**Top Ten Articles  AACPDM 2014**

**Obstructive sleep apnea syndrome and cognition in Down syndrome**

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**AIM:** Good-quality sleep is essential for normal learning and memory. Sleep fragmentation and disrupted sleep architecture are commonly observed throughout the lifespan of individuals with Down syndrome, a condition marked by cognitive deficits emerging within the first months of life. While obstructive sleep apnea syndrome (OSAS) is known to contribute to the loss of sleep quality in Down syndrome, its relation to cognitive and behavioral impairment remains poorly understood.

**Method:** Using ambulatory polysomnography, we measured sleep in an unreferred community-based sample of 38 individuals with Down syndrome (15 males, 23 females; mean age 9 y 7mo (SD 1y 9mo), range 7-12y). Cognitive outcomes were assessed with the Arizona Cognitive Test Battery, a set of psychometric measures designed and validate for this population.

**Results:** Among children with Down syndrome, mean Verbal IQ score ($p=0.006$) was 9 points lower in those with comorbid OSAS (apnea-hypopnea index >1.5) than in those without OSAS, and performance on measures of cognitive flexibility was poorer ($p=0.009$) at the expense of slow-wave sleep ($p=0.04$).

**Interpretation:** These findings demonstrate a relation between OSAO and cognitive outcomes in Down syndrome. More is required to fully understand the mechanisms underlying the links between poor sleep and impaired cognitive function. Overall, these findings highlight the importance of adequate sleep in typically and atypically developing populations.
Objective: To evaluate adulthood function following chronic iron deficiency in infancy.

Study design: At 25 years, we compared 33 subjects with chronic iron deficiency in infancy to 89 who were iron-sufficient before and/or after iron therapy. Outcomes included education, employment, marital status, and physical and mental health.

Results: Adjusting for sex and socioeconomic status, a higher proportion of the group with chronic iron deficiency did not complete secondary school (58.1% vs 19.8% in iron-sufficient group; Wald value = 8.74; \( P = .003 \)), were not pursuing further education/training (76.1% vs 31.5%; Wald value = 3.01; \( P = .08 \); suggestive trend), and were single (83.9% vs 23.7%, Wald value = 4.49; \( P = .03 \)). They reported poorer emotional health and more negative emotions and feeling of dissociation/detachment. Results were similar in secondary analyses comparing the chronic iron-deficient group with subjects in the iron-sufficient group who had been iron-deficient before treatment in infancy. Path analysis showed direct paths for chronic iron deficiency in infancy and being single and more detachment/dissociation at 25 years. There were indirect paths for chronic iron deficiency and not completing school via poorer cognitive functioning in early adolescence and more negative emotions via behavior problems in adolescence, indicating a cascade of adverse outcomes.

Conclusion: The observational nature of this study limits our ability to draw casual inference, even when controlling for background factors. Nonetheless, our results indicate substantial loss of human potential. There may be broader societal implications, considering that many adults worldwide had chronic iron deficiency in infancy. Iron deficiency can be prevented or treated before it becomes chronic or severe.
Clinical assessment of PTSD in children with mild to borderline Intellectual disabilities: A pilot study
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Objective: There are few studies regarding assessment and treatment of trauma-related disorders in people with intellectual disabilities (ID). The aims of this study were to determine (1) the feasibility of an adapted version of a post-traumatic stress disorder (PTSD)-clinical interview and (2) to what extent manifestation of PTSD in a sample of children with mild to borderline ID corresponds with four existing PTSD algorithms.

Method: Fifteen children who visited a special need school were interviewed.

Results: In all children, the full interview could be completed. Potentially traumatic events (A1 criterion), and PTSD symptoms for children with mild to borderline ID were similar to those observed in children without ID.

Conclusions: The manifestation of PTSD in children with mild to borderline ID corresponds with the manifestation of PTSD in children without ID. The data provide no reason to broaden PTSD criterion A1 for children with mild to borderline ID.
Maternal Behaviors Promoting Language Acquisition in Slow-to-Talk Toddlers: Prospective Community-based Study
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**Objective:** To determine, in a community-based sample of slow-to-talk toddlers, the extent to which specific maternal responsive behaviors at 24 months predict child language at 24 and 36 months.

**Methods:** Mother-child dyads were recruited for this prospective longitudinal study from 3 local government areas spanning low, middle, and high socioeconomic status in Melbourne, Australia. At child age 18 months, 1138 parents completed a 100-word expressive vocabulary checklist; the 251 (22.1%) children scoring <20th percentile were then followed up to comprise the study.

**Predictors:** Six maternal responsive behaviors (imitations, interpretations, labels, expansions, supportive directives and responsive questions) were derived from mother-child free-play videos collected at 24 months of age and coded using the Observer XT system.

**Outcomes:** Expressive and receptive language measured at 24 and 36 months of age (Preschool Language Scale-4), blind to maternal responsiveness ratings.

**Results:** Two hundred and twenty-six of the 251 (90.0%) mother-child dyads were followed up at 36 months. In confounder-adjusted linear regression analyses, expansions, limitations, and responsive questions were strongly associated with better receptive and expressive language at 24 and 36 months. Labels unexpectedly predicted poorer expressive language at 36 months. Expansions are the only maternal behavior that predicted improvement in language between 24 and 36 months.

**Conclusions:** Maternal responsive behaviors, particularly expansions, offer promise in enhancing early language learning in slow-to-talk toddlers. Parent-child interactions characterized by frequent use of maternal labels at 24 months could also be a predictive marker of those slow-to-talk toddlers at greater risk of persistent language problems.
Reducing Distress in Mothers of Children With Autism and Other Disabilities: A Randomized Trial


**Background:** Compared with other parents, mothers of children with autism spectrum disorder or other neurodevelopmental disabilities experience more stress, illness, and psychiatric problems. Although the cumulative stress and disease burden of these mothers is exceptionally high, and associated with poorer outcomes in children, policies and practices primary serve the identified child with disabilities.

**Methods:** A total of 243 mothers of children with disabilities were consented and randomized into either Mindfulness-Based Stress Reduction (mindfulness practice) or Positive Adult Development (positive psychology practice). Well-trained, supervised peer mentors led 6 weeks of group treatment in 1.5-hour weekly sessions, assessing mothers 6 times before, during, and up to 6 months after treatment. Mothers had children with autism (65%) or to other disabilities (35%). At baseline, 85% of this community sample had significantly elevated stress, 48% were clinically depressed, and 41% had anxiety disorders.

**Results:** Using slopes-as-outcomes, mixed random effects models, both treatments led to significant reductions in stress, depression, and anxiety, and improved sleep and life satisfaction, with large effects in depression and anxiety. Mothers in Mindfulness-Based Stress Reduction versus Positive Adult Development had greater improvements in anxiety, depression, sleep, and well-being. Mothers of children with autism spectrum disorder improved less in anxiety, but did not otherwise differ from their counterparts.

**Conclusions:** Future studies are warranted on how trained mentors and professionals can address the unmet mental health needs of mothers of children with developmental disabilities. Doing so improves maternal well-being and furthers their long-term caregiving of children with complex development, physical, and behavioral needs.
Aim: The aim of this study was to examine the relationship between vocational rehabilitation services provided and work outcomes among people with cerebral palsy (CP), taking into account demographic characteristics.

Method: From the US Department of Education Rehabilitation Service Administration Case Service Report (RSA-911) database, data from 3162 individuals with CP (1820 males [57.6%] and 1342 females [42.4%] age range 16–54y) whose cases were closed in 2009, were used in this study. A total of 1567 cases (49.6%) were closed with clients being categorized as ‘successful employment’ and 1595 cases (50.4%) were closed with clients being classified as unemployed.

Results: Multivariate logistic regression was used to examine the relationship between services provided and work outcomes with regard to demographic characteristics. Males aged between 26 and 54 years old with higher education attainment were more likely to be employed. Individuals receiving disability benefits were less likely to be employed. After controlling for the effect of demographic and work disincentive variables, five vocational rehabilitation services significantly predicted employment outcomes ($p<0.05$), including (1) on-the-job training; (2) job placement assistance; (3) on-the-job support; (4) maintenance services; and (5) rehabilitation technology.

Interpretation: Medical and health professionals need to be aware of vocational rehabilitation agencies as a resource for providing medical, psychological, educational, and vocational interventions for adults with CP to help them maximize their employability, to address their much needed work adjustment skills, to establish independent living, and to eventually reach their full potential in participation in society.
Botulinum Toxin A for Nonambulatory Children with Cerebral Palsy: A Double Blind Randomized Controlled Trial


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**Objectives:** To examine the efficacy and safety of intramuscular botulinum toxin A (BoNT-A) to reduce spasticity and improve comfort and ease of care in nonambulant children with cerebral palsy (CP).

**Study design:** Nonambulant children with CP (n = 41; Gross Motor Function Classification System level IV = 3, level V = 38; mean age 7.1 years, range 2.3-16 years, 66% male) were randomly allocated to receive either intramuscular BoNT-A injections (n = 23) or sham procedure (n = 18) combined with therapy. The analysis used generalized estimating equations with primary outcome the Canadian Occupational Performance Measure (COPM) at 4 weeks postintervention and retention of effects at 16 weeks. Adverse events (AE) were collected at 2, 4, and 16 weeks by a physician masked to group allocation.

**Results:** There were significant between group differences favoring the BoNT-A-treated group on COPM performance at 4 weeks (estimated mean difference 2.2, 95% CI 0.8, 3.5; *P* = .002) and for COPM satisfaction (estimated mean difference 2.2, 95% CI 0.5, 3.9; *P* = .01). These effects were retained at 16 weeks for COPM satisfaction (estimated mean difference 1.8, 95% CI 0.1, 3.5; *P* = .04). There were more mild AE at 4 weeks for the BoNT-A group (*P* = .002), however, there were no significant between-group differences in the reporting of moderate and serious AE.

**Conclusions:** In a double-blind randomized sham-controlled trial, intramuscular BoNT-A and therapy were effective for improving ease of care and comfort for nonambulant children with CP. There was no increase in moderate and severe AE in the children who had BoNT-A injections compared with the sham group.
Early Adversity, Socioemotional Developmental, and Stress in Urban 1-Year-Old Children
Palmer FB, Anand KJS, et al


**Objective:** To determine demographic, maternal, and child factors associated with socioemotional (SE) problems and chronic stress in 1-year-old children.

**Study design:** This was a prospective, longitudinal, community-based study, which followed mother-infant dyads (n=1070; representative of race, education, and income status of Memphis/Shelby County, Tennessee) from mid-gestation into early childhood. Child SE development was measured using the Brief Infant-Toddler Social and Emotional Assessment in all 1097 1 year-olds. Chronic stress was assessed by hair cortisol in a subsample of 1-year-olds (n=297). Multivariate regression models were developed to predict SE problems and hair cortisol levels.

**Results:** More black mothers than white mothers reported SE problems in their 1-year-oldss (32.9% vs 10.2%; *P* < .001). In multivariate regression, SE problems in blacks were predicted by lower maternal education, greater parenting stress and maternal psychological distress, and higher cyclothymic personality score. In whites, predictors of SE problems were Medicaid insurance, higher maternal depression score at 1 year, greater parenting stress and maternal psychological distress, higher dysthymic personality score, and male sex. SE problems scores were associated with higher hair cortisol levels (*P* = .01). Blacks had higher hair cortisol levels than whites (*P* < .001). In the entire subsample, increased hair cortisol levels were associated with higher parenting stress (*P* = .001), lower maternal depression score (*P* = .003)

**Conclusion:** Differences in maternal education, insurance, mental health, and early stress may disrupt SE development in children. Complex relationships between hair cortisol level in 1-year-olds and maternal parenting stress anti-depression symptoms dysregulation of the child’s hypothalamic-adrenal axis.
Communication Interventions for Minimally Verbal Children With Autism: A Sequential Multiple Assignment Randomized Trial

Connie Kasari, PhD, Ann Kaiser, PhD..et al.


Objective: This study tested the effect of beginning treatment with a speech-generating device (SGD) in the context of a blended, adaptive treatment design for improving spontaneous, communicative utterances in school-aged, minimally verbal children with autism.

Method: A total of 61 minimally verbal children with autism, aged 5 to 8 years, were randomized to a blended developmental/behavioral intervention (JASP+_EMT) with or without the augmentation of a SGD for 6 months with a 3-month follow-up. The intervention consisted of 2 stages. In stage 1, all children received 2 sessions per week for 3 months. Stage 2 intervention was adapted (by increased sessions or adding the SGD) based on the child’s early response. The primary outcome was the total number of spontaneous communicative utterances; secondary measures were the total number of novel words and total comments from a natural language sample.

Results: Primary aim results found improvements in spontaneous communicative utterances, novel words, and comments that all favored the blended behavioral intervention that began by included an SGD (JASP+EMT+SGD) as opposed to spoken words alone (JASP+EMT). Secondary aim results suggest that the adaptive intervention beginning with JASP+EMT+SGD and intensifying JASP+EMT+SGD for children who were slow responders led to better post treatment outcomes.

Conclusion: Minimally verbal school-aged children can make significant and rapid gains in spoken spontaneous language with a novel, blended intervention that focuses on joint engagement and play skills and incorporates an SGD. Future studies should further explore the tailoring design used in this study to better understand children’s response to treatment.

Clinical trial registration information-Developmental and Augmented Intervention for Facilitating Expressive Languages (CCNIA); http://clinicaltrials.gov/; NCT01013545.
Population Pharmacokinetics of Oral Baclofen in Pediatric Patients with Cerebral Palsy
Yang He, PhD¹, Janice E. Brunstrom-Hernandez, MD², et al.


**Objective:** To characterize the population pharmacokinetics (PK) of oral baclofen and assess impact of patient-specific covariates in children with cerebral palsy (CP) in order to support its clinical use.

**Subject design:** Children (2-17 years of age) with CP received a dose of titrated oral baclofen from 2.5 mg 3 times a day to a maximum tolerated dose of up to 20 mg 4 times a day. PK sampling followed titration of 10-12 weeks. Serial R- and S- baclofen plasma concentrations were measured for up to 16 hours in 49 subjects. Population PK modeling was performed using NONMEN 7.1 (ICON PLC; Ellicott City, Maryland).

**Results:** R- and S- baclofen showed identical concentration-time profiles. Both baclofen enantiomers exhibited linear and dose/kg-proportional PD, and no sex differences were observed. Average baclofen terminal half-life was 4.5 hours. A 2-compartment PK model with linear elimination and transit absorption steps adequately described concentration-time profiles of both baclofen enantiomers. The mean population estimate of apparent clearance/F was 0.273 L/h/kg with 33.4% inter-individual variability (IIV), and the apparent volume of distribution (Vˢˢ/F) was 1.16 L/Kg with 43.9% IIV. Delayed absorption was expressed by a mean transit time of 0.389 hours with 83.7% IIV. Body weight, a possible genetic factor, and age were determinants of apparent clearance in these children.

**Conclusion:** The PK of oral baclofen exhibited dose-proportionality and were adequately described by a 2-compartment model. Our population PK findings suggested that baclofen dosage can be based on body weight (2 mg/kg per day) and the current baclofen dose escalation strategy is appropriate in the treatment of children with CP older than 2 years of age.

Effect of Extracorporeal Shock Wave Therapy on Gait Pattern in Hemiplegic C P
El-Shamy SM, Eid MA, El-Banna MF


**Abstract:** Effect of extracorporeal shock wave therapy on gait pattern in hemiplegic cerebral palsy: a randomized controlled trial.

**Objective:** The aim of this study was to investigate the effects of shock wave therapy on gait pattern in children with hemiplegic cerebral palsy.

**Design:** Fifteen children were assigned to the study group, whose members received shock wave therapy (1500 shots/muscle, frequency of 5Hz, energy of 0.030 mJ/mm², one session/wk). Another 15 were assigned to the control group, whose members participated in a conventional physical therapy exercise program for 3 successive months. Baseline and post treatment assessments were performed using the Modified Ashworth Scale to evaluate spasticity degrees and using a three-dimensional gait analysis to evaluate gait parameters.

**Results:** Children in the study group showed group showed a significant improvement when compared with those in the control group (P< 0.005). The Modified Ashworth scores after treatment were 1.86 (0.22) and 1.63 (0.23) for the control and study group, respectively. The gait parameters (stride length, cadence, speed, cycle time, and stance phase percentage) after treatment were 0.5 m, 125 steps/min. 0.6 m/sec, 0.48 sec, and 50.4% and 0.74 m, 119 steps/min, 0.75 m/sec, 0.65 sec, and 55.9% for the control group and the study group, respectively.

**Conclusions:** Shock wave therapy may be a useful tool for improving spasticity and gait pattern in children with hemiplegic cerebral palsy.