

12th international CHARGE Syndrome Conference Proceedings

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Abstract

The CHARGE Syndrome Foundation holds an International conference for families and professionals every other summer. In July, 2015, the 12th meeting was held in Schaumburg, Illinois, at the Renaissance Schaumburg Hotel. Day one of the

four-day conference was dedicated to professionals caring for and researching various aspects of CHARGE, including education, medical management, animal models, and stem cell based approaches to understanding and treating individuals with CHARGE. Here we summarize presentations from the meeting, including a synopsis of each of the three different breakout sessions (Medical/Clinical, Basic Science/CHD7 and Education), followed by a list of abstracts and authors for both platform and poster presentations.

INTRODUCTION

The 12th International meeting of the CHARGE Syndrome Foundation was held July 30-August 2, 2015, in Schaumburg, Illinois at the Renaissance Schaumburg Hotel. There were 1200 participants at the meeting, including 234 individuals with CHARGE. The first day of the four-day meeting was dedicated to Professionals interested in learning more about CHARGE and presenting novel observations from research, clinical care, education, and therapeutic approaches for individuals with CHARGE. There were 150 participants at Professional Day. Included below is a brief history of the meeting, followed by summaries of breakout sessions and abstracts from platform and poster presentations.

The CHARGE Syndrome Foundation was incorporated in 1993 to coincide with the first International CHARGE Syndrome Conference for Families and Professionals in St. Louis, Missouri. By then, a dedicated group of professionals originating in Columbia, Missouri (Joyce Mitchell, PhD, Sandra Davenport, MD, James Thelin, PhD and

Margaret Hefner, MS), had been working on CHARGE for about 10 years. A Booklet for Families had been produced in 1986, followed by a newsletter in 1989. At the first conference, 250 people registered: 77 families with 86 children, 46 of whom had CHARGE. Since the first meeting, conference attendees have included dedicated family members, professionals, doctors, nurses, social workers, audiologists, teachers, and therapists from around the world. In addition, dozens of local volunteers participate to assist with childcare, support, and sign language interpretation. The CHARGE Syndrome Foundation is currently led by President David Wolfe, board members (Lisa Weir, Brownie Shott, Neal Stanger, Joanne Lent, Amrit Mehta, Pamela Ryan, Karin Dagley, Christian Lobaugh, Minnie Lambert), and numerous volunteers, all of whom work toward the mission of education, service, and community for individuals with CHARGE.

Research has always taken place at conference, including questionnaires in St. Louis in 1993, an on-site clinic in Portland in 1995, and examination of toes and feet in 2007 in Costa Mesa. In 1999, John Belmont and colleagues from Baylor College of Medicine drew blood on individuals with CHARGE and their family members as part of the search for a gene for CHARGE. Professionals attending conference recognize that that this gathering of individuals with CHARGE and their families provides a wealth of opportunity for research. In 2015, research for conference was coordinated in advance and space was set aside specifically for 11 research teams to gather data.

The CHARGE Syndrome Foundation has provided many grants over the years to help support research. Previously, resources of the Foundation were dedicated primarily to subsidizing conference, and research grants were limited to small projects

such as assistance with large questionnaire based studies. In 2009, the Foundation made a commitment to dramatically increase fundraising towards the goal of supporting major basic science research on CHARGE and *CHD7*. The hope was that by funding pilot awards, the Foundation could facilitate the ability of researchers to obtain larger grants to support their work. A Scientific Advisory Board (SAB) was formed to advise the Foundation and review grant applications. The first pilot grants were awarded in 2012, and the Foundation has continued to provide funds for basic science research on an annual basis.

PLENARY SESSION

The opening plenary session highlighted three different topics: genetics, basic neurobiology, and intervention strategies. The first presentation by Caitlin Hale (University of Michigan) discussed a proposed revision of the diagnostic criteria for CHARGE Syndrome, which includes consideration of *CHD7* mutation status as a major criterion for diagnosis. The second presentation, by Daniel Marendia (Drexel University) showed that glutamatergic neurotransmission and synapse formation is disrupted with loss of *kismet*, the *Drosophila* *CHD7* ortholog. The third presentation of the plenary session was by Nancy Steele (National Center on Deaf-Blindness) and a panel of experts who discussed interveners and their utility in enhancing communication for individuals with CHARGE. After these presentations, Claudia Junghans and Julia Benstz (German CHARGE family support group) presented excerpts from a video "We have CHARGE, so what!" showing a group of German teens with CHARGE on a weekend retreat, including a hike and discussions about their experiences as young people with CHARGE.

Concurrent Sessions: Basic Science/CHD7

This session was chaired by Peter Scacheri (Case Western Reserve University). Themes included animal models (flies, mice, fish and frogs), and stem cell based studies to identify common mechanisms underlying CHARGE. Presentations focused on roles for CHD7 in neurotransmission and learning/memory, generation of new mouse models to perform lineage tracing of CHD7 cell fates, and interactions between CHD7 and members of the SOX gene family of transcription factors. One presentation centered around development of biological treatments for deafness and balance disorders, through study of viral vectors to treat genetic forms of deafness in developing mice. In another study, researchers described abnormalities in neural crest-derived enteric neurons in *chd7* morphant zebrafish, which were associated with reduced gut motility and altered gastrointestinal tract morphology. Other researchers discussed the role of *kismet* in promoting proliferation of stem cells of the *Drosophila* gut. Results of studies in mice showed that *Chd7* controls cerebellar growth, via changes in Reelin and *Fgf8* expression, suggesting important links between signaling pathways and locomotion or cognition. In *Xenopus*, knockdown of *chd7* was shown to disrupt formation of neural crest cells, providing a potential explanation for craniofacial dysmorphisms and heart defects in CHARGE.

Concurrent Sessions: Education

The Education session was chaired by Nancy Salem-Hartshorne (Delta College). General themes for this session were implementation of novel approaches and review of existing methodologies. One presentation covered adaptive books, which are used to promote early concept development since people who are deafblind experience the

world only as far as their fingertips can reach. Thus, they literally “grasp” concepts, and touch is extremely important. Books are a rich tool for teaching because they require mutual attention, shared language, and controlled and predictable vocabulary. Another group presented a video entitled “Hello to the Future” highlighting conversations between two adolescent girls who have CHARGE syndrome. The girls seemed to be more interested in social topics like friends, hobbies and parties than they were about sharing experiences of having CHARGE syndrome. They were hopeful and optimistic about the future, and were excited about providing their message to conference participants. There was also a panel presentation entitled “Lived Experience of Parents of Children with CHARGE” in which four parents presented their experiences, including legal battles with a school district, experience with doctors, learning how to ask questions, and keeping in mind that doctors and parents work as a team. Another parent spoke about difficulties with early intervention services and case coordination. Many therapists have little or no experience with deaf-blindness, yet there is a need to trust the expertise of the professionals. Another presenter spoke about an educational model aimed at decreasing passivity and increasing self-determination through use of direct learning: “touch it, move it, use it.” This method was presented as effective for educators and parents. Positive behavioral supports also help with emotion regulation and anxiety, and were incorporated into cognitive behavior therapy with young adults who were deafblind, five of whom had CHARGE syndrome. Supporting students to cope with anxiety and providing adult language to support positive behavior had the highest impact on behaviors. Another group presented development of a staff training program in Europe, which trains skills in video analysis, congenital deaf-blindness and

social interaction. Finally, there was a discussion about intervener services for children and young adults including general and deafblind learning styles. For individuals who are deafblind, there is minimal incidental learning, and most learning comes from direct instruction. An intervener who works consistently with individuals who are deafblind can help facilitate incidental learning.

Concurrent Sessions: Medical/Clinical Approaches

This session was summarized by Timothy Hartshorne (Central Michigan University). General themes for this session were updates to guidelines and diagnostics. There was a checklist for “Guiding health screening and management” which was organized by age into 9 categories ranging from “neurology” to “self-management”. This provided a starting point for other presentations about monitoring risks associated with CHARGE, including vascular ring and aortic arch vessel anomalies which can be difficult to detect yet can create complications such as swallowing issues from a vascular difficulties. Neurology is an area that is understudied in CHARGE. Two presentations discussed brain anomalies; one focused on the cerebellum and the other on defects of the clivus, part of the base of the skull. Another group considered the importance of considering pain when a child with CHARGE exhibits challenging behavior. Aspects of immunology in CHARGE were also discussed in a presentation on immunoglobulins and T-cell function, and endocrine issues related to pubertal delays and hormone replacements were also explored. Other topics included sleep disorders, timing and decision-making about gastrostomy tubes, risks and benefits of psychotropic medications, social play, and developmental delays. Emphasis was placed on developing recreational opportunities for children with

CHARGE, the need for more family based research, and recent advice from siblings of children with CHARGE.

ABSTRACTS:

PLENARY SESSION

Atypical features associate with CHD7 mutations and CHARGE syndrome: a proposal for revised clinical diagnostic criteria

Caitlin L Hale, Jane Schuette, Stephanie Bielas, and Donna M Martin. University of Michigan, Ann Arbor

Since the discovery of *CHD7* as the causative gene for CHARGE syndrome in 2004, the phenotypic spectrum associated with *CHD7* mutations has greatly expanded to include individuals with *CHD7* and mild or atypical clinical features that do not meet clinical diagnostic criteria for CHARGE. Since 2004, the phenotypic spectrum associated with *CHD7* mutations has greatly expanded to include individuals with nonsyndromic autism, GnRH deficiency, or other subsets of features of CHARGE. This raises the question of whether CHARGE syndrome should be considered a clinical or molecular diagnosis, or both. The most recent clinical criteria for CHARGE were published by Verloes and colleagues in 2005, and did not consider *CHD7* mutation status. In this presentation, we review atypical clinical phenotypes reported with CHARGE or *CHD7* mutations, including clinical data from individuals who were evaluated at the University of Michigan. We also present ongoing genetic studies to identify new genetic contributions in CHARGE, and propose a revision of CHARGE clinical diagnostic criteria.

Synaptic abnormalities in a Drosophila model of CHARGE syndrome

Daniel R. Marendia, Drexel University, Philadelphia

In this presentation, I discuss the work my lab has accomplished in understanding the function of the *kismet* gene in the development of the fly nervous system, and how this relates to normal fly behavior in the context of further understanding CHARGE syndrome by using this animal. The *Drosophila* neuromuscular junction (NMJ) is a glutamatergic synapse that is highly similar to mammalian glutamatergic synapses. *Kismet* is important for synaptic morphology and transmission at this synapse, suggesting that *Kis* is part of the machinery that modulates the function of the NMJ. Glutamate is a neurotransmitter that mediates the majority of excitatory synaptic transmission in the human brain. Understanding the mechanisms by which *kismet* controls this signaling may help understand *kismet* (and by association, *CHD7*) function in nervous system development and function. Our data also suggests novel avenues of investigation for potential synaptic defects associated with CHARGE syndrome

Open-Hands, Open Access, Deaf-Blind Intervener Learning Modules: Using a national resource to meet state-specific training needs

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1 National Center on Deaf-Blindness; 2 Illinois Deaf-Blind Project

The Open Hands, Open Access (OHOA) Deaf-Blind Intervener Learning Modules are a national resource that has been created and refined by members of the national deafblind community. Parents have played a central role in their creation, field-testing and adoption. This presentation will describe the ways in which OHOA is being used within states to meet unique training needs using the OHOA modules within the Moodle system. From their first release, there were several state partners who wanted to host the OHOA modules with groups of adult learners. Some states are using the modules to develop broad statewide awareness of intervention practices for students who are deafblind while other states are using modules as a part of intensive technical assistance to teams. Another state partner is using the OHOA modules as a prerequisite to providing classroom based technical assistance (Durando, 2014). A university partner in collaboration with a state partner has embedded OHOA modules within the state's current preparation structure for interveners (Nelson & Sanders, 2014). In September 2014, there were 10 state deaf-blind partners and two university partners who were actively using the modules as a part of their outreach, technical assistance or personnel preparation. Families who have participated in the modules with state adopters or as a part of a special training opportunity provided through the National Family Association on Deaf-Blindness and NCDB have expressed appreciation for the depth of the modules and how much the content has helped them reflect on their own interactions with their children (McGowan & Malloy, 2014). Partnership with state adopters has led to a tremendous understanding of how the modules may be used effectively with learners. It has also led to the creation of tip-sheets, screen casts and other guiding tools for state partners to use. NCDB staff has partnered with an educational technologist to refine and systematically support our outreach and engagement with states in the use of the Moodle system and with the OHOA materials. Quarterly Moodle Users meetings help sustain not only NCDB's targeted technical assistance to states but are a mechanism for creating engagement across partners who are learning from each others' experiences.

German CHARGE youth-week-ends "We have CHARGE – so what?!"
Claudia Junghans & Julia Benstz, CHARGE Syndrom e.V., Germany

In previous German conferences, our teens and young adults with CHARGE syndrome voiced their wish to have a weekend "away". The purpose of the weekend is to find a way to communicate to our society what living with CHARGE syndrome means and share their everyday difficulties. Nine teens and young adults (age 15-26) with CHARGE syndrome met in a youth hostel for the first German CHARGE youth-week-end. They were accompanied by the two presidents of the German CHARGE self-help group, a film team, a team of climbing guides, and some other people able to assist individuals with disabilities. On Friday night, they started with some introductory games and started preparations for the climbing excursion, which was planned for the next morning. The next day the group went on a climbing steep path, with very challenging moments for each of them. At the end, everyone was very proud of what had achieved! In the afternoon, interviews with the film team took place. They could distinctly express

how life is with CHARGE syndrome and which difficulty they face, which hope and dreams they have. The last day began in an adventurous setting and once again these young adults showed their enormous potential. The film of this first CHARGE youth weekend became a great success. It was presented on the homepage of the self-help group and also on the following German CHARGE Conference. At this event, the performers had the opportunity to introduce their film to the audience and to answer their questions. Owing to the overwhelming response to the weekend, an annual meeting was established. Among several aspects that may be highlighted, there is indeed something special and is precisely the possibility of this youth to develop friendships and the unique chance to realize their dreams and wishes.

Basic Science/CHD7 SESSION

Chd7 controls cerebellar growth via Reelin

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CHD7 is expressed in proliferating granule neuron progenitors (GNPs) in the early postnatal cerebellum. Using conditional gene deletion strategies in mice, we have deleted *chd7* specifically from these progenitors and identified defects in cell proliferation and differentiation resulting in cerebellar hypoplasia. We identified the Reelin gene as a functional target of *chd7* in these cells and observed mild motor deficits in some of the mice.

Modeling CHARGE syndrome in zebrafish: A look at the innervation and function of the gastrointestinal system

Kellie Cloney, Shelby L Steele, Matthew Stoyek, Roger P Croll, Frank M Smith, Kim Blake, and Jason N Berman, Dalhousie University, Halifax NS Canada

CHARGE syndrome has been linked to mutations in the *CHD7* gene and results in a number of physiological and structural abnormalities. Of these challenges, eating problems often have a profound impact throughout a child's life and can lead to complications and even death. A corresponding *chd7* gene has been identified in the zebrafish, the loss of which results in the fish displaying many of the features of the human disease. Using morpholinos to eliminate the function of *chd7* in zebrafish, we investigated changes in the nerves of the gastrointestinal tract using a nerve labeling technique called immunohistochemistry. As zebrafish embryos are transparent, we directly observed the consequences when *chd7* is lost, something that is not possible in many other animal models. We have shown that zebrafish lacking *chd7* display changes in the anatomy of their gut, nervous system, and yolk sac. We successfully labeled the cranial nerves that supply the head and the nerves of the gastrointestinal (GI) system. With these nerves labeled, we observed a decrease in the branching of the GI nerve network surrounding the stomach. This more limited nerve network might contribute to

decreased stomach emptying and, in combination with a smaller stomach, may account for the increased gastrointestinal reflux and other feeding problems often seen in patients with CHARGE. In summary, we have demonstrated how loss of the *chd7* in zebrafish results in physical changes in the gastrointestinal tract and abnormalities in nerve patterning. These observations may help provide explanations for some of the feeding difficulties that occur in CHARGE syndrome and have potential to ultimately impact the monitoring and management of these patients.

Novel treatments for deafness and balance disorders

Yehoash Raphael & Donna M Martin, University of Michigan, Ann Arbor

Our objective is to develop novel therapies for repair and regeneration of the cochlear epithelium and the auditory nerve in deaf ears. The objective of one set of experiments was to assess the influence of neurotrophin gene therapy on auditory neurons in deaf ears. Neurotrophin experiments were performed on guinea pigs deafened with an ototoxic lesion and on mice with a deafness mutation modeling human hereditary hearing loss. Adult guinea pigs were deafened by neomycin or kanamycin and furosemide. Adeno-associated viral vectors (AAV) with BDNF or NTF3 gene insert were injected into the perilymph one week later. In cochleae that were obtained three months later, the extent and pattern of nerve sprouting was assessed, along with spiral ganglion nerve survival. Similar experiments were performed using a mouse model for a connexin 26 (Cx26) mutation, in which cre-Sox10 drives excision of the Cx26 gene from supporting cells of the auditory epithelium. In this model the peripheral fibers of the auditory nerve die back, followed by death of the neurons. Overall, the results suggest that gene therapy with either BDNF or NT-3 leads to peripheral auditory nerve fiber re-growth, and treatment with BDNF leads to enhanced SGN survival. In Gjb2-CKO mice injected with Ad.BDNF at 1 month of age spiral ganglion neurons in the basal cochlear turn were rescued. The goal of the other experiments was to test methods for integrating exogenous cells in the mature deaf cochlea, in preparation for stem cell implantation. Specifically, we tested whether deaf cochleae can be “conditioned” to “accept” implanted exogenous cells and promote their survival and integration. To condition the cochlea, we used guinea pigs deafened with neomycin and performed procedures aimed at transiently lowering potassium levels in endolymph and opening the apical junctions in the auditory epithelium. We determined that exogenous cells injected into scala media survived in the conditioned cochleae for at least 7 days, but in un-conditioned (control) cochleae they promptly degenerated. Together, our data show that the cochlea can be manipulated to enhance nerve survival and sprouting and to accept and maintain exogenous cells. This can be accomplished in ears both environmentally and genetically caused cochlear pathologies.

Generation and characterization of Chd7-iCre transgenic mice as a tool for lineage tracing and gene deletion

Jennifer M. Skidmore, Donald L Swiderski, and Donna M. Martin. University of Michigan, Ann Arbor

Chd7, the gene involved in CHARGE syndrome, is highly expressed in embryonic stem cells, and is gradually restricted to organs and tissues known to be affected in CHARGE. Importantly, contributions of CHD7-positive cells to specific organs and tissues during embryonic development have not been defined. Here we describe the generation of a new transgenic mouse line, *Chd7-iCre*, which can be used to (a) identify CHD7-positive cells and their progeny and (b) delete genes in a CHD7-dependent manner. Our objective was to generate a tool that can be used to investigate the temporal and spatial expression of *Chd7* during embryonic development. Using a *Chd7*-containing BAC that was previously used to generate *Chd7GFP* transgenic mice, we designed a transgene in which *iCre* was inserted at the ATG translation start codon for *Chd7* in exon 2. The resulting BAC transgene was injected into mouse blastocysts, and resulted in eight different transgenic lines. Each *Chd7-iCre* line was analyzed in crosses with *R26;lacZ* and *R26;EYFP* Cre reporter mice to identify sites of Cre activity, and with *Chd7^{flox/flox}* mice to test for *Chd7* deletion phenotypes. Ears from *Chd7-iCre;Chd7^{flox/+}* embryos were paint-filled and compared to inner ear phenotypes in *Chd7^{Gt/+}* embryos. Seven of eight lines exhibited germline transmission of the transgene. Two of the eight lines were eliminated due to inefficient transmission, and a third line was eliminated due to incomplete penetrance. Cryosections of E12.5 *Chd7-iCre;R26lacZ* embryos showed X-gal staining in tissues known to express *Chd7*. *Chd7-iCre;Chd7^{flox/+}* embryos exhibited inner ear phenotypes similar to those previously reported in *Chd7^{Gt/+}* embryos. We conclude that *Chd7-iCre* transgenic mice will be useful for studies aimed at carefully identifying *Chd7*-positive cell lineages during development and in the postnatal period. These mice also will be valuable for deleting other genes (such as CHD7 interacting factors or targets) in a *Chd7*-dependent fashion.

Developing Zebrafish resources for CHARGE syndrome analysis and drug screening

Yuhan Sun, William Ciozda, Mallory Holland and Ruchi Bajpai, University of Southern California, Los Angeles

CHARGE syndrome is a multi-sensory and structural birth defect syndrome. CHARGE is different for each patient, with the variability and severity of each affected tissue resulting in a very broad phenotypic spectrum posing unique challenges for each individual and requiring distinct medical interventions. This poses a challenge for identifying potential small molecules that may serve to improve one or a set of affected functions in patients with CHARGE, thereby significantly improving quality of life for some or many patients. To overcome these problems we have developed a series of CHARGE syndrome relevant Zebrafish reporter lines carrying human regulatory genomic regions (enhancers) upstream of a green fluorescent protein (GFP). The selected enhancers are (i) either direct targets of *CHD7* (the gene mutated in patients with CHARGE syndrome) or near genes affected by *CHD7* downregulation during human development (ii) transiently activated in a subset of organs/tissues commonly affected in patients with CHARGE. In addition we have generated Zebrafish mutants of *chd7* to model CHARGE syndrome. Together the tissue specific reporters and *chd7* mutants will be an invaluable resource for integrated high-throughput assays and for future drug screening.

This part of the work was supported by Pilot grant to RB from the CHARGE Syndrome

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EDUCATION SESSION

Identifying effective positive behavioral supports for young adults with CHARGE syndrome

Susan M. Bashinski, Missouri Western State University, St. Joseph, MO, and Susan M. Bruce, Boston College, Boston

Many individuals with CHARGE syndrome experience heightened levels of fatigue due to lack of sleep or the extra effort expended to concentrate when both distance senses are impaired. Communication frustrations often trigger socially inappropriate behaviors. Additionally, many individuals who have CHARGE syndrome experience high levels of anxiety (Davenport & Hefner, 2010) or display autistic-like behaviors and difficulties with self-regulation (Hartshorne & Salem-Hartshorne, 2010). Extant literature verifies the efficacy of positive behavioral interventions and supports (PBIS) for preventing challenging behavior through application of *proactive* strategies. This collaborative action research study employed a collective case design to examine three elements of PBIS: adult use of language, environmental arrangement, and sensory system sensitivities and needs. Participants were five young adults (18-21 years) with CHARGE syndrome. The primary research question sought to determine what PBIS strategies are most effective with each of the young adults with CHARGE? Sub-questions addressed the three elements listed above and the identification of individually effective proactive and reactive strategies. Data sources included videotaped observations, teacher journals, PBIS and other data charts, notes from discussion groups, and individualized PBIS profiles developed for each learner. Constant comparative analysis (Glasser & Strauss, 1967; McHatton, 2009) was conducted, integrating elements of grounded theory (open coding, axial coding, and in vivo coding). Member checks were conducted on the final profiles. Findings included the identification of a number of effective strategies for this group of five young adults with CHARGE syndrome. Examples of effective strategies, in each of the three primary categories, for the largest number of learners included: 1) *Adult use of language (verbalizations OR manual sign)* - Keep the learner informed; choose vocabulary selectively; avoid trigger words and topics; and assist the learner to reflect on her behavior as “mature” / “not mature.” 2) *Environmental arrangement* - Provide structure; provide clearly defined physical spaces; and avoid situations that might cause unexpected touching by others (e.g. crowded hallway or elevator). 3) *Sensory system sensitivities and needs* - Provide style of chair matched to learner (e.g. chair with no arms, chair that will mold to learner’s body); employ periodic opportunities for physical exertion; and make available weighted / deep pressure materials (e.g. vest, backpack, body sock).

The lived experience of parents of children with CHARGE syndrome in advocating and navigating systems

Seth Harkins, Philip J. Rock Center & School, Glen Ellyn, IL & National Louis University, Chicago, IL

Parents of children with complex disabilities are particularly challenged in advocating for their youth as they navigate the complex maze of special education and human service systems. The presentation explored the ways educational and human service systems interact with family systems regarding fears, anxieties, and other emotions regarding children with CHARGE syndrome. The parents' advocacy stories of parents highlight points of tension and stress as they navigate medical, educational, and human service systems. David Winnecott's (1965) concept of the "good enough parent" and "good enough system" is used as a framework for understanding the challenge of human service systems in providing for the complex needs of children with CHARGE. This framework is also helpful in understanding and shaping family empowerment and leadership. Parent narratives focus on advocacy and navigation of: 1) medical; 2) early intervention; 3) school; 4) post-secondary planning. Parents tell the salient aspects of their stories, including their struggles and successes. The presentation concluded with a dialogue with the audience regarding leadership and advocacy strategies. These narratives highlight efforts to build relationships with professionals, other parents, and public and private providers.

Making it happen: Intervener services for children and young adults who have vision and hearing losses

Beth Kennedy and Linda Alsop, DeafBlind Central: Michigan's Training & Resource Project, Mount Pleasant, MI

Interveners have training and specialized skills in deafblindness that enable them to work effectively with children and young adults who are deafblind. The practice of using interveners as individualized supports for students with combined vision and hearing loss in educational settings is growing across the United States. This is creating an ongoing need to provide information and training to parents and professionals about the critical role that interveners play in providing access. Parent advocacy has, and will continue to play, an important role in the increased understanding of intervention and the expanded use of this service delivery model.

The training of interveners is a critical issue, and competency-based higher education programs play an important role in producing interveners who are highly qualified and recognized as part of a professional discipline. There are now a growing number of interveners around the country who have completed an intervener training program and have earned the National Intervener Credential. They are providing skilled intervention services that result in improved educational outcomes for children and young adults who are deafblind.

An educational model to reduce passivity and increase self-determination in deafblind learners resulting in improved connection, communication, and learning

Kimberly Lauger, Redtail Neurodevelopmental Center, Tuscon, Consultant for the Arizona Deafblind Project, Phoenix, AZ

Emerging from one team's efforts to meet the needs of Dylan, a 17-year old boy with CHARGE syndrome, this session will cover an educational model that supports

connection, communication, and learning in deafblindness. Committed to following Dylan's interests and measuring smiles and laughter instead of goals, his team was encouraged to see the improvements in health, mood, communication, literacy, learning, and friendships that emerged, as he became an active participant in school and home. Initially focused on reducing stress and improving Dylan's health, Dylan's team started with some general principles: 1) A team with Dylan at the center, all committed to following his lead 2) An environment set up to support Dylan's visual focus and attention 3) A team that honored the cues from Dylan's body, and provided the necessary sensory and physical supports he needed to maintain engaged learning 4) Deafblind principles and practices so embedded into the daily routine that we didn't even know we were doing them 5) Daily opportunities to learn through hands on activities and experiences . Communicating well through acting on people and objects, Dylan's progress towards formal language had previously been slow in spite of his family and school-teams' ongoing commitment to support it. As Dylan began to actively use his communication symbols to express his preference, to use his eyes to get - and direct -- attention, to initiate signs, to recognize a word in print and sign the word (read), and to initiate writing familiar words without a model, Dylan's team realized they had inadvertently created a truly active and responsive environment, which allowed him to make choices about his own life and to act on them. As Dylan's ability to act on his own world increased, his self-expression - including language - increased. In this session an overview of the model will be shared through the example of Dylan emphasizing the synergistic impact of each element in creating a reactive and responsive environment and the corresponding reduction in passivity and increased self-determination. Data documenting Dylan's change in function will be shared.

Hello to the future!

Eva Seljestad and Wenche Andersen, Deafblindness and Dual Sensory Impairment, Oslo, Norway

We will present some themes in a conversation between two girls (ages 12 and 14) with CHARGE syndrome. We highlight how they reflect upon the syndrome, and what they know about facts and myths about CHARGE. We also note how they manage to listen to each other, exchange information and ask following-up questions. When we analyze their conversations, we focus on both facts and more philosophical aspects of their understanding. This might give a valuable contribution to our counseling. At this age, questions like; "Who am I?" arise. The main issue at this age is related to identity and self-esteem. Having CHARGE syndrome raises more issues than usual in building an identity. When and how they are informed about the syndrome might influence upon the existential pain following with the information. Having CHARGE syndrome is a lifelong challenge. How you manage to accept this has a great influence on your quality of life. Acceptance is the golden key. Participating in a conversation demands communication skills that make it possible to maintain focus. Those skills might be missing. The dual sensory loss is one difficulty. Secondly, to maintain attention and to keep your body under control is challenging. Also to be deflected by your "special interests", might blur the focus. The two girls have little experience in having conversations with others their age. This time they were challenged to maintain a

conversation over some time. In spite of some misunderstanding we think the two girls had some joint experience discussing CHARGE. They had some reflections that were rather philosophical when we videotaped them. They suggested that they would like to see the video again in the future. Our hope is that they will continue to discuss experiences, writing letters/ emails and perhaps meet again. The inclusion of knowledge about their experience of having CHARGE is one important theme in building identity and self-esteem.

What shall professionals know – and how can we teach them in a sustainable way for working with people with CHARGE syndrome?

Andrea Wanka, Foundation St. Francis Heiligenbronn, Germany

An international working group is developing a staff training program. One module in this program is on CHARGE syndrome. The main focus of the working group is based on the selection of the topics (separated into learning areas) with simultaneous considerations of new learning theories (like principals of teaching based on neurology) to make sure that staff gets sustainable knowledge while taking part in the program. Contents and the way of imparting will be presented. A working group from Germany, Switzerland, Austria and the Netherlands (EU project „PropäK“) is currently working on the program which is mainly based on the booklets, but also takes further topics in special modules into consideration like the one on CHARGE syndrome, which will be presented or one on Usher syndrome or another on tactile signing. First a short description of the history and within for the reasons of the project is described. Second a short overview about the staff training program is given. Third the selection of the topics and here the learning areas are presented and fourth the chosen ways of imparting are described. The staff training program is in progress. We try to make sure that it stays pragmatic and realizable.

MEDICAL/CLINICAL SESSION

Congenital arch vessel anomalies in CHARGE syndrome: a frequent feature with risk for co-morbidity

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CHARGE syndrome is mainly caused by mutations in the *CHD7* gene. We previously studied heart defects in patients with CHARGE syndrome and a proven *CHD7* mutation. Heart defects occur in 74% of the patients with a *CHD7* mutation, with overrepresentation of atrioventricular septal defects and conotruncal defects, including congenital arch vessel anomalies. In this study we will describe CHARGE patients with arch vessel anomalies and focus on the problems that might be caused by arch vessel anomalies in this patient's category *Methods and Results*: We report a patient with an arch vessel anomaly, underlying serious feeding problems, which resolved after arch vessel surgery. This patient made us focus on arch vessel anomalies in our previously studied cohort of 299 patients with a *CHD7* mutation. Forty two patients (14%) had an

arch vessel anomaly, mostly right aortic arch or aberrant subclavian artery. The arch vessel anomalies usually occurred in combination with other congenital heart defects (81%). The majority of the patients had feeding problems. These feeding problems may be linked to their arch vessel anomaly, but insufficient information was available to exclude other causes. *Conclusions:* Arch vessel anomalies occur in a significant proportion of patients with a *CHD7* mutation. They may cause problems due to compression of the esophagus or trachea. Since symptoms of vascular compression may mimic those caused by other abnormalities in CHARGE syndrome, it is important to be aware of arch vessel anomalies in patients with this syndrome. However, future studies are needed to exactly identify the frequency of symptomatic arch vessel anomalies in CHARGE syndrome.

Cerebellum abnormalities, the 5th C in CHARGE syndrome

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Introduction and background: Children with CHARGE syndrome often have balance problems due to hypoplasia of the semicircular canals. Balance involves the complex task of integrating postural responses and multisensory (visual, labyrinthine from the semi-circular canals, and proprioceptive) feedback. The cerebellum plays an important role in coordination of movements and balance, but little is known about the effect of *CHD7* mutations on cerebellum development and function. Recently, it was shown that loss of *Chd7* resulted in decreased *Fgf8* expression in mice. Combined loss of *Chd7* and *Fgf8* resulted in abnormal cerebellum development in mice. This prompted us to critically evaluate MRI scans of children with CHARGE syndrome for cerebellar defects. Methods: MRI scans of patients with a proven *CHD7* mutation were collected and evaluated by an experienced neuroradiologist using a standard protocol. Only MRI scans that allowed a reliable interpretation of the cerebellum, that is the presence of sagittal and axial images of the cerebellum, were included in this study (n = 20). MRI images of CHARGE patients were compared with images of age-matched controls. *FGF8* was analyzed for variants in the same 20 patients. Results: We found cerebellum abnormalities in 55% of the 20 patients. Patients exhibited cerebellar vermis hypoplasia, varying from slight to pronounced hypoplasia (35%) and an anticlockwise rotated vermis (35%). Fluid-filled spaces surrounding the cerebellum appeared larger: a large foramen of Magendi and fourth ventricle (50%) and large subcerebellar cistern (25%) were seen. Two patients with vermis hypoplasia exhibited broad gait or ataxia, consistent with defects that disrupt cerebellar function. Furthermore, 25% of the patients had foliation abnormalities, implying additional roles for *CHD7* during the process of foliation. The presence or absence of cerebellum abnormalities could not be explained by the type of *CHD7* mutation or by additional variants in *FGF8*. Conclusion: *CHD7* plays a role in cerebellum development. Cerebellum defects are a clinical feature in CHARGE syndrome, being the 5th C after coloboma, choanal atresia, cranial nerve defects and cardiac abnormalities. The involvement of the cerebellum may have important implications for amongst others posture and gait, and future studies are needed to explore the effect on balance in CHARGE syndrome.

The CHARGE Syndrome Research Lab at Central Michigan University

Timothy Hartshorne, Benjamin Kennert, Megan Schmittle, Rachel Malta, Hayley Hoesch, Gretchen Imel, Amanda Odren, Claire Latus-Kennedy, Central Michigan University, Mount Pleasant, Michigan

The CHARGE syndrome research lab at Central Michigan University began in 1999. The lab is headed by Tim Hartshorne, Ph.D. Children with CHARGE syndrome frequently engage in behavior that is challenging to those who work or live with them. The behavior is often described as obsessive compulsive, autistic-like, and stereotypical. The function of the lab is to investigate the biological, environmental, and individual factors that may be implicated in the etiology of these behaviors, with the aim of better describing the behavior and developing appropriate strategies for intervention and prevention. Current projects include: intervention for sleep issues, the development of social play, the decision-making process around g-tube removal, reviewing what is known about the brain in CHARGE, the experience of siblings, psychotropic medication use, Tai Chi as an intervention for sleep and emotion-regulation, and recreational activity engagement by children with CHARGE.

Sex hormones in CHARGE

Jeremy Kirk, Diana, Princess of Wales Children's Hospital, Birmingham, UK

Problems of puberty (delay, arrest or absence) are common in adolescents, and especially in boys. Dr. Kirk will present data on puberty problems in CHARGE syndrome, and the implications not only for development of sexual characteristics but also long-term osteoporosis. A variety of therapies are available, and the pros and cons of each will be described, which can where necessary be individually tailored, but the overall benefits must be balanced against any potential side effects

Pain and coping: Identifying and easing pain

Kasee Stratton, Mississippi State University, Starkville, MS

Understanding when and where a child or individual with CHARGE experiences pain can be perplexing due to their often limited communication and limited facial reactions to pain as a result of facial palsy. Davenport (2002) suggested that individuals with CHARGE might experience a higher-threshold for pain, also adding to the difficulty of identifying pain early. Stratton and Hartshorne (2010) found that children with CHARGE experience acute pain (e.g. migraine, surgery pain) and chronic pain (e.g. abdominal migraines, gastroesophageal reflux, hip/back pain) and hypothesized that individuals with CHARGE exhibit a high pain tolerance due to the significant number of days each year that they experience pain. Individuals with CHARGE may learn to cope with the pain experience and fail to communicate the degree of their pain. Further, Stratton has suggested pain behaviors for individuals with CHARGE, similar to individuals with vision impairment, are different than those of the general population due to their sensory deficits. As a result, a non-vocal pain assessment was developed specifically for individuals with CHARGE: *The CHARGE Non-Vocal Pain Assessment* (CNVPA, Stratton & Hartshorne, 2012). The results of the validation study for this 30-item

measure were found to be reliable and valid and serve as a helpful resource to parents, teachers, and nurses. Variation in items discriminating pain from non-pain by age suggests additional modification of the CNVPA is needed based on age. Once pain is identified, parents, caregivers, and medical professionals can assist children with CHARGE in easing their pain by using active distraction techniques, sharing information about procedures with the child before a medical exam, surgery and the like, and by teaching specific words, phrases, signs, gestures, or pictures to communication pain.

Development of a comprehensive Checklist guiding health screening and management considerations in individuals with CHARGE syndrome: a Delphi technique

Carrie-Lee Trider 1, Angela Arra-Robar 2, Kim Blake2, 1 Queen's University, Kingston, Ontario; 2 Dalhousie University, Halifax, Nova Scotia, Canada

There is a wide spectrum of medical, physical and psychological diagnoses in individuals with CHARGE syndrome. No simple guidelines for an approach to screening and management of clinical problems have previously been published for CHARGE syndrome. Health care providers could benefit from guidance to an approach to health supervision of individuals with CHARGE. We developed a one-page user-friendly checklist guiding health screening and management considerations in individuals with CHARGE across their lifespan, in a head to toe format. Consensus was obtained using the Delphi method. This is accompanied by a user-friendly one-page document providing further information about the clinical problems and supporting screening and management suggestions. This checklist could be utilized by the general practitioner as well as the multi-disciplinary team, including specialists and therapists to ensure comprehensive care and to help prioritize issues. We present and encourage discussion of the results of our consensus-based checklist and one-page supporting document. This discussion is intended for parents and all members of the multi-disciplinary team involved in the care of an individual with CHARGE syndrome. After additional feedback and revision the questionnaire will be published.

Aspects of immunological and adrenal function in CHARGE syndrome

Monica Wong, Gianni Bocca, Annechien Lambeck, Mirjam van der Burg, Sasha laBastide-van Gemert, Lianne Hogendorf, Elisabeth Schölvinc, Conny van Ravenswaaij-Arts, University Medical Center Groningen, and Erasmus Medical Center, Rotterdam, the Netherlands

Introduction and background: Children with CHARGE syndrome have frequent infections, which increase their morbidity and mortality. Anomalies in the upper airway contribute to this susceptibility to infections. Immunological abnormalities may also be a contributing factor as has been shown in the clinically overlapping 22q11.2 deletion syndrome. Moreover, unknown subtle adrenal insufficiency may complicate the course of infections, as has been reported in children with Prader-Willi syndrome. The aim of this study is to explore the presence of immune as well as central adrenal dysfunction in children with CHARGE order to optimize the management of care in these patients. **Methods:** Patients with molecularly proven CHARGE syndrome, aged 20 months till 18 years, were recruited from the Dutch Expert Clinic for CHARGE Syndrome. All patients

completed a questionnaire on infectious history, and their immune system was studied extensively and adrenal function was assessed by the low dose ACTH test and, if abnormal, followed by a glucagon stimulation test. Results: Twenty-four patients were included in the study. Otitis media (n =16, 67%) and pneumonia (n=7, 29%) were the most frequently reported infections. The most important findings of the immunological studies were: 1) decreased T-cells (n=12, 50%), 2) impaired formation of memory B-cells, and 3) reduced immune responses to vaccines given in childhood (n=19, 83%). Adrenal function was tested in 23 patients and insufficiency was confirmed in only one patient of the seven patients who had undergone both adrenal function tests. Conclusions: Frequent infections in combination with a high percentage of immunological abnormalities indicate that further research is needed to develop evidence-based guidelines to protect these children from excess morbidity and mortality due to infections. Based on our results, we recommend specific immunological laboratory tests in children with recurrent infections. Booster vaccinations are advised for children with reduced immune responses to vaccines. However, central adrenal insufficiency is not common in CHARGE syndrome. There is thus no need to screen and to take preventive measures regarding the adrenal function in children with CHARGE syndrome.

ABSTRACTS-POSTERS

Expressive communication skills of children with CHARGE syndrome

Alexandria Cook and Charity Rowland, Oregon Health and Science University, Portland OR

The *Communication Matrix* (Rowland, 1990, 2004), available without cost at www.communicationmatrix.org, is an assessment tool for children and adults with complex communication needs that is used world-wide to show how individuals at the earliest stages of communication development express themselves. It is used by parents and professionals from many countries to assess the expressive communication skills of early communicators, especially those who use augmentative and alternative communication. This assessment is unique in measuring all possible communicative behaviors used by individuals who have no speech or who have minimal speech. Assessment data are captured in a database that currently contains over 90,000 assessments, many of which were conducted on children who experience rare disorders associated with communication challenges. At this writing, assessments on over 169 children ages 0-21 years residing in the U.S. are included in the database. Through these data a portrait of communication skills in children with CHARGE syndrome is presented. While many studies present data collected from either parents or professionals, we include data from educators, speech-language pathologists and parents. Similar to the findings of Thelin and Fussner (2005) derived from parent surveys, the Communication Matrix data indicate that the majority of individuals with CHARGE have mastered pre-intentional behaviors, intentional behaviors, and unconventional communication. Many also have emerging skills using conventional communication and concrete symbol systems to communicate messages related to refusing unwanted items and obtaining desired items. A composite portrait of

communicative behavior in children with CHARGE syndrome, to which stakeholders across the U.S. have contributed, is the major purpose of this poster.

CHARGE Syndrome Clinical Database Project (CSCDP): findings and future direction of a web-based, parent-report registry.

Margaret Hefner, Emily Fassi and Kevin Ballard, Saint Louis University, St. Louis MO

CSCDP is a web-based, parent-completed database project. This database and registry of individuals with CHARGE syndrome (CS) will help to better describe the syndrome and its natural history and will greatly facilitate CHARGE syndrome research. It went live May 15, 2013. As of July 1, 2015, more than 100 participating families had entered complete information on their children with CHARGE. Validity of parent-entered data is demonstrated by frequency of features (e.g. coloboma, choanal atresia, heart defects, and kidney abnormalities) matching what is reported in the medical literature. The database currently has 13 sections, including demographics, birth history, CHARGE features and genetic testing and milestones such as walking, acquisition of language and growth. Interesting and somewhat unexpected findings include the high reported incidence of seizures (39%), gastrostomy or g-j feeding (66%) and tracheostomy (25%). Seeing the distribution – rather than simply average - of milestones such as age of walking or potty training can be helpful for parents whose children have not yet reached those milestones. In the future, we expect to add sections to the database and hope to be able to collect longitudinal data on individuals with CHARGE syndrome. Data from CSCDP will be made available as baseline information to CHARGE research studies with IRB approval and Data Use Agreements with CSCDP and Saint Louis University. This will benefit families by making it possible for them to participate in multiple research studies without answering the same basic questions over and over.

Advice from siblings of persons with CHARGE

Hayley Hoesch & Timothy S. Hartshorne, Central Michigan University, Mount Pleasant, MI

There exists little published research on the experience of siblings of children with disabilities. We asked siblings “What advice would you give to others who have a sibling with CHARGE?” This is a sampling of what they said. *General advice:* People are people; Don't be depressed, because it's not a bad thing to have a sibling with CHARGE; Get the facts when you're young, this will make it easier to understand; Try not to be embarrassed of them - it wasn't their choice to be born with CHARGE; Love them unconditionally. *Patience:* Don't flip over every little thing; Some days will be awesome, and other days, the crap will hit the fan; Just take everything one step at a time, and you'll do fine; Be patient, understanding, and put yourself in their shoes. *Acceptance:* Accept who they are, not what they're not, the more you understand them, the more you grow to love them. *Social:* Don't be afraid to bring your friends around. In most cases, they are interested more so than scared; If you act at ease, so will those around you; Feel free to tell people about your sibling and what holds them back in life. *Family:* Don't let your parents treat siblings differently; Remember they are still a wonderful, smart, and energetic part of the family; They don't express it the same way

we do, but they understand and can teach us a lot! *Skills*: Learn sign language; Try to find something you can do together, like video games or rock climbing. *“Go with the Flow”*: Be thankful for everything you are capable of and learn to go with the flow; Don't take life too seriously (but stay driven and focused on your own goals); There are happy moments when things make them "more normal", but there are also so many hard times; Having a brother with CHARGE has helped shape the person that I am today! He is the most wonderful person I know- he is loving, funny, and can find enjoyment out of the smallest things; Embrace the journey.

Experiences with mouth over-stuffing and pocketing of food in cheeks during eating in individuals with CHARGE syndrome

Alexandra Hudson, Meghan Macdonald, Kim Blake, Dalhousie University, Halifax, Nova Scotia, Canada

OBJECTIVE: Individuals with CHARGE syndrome commonly experience adverse oral eating behaviors. These include over-stuffing their mouth or pocketing food in their cheeks, which is not well described and may have serious consequences such as aspiration. These feeding issues may be associated with CHARGE syndrome characteristics such as oral sensory impairment. In this study, we interviewed parents to help better describe the mouth over-stuffing and food pocketing feeding behaviors in individuals with CHARGE syndrome and assessed the resulting parental impact. **METHODS:** Parents of individuals with CHARGE syndrome who experienced mouth over-stuffing and/or food pocketing in cheeks during eating completed an in-depth semi-structured interview and a Feeding/Swallowing Impact Survey. **RESULTS:** Twenty parents were interviewed, each detailing their child/adult's (age range 2-31 years) experiences with eating and swallowing over their life. Fifteen individuals with CHARGE syndrome (75%) pocketed food in their cheeks and palate, and several (n=7, 35%) pocketed food for hours after a meal. Three individuals (15%) also pocketed saliva in their cheeks. Qualitative interview transcript analysis revealed 3 main themes of mouth over-stuffing: (1) increased risk of choking (2) time to eat a meal was decreased or increased and (3) the presence of structured and repetitive feeding behaviors. Cranial nerve dysfunction, abnormal tongue movement, and cleft palates negatively impacted the individuals' feeding difficulties. **CONCLUSION:** This is the first in-depth study to describe mouth over-stuffing and food pocketing feeding behaviors in individuals with CHARGE syndrome. Oral feeding therapy should target interventions to specifically address these problematic feeding issues.

Role of CHD7 in nerve formation

Fumiaki Imamura, Pennsylvania State University, Hershey, PA

Mutations in *CHD7* gene have been detected in more than half of all children with CHARGE tested to date. *CHD7* is a member of the chromodomain helicase DNA-binding (chd) family that regulates gene transcription, and most of the chd family members play critical roles during developmental processes. We are studying the development of mouse brain, and focusing on the molecular mechanisms underlying olfactory tract formation. The olfactory tract is a bundle of axons of projection neurons of

the olfactory bulb, and abnormal olfactory tract is observed by *chd7* mutation. Results of our *chd7* suppression experiments suggest that *chd7* plays a major role in olfactory tract formation. However, almost nothing is known about the role of *chd7* in neural circuit formation. My research aims to reveal the role of *chd7* in olfactory tract formation during mouse brain development. Specifically, I am currently conducting a research project to identify molecules whose expression is regulated by *chd7* in developing olfactory bulb projection neurons. In this project, *chd7* expression is suppressed by RNA interference (RNAi) technique in developing projection neurons, and the transcriptome profile of the neuron will be determined by RNA-seq analysis to create a list of molecules whose expression level is affected by *chd7* knockdown. This project is kindly supported by 2014 Pilot Grant from the CHARGE Syndrome Foundation.

CHARGE syndrome: Inclusive recreation

Gretchen Imel and Timothy S. Hartshorne, Central Michigan University, Mount Pleasant, MI

Recreation and leisure activities comprise a critical dimension of the quality of life for all people, a vital component of personal expression and interaction that can open paths to adventure, confidence, and health. However, some children have never run a mile, batted a ball, jumped off a diving board, or been asked to play in a soccer game – all because they have some sensory impairment. This is true for individuals diagnosed with CHARGE syndrome. Nonetheless, almost any sport can be modified using technology or adaptive equipment to accommodate participation at any ability level (www.atra-online.com). This poster reviews four programs: Challenge Mountain is an adaptive ski slope in Michigan that guarantees any person can experience skiing. Camp Abilities Brockport is a one-week developmental sports camp for children and teens who are blind, visually impaired, and deafblind. The mission of Camp Abilities Brockport is to empower children and teens with visual impairments to be physically active and productive member of their communities, as well as to improve the health and well-being of people with sensory impairments. Equestrian therapy, which exists in many places, is the use of horses and equine-assisted activities in order to achieve goals that enhance physical, emotions, social, cognitive, behavioral, and educational skills for people who have disabilities. The Ethan Wolfe Recreational Assistance Program provides individuals with CHARGE syndrome the opportunity to participate in recreational activities. This program is need-based and funded through a generous gift from The Wolfe family and friends.

Family demographics and parent relationships in CHARGE syndrome

Dominik Keller, Madison Sully & Kasee Stratton. Mississippi State University, Starkville, MS

The dynamics and demographics of families have undergone many changes over time. To the best of our knowledge, no previous investigations have reviewed family demographics or family dynamics in CHARGE syndrome. The following research questions are posed: 1) What are the most common family composition patterns

among families who have a child with CHARGE syndrome (i.e. two-parent, divorce-remarried, single)? 2) Is there a “CHARGE syndrome advantage” or reduced risk of divorce/ separation, similar to families who have a child with Down syndrome? 3) Do families of children with CHARGE have subsequent children and what is the birth order? 4) How do parents believe their family composition has changed since having a child with CHARGE? Previous literature by Burke and colleagues (2011) have found families of children with Down syndrome and with spina bifida were more likely to have subsequent children and larger family sizes than the general population. We hypothesize that families with a child with CHARGE will have subsequent children. Secondly, Urbano (2007) described what is known as the “Down syndrome advantage,” based on research suggesting that individuals who have a child with Down syndrome separated less than parents who had a child who did not have disability or compared to couples who had a child with a birth defect. We hypothesize that families of children with CHARGE will have a divorce/separation rate equivalent or less than that of the general population. Our research will present literature related to divorce/separation, family demographics, and disability as it relates to CHARGE.

Review of two research-based methods for improving sleep in children with developmental disabilities

Benjamin Kennert and Timothy S. Hartshorne, Central Michigan University, Mount Pleasant, MI

Sleep problems are common among children with various developmental disabilities, and has been indicated as a problem among children with CHARGE syndrome, with the most common category of sleep difficulty being initiating and maintaining sleep (Hartshorne et al., 2008). In addition, a survey of adolescents and adults with CHARGE has shown that half continue to report sleep difficulties (Blake et al., 2005). It is important to address sleep problems of children, because child sleep problems have been shown to be related to poorer quality of life, lower caregiver well-being, poorer daily functioning of the child, behavioral difficulties, and school difficulties (Sung et al., 2008; Hartshorne et al., 2008). Two treatments for sleep problems that have been reported to be effective with children with developmental disabilities are melatonin and positive bedtime routines. These treatments are most useful for problems related to initiating and maintaining sleep. Melatonin is often produced at lower rates in individuals with visual impairments, and this can result in irregular sleep cycles (Heussler, 2011). Positive bedtime routines are consistent routines before bedtime that promote sleep and may help to regulate sleep cycles (Durand, 1998). Although these treatments have not yet been studied in children with CHARGE syndrome, they may be useful treatments for this population.

Psychotropic drugs used in children with CHARGE syndrome

Claire Latus-Kennedy and Timothy S. Hartshorne, Central Michigan University, Mount Pleasant, MI

The purpose of this poster was to inform viewers of the published effects and side effects of psychotropic drugs commonly prescribed for children with CHARGE

syndrome. Parents were asked on the CHARGE facebook page what psychotropic medications their child uses. The most commonly mentioned were Zyprexa, Risperdal, Catapres, Prozac, Lamictal and Zoloft. The active ingredients, typical reasons for prescribing, and major side effects were listed for each. There is little research available regarding the effects of these drugs on children. Furthermore, there is no research to be found on the effects of these medications on children with CHARGE syndrome. Dosage of the drugs given to children should be monitored very closely for the safety of the child. The lack of research means that psychiatrists have limited guidance in prescribing for children with CHARGE. In order to assist the child they may prescribe “off label” (using a medication for other than specific purpose for which it was developed). Parents should have conversations with their child’s physician regarding the specific medications being prescribed.

Experiences with feeding and gastrointestinal motility in children with CHARGE syndrome

Meghan Macdonald, Alexandra Hudson, Elyanne Ratcliffe², Angela Bladon², Kim Blake¹, ¹ Dalhousie University, Halifax, Nova Scotia, ²McMaster University, Hamilton, Ontario, Canada

Background: Feeding and gastrointestinal (GI) motility issues are very common and concerning problems in individuals with CHARGE syndrome. Despite the importance of this issue, there is little empirical research on GI motility in this population. Objective: The aim of this study was to expand upon the limited knowledge base of feeding and GI issues in children with CHARGE syndrome. Methods: Parents of individuals with CHARGE syndrome were recruited through CHARGE syndrome groups and CHARGE Syndrome Facebook pages. Participants completed questionnaires including: CHARGE characteristics; open-ended questions regarding feeding; Pediatric Assessment Scale for Severe Feeding Problems © (PASSFP); and PedsQL™ Gastrointestinal Symptoms Scale. Results: The CHARGE characteristic information confirmed that our population was representative of a typical CHARGE syndrome group. The PASSFP compared tube feeding, partial oral feeding, and complete oral feeding. One-way ANOVA revealed a significant effect of feeding type on the mean PASSFP score. Student’s t-tests of the PedsQL™ Gastrointestinal Scale revealed that children who were tube fed had significantly more GI symptoms compared to oral feeders in the following domains: stomach hurt and pain; stomach discomfort when eating; food and drink limits; trouble swallowing; nausea and vomiting; and constipation. Children with choanal atresia/stenosis had significantly more GI symptoms than children without this feature. Children with cranial nerve IX, X, and XI dysfunction had significantly more GI symptoms than participants without. The greatest feeding challenges reported were bowel regulation (n=19, 30%), vomiting (n=12, 19%), and choking (n=11, 17%). Discussion: Feeding difficulties are present throughout the entire GI tract in many individuals with CHARGE syndrome. Children who were tube-fed had the most severe feeding problems and GI symptoms. The clinical features of choanal atresia/stenosis and cranial nerve dysfunction IX, X, and XI were found to be associated with more severe GI symptoms, which may relate to GI tract innervation.

"Wow, that sounds familiar": Parent-child playgroups for families of children with deaf-blindness

Julie Maier, California Deaf-Blind Services, San Francisco, CA

This poster presents the components and outcomes of biweekly Parent-Child Playgroup facilitated by an early intervention specialist from Center on Early Intervention on Deafness (CEID) and educational specialists from California Deaf-Blind Services (CDBS) in the San Francisco Bay Area. The group included the facilitators and approximately five families. The families had children ranging from 8 months to 5 years of age. Three families had a child with CHARGE syndrome. The initial purpose of the group was to provide an interactive forum for information provision, modeling, and practice of skills and strategies parents could use at home to support their child's early development. Two additional outcomes of these regular playgroup meetings have included 1) parents' enhanced confidence in advocating for their child's educational needs and rights and 2) the development of a strong support network for these families. It is not always easy to find another family in your community who understands what it's like to raise a child with CHARGE or deaf-blindness. We discovered that the opportunity to be around other families who "get it" and also wanted to learn more about deaf-blindness was very appealing to these families. The components of the presentation include information about the local Early Start grant that funded this project; collaborative planning that occurred between the two agencies; recruitment of families to join the playgroup; initial goals of the group; training topics covered during the group meetings; a typical schedule of group meeting; special events that occurred at some meetings; and final outcomes. Special attention is paid to identifying potential funding sources; components that we found to be most successful related to useful information and resources, modeling, and supportive discussions; and the growth in confidence and advocacy we saw develop among the parents in the group.

Parental decision-making in the removal of gastrostomy tubes or buttons

Rachel Malta and Timothy S. Hartshorne, Central Michigan University, Mount Pleasant, MI

Gastrostomy tubes are often used to maintain adequate nutrition for children with CHARGE from young ages, but many parents decide to have the tube removed over time. Due to a lack of literature on the parent decision-making surrounding the removal of the tube in CHARGE syndrome, a survey was distributed via SurveyMonkey® to parents of these individuals through social media. The survey addressed parental support needs and decision-making process through retrospective and prospective questions. The most common reasons for removal included: majority of nutrition through oral feed (tube no longer needed), granulation build-up at site of stoma, leakage from stoma, continuous infections at site of g-tube, and social reasons. The most common reasons against removal included: inability to orally maintain adequate intake or maintain hydration, underweight/less than normal weight, takes medications primarily through g-tube. Participants indicated professionals who were most helpful to them included: occupational therapist, nutritionist, surgeon, pediatrician, and gastrointestinal specialist. 63% of participants indicated they did not use social media to gather opinions

and advice, though many indicated in additional responses that other parents within the CHARGE community were able to answer questions in a more satisfactory way than other medical professionals. Information from this survey may be helpful to parents as they go through this process as well as to health professionals as they consult with parents to provide good decision-making.

What we know of the CNS in CHARGE syndrome

Amanda Odren and Timothy S. Hartshorne, Central Michigan University, Mount Pleasant, MI

Any brain and/or cranial nerve anomaly can be consistent with CHARGE syndrome. Many brain disorders in CHARGE are diagnosed or presumed solely on the basis of behavioral observation. This poster presentation provides an overview of the known brain anomalies seen in CHARGE, highlights the discrepancies in the current research, and focuses on promoting a greater awareness of the need for up-to-date research involving the central nervous system (CNS) in CHARGE syndrome. The relationship between functional deficits and CNS malformations in CHARGE syndrome has not been described well in the literature, and CNS malformations have not been studied extensively. Current research claims that CNS defects, such as arhinencephaly, hypoplasia of the cerebellum, and brainstem and cerebellar heterotopia are detected in 70–80% of CHARGE syndrome cases. This incidence is in the same range as other more regularly reported clinical features of CHARGE syndrome: coloboma (82%), atresia of the choanae (57%), ear abnormalities and deafness (95%), cranial nerve dysfunction (61%), heart defects (80%), retardation of growth/development (90%), and genito-urinary anomalies (60%). CNS defects are likely to represent a significant component of the clinical spectrum that typifies CHARGE syndrome, but without additional research, the exact scope of CNS defects associated with CHARGE syndrome and CHD7 deficiency is unknown.

How do we raise awareness for CHARGE? A study of Facebook and Twitter outcomes

Hailey Ripple, Daniel Gadke and Kasee Stratton, Mississippi State University, Starkville, MS

The world of social media offers a unique outlet for raising awareness of CHARGE syndrome. For example, a recent investigation by Gadke, Stratton, & Butts (in preparation) found that 4,928 tweets were collected in a 24-hour period on the topic of autism. Our study involved the use of a Social Media Tracking and Analysis System (SMTAS), in a big data laboratory to collect data on tweets from Twitter on CHARGE syndrome from January to April, 2015. Simultaneously, additional data collection occurred on the CHARGE Syndrome Facebook page. SMTAS allows the user to choose key words and phrases, location, and other identifiers to track tweets related to a desired topic. Key words and phrases for this study included “CHARGE syndrome.” Data were collected internationally and was not limited to English. For the CHARGE Syndrome Facebook page, data analysis involved examining the frequency of certain topics discussed, ultimately resulting in fifteen of the most popular topics, and was limited to English. The most popular themes from Twitter and Facebook were

compared. Twitter data were analyzed by creating “buckets” on the SMTAS software, allowing the user to exclude certain tweets or phrases not related to CHARGE syndrome. After excluding tweets unrelated to CHARGE, the remaining tweets were exported to an excel file where they could be more easily analyzed and divided into themes. It was hypothesized that Twitter would be used less frequently, despite having the potential for greater awareness of CHARGE; whereas, Facebook would serve to connect individuals with CHARGE and their families to share resources and support. The top six themes identified on Facebook included: videos/photo sharing, sharing resources, feeding, fundraising, academic and school issues, and discussion of the (then upcoming) CHARGE conference. Twitter themes included CHARGE awareness, personal tweets about individuals, resource sharing, fundraising, specific features of CHARGE, and discussion of the CHARGE conference. A total of 440 tweets were collected from January to April, 2015. Such data suggests a much smaller population is using Twitter to raise awareness of CHARGE when compared to the 4,630 members of the CHARGE Syndrome Facebook Page. Ultimately, Facebook serves as a resource to those in the CHARGE community already familiar with CHARGE; however, Twitter can serve as the primary awareness tool for the general population.

Genetic testing in patients suspected of having CHARGE syndrome

Cheryl Scacheri, Chris Lauricella, Toni Lewis, Rebecca Fowler, Jennifer Siegel, Jane Juusola, Sherri Bale. GeneDx, Inc, Gaithersburg, MD

Genetic testing for patients with features of CHARGE syndrome may provide helpful information to families and health care providers. Our laboratory has analyzed the *CHD7* gene in over 1,000 samples that were referred for sequence analysis and/or deletion and duplication analysis. We have also performed whole exome sequencing (WES) on samples from several patients with some features of CHARGE syndrome. In some of these cases, *CHD7* mutations were identified. In others, however, other genes were likely to be the underlying cause of their CHARGE-like features. Aside from *CHD7*, no single gene has yet been shown to have a recurring association with CHARGE syndrome. However, the diverse genetic diagnoses provided by WES may be helpful to some patients, particularly those who are negative for *CHD7* mutations and present with atypical findings.

The development of play in CHARGE syndrome

Megan Schmitt and Timothy S. Hartshorne, Central Michigan University, Mount Pleasant, MI

Play is a fundamental aspect of development. As children age they progress through different stages of play supporting their social, emotional, and cognitive development. Many factors affect play and the way a child progresses through play. Conditions that may inhibit the development of play include sensory impairment, motor problems, communication delays and cognitive impairment. Children with disabilities involving sensory limitations typically spend less time playing compared to typically developing peers (Gowen, Goldman, Johnson-Martin, & Hussey, 1989). Children with a hearing impairment seem to spend less time in higher stages of social play and more time in

lower stages of social play compared to hearing peers. Specifically, children with a hearing impairment engaged more frequently in solitary play (Johnson, Christie, Wardle, 2005) and less time in cooperative play compared to hearing peers. Children with visual impairment reportedly progress through play stages at later ages than typically developing children. This could be because a child with vision impairment does not begin engaging in social play until a later age or spends more time in different stages of social play (Troster & Brambring, 1994). It has been found that children with motor impairments experience a significantly lower developmental play age for social play and cooperation compared to typically developing peers (Kennedy-Behr, Rodger, & Mickan, 2013). Overall, children with an intellectual disability interact less frequently with their peers compared to typically developing children. Instead, they commonly participate more in solitary play or unoccupied and onlooker behavior (Guralnick & Groom, 1987; Leach, Pratt, & Roberts, 1990). Interventions have been developed to assist with the development of social play. Studying play in individuals with CHARGE syndrome can help to develop interventions for these children to aid in their development.

CHARGE syndrome and characteristics of autism spectrum disorder: examining similarities and differences

Hallie Smith, Daniel Gadke, MacKenzie Sidwell, & Hallie Smith. Mississippi State University, Starkville, MS

Many families with a child with CHARGE syndrome report their children have been given a comorbid diagnosis of Autism Spectrum Disorder (ASD). Previous research has shown a significant over-representation of ASD among individuals with a congenital condition (e.g. Mobius syndrome, Joubert syndrome; Johansson et al., 2001; Azonoff et al., 1999). The cognitive, social, and communication deficits that are present in children with ASD are very similar to the deficits experienced by individuals with vision and hearing loss or other sensory impairments, such as individuals with CHARGE (Vervloed, Hoevenaars-van den Boom, Knoors, van Ravenswaaij, & Admiraal, 2006). This begs the question, could ASD be over-diagnosed or misdiagnosed among individuals with CHARGE syndrome? CHARGE syndrome is the leading genetic cause of congenital deaf-blindness and further presents with additional sensory deficits (e.g. anosmia). This high prevalence of ASD in children with sensory deficits has led researchers in the field to suggest that there may be an over-diagnosis of ASD among children who have sensory impairments, due to the similarities of behavior expression of these diagnoses (Andrews & Wyver, 2005; Cass, 1998; Hobson, Brown, Minter, & Lee, 1997). In order to meet diagnostic criteria for ASD, individuals must present with deficits in social communication and interaction along with restricted, repetitive patterns of behavior, interests or activities (American Psychiatric Association, 2013). We hypothesize that individuals with most often CHARGE do not meet full diagnostic criteria given their level of social engagement. The CHARGE syndrome behavior phenotype states that individuals with CHARGE are socially interested, but immature in presentation, which is suspected to be related to sensory deficits. The proposed study is designed to better understand the similarities and differences between CHARGE and ASD with a larger sample size than has been previously reported in the research literature, and including gold standard ASD assessment tools (e.g. Autism Diagnostic

Interview-Revised).

The Bulldog CHARGE Syndrome Research Lab at Mississippi State University

Kasee Stratton, Hailey Ripple, MacKenzie Sidwell, Hallie Smith, Mady Sully, & Dominik Keller, Mississippi State University, Starkville, MS

The Bulldog CHARGE Syndrome Research Lab at Mississippi State University conducts research and helps to spread awareness of CHARGE Syndrome. The lab is composed of graduate students in school psychology and undergraduate students in psychology, pre-medicine, and related fields. The Bulldog CHARGE Research Lab is under the direction of Dr. Kasee Stratton, an assistant professor and licensed psychologist who has researched CHARGE for over 10 years. Our mission is to improve the lives of individuals with CHARGE in the school, home, and hospital. We seek to investigate areas that are important to families, professionals, and individuals with CHARGE. Additionally, the lab is designed to create a diverse group of advocates and future professionals who are well informed of CHARGE Syndrome and can provide evidence-based interventions to support this community. Our current research agenda includes the following projects: non-vocal identification of pain, comorbid diagnoses, and educational plans and interventions. We also partner with other CHARGE researchers and welcome collaboration across disciplines.

Take time for yoga

Rebekka Valian, W. Ross Macdonald School for the Blind, Brantford Ontario, Canada

Creating time and space for yoga can be invaluable to your student's growth. Adapting the class for your individual student's preferences and strengths can be easy if you keep a few guidelines in mind, if you are a yoga teacher as well. I'd like to share the film showing one such class. My yogi is a young man, sixteen years old, with CHARGE. He is in a school for students with deafblindness. Watch the magic unfold.

Assessing attachment in mother-child relationships in rare syndrome contexts

Nicole Vian, Milano-Bicocca University, Italy

The role of attachment proves to be one of the mediation factors in the relationship between child trauma and the overcoming of the trauma itself. The short and long term effects of traumatic experiences linked to numerous hospitalizations, as lived outside the family, should be mediated by the mental models developed by the subject in relation to her/his own attachment relationships with adults caregivers. Thus it is important to highlight the mother-child attachment patterns in rare syndrome contexts, so as to implement intervention plans aimed at increasing mothers' awareness of their caring style and at improving mother-child dyadic relationship. The present research aims at investigating mother-child attachment styles in rare syndrome contexts. Methods uses are the Attachment Q-sort (AQS, Waters & Deane, 1985) and Attachment Style Questionnaire (ASQ; Feeney, Noller & Hanrahan, 1994) and written autobiographies.

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