjective. TheAutoquestionnaireQualité de Vie Enfant Imagé (AUQEI) is a QL assessment designed for children to self-report-it uses images to facilitate the reporting process. OBJECTIVE: evaluate the psychometric properties of AUQEI when responses are given by children with CP. FINDINGS: Children aged 4 to 12 years (45 with CP and 45 healthy children) gave responses to the questionnaire. The data quality, reliability and validity were assessed. The data loss rate ranged from 8.8% to 46.7%, and was highest for the "autonomy" factor. No floor or ceiling effect was detected. The success rate for reliability of the internal consistency of the items was less than 80% for the "autonomy" factor. Cronbach's alpha coefficient was 0.71 for the instrument and less than 0.5 for the factors. All the factors had a success rate of greater than 80% for the discriminating validity of the items. The factors did not have correlations between each other, thus indicating adequate discriminating validity. Convergent validity was tested and a significant correlation was demonstrated only between the AUQEI "functioning" factor and the Child Health Questionnaire-50-Item (CHQ-PF50) physical summary score ($r = 0.31$, $p = 0.042$). The AUQEI scores did not have correlations with the gross motor function scores ($p>0.05$) as expected for divergent validity. Regarding construct validity, the total AUQEI score obtained by the CP group was lower (median: 47.3) than that of the healthy group (median: 51.0) ($p<0.01$). CONCLUSION: The AUQEI was shown to be a reliable and valid instrument for assessing children with CP when the total score was used. Convergent validity should continue to be tested in future studies.

PMID: 25671523 [PubMed - in process] Free full text

Prevention and Cure

14. Mol Psychiatry. 2015 Feb 10. doi: 10.1038/mp.2014.189. [Epub ahead of print]

Whole-exome sequencing points to considerable genetic heterogeneity of cerebral palsy.

McMichael G1, Bainbridge MN2, Haan E3, Corbett M4, Gardner A4, Thompson S5, van Bon BW6, van Eyk CL1, Broadbent J1, Reynolds C1, O'Callaghan ME1, Nguyen LS7, Adelson DL8, Russo R9, Jhangiani S2, Doddapaneni H2, Muzny DM2, Gibbs RA2, Gecz J4, MacLennan AH1.

Cerebral palsy (CP) is a common, clinically heterogeneous group of disorders affecting movement and posture. Its prevalence has changed little in 50 years and the causes remain largely unknown. The genetic contribution to CP causation has been predicted to be ~2%. We performed whole-exome sequencing of 183 cases with CP including both parents (98 cases) or one parent (67 cases) and 18 singleton cases (no parental DNA). We identified and validated 61 de novo protein-altering variants in 43 out of 98 (44%) case-parent trios. Initial prioritization of variants for causality was by mutation type, whether they were known or predicted to be deleterious and whether they occurred in known disease genes whose clinical spectrum overlaps CP. Further, prioritization used two multidimensional frameworks-the Residual Variation Intolerance Score and the Combined Annotation-dependent Depletion score. Ten de novo mutations in three previously identified disease genes (TUBA1A (n=2), SCN8A (n=1) and KDM5C (n=1)) and in six novel candidate CP genes (AGAP1, JHDM1D, MAST1, NAA35, RFX2 and WIPI2) were predicted to be potentially pathogenic for CP. In addition, we identified four predicted pathogenic, hemizygous variants on chromosome X in two known disease genes, L1CAM and PAK3, and in two novel candidate CP genes, CD99L2 and TENM1. In total, 14% of CP cases, by strict criteria, had a potentially disease-causing gene variant. Half were in novel genes. The genetic heterogeneity highlights the complexity of the genetic contribution to CP. Function and pathway studies are required to establish the causative role of these putative pathogenic CP genes.Molecular Psychiatry advance online publication, 10 February 2015; doi:10.1038/mp.2014.189.

PMID: 25666757 [PubMed - as supplied by publisher]

15. Arch Dis Child Fetal Neonatal Ed. 2015 Feb 12. pii: fetalneonatal-2014-307521. doi: 10.1136/archdischild-2014-307521. [Epub ahead of print]

Do recommended protein intakes improve neurodevelopment in extremely preterm babies?

Cester EA1, Bloomfield FH2, Taylor J3, Smith S3, Cormack BE2.

OBJECTIVE: To determine whether achieving recommended protein intakes for extremely low birthweight (ELBW; birth weight <1000 g) babies, resulting in better growth, improves neurodevelopmental outcomes. DESIGN: A prospective cohort study of ELBW babies before and after the introduction of a new nutritional policy designed to meet international consensus protein recommendations. Forty-five children born 'before' and 42 born 'after' the policy change were assessed at 2 years' corrected age (CA). Associations between nutritional intakes, growth and neurodevelopmental outcome (Bayley Scales of Infant and Toddler Development, Third edition (Bayley-III), motor and sensory impairment) were assessed using univariate and multivariate analyses. RESULTS: Bayley-III cognitive (mean (SD) 96 (12) vs 96 (15)), motor (96 (13) vs 95 (15)) or language scores (89 (11) vs 91 (17)) were not different between the 'before' and 'after' cohorts. In the 'before' cohort, motor scores were positively associated with enteral nutrition intakes and growth velocity. Neither were sensory impairments different between groups (visual impairment 4 vs 2, hearing impairment 2 vs 0) nor was the gross motor function classification score (any cerebral palsy 2 vs 1). CONCLUSIONS: In this prospective cohort study, increasing intravenous and enteral protein intakes to recommended levels in the first month after birth was not associated with improved cognitive, language or motor scores or decreased sensory impairments at 2 years' CA despite significantly improved early growth and reduced postnatal faltering growth. Appropriate randomised controlled trials are needed to answer definitively whether higher early protein intakes improve neurodevelopmental outcome in this population.

PMID: 25678631 [PubMed - as supplied by publisher]

16. J Neurosci. 2014 Nov 12;34(46):15347-55. doi: 10.1523/JNEUROSCI.1935 -14.2014.

Mammalian target of rapamycin's distinct roles and effectiveness in promoting compensatory axonal sprouting in the injured CNS.

Lee DH1, Luo X1, Yungher BJ1, Bray E1, Lee JK2, Park KK2.

Mammalian target of rapamycin (mTOR) functions as a master sensor of nutrients and energy, and controls protein translation and cell growth. Deletion of phosphatase and tensin homolog (PTEN) in adult CNS neurons promotes regeneration of injured axons in an mTOR-dependent manner. However, others have demonstrated mTOR-independent axon regeneration in different cell types, raising the question of how broadly mTOR regulates axonal regrowth across different systems. Here we define the role of mTOR in promoting collateral sprouting of spared axons, a key axonal remodeling mechanism by which functions are recovered after CNS injury. Using pharmacological inhibition, we demonstrate that mTOR is dispensable for the robust spontaneous sprouting of corticospinal tract axons seen after pyramidotomy in postnatal mice. In contrast, moderate spontaneous axonal sprouting and induced-sprouting seen under different conditions in young adult mice (i.e., PTEN deletion or degradation of chondroitin proteoglycans; CSPGs) are both reduced upon mTOR inhibition. In addition, to further determine the potency of mTOR in promoting sprouting responses, we coinactivate PTEN and CSPGs, and demonstrate that this combination leads to an additive increase in axonal sprouting compared with single treatments. Our findings reveal a developmental switch in mTOR dependency for inducing axonal sprouting, and indicate that PTEN deletion in adult neurons neither recapitulates the regrowth program of postnatal animals, nor is sufficient to completely overcome an inhibitory environment. Accordingly, exploiting mTOR levels by targeting PTEN combined with CSPG degradation represents a promising strategy to promote extensive axonal plasticity in adult mammals.

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