11th International CHARGE Syndrome Conference Thursday, July 25, 2013 Professional Day Program Handouts

CHARGE Syndrome Foundation, Inc.

Category: Medical Genetics

Thursday
9:15-9:40
Palomino 1-3

Functions for CHD7, the Gene Altered in CHARGE, in Developing Cells and Tissues

Donna Martin, Joseph Micucci, and Ethan Sperry

The University of Michigan Medical School

Presenter Information:
Mutations in the *CHD7* gene are a common cause of CHARGE. Our laboratory has been studying mice with mutations in the *Chd7* gene. We will discuss recent data indicating roles for CHD7 in development of skeletal structures and in stem cells of the ear, nose, and brain.

Presentation Abstract:
CHD7, the gene for chromodomain DNA-binding protein 7, is a common genetic cause of CHARGE Syndrome. CHD7 is highly expressed in developing human and mouse embryos, especially in stem cells and tissues that are affected in CHARGE. In order to identify the underlying mechanisms by which CHD7 regulates organ growth and development, our laboratory has generated and analyzed mice with mutations in the mouse *Chd7* gene. Mice with reduced *Chd7* function have many of the same structural and functional deficits as those observed in CHARGE; thus, detailed understanding of *Chd7* function in mice can provide critical information for designing effective therapies. We will present recent data show CHD7 functions in the development of stem cells of the ear, nose, and brain and in development of craniofacial structures. We will also discuss progress using induced pluripotent stem cells generated from skin cells of children with CHARGE and *CHD7* mutations. Together, these studies are helping to pave the way for novel, innovative strategies to develop regenerative therapies for individuals with CHARGE.

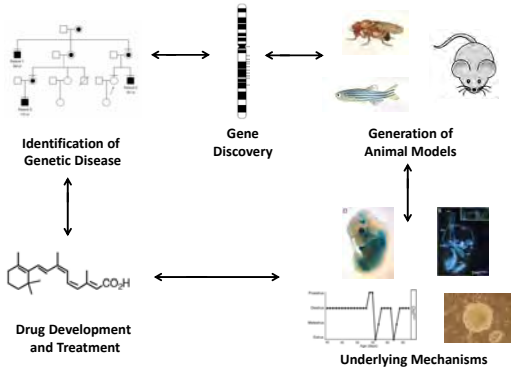
CHARGE Syndrome: Advances in Research

C.S. Mott Children's and von Voigtlander Women's Hospital, The University of Michigan

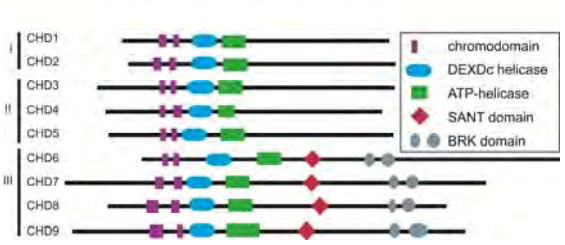
Donna M. Martin MD, PhD
Joe Micucci, BS
Ethan Sperry, BS

The University of Michigan Departments of Pediatrics, Human Genetics, and the Medical Scientist Training Program

Exploring Genetic Mechanisms in CHARGE

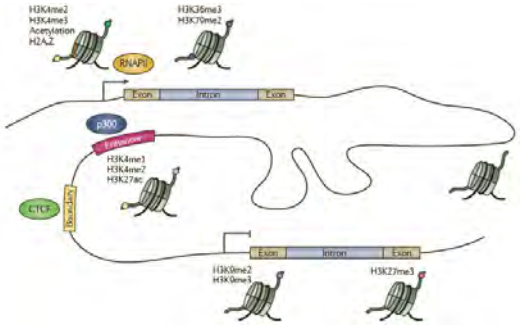


Chromodomain Helicase DNA-binding (CHD) Family



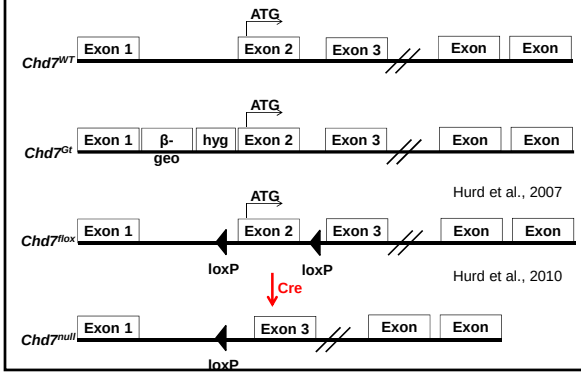
Layman et al. *Clin Genetics* 2010

Gene Structure and Chromatin Modifications



Zhou, VW. et al. *Nature Reviews Genetics*. 2011.

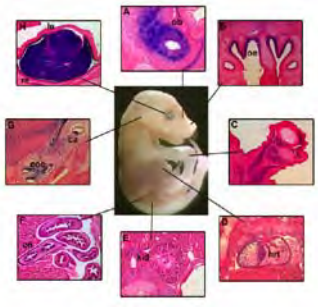
Chd7 alleles



Hurd et al., 2007

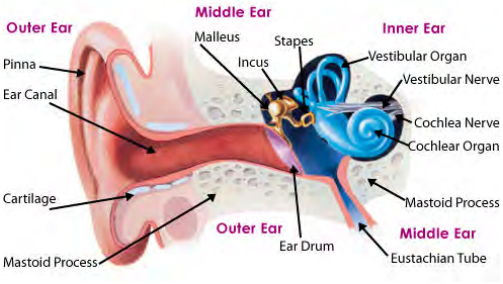
Hurd et al., 2010

Chd7 expression is tissue-restricted during development



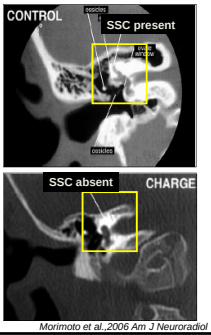
Liz Hurd

Layman et al., *Clin Genetics*, 2010



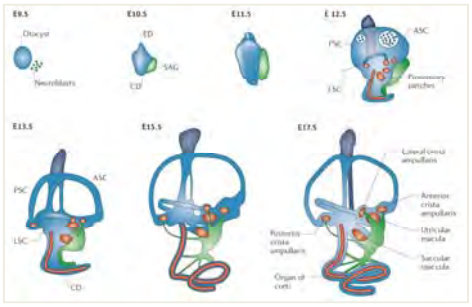
CHARGE is associated with semicircular canal hypoplasia

- Semicircular canal hypoplasia with vestibular dysfunction is common (temporal bone CT scan)
- Lateral SCC is always involved, while the superior or posterior may be normal
- Patients display abnormal canal vestibulo-ocular responses (>90%)



Morimoto et al.,2006 Am J Neuroradiol

Inner Ear Development

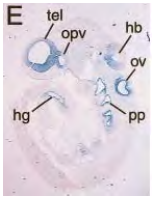


Kelley, 2006 Nat Rev. Neurosci.

Conditional Mutant Mice

$Chd7^{flox/flox}$ × $Foxg1\text{-}Cre;Chd7^{Gt/+}$

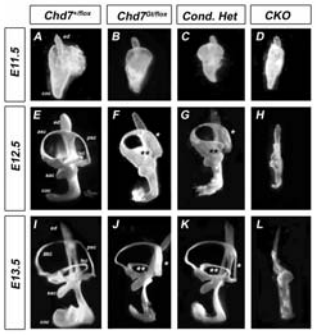
$Chd7^{+/flox}$ $Chd7^{Gt/flox}$ $Foxg1\text{-}Cre;Chd7^{+/flox}$ $Foxg1\text{-}Cre;Chd7^{Gt/flox}$



Hurd et al., 2010

Hebert and McConnell, 2000

Inner ear formation requires *Chd7*

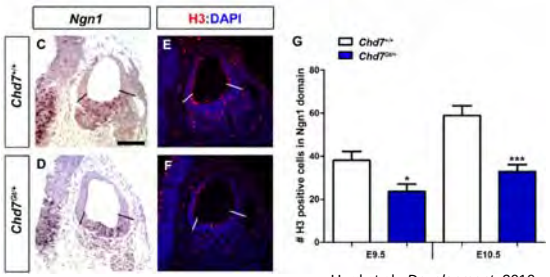


Liz Hurd

Elyse Reamer

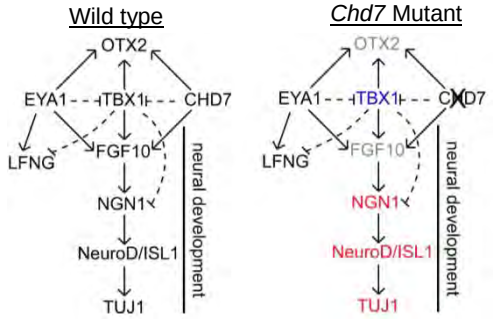
Hurd et al., *Mechanisms of Development* 2012

Chd7 mutants have reduced proliferation in the neurogenic domain



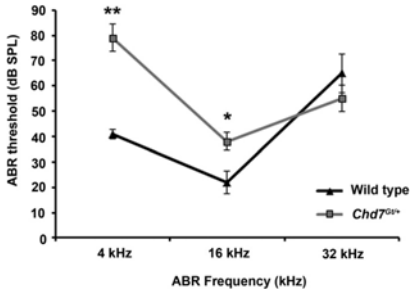
Hurd et al., *Development*, 2010

Model for CHD7 Developmental Gene Regulation in Inner Ear



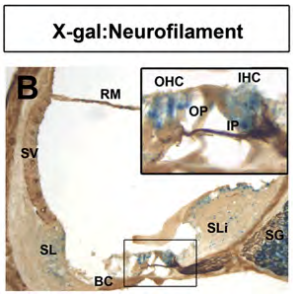
Hurd et al., *Development*, 2010

Chd7$^{Gt/+}$ mice have mild hearing loss



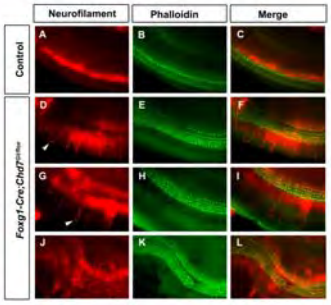
Hurd et al., *Hearing Research* 2011

Chd7 is expressed in the mature cochlea



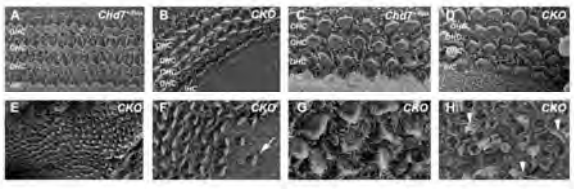
Hurd et al., *Hearing Research* 2011

Cochlear innervation is abnormal with complete loss of *Chd7*



Hurd, unpublished

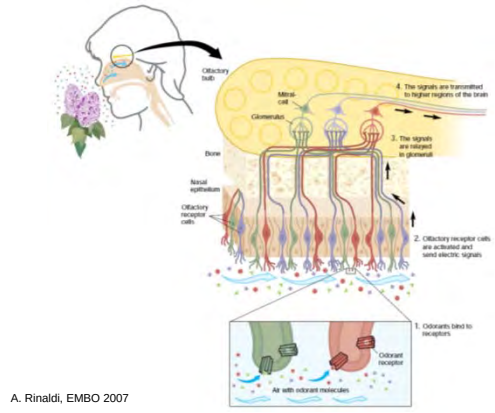
Cochlear hair cells are disorganized with loss of *Chd7*



Hurd, unpublished

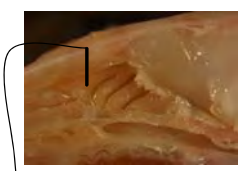
Lessons Learned

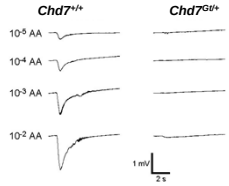
- CHARGE is a genetic disorder caused by *CHD7* mutations
- Mice are an excellent model of CHARGE
- The mouse *Chd7* gene is required for proper inner ear development and for hearing



A. Rinaldi, EMBO 2007

Electro-olfactograms show severely impaired olfaction in *Chd7* mutant mice

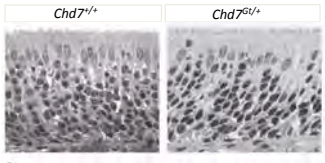


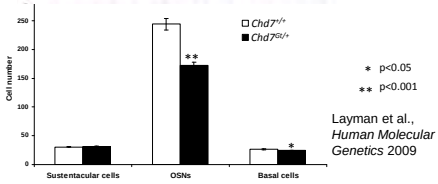


www.roscreaonline.com

Wanda Layman et al., *Hum Mol Gen,* 2010

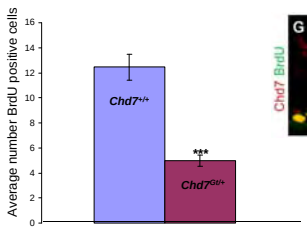
Olfactory sensory neurons are reduced in *Chd7*$^{Gt/+}$ mice

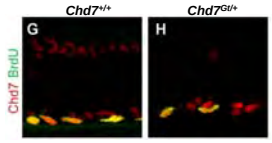




Layman et al., *Human Molecular Genetics* 2009

Cellular proliferation is reduced in the *Chd7* mutant olfactory epithelium

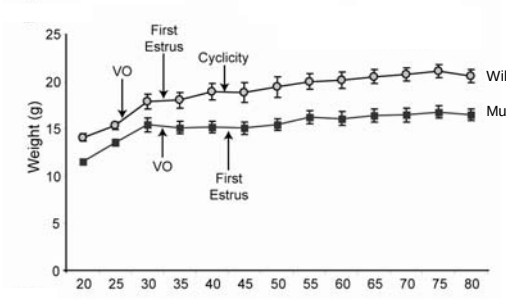




Chd7 is expressed in proliferating basal cells

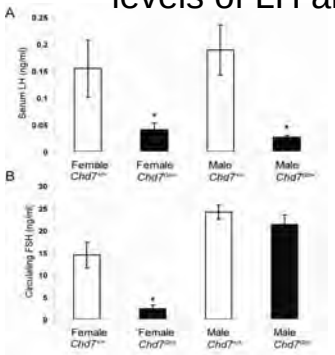
Cellular proliferation in basal cells is reduced by >50% in adult *Chd7*$^{Gt/+}$ mice

Chd7$^{Gt/+}$ female mice have delayed puberty



Layman et al., *Human Molecular Genetics* 2011

Chd7$^{Gt/+}$ mice have decreased levels of LH and FSH

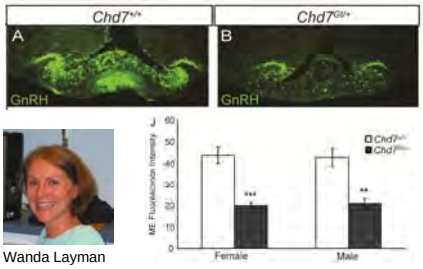


Chd7$^{Gt/+}$ females and males have reduced LH

Chd7$^{Gt/+}$ females have reduced FSH

Layman et al., Human Molecular Genetics 2011

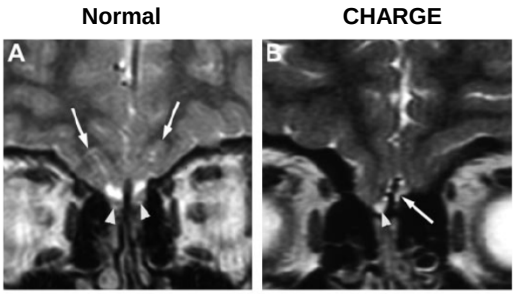
GnRH is reduced in the median eminence of *Chd7*$^{Gt/+}$ mice



Wanda Layman

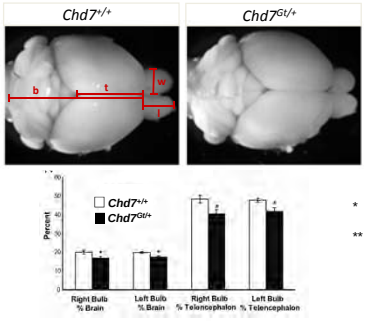
Layman et al., *Hum Mol Gen* 2011

Olfactory bulb defects in CHARGE



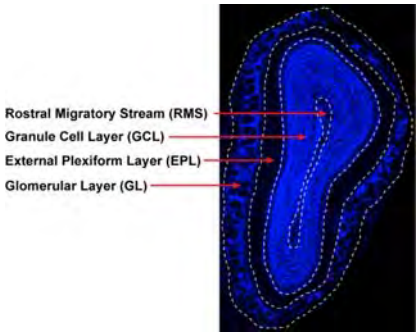
Pinto et al., *J. Clin. Endocrinol. Metab.* 2005

Chd7$^{Gt/+}$ mice have olfactory bulb hypoplasia

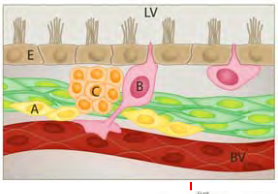


Layman et al., *Human Molecular Genetics* 2009

Olfactory bulb anatomy



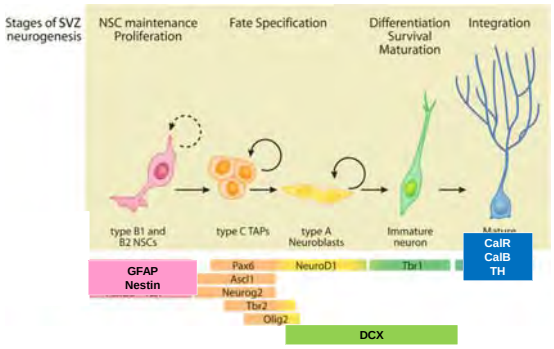
Stem Cells in the Subventricular Zone (SVZ) Give Rise to All Olfactory Bulb Interneurons



LV: Lateral Ventricle
E: Ependymal Cell
B: Type B stem cell
C: Type C transit amplifying cell
A: Type A neuroblast
BV: Blood Vessel

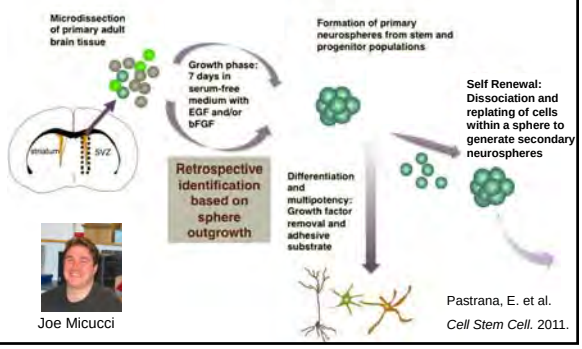
Hsieh J. *Genes and Development* 2012.

Many Cell Types are Present in the SVZ



Adapted from Hsieh J. *Genes and Development* 2012.

Neurosphere Assay



Joe Micucci

Pastrana, E. et al. *Cell Stem Cell.* 2011.

Individuals with CHARGE syndrome have skeletal abnormalities

- 30%-50% of patients present with skeletal abnormalities (Brock et al., 2003; Tellier et al., 1998)
- Isolated cases
  - Neck and shoulder abnormalities (Issekutz et al., 2005)
  - Spine anomalies (Stromland et al., 2005)
  - Hypoplastic vertebrae (Jongmans et al., 2006)
  - Tracheoesophageal fistula (Lee et al., 2008)
  - Other hand and foot deformities (various authors)

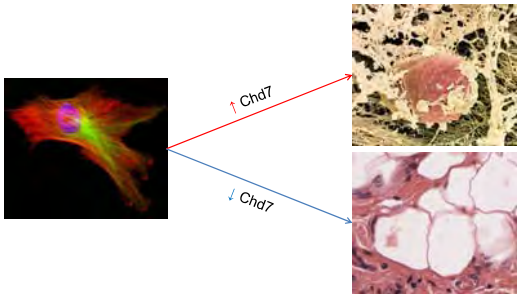
Hartshorne et al., 2011

Craniofacial features in CHARGE

- External ear abnormalites
- Micrognathia, glossoptosis (>95%)
- Cleft lip and/or palate (20%)
- Cranial nerve dysfunction (VII, VIII, IX, X)
- Dental abnormalities
- Tracheomalacia and/or laryngomalacia

Hartshorne et al., 2011; Hall and Hefner, 1999; CHARGE Syndrome Foundation

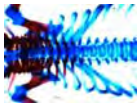
Chd7 is necessary for proper bone development



Adapted from Takada et al., 2007; Nature Publishing Group (Dennis Discher); Science Photo Library (Paul Gunning); University of Michigan Medical School (Michael Hortsch, Ph.D.)

Skeleton Preparations

- Isolation of bone and cartilage from post-natal mice
- Stain with Alizarin red (for bone) and Alcian blue (for cartilage)
- De-stain using gradient mixtures of glycerol and potassium hydroxide



Ethan Sperry

Lessons Learned

- Mice with heterozygous *Chd7* mutations have anosmia, fewer olfactory sensory neurons, and fewer GnRH neurons
- *Chd7* is required for normal proliferation and neurogenesis in the olfactory epithelium
- *Chd7* appears to be necessary for subventricular zone neural stem cell function and for skeletal development

Current Research Goals

- Identify critical target genes and interacting partners that mediate CHD7 function
- Characterize roles for CHD7 in adult cells and tissues using induced pluripotent stem cells
- Design regenerative strategies for treating CHARGE-related disorders
- Determine the cause of the remaining 15-25% of CHARGE cases not due to *CHD7* mutations

Acknowledgements

Current lab members
Jennifer Skidmore
Joe Micucci
Ethan Sperry
Mark Durham
Sophia Frank

Former lab members
Elizabeth Hurd
Wanda Layman
Elyse Reamer
Heather Poucher

UM Collaborators
Yehoash Raphael
Jeff Martens

Other Collaborators
Peter Scacheri (CWRU)
Bob Hevner (U Washington)

Funding
-NIH-NIDCD
-National Organization for Hearing Research (NOHR)
-Hearing Health Foundation
-The CHARGE Syndrome Foundation

Category: Medical/Genetics

Thursday
9:40-10:05
Palomino 1 - 3

Phenotypes in a Drosophila model of CHARGE Syndrome

Daniel R. Marenda, Ph.D.
Assistant Professor
Drexel University

Presenter Information:

Dr. Marenda is an Assistant Professor in the Department of Biology at Drexel University with a joint appointment in the Department of Neurobiology and Anatomy at the Drexel University College of Medicine. He has been working in the field of developmental neurobiology using the fruit fly *Drosophila melanogaster* for more than a decade.

Presentation Abstract:

In human disease, animal models (called model organisms) often act as surrogates for patients when experimentation on humans is unfeasitble or unethical. The fruit fly, *Drosophila melanogaster*, has been a powerhouse model organism in studying human disease. Using Drosophila, my lab inactivated the fly equivalent of the Chd7 gene (called *kismet*). In this presentation, I will 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. I will show data on *kismet* dependent regulation of steroid hormone signaling, and how this affects the proper development of neural circuits in the brain that control learning and memory behavior. Steroid hormones are critical regulators of normal development, and *kismet*-mediated regulation of steroid hormone function is an important observation that may have significant and broad reaching impact.

Category: Medical/Genetics

Thursday
10:05-10:30
Palomino 1 - 3

Epigenetic regulation of neural crest cell development by Brg1 and Chd7

Ching-Pin Chang, M.D.,Ph.D.
Stanford University

Presenter Information:

CHARGE syndrome, which includes congenital defects in the cardiac outflow tract, is caused by CHD7 mutation. Our studies of Brg1, a chromatin-remodeling factor, demonstrate a molecular interaction between Chd7 and Brg1 to control mammalian fetal heart development. Brg1 and Chd7 are chromatin-regulating factors that structure the epigenome to program gene expression. Within neural crest cells, Brg1 partners with Chd7 on the promoter of PlexinA2 to program its expression, which is essential for guiding neural crest cells o the heart to control the development of cardiac outflow tract. In addition, Brg1 is necessary for maintaining neural crest cell pool for heart development. These studies thus uncovers a new layer of regulation related to the pathogenesis of CHARGE syndrome.

Presentation Abstract:

Development of the cerebral vessels, pharyngeal arch arteries (PAAs) and cardiac outflow tract (OFT) requires multipotent neural crest cells (NCCs) that migrate from the neural tube to tissue destinations. However, little is known about how mammalian NCC development is orchestrated by gene programming at the chromatin level. Here we show that Brg1, an ATPase subunit of the BAF chromatin-remodeling complex, is required in NCCs to direct cardiovascular development. Mouse embryos lacking *Brg1* in NCCs display immature cerebral vessels, aberrant PAA patterning, and shortened OFT. Brg1 suppresses an apoptosis factor *Ask1* and a cell cycle inhibitor $p21^{cip1}$ to inhibit apoptosis and promote proliferation of NCCs, thereby maintaining a multipotent cell reservoir at the neural crest.

Also, Brg1 supports *Myh11* expression for NCCs to develop into mature vascular smooth muscle cells of cerebral vessels. Within NCCs, Brg1 partners with a chromatin remodeler Chd7 on the *PlexinA2* promoter to activate *PlexinA2,* which encodes a receptor for semaphorin to guide NCCs into the OFT. Our studies thus reveal a new role of Brg1 and its downstream pathways in the survival, differentiation, and migration of the multipotent NCCs, critical for mammalian cardiovascular development.

3rd Professional Day & 11th International CHARGE Syndrome Conference
Fairmont Scottsdale Princess Hotel, Scottsdale, AZ July 25-28, 2013

Category: Medical/Genetics

Thursday
11:00-11:25
Palomino 1 - 3

Chd7 in neural crest-mediated cardiac development

Adam Stein
Assistant Professor of Medicine
Dept of Medicine, Division of Cardiology
University of Michigan

Presenter Information:
Adam B. Stein, M.D.
Assistant Professor of Medicine
Dept of Medicine, Division of Cardiology
University of Michigan

Presentation Abstract:
CHD7-mutation positive CHARGE patients display a range of clinical abnormalities including temporal bone defects, hearing defects, heart defects, craniofacial defects and choanal atresia. Although CHARGE Syndrome results in a seemingly diverse spectrum of congenital abnormalities, one unifying explanation is that the phenotypic traits result from abnormal neural crest cell (NCC)-mediated differentiation and/or migration. Cardiac NCCs (CNCCs) are a NCC population that migrate to the heart and great vessels where they are important for the development of the aorta and pulmonary artery from the pharyngeal arch arteries (PAAs) as well as the septation of the conotruncus into the ventricular outflow tract. We hypothesized that the absence of Chd7 in murine cardiac neural crest cells could recapitulate the congenital abnormalities seen in patients with CHARGE Syndrome. Using a Wnt1-Cre mouse model and a floxed Chd7 allele, Chd7 was conditionally deleted from neural crest cells (Wnt1-Cre) in vivo. We observed that a lack of Chd7 in Wnt1-Cre expressing neural crest cells does not compromise the ability of these cells to migrate and differentiate into normal cardiac structures. Thus, we conclude that Chd7 is not necessary for the development of neural crest-derived cardiac structures in our murine model.

People with CHARGE Syndrome often have congenital cardiovascular defects. Mutations in *CHD7*, the gene encoding chromodomain helicase DNA binding protein 7, have been identified in CHARGE Syndrome in a majority of cases. In an effort to understand more about this syndrome, scientists have created mice that have only one functioning copy of the *Chd7* gene. Mice with a loss of *Chd7* function display CHARGE-like phenotypes and are an excellent model of human CHARGE Syndrome. Several of the murine models with one functioning *Chd7* gene display congenital cardiac abnormalities. In patients with CHARGE Syndrome, observed congenital heart problems are likely a result of abnormal development of the conotruncal region (outflow tract- i.e. where the pumping chambers of the heart give rise to pulmonary artery and the aorta) and the great vessels (aorta and pulmonary artery).

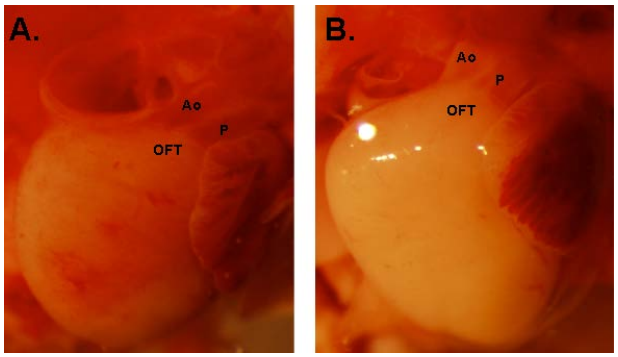


Figure 1. Grossly intact septation and structure of the outflow tract (OFT), aorta (Ao), and pulmonary trunk (P) in mice with *Chd7* still present in NCCs (Panel A) and with *Chd7* deleted in NCCs (Panel B).

During development, the conotruncal region and the great vessels are derived from several different populations of early progenitor cells. Neural crest cells (NCCs) are one developmental cell population that is necessary for the proper development of these cardiac structures. NCCs are an interesting cell type that originates near the neural tube. NCCs migrate to many different parts of the developing embryo where they differentiate into a diverse array of tissues. Thus, it is plausible that many of the clinical features of CHARGE Syndrome may be a result of an inability of NCCs to migrate and differentiate into various tissues. Interestingly, it has been shown that one

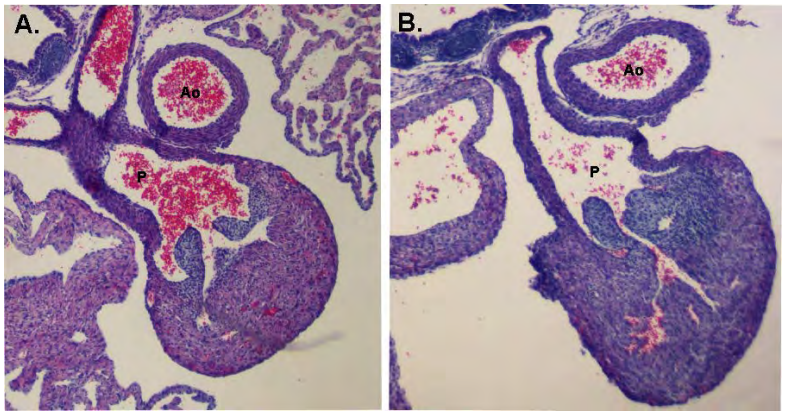


Figure 2. H&E staining of embryonic sections from mice with *Chd7* present in neural crest cells (Panel A) and in mice with *Chd7* absent from NCCs revealed intact septation and overall structure of the pulmonary trunk (P) and the aorta (Ao).

group of NCCs, namely cardiac NCCs, migrate from the neural tube to the heart where they are important for the normal development of the heart and the great vessels. The objective of our study was to determine whether *Chd7* is important for NCCs to migrate to the heart region and successfully participate in the development of the outflow tract and the great vessels.

We created a unique mouse model in which we could breed mice to selectively delete *Chd7* (*Chd7*^{flox}) from NCCs (*Wnt1-Cre*). We found that we were not able to generate viable pups that have *Chd7* deleted from the NCC population (*Wnt1-Cre:Chd7*$^{flox/flox}$). The pups died shortly after birth, and our observations revealed that the pups likely died due to abnormal brain development and oral palate defects that prevented them from feeding properly. In order to determine if mice without *Chd7* in the NCC population have abnormalities in the development of the conotruncal region and the great vessels, we studied at embryonic mice just before birth (e16 and later). As shown in figure 1, at embryonic day 18, we observed normal development of the outflow tract and normal septation of the aorta and pulmonary trunk. In order to further visualize the structure of the outflow tract, pulmonary trunk and aorta of these structures, we fixed and cut tissues from mice with and without *Chd7* in the NCCs. As shown in figure 2, staining revealed that the aorta and the pulmonary trunk were septated.

Thus far, our results suggest that *Chd7* deletion in NCCs using a *Wnt1-Cre* driver is not critical for the development of the outflow tracts and the septation of the pulmonary trunk and the aorta. We are currently looking at earlier time points to see if the development of the pharyngeal arch arteries is impacted by the deletion of Chd7 in NCCs. We are also using other murine models to delete *Chd7* from a variety of early cell populations that participate in the development of the cardiac structures that are often impacted in patients with CHARGE Syndrome.

Category: Medical/Genetics

Thursday
11:25-11:50
Palomino 1 - 3

Role of CHD7 in Development of Midbrain and Hindbrain

Mark Durham
Undergraduate Student
Cellular and Molecular Biology
University of Michigan

Presenter Information:

Currently, I am a junior at the University of Michigan studying Cellular and Molecular Biology. For the past two and a half years I have worked with Dr. Donna Martin studying the molecular mechanisms causing CHARGE Syndrome. My research interests include Neurodevelopmental disorders, Biochemistry, Genetics, and Genomics. After my undergraduate education I plan to attend an M.D. PhD. program and pursue a career as a physician-scientist in the field of medical genetics.

Presentation Abstract:

Recent studies have linked CHARGE Syndrome to developmental defects of the midbrain, hindbrain, and cerebellum. To investigate this further, our lab is studying the inner ear and central nervous system of mice with *Chd7* mutations. We will present our results showing that reduced *Chd7* leads to central nervous system abnormalities.

Category: Medical/Genetics

Thursday
11:50-12:15
Palomino 1 - 3

Identification of Molecular Markers to Predict Auditory Neuron Function for CHARGE Syndrome

Kelvin Y. Kwan
Assistant Professor of Cell Biology & Neuroscience
Rutgers University

Presenter Information:

Kelvin Kwan is an Assistant Professor in the Department of Cell Biology and Neuroscience at Rutgers University. His lab is located in the Rutgers University Stem Cell Center. Dr. Kwan's lab is interested in regenerating the sensory and nerve cells of the inner ear. He is working closely with the Rutgers University Cell and DNA Repository, the largest university based cell and DNA biobank, to generate induced pluripotent stem cells from archived cells.

Presentation Abstract:

Encased in a bony labyrinth, the cochlea residing within the inner ear allows us to discriminate and hear complex sounds. Hair cells in the cochlea are the sensory cells that convert sound into neural signals, which are then relayed to the brain by auditory neurons. Patients with CHARGE are frequently affected by sensorineural hearing loss resulting from hair cells or auditory neuron dysfunction. Currently, the only treatment for hearing loss is the use a cochlear implant or a hearing aid. A major factor for auditory prosthesis candidacy is a functional auditory nerve. Since auditory neuron impairment can vary dramatically in CHARGE, it would be ideal to determine functional activity of neurons from individuals. However, direct recording from the auditory nerve is invasive and difficult because the inner ear is small, encased in bone and difficult to access. Instead, we have established a progenitor cell line that continually proliferates and can differentiate into auditory neurons. I propose to use progenitor-derived auditory neurons as a platform for identifying a panel of genes that correlates to auditory neuron function. In the future, when samples from patients with become available, induced pluripotent stem cells (iPSCs) can be made. Auditory neurons generated from iPSCs from patients with CHARGE can be used to determine their candidacy for auditory prosthesis.

Category: Behavior, Family Support

Thursday
Poster Session
1:15-2:30

Getting Ready to Talk to a Psychiatrist

Laurie S. Denno, Ph.D., BCBA-D
Behavior Analyst
Perkins School for the Blind

Presenter Information:

Laurie S. Denno, Ph.D., is a behavior analyst at the Perkins School for the Blind, Deafblind Program, and also in private practice serving adults with developmental disabilities in residential and day programs. She has worked with children and young adults with CHARGE syndrome and behavior challenges for 20 years.

Poster Abstract:

This poster outlines Laurie's dissertation research that taught parents who were considering a psychiatric consultation how to present their child's challenging behavior to a psychiatrist in a specific and organized manner. A self-directed teaching program was used. Data for all six participants is presented. This is an educational presentation.

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Category: Medical, Family Support, Education

Thursday
1:15-2:30
Poster Session

A CHARGE information pack for practitioners

Gail Deuce (M.Ed)
Principal MSI Consultant
Children's Specialist Services, Sense UK

Presenter Information:

Gail has a B.Ed in Special Education, is a qualified teacher of the deaf and also has a M.Ed. in Multi-sensory Impairment.
Gail works in the UK and has over twenty-five years experience in the field of special education, working initially in schools for children with severe learning difficulties and then a school for the deaf before moving into peripatetic work focusing on learners who are deafblind. Joined Sense in December 2001 and is working in the Children's Specialist Services as a Principal MSI Consultant.
Gail has a particular interest in CHARGE and is on the committee for the CHARGE Family Support Group in the UK. She is currently undertaking a PhD, focusing on the educational environment for children with CHARGE Syndrome.

Presentation Abstract:

This pack of information arose from parental request for information to share with professionals who become involved with their child following diagnosis.
The aim is to have a web-based package of information that parents of children with CHARGE, or other interested parties, can pass to the varied professionals that work with their children. It will be possible to download the pack either by section or in its entirety.
Each topic is essentially a summary of immediately relevant information for each professional area with suggestions for further reading and where additional information and advice can be found. The topics were chosen following consultation with a range of professionals who work with children with CHARGE and as a result of a questionnaire returned by approximately 70 families.

Category: Family Support

Thursday
1:15-2:30
PosterSession

CHARGE syndrome in German speaking countries

CHARGE Syndrom e.V.
(German CHARGE Family Support Group)
Claudia Junghans, Dr. Julia Benstz,
Dr. Phil. Andrea Wanka

Presenter Information:

Claudia Junghans, President of the German CHARGE Family Support Group and mother of a 9 year old son with CHARGE syndrome (non-attendant).

Dr. Julia Benstz is Vice President of the German CHARGE Family Support Group and mother of a 14 year old daughter with CHARGE syndrome.

Co-presenter **Dr. Phil. Andrea Wanka** is representative for deaf blindness and hearing impairment at the foundation St. Franziskus Heiligenbronn and educational consultant of the German CHARGE Family Support Group. She works with affected families above all in the area of communication and the behaviour of children with CHARGE syndrome.

Presentation Abstract:

The poster is about the foundation “CHARGE Syndrom e.V.”, the Family Support Group for German speaking countries and exposes the most important information on the formation.
Focus of attention will be the possibilities of support for affected families, which shall help to cope with the CHARGE Syndrome. These include for example the offer of topic based weekends for a smaller number of families up till about 5 (weekends on communication and behavior, for siblings, for mothers, for CHARGE youngsters, on music and animals).

Category: Behavior

Thursday
1:15-2:30
Poster Session

Understanding Behavioral Self-Regulation in CHARGE

Sarah Haney and
Dr. Tim Hartshorne
Central Michigan University, Psychology Department

Presenter Information:

Sarah Haney is a senior at Central Michigan University studying Psychology and Child Development. She plans on attending graduate school to pursue a degree in Applied Behavior Analysis. She has been researching CHARGE for one year now and has presented a poster of her research at the Australian CHARGE Syndrome conference in 2012.

Tim Hartshorne is a professor of psychology, specialized in school psychology, at Central Michigan University. He is the grant holder for DeafBlind Central: Michigan's Training and Resource Project, which provides support to children who are deafbind in Michigan. He has been researching and presenting about CHARGE syndrome since 1993, motivated by the birth of his son with CHARGE in 1989. He has been awarded the Star in CHARGE by the CHARGE Syndrome Foundation. He is first editor of the book CHARGE Syndrome.

Presentation Abstract:

Nicholas and Hartshorne have proposed four areas of functioning that are impacted by problems with self-regulation. This poster focuses on one of these, the area of behavior. It will describe the difficulty, and offer parents, educators, and others insight into how to help these individuals learn to self-regulate their behavior. This is one of four companion posters illustrating areas of self-regulation.

Category: Behavior,
Family Support

Thursday
1:15-2:30
Poster Session

Physiological Self- Regulation in CHARGE

Tim Hartshorne, Ph.D.
Central Michigan University
and
Andrea Larson

Presenter Information:

Tim Hartshorne is a professor of psychology, specialized in school psychology, at Central Michigan University. He is the grant holder for DeafBlind Central: Michigan's Training and Resource Project, which provides support to children who are deafbind in Michigan. He has been researching and presenting about CHARGE syndrome since 1993, motivated by the birth of his son with CHARGE in 1989. He has been awarded the Star in CHARGE by the CHARGE Syndrome Foundation. He is first editor of the book *CHARGE Syndrome*.

Andrea Larson is a graduate of Central Michigan University with a major in psychology. She is taking a year off before pursuing a medical education.

Presentation Abstract:

Nicholas and Hartshorne have proposed four areas of functioning that are impacted by problems with self-regulation. This poster focuses on one of these, the area of physiological experience. It will describe the difficulty, and offer parents, educators, and others insight into how to help these individuals learn to self-regulate their behavior. This is one of four companion posters illustrating areas of self-regulation.

Category: Medical

Thursday
1:15-2:30
Poster Session

Headaches in CHARGE

Tate Jenkins & Tim Hartshorne
Central Michigan University

Presenter Information:

Tate Jenkins is a psychology student at Central Michigan University. She is a senior and studying for Medical School.

Tim Hartshorne is a professor of psychology, specialized in school psychology, at Central Michigan University. He is the grant holder for DeafBlind Central: Michigan's Training and Resource Project, which provides support to children who are deafbind in Michigan. He has been researching and presenting about CHARGE syndrome since 1993, motivated by the birth of his son with CHARGE in 1989. He has been awarded the Star in CHARGE by the CHARGE Syndrome Foundation. He is first editor of the book*CHARGE Syndrome*.

Presentation Abstract:

There is little information about the experience of individuals with CHARGE Syndrome and headaches. Headaches may be the result of cranial nerve anomalies, dental complications, and migraines. Classification of headaches, possible sources of headaches due to CHARGE, data collection strategies, and estimation of incidence will be addressed.

Category: Family Support

Thursday
1:15-2:30
Poster Session

Fathers and CHARGE: Work and Friendships

Shantell Johnson, Kirsten Hissong
(with Timothy Hartshorne)
Central Michigan University

Presenter Information:

Shantell and Kirsten are both students at Central Michigan University.

Tim Hartshorne is a professor of psychology, specialized in school psychology, at Central Michigan University. He is the grant holder for DeafBlind Central: Michigan's Training and Resource Project, which provides support to children who are deafbind in Michigan. He has been researching and presenting about CHARGE syndrome since 1993, motivated by the birth of his son with CHARGE in 1989. He has been awarded the Star in CHARGE by the CHARGE Syndrome Foundation. He is first editor of the book *CHARGE Syndrome*.

Presentation Abstract:
Familial research traditionally is centered around the maternal viewpoint; paternal research is extremely underrepresented across subject fields. Commonly, their viewpoints are synonymously linked to the views, thoughts, stresses of the mother. It is known that fathers and mothers have very different thoughts regarding parenthood and their children. Further, fathers differ significantly in the prioritizing of work over family. Women are more likely to put their family above any work related events. The work more, play less language of the father often translates into fewer friendships. Male-male friendships often exhibit weaker, fewer intimate and superficial relationships. This has been found for fathers of developmentally on-track and fully able children, but does the same idea hold true for fathers of children with disabilities? More specifically, does this hold true for fathers of children with CHARGE? CHARGE is a rare, genetic disorder in which the child has pronounced birth and developmental deficits. This study aims to examine whether fathers with CHARGE parallel the work practice and male-male friendship patterns of fathers with non-disabled children.

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Category: Medical/Genetics

Thursday
Poster Session
1:15-2:30

Chromatin remodeling by the CHD7 protein is impaired by mutations that cause human developmental disorders

Karim Bouazoune, Ph.D.
Massachusetts General Hospital/
Harvard Medical School

Presenter Information:
Karim Bouazoune, Ph.D.
Post-doctoral fellow in Prof. Robert E. Kington's lab
Department of Molecular Biology, Massachusetts General Hospital
Department of Genetics, Harvard Medical School

Richard Simches Research Center
185 Cambridge Street, CPZN 7412
Boston, MA 02114
bouazoune@molbio.mgh.harvard.edu
Tel: +1-617-643-3282

Presentation Abstract:

Background

Mutations in the CHD7 gene cause CHARGE syndrome. To understand how the CHD7 protein achieves its function and how mutation of CHD7 leads to developmental disorders, it is critical to characterize wild-type and mutant CHD7 proteins biochemically. However to date, CHD7 has not been characterized for activity, as it is extremely large and has resisted purification.

Approach

We used the baculovirus system and a dual-tag strategy to purify intact recombinant WT and mutant CHD7 proteins. We subjected these polypeptides to nucleosome remodeling and ATPase assays to characterize the CHD7 basic properties, perform a structure-function analysis of CHD7 and examine point mutants reported in human patients.

Results

We show that CHD7 is an ATP-dependent nucleosome remodeling factor with distinct characteristics. Further investigations show that CHD7 patient mutations have consequences that range from subtle to complete inactivation of remodeling activity, raising the possibility that even partial impairment of remodeling function has a significant impact on human biology. In addition, we find that patient mutations leading to protein truncations upstream of amino acid 1899 of CHD7 are likely to cause a hypomorphic phenotype for remodeling.

Conclusions

We propose that nucleosome remodeling is a key function for CHD7 during developmental processes and provide a molecular basis for predicting the impact of disease mutations on that function.

Category: Behavior

Thursday
1:15-2:30
Poster Session

Cognitive Self-Regulation in CHARGE Syndrome

Benjamin Kennert, Doctoral student
Tim Hartshorne, Ph.D.
Central Michigan University

Presenter Information:

Benjamin Kennert is a first year graduate student in the School Psychology Ph.D. program at Central Michigan University. He has been working with Dr. Tim Hartshorne on research involving self-regulation and CHARGE Syndrome.

Tim Hartshorne is a professor of psychology, specialized in school psychology, at Central Michigan University. He is the grant holder for DeafBlind Central: Michigan's Training and Resource Project, which provides support to children who are deafbind in Michigan. He has been researching and presenting about CHARGE syndrome since 1993, motivated by the birth of his son with CHARGE in 1989. He has been awarded the Star in CHARGE by the CHARGE Syndrome Foundation. He is first editor of the book *CHARGE Syndrome*.

Presentation Abstract:

Nicholas and Hartshorne have proposed four areas of functioning that are impacted by problems with self-regulation. This poster focuses on one of these, the area of cognition. It will describe the difficulty, and offer parents, educators, and others insight into how to help these individuals learn to self-regulate their behavior. This is one of four companion posters illustrating areas of self-regulation.

Category: Behavior

Thursday
1:15-2:30
Poster Session

Self-Regulation of Emotion in CHARGE Syndrome

Benjamin Kennert, doctoral student
Maria Ramirez, doctoral student
Tim Hartshorne, Ph.D.
Central Michigan University

Presenter Information:

Benjamin Kennert is a first year graduate student in the School Psychology Ph.D. program at Central Michigan University. He has been working with Dr. Tim Hartshorne on research involving self-regulation and CHARGE Syndrome.

Tim Hartshorne is a professor of psychology, specialized in school psychology, at Central Michigan University. He is the grant holder for DeafBlind Central: Michigan's Training and Resource Project, which provides support to children who are deafbind in Michigan. He has been researching and presenting about CHARGE syndrome since 1993, motivated by the birth of his son with CHARGE in 1989. He has been awarded the Star in CHARGE by the CHARGE Syndrome Foundation. He is first editor of the book *CHARGE Syndrome*.

Maria Ramirez is a Doctoral student in the School Psychology program at Central Michigan University. For the past three and a half years she has been working with Dr. Tim Hartshorne exploring self-regulation in children with CHARGE. Her current research focuses on the assessment and validation of a Fun Chi video to be used in future research to assess the effects of Fun Chi on sleep, balance, and self-regulation in children with CHARGE.

Presentation Abstract:

Nicholas and Hartshorne have proposed four areas of functioning that are impacted by problems with self-regulation. This poster focuses on one of these, the area of emotion. It will describe the difficulty, and offer parents, educators, and others insight into how to help these individuals learn to self-regulate their behavior. This is one of four comanion posters illustrating areas of self-regulation.

Category: Family Support

Thursday
1:15-2:30
Poster Session

Microenterprises – Building on Strengths and Promoting Self-Sufficiency: Factors to Consider with Individuals with CHARGE syndrome

Seraphim Mork, doctoral student
Maria Ramirez, doctoral student
Tim Hartshorne, Ph.D.
Central Michigan University

Presenter Information:

Seraphim Mork is a Doctoral student in the School Psychology program at Central Michigan University.
She is currently examining the concurrent validity of the Bayley Scales of Infant and Toddler Development, Third Edition; the most commonly used measure of cognitive development with the Cognitive Abilities Scale-Second Edition; a test that has considerable support for its validity. Her research interests are in early literacy especially for individuals with developmental impairments.

Maria Ramirez is a Doctoral student in the School Psychology program at Central Michigan University. For the past three and a half years she has been working with Dr. Tim Hartshorne exploring self-regulation in children with CHARGE. Her current research focuses on the assessment and validation of a Fun Chi video to be used in future research to assess the effects of Fun Chi on sleep, balance, and self-regulation in children with CHARGE.

Tim Hartshorne is a professor of psychology, specialized in school psychology, at Central Michigan University. He is the grant holder for DeafBlind Central: Michigan's Training and Resource Project, which provides support to children who are deafbind in Michigan. He has been researching and presenting about CHARGE syndrome since 1993, motivated by the birth of his son with CHARGE in 1989. He has been awarded the Star in CHARGE by the CHARGE Syndrome Foundation. He is first editor of the book *CHARGE Syndrome*.

Presentation Abstract:
Currently there is a movement towards promoting more choices and self-sufficiency among people with disabilities using microenterprises. This is an area that has not yet been explored in individuals with CHARGE syndrome. Microenterprises offer a viable opportunity for self-determination and self-sufficiency. This poster provides a brief overview of things the processes, benefits and barrier in starting microenterprises.

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Category: Behavior

Thursday
1:15-2:30
Poster Session

Models of Conceptualizing Self-Regulation in CHARGE syndrome

Maria Ramirez, doctoral student
Tim Hartshorne, Ph.D.
Central Michigan University

Presenter Information:

Maria Ramirez is a Doctoral student in the School Psychology program at Central Michigan University. For the past three and a half years she has been working with Dr. Tim Hartshorne exploring self-regulation in children with CHARGE. Her current research focuses on the assessment and validation of a Fun Chi video to be used in future research to assess the effects of Fun Chi on sleep, balance, and self-regulation in children with CHARGE.

Tim Hartshorne is a professor of psychology, specialized in school psychology, at Central Michigan University. He is the grant holder for DeafBlind Central: Michigan's Training and Resource Project, which provides support to children who are deafbind in Michigan. He has been researching and presenting about CHARGE syndrome since 1993, motivated by the birth of his son with CHARGE in 1989. He has been awarded the Star in CHARGE by the CHARGE Syndrome Foundation. He is first editor of the book *CHARGE Syndrome*.

Presentation Abstract:

Individuals with CHARGE syndrome have difficulties with self-regulation, or the voluntary management of goal directed behavior. This poster provides an overview of what self-regulation is and why it can be problematic for individuals with CHARGE. Four areas of self-regulation are described: cognitive, behavior, emotion, and physiological. This poster serves to introduce four other posters which focus on each one of these areas.

Category: Medical/Genetics

Thursday
2:30-2:55
Palomino 1 - 3

The Cerebral Cortex in CHARGE Syndrome

Robert F. Hevner, MD, PhD
Credentials & Organization
Professor, University of Washington and Seattle Children's Research Institute

Presenter Information:

Dr. Hevner is a pediatric neuropathologist at Seattle Children's Hospital. His lab studies development and malformations of the cerebral cortex, using mice as a model system. Dr. Hevner obtained his B.S. in Cellular and Molecular Biology (with High Honors) from the University of Michigan, and M.D. and Ph.D. degrees from the Medical College of Wisconsin. He completed residency in Anatomic Pathology at Brigham and Women's Hospital, and fellowship in Neuropathology at Stanford University. He then performed postdoctoral research at UCSF. He has been at the University of Washington since 2000, and at Seattle Children's Research Institute since 2008.

Presentation Abstract:

CHARGE syndrome is caused in most cases by mutations in *CHD7*, a gene that is highly expressed in many areas of the developing brain, including the cerebral cortex. The cerebral cortex may develop abnormally in CHARGE syndrome, contributing to cognitive and behavioral problems in some affected individuals. To investigate this possibility, we have studied mice with *Chd7* gene mutations to evaluate cortical development. The cortex in these mice indeed shows multiple anomalies of cortical gene expression during development, including defects of neuronal differentiation and cell migration. Both projection neurons (excitatory neurons with long axons) and interneurons (inhibitory neurons with short axons) are affected. Our findings suggest that cortical development may be perturbed in CHARGE syndrome and contribute to disease symptoms.

Category: Medical/Genetics

Thursday
2:55-3:20
Palomino 1 - 3

Gene therapy induces nerve fiber regeneration in the inner ear of deaf mutant mice

Yehoash Raphael, Hideto Fukui, Yohei Takada, Donna M. Martin
The University of Michigan, Ann Arbor

Presenter Information:

Yehoash Raphael is Professor of Otolaryngology, Head & Neck Surgery, working in Kresge Hearing Research Institute at The University of Michigan. He specializes in inner ear biology, with a special focus on ear trauma, repair and regeneration. The lab personnel study both hereditary and environmental ear disease and design therapies for prevention and for hearing restoration.

Drs. Hideto Fukui and Yohei Takada have performed the laboratory work presented at the meeting. They are Otolaryngology specialists originally from Kansai Medical University in the Osaka area, Japan.

Dr. Donna Martin is a colleague who works with Dr. Raphael on characterizing ears of a mouse model for CHRAGE. Dr. Martin is also a spouse, and together, Donna and Yehoash are parents of a 19 year-old son, Noam Raphael, with CHARGE, and a 17-year old daughter, Maya Raphael. Both Noam and Maya are also attending the meeting

Presentation Abstract:

The outcome of cochlear implant therapy depends on a healthy auditory nerve. We tested whether *BDNF* gene transfer into the cochleae of deaf mice can influence the fate of neurons. We determined that the diameter and number of nerve fibers in the auditory epithelium were increased compared to non-treated ears, and that spiral ganglion cell density in Rosenthal's canal was also increased. The data suggest that nerve fiber regeneration treatment may augment cochlear implant therapy.

Category: Medical/Genetics, Family Support

Thursday
3:20-3:45
Palomino 1 - 3

Study of CHARGE syndrome clinical studies:
UK Survey & the
Clinical Database Project

Gail Deuce, M.Ed
Steve Rose M.Ed
Simon Howard

Meg Hefner, MS
Emily Fassi

Presenter Information:

Gail is a qualified teacher of the deaf with expertise in multi-sensory impairment with25 years experience in the field of special education in the UK. She is on the committee for the CHARGE Family Support Group in the UK. She is currently undertaking a PhD, focusing on education of children with CHARGE Syndrome.

Steve is a speech and language therapist specialising in deafblindness. He has worked as an intervenor family support groups for Sense. Steve has particular interest in the development of eating and drinking skills and early interventions, including parent-child interaction therapy.

Simon has a daughter, Jessica (now 12), with CHARGE. He is the point of contact and newsletter organizer for the CHARGE Family Support Group. He has worked closely with Sense in the UK regarding CHARGE including organising a UK conference in 2011.

Meg is a genetic counselor with 30 years experience with CHARGE and started the CHARGE Syndrome Foundation. She started the first CHARGE Syndrome Clinic in the US in 2011.

Emily is about to start formal training as a genetic counselor. She became interested in CHARGE working with Meg and has been instrumental in the development of the Clinical Database Project.

Presentation Abstract:
UK study: This presentation will briefly report a few findings of a paper questionnaire completed by families living in the UK with a child (aged 15 years or younger) with a medical diagnosis of CHARGE syndrome. The questionnaire contained three sections: Diagnosis & medical issues, child development; and educational provision (including identification of educational need in relation to multi-sensory impairment/deafblindness, support from specialist teachers and other professionals, and parental satisfaction.

Clinical Database Project: an Internet-based survey of a very broad specturm of CHARGE features launched in May, 2013. The presentation will show the features collected in the survey, current status of data entry, and intended uses of the database. The intent of this project is to provide as much information on CHARGE as possible to as broad an audience as possible: families, medical and educational professionals and other doing research on CHARGE syndrome.

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CHARGE Syndrome Clinical Database Project

Principal Investigator: Meg Hefner, MS
Saint Louis University School of Medicine
Department of Pediatrics, Division of Medical Genetics

We have developed a comprehensive database of clinical information on CHARGE syndrome (CS). If you or your child has been diagnosed with CS, you may be eligible to participate.

What is this for? The purpose of this study is to create a comprehensive clinical database and registry of individuals with CS of all ages from all over the world. Information from this database will provide meaningful contributions to CS knowledge and research.

Who can do this? Any adult with CS or parent/guardian of an individual with CS is eligible.

How would I do it? Participation in this project involves entering data (mostly medical information) into a web-based questionnaire. There are opportunities to directly upload photographs and certain medical records in some sections.

How long will it take? Completing the entire questionnaire will take several hours. It can be done in multiple sittings over several weeks. We may ask for yearly updates.

What do I need? You must have email and Internet access to participate in this project. You will need access to your/your child's medical history. The study is in English only.

Will I get paid? No. Your participation is strictly voluntary.

I want more information. What do I do now? If you are interested in learning more about this project, or if you have questions, you can go to the Clinical Database Project link at ***chargeysndrome.org***, or contact Meg Hefner directly at ***hefnerma@slu.edu***. Thank you for your interest in this study.

This project is endorsed by the CHARGE Syndrome Foundation and Saint Louis University.

A study of CHARGE syndrome in the UK
by Deuce, Howard, Rose & Fuggle

Steve Rose (Head of Service) and Gail Deuce (Principal MSI Consultant)
Children's Specialist Services, Sense

Purpose of study:

- Build upon existing knowledge of CHARGE syndrome
- Help recognize areas of need
- Improve the support we can give to children, young people and their families and to the professionals working with them

2

Survey:
- Designed following an earlier pilot (Deuce 2009)
- A questionnaire sent out by post or email
- Families with a family member with CHARGE under the age of 16

3

The questionnaire was divided into three parts:

1. Diagnosis:
-Presence of major and minor characteristics (according to Sanlaville & Verloes 2007)
-Prevalence of other conditions
-Provision of aids for vision and hearing
-Genetic testing and prevalence of CHD7 genetic defect
-Medication

4

2. Child development
- Hospitalisation following birth
- Early developmental milestones
- Eating and drinking

3. Educational provision
- Types of provision
- Range of professionals involved and levels of support
- Statutory assessment
-Parental satisfaction

5

Collation and analysis

- A framework set up using Microsoft Excel to record quantitative and qualitative information
- Structured to code the responses so that the outcomes could be identified and cross reference analysis undertaken
- Data was collated by an external company on a pro bono basis
- Analysed by the authors

6

Issues for consideration:

- How to gain information from a wider cohort or allows for easy comparison

- Over 15's- real need to develop knowledge of late teens and adulthood

- Need for empirical research to support anecdotal evidence

- Time! Very few have clear dedicated time for research that is not impinged upon by other work commitments

7

Part 1 is reported in:

Deuce G., Howard S., Rose S. & Fuggle C. (2012)

A Study of CHARGE syndrome in the UK

The British Journal of Visual Impairment 30(2) 91–100

8

Category: Behavior

Thursday
4:10-4:35
Palomino 1 - 3

Behavior as self-regulatory adaptation, or "I can't believe my child just did that!

Tim Hartshorne, Ph.D.
Central Michigan University

Presenter Information:

Tim Hartshorne is a professor of psychology, specialized in school psychology, at Central Michigan University. He is the grant holder for DeafBlind Central: Michigan's Training and Resource Project, which provides support to children who are deafbind in Michigan. He has been researching and presenting about CHARGE syndrome since 1993, motivated by the birth of his son with CHARGE in 1989. He has been awarded the Star in CHARGE by the CHARGE Syndrome Foundation. He is first editor of the book *CHARGE Syndrome*.

Presentation Abstract:

Individuals with CHARGE often show odd, sometimes challenging, behaviors. These can lead to various psychiatric diagnoses. However, behavior is rarely random, and in fact humans actively attempt to adapt to their experience. The concept of self-regulation is a way to view "CHARGE behavior" as adaptation, and leads to avenues for intervention. This is the first of three presentations on self-regulation and intervention for behavioral challenges.

Behavior as self-regulatory adaptation, or "I can't believe my child just did that!"

Tim Hartshorne
Central Michigan University

Typical Deafblind Behavior

- Eye pressing
- Finger flicking
- Rocking
- Tapping body/objects
- Self-injurious behavior
- Mouthing objects
- Tactile defensiveness
- Clinging
- Spinning
- Vocal tics
- Feces smearing
- Lining things up
- Extreme preferences
- Darting/running off
- Learned helplessness
- Submissive
- Stare at lights
- Inappropriate vocalization

How to make sense of it

- The kid has a syndrome!
- It's pathological and should be eliminated
- It's due to frustration and pain
- It's communication
- It works for the kid

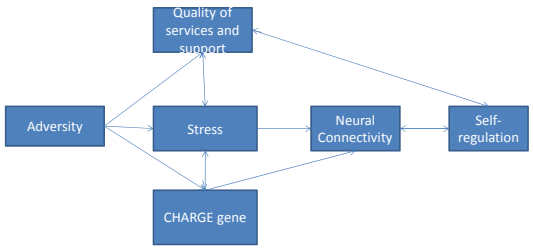
Not because they guarantee success, but because they serve a purpose

Self-regulation problems in CHARGE

- Rapid changes in arousal levels
- Melt downs
- Unfocused behavior
- Diagnoses
  - OCD – a way to reduce stimulation and exercise control
  - ADHD – a problem with regulating sensory and behavioral stimulation and focusing on a goal
  - Tic disorder – a stress response to lack of control over environment
  - Autistic-like behavior – the failure of regulation strategies, and the adoption of dysregulated behavior

Definition

The primarily voluntary regulation of cognition, behavior, emotion, and physiological states for the purpose of goal-directed actions



After Blair & Raver, 2012

Adversity

- Fragile health
  - Breathing problems
  - Multiple hospitalizations
  - Multiple surgeries with anesthesia
  - Multi-sensory impairment
  - Defects in major organs
- Nervous parents
- Sources of stress
  - Social relationships
  - School
  - Family
  - Abuse

Quality of Services and Support

- Lack of medical or specialist knowledge
- Needs multi-disciplinary medical and educational teams
- Parent-Professional relationships
- Lack of social support
- Parent and family resilience

CHD7 Gene

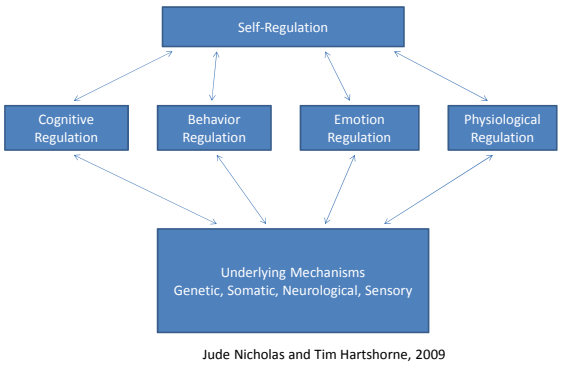
- Regulatory gene
  - Neural crest
  - Placode cells
- Multisensory impairment
- Major organs may be affected
- Vestibular functioning impaired

Stress

- Endocrine regulatory system
- Perception of adversity
- Availability of resources
- Response of professionals
- Response of family

Neural Connectivity

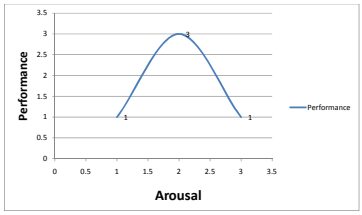
- Prefrontal cortex and executive function
  - Reactive forms of learning and behavior
  - Reflective forms of learning and behavior
- Neuropsychological control over behavioural schemas
  - Routine control
  - Supervisory attentional system



Jude Nicholas and Tim Hartshorne, 2009

Dunn Conceptual Model

Arousal of thoughts, behavior, feelings, sensations	PASSIVE Self-regulation Strategies	ACTIVE Self-regulation Strategies
Habituation	Non-reactive Tune it out	Sensation Seeking
Sensitization	Reactive to Stimuli	Sensation Avoiding



Self-regulation is used to manage arousal levels

With a regulatory disorder, child is challenged to manage
- Cognitive – unfocused vs. obsessive
- Behavior – hyperactive vs. hypoactive
- Emotion – reactive vs. passive
- Physiological – overwhelmed vs. underwhelmed

Self-regulation begins with a goal

– What do you want to have happen?
– What must you do to make it happen?

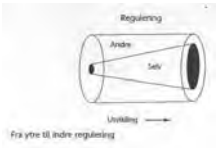
Study for an exam

- Cognitive
- Behavioral
- Emotion
- Physiological

Strategies?

Supporting self-regulation

- Because self-regulation skills are hard for children with significant disabilities to develop
- We have to provide the external support for what will become an internal self-regulatory process



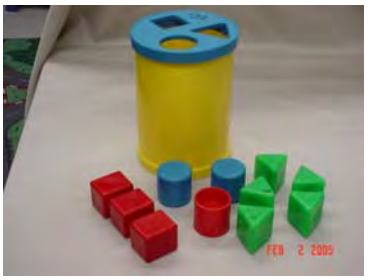
Scaffolding

- The process of planning and organizing the activity of children so that they can execute a task that is beyond their current level of ability.

Components of Scaffolding

1. Identification of the problem to be solved
2. Focus activities on outcomes and goals
3. Frustration control
4. Reducing the complexity of the task
5. Marking critical relevant features
6. Modeling

The Shape Sorter



1. Problem Identification
2. Focus on outcomes
3. Frustration control
4. Reducing complexity
5. Marking features
6. Modeling

Examples

- Cognitive self-regulation
  - Break down larger goals into shorter (pie)
- Behavioral self-regulation
  - Feedback on reactions from others (consequences)
- Emotional self-regulation
  - Creating an environment for self-soothing
- Physiological self-regulation
  - Squeeze technique; hand on arm or leg

Summary

- Children with disabilities often have poorly regulated systems
- This is centrally related to stress, deriving from adversity, quality of supports, and genetics
- The child's attempts to self-regulate manifest as peculiar behavior, often labeled as challenging
- They will do better socially and academically if they can learn to self-regulate
- They can only develop self-regulation skills slowly while they experience a lot of scaffolding from the adults in their lives

Thanks to my Lab

- Maria Ramirez
- Andrea Larson
- Sarah Haney
- Kayla Hilyard
- Ben Kennert

www.chsbs.cmich.edu/timothy_hartshorne

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Category: Behavior

Thursday
4:10-4:35
Palomino 1 - 3

"Why self-stimulation is a good thing, and how and why we should interpret it"

David Brown
Educational Specialist
California Deaf-Blind Services
San Francisco State University

Presenter Information:

David Brown is a special education teacher who has been working with children with CHARGE syndrome for 30 years. He has written extensively about CHARGE, and travels the world giving presentations about various aspects of the syndrome, and helping to assess children alongside their families and local professional teams. In 2013 David will be spreading the word about CHARGE in person on visits to New Jersey, Sweden, Maryland, Minnesota, Arizona, Tennessee, and Germany.

Presentation Abstract:

As the most multi sensory impaired of syndromes, people with CHARGE are challenged to explore a range of apparently unusual behaviors in order to function effectively to satisfy their own needs. Many of these unusual behaviors seen in people with CHARGE are attempts to compensate for sensory losses and obtain the best and most reliable information possible, both from the environment and also from their own bodies. Other of these behaviors originate as attempts to modulate arousal levels – what we would call self-regulation. All these behaviors can be characterised as 'self stimulation', which is a normal part of human behavior but often occasions extreme and persistent opposition when seen in people with CHARGE. Indeed, in the field of special education self-stimulation, or 'stimming', is often regarded as a cardinal sin to be opposed and removed at all costs. This presentation will try to clarify the role of unusual postures and self stimulation behaviors, and will encourage more careful and informed observation as the essential prelude to any intervention.

Category: Behavior

Thursday
4:10-4:35
Palomino 1 - 3

Self-regulatory strategies for children with CHARGE syndrome

Maria A Ramirez
Doctoral Student
Central Michigan University

Presenter Information:

Maria Ramirez is a Doctoral student in the School Psychology program at Central Michigan University. For the past three and a half years she has been working with Dr. Tim Hartshorne exploring self-regulation in children with CHARGE. Her current research focuses on the assessment and validation of a Fun Chi video to be used in future research to assess the effects of Fun Chi on sleep, balance, and self-regulation in children with CHARGE.

Presentation Abstract:

The four windows of self-regulation (physiological, behavioral, cognitive, and emotional) provide the perfect areas for intervention in children with CHARGE. Although individuals with CHARGE may often use compensatory behaviors to aid in regulating their behavior, because of the presence of multisensory impairments and maladaptive patterns of behavior, positive self-regulatory strategies may at times be compromised. Using the four windows of self-regulation may prove to be an invaluable tool in understanding the function of the child's behavior, identifying the child's behavioral strengths that we can build up on, and in identifying specific self-regulatory areas to target for intervention. Strategies to enhance self-regulation in both the school and home will be presented. This presentation will be the third, preceded by Tim Hartshorne and David Brown.

FOSTERING SELF-REGULATORY STRATEGIES IN CHILDREN WITH CHARGE SYNDROME

Maria Alejandra Ramirez
School Psychology Doctoral Student
Central Michigan University

Agenda

1. Overview of 4 areas/windows of Self-Regulation
2. Example of Self-Regulation
3. What we know about Self-Regulation in children with CHARGE syndrome
4. Using the Windows of Self-Regulation to *identify strengths* and *identify difficulties*
5. Using the window of self-regulation to *prioritize areas to target*
6. In Detail: Specific strategies to foster each window of self-regulation

Discussion Goal 1:

Quick Overview Self-Regulation and the 4 Windows of Self-Regulation

What is Self-Regulation?

- Adaptive and flexible management of four domains.
  - Physiological, behavioral, cognitive, and emotion
- In order to describe regulation as "self-regulation" two components are necessary:
  - 1) self-awareness of the process
  - 2) a subsequent goal-directed action.
- Self-regulation must begin with a goal, and that goal describes what you want to have happen and what you must do to make that goal happen.
- Self-regulation involves gauging internal and external stimuli and responding appropriately under environmental expectations.

Self-Regulation:

→ **Goal** →

What are the 4 Windows of Self-Regulation?

Physiological

Behavior

Cognitive

Emotion

What is Physiological Self-Regulation?

Physiological

- Self's ability to react and alter its own states and responses to meet the needs of the body.
- In great part under the control of the somatic, endocrine and autonomic nervous systems.

What is Behavioral Self-Regulation?

Behavior

- Awareness of a behavior
- And choosing those behaviors most adaptive toward achieving a goal.
- Goal directed and purposeful behavioral patterns consisting of:
  - one's ability to inhibit,
  - regulate, pace, and delay gratification
    - Jahromi and Stifter (2008)

What is Cognitive Self-Regulation?

Cognitive

- Voluntarily regulating thoughts and mental processes by balancing inhibition and initiation of behavior in order to achieve a goal
- Involves
  - Attention
  - Memory
  - Learning (as well as using prior learning)
  - Reasoning
  - Problem-solving
  - Decision-making
  - Metacognition

What is Emotion Self-Regulation?

Emotion

- Using emotion regulation, the individual analyzes, controls, alters, or prevents behaviors related to the adaptive expression of emotions
  - (Lam & Lewis, 2010).
- May occur at different points in time during the emotional response

Discussion Goal 2:

Example of Self-Regulation

Example: Dentist Appointment

- **Physiological:**
  - You make sure to brush and floss your teeth really well a couple days before the appointment
- **Behavioral:**
  - You make sure to put the appointment time/day in your planner
  - You get a babysitter
- **Cognitive:**
  - You mentally prepare yourself for the procedure
- **Emotion:**
  - You tell yourself the pain will be over soon
  - You ask for a lot of pain medicine to make sure you feel no pain

Discussion Goal 3:

What we know about Self-Regulation in children with CHARGE syndrome

What do we know about Self-Regulation in CHARGE?

- Multi-sensory difficulties may limit exposure to environmental stimuli, their exposure to interactions and reactions to the environment.
- As DeGangi (2000) states, early deficiencies in self-regulation may lead to challenging behavior, and deficits in attention and inhibition.

What do we know about Self-Regulation in CHARGE?

- **Physiological:**
  - Brown (2005) notes that individuals with CHARGE syndrome are truly multi-sensory impaired, often having challenges with vision, hearing, balance, touch, temperature, pain, pressure, smell, breathing, swallowing, eating, drinking, digestion, and temperature control

What do we know about Self-Regulation in CHARGE?

- **Behavior:**
  - May display behaviors typical of individuals with: Autism Spectrum Disorder, ADHD, OCD, Tourette's syndrome, and Deaf Blindness (Hartshorne & Cypher ,2004).
  - These may include: restricted range of interest, stereotyped movements, fidgeting with objects, preference for certain objects or people, tactile defensiveness, staring at lights, vocal stimulation.

What do we know about Self-Regulation in CHARGE?

- **Cognitive:**
  - Children with CHARGE may present with executive *dys*function.
  - Specifically in the areas of *shifting, monitoring, and inhibiting.*
    - Hartshorne, Nicholas, Grialou, and Russ (2007)

What do we know about Self-Regulation in CHARGE?

- **Emotion:**
  - This area is much less explored than the other areas of self-regulation
  - Given that children with CHARGE have difficulty in the other areas of self-regulation and all the areas are related….it is possible that this may also be an area of difficulty.

Discussion Goal 4:

Using the Windows of Self-Regulation to:

1. *identify strengths*
2. *identify difficulties*

Identifying Regulatory Strengths/Difficulties in YOURSELF

Physiological

Behavior

Cognitive

Emotion

Identifying Regulatory Strengths/Difficulties in YOUR CHILD

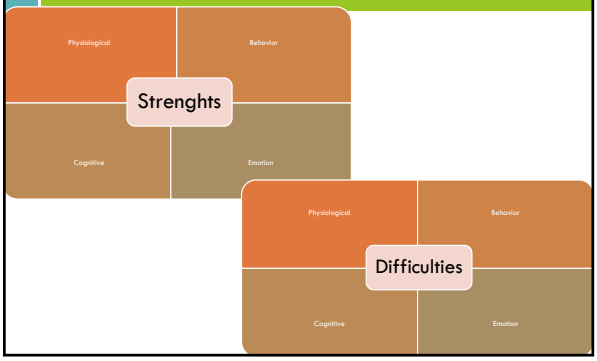
Physiological

Behavior

Cognitive

Emotion

Complete handouts for yourself and child



Discussion Goal 5:

Using the Windows of Self-Regulation to

Prioritize areas to target

Prioritizing Areas to Target

Things to consider:

- What would increase the most function?
- What would increase quality of life?
- What would save time?
- What would save resources?
- Do I have time to target this area?
- Do I have the resources to target this area?
- Are the final outcomes worth it?

Example:

Discussion Goal 6:

Specific Regulatory Strategies to Foster Each Window

Strategies: Behavior

Factors to consider:

- ID problematic Behavior
- What preceded the behavior?
- What follows the behavior?
- Who is present when the behavior occurs?
- Where does the behavior take place?

Strategies: Behavior

- Modeling, Role-playing, and Reinforcement
- Predictable routines
- Visual Schedule
- Increasing choices
- Pre-correction
- Red Dot Timer
- First-Then Statements
- Scaffolding
- Requesting breaks with visuals
- Pressure vests and deep tissue massages

Strategies: Physiological

- Sensory stimulation
- Environmental modifications
- Relaxation Therapies
- Diet
- Feeding
- Toileting
- Sleep issues

Strategies: Cognitive

- Modeling thinking, planning, and inhibitory strategies
- Modification of stressful environments
- Preparation to enter stressful environments
- Use of mind-body and technology practices to foster concentration and inhibition
- Take advantage of the child's favorite activities to imbed teaching of waiting and engaging.

Strategies: Emotion

- To develop awareness of emotion: teaching feeling vocabulary (modeling, scaffolding, and reinforcement)
- Mirroring feeling and modeling appropriate emotional responses
  - "I am happy, this is what happy looks like"
  - "You look upset, like this"
- Repetition and rehearsal of skills
- Use of visuals: colors, faces, traffic lights – to represent feeling or state
- Recognizing triggers that produce emotional response
- Teaching strategies to deal with emotions (deep breathing, location to calm down, attachment objects, etc.)
- Using all daily events to teach feelings, reactions, and modeling appropriate ways of coping

Strategies: Emotion

Remember to:

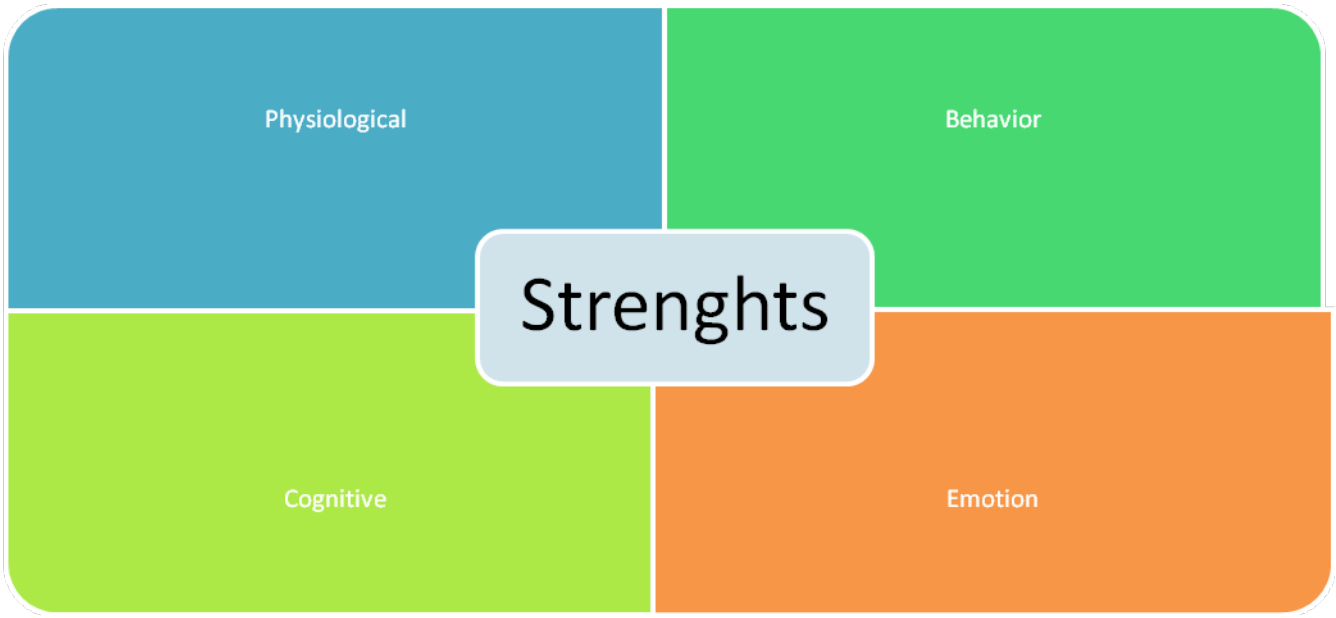
- Teach in different environments (home, school, grocery store)
- Teach with different people (peers, parents, siblings, etc.)
- Reinforce all appropriate behaviors in new environments

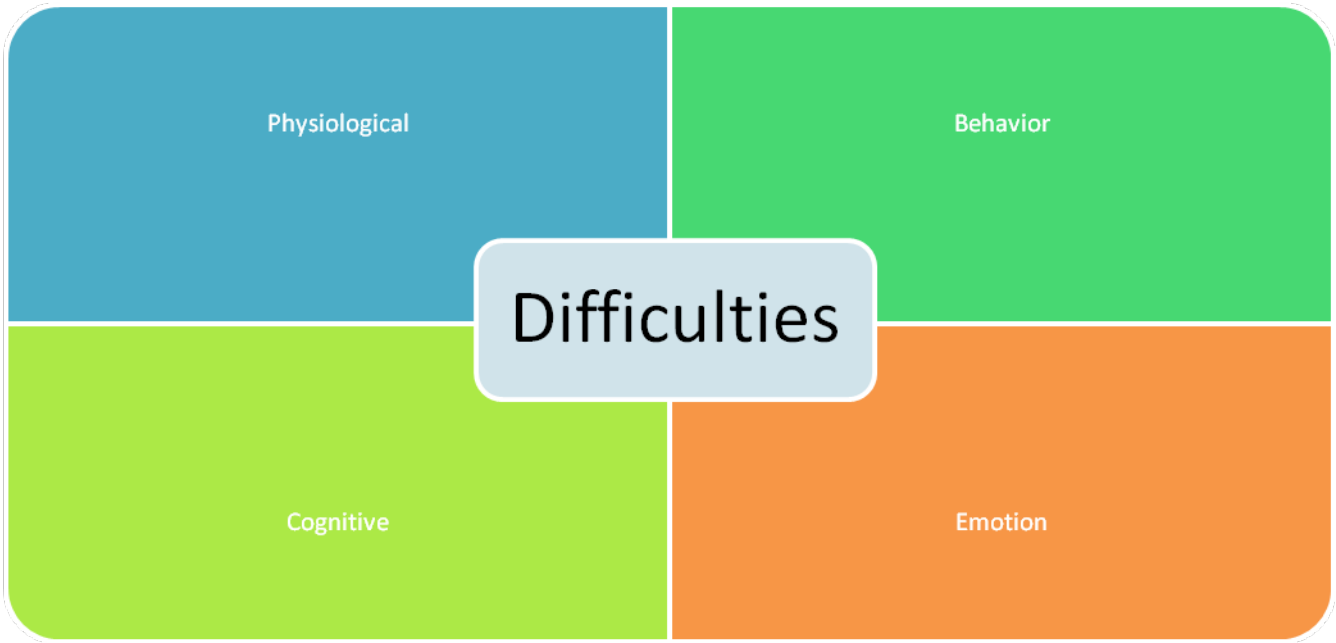
Thank you for your time!!!

If you have questions, please contact me at:

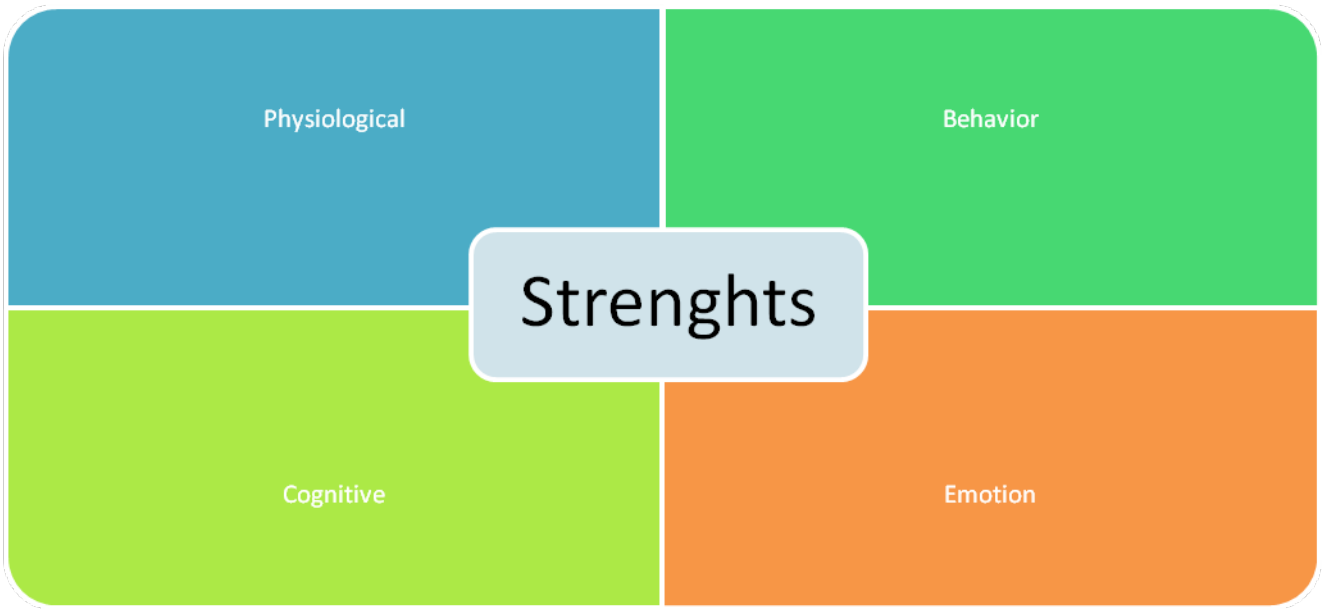
ramir1ma@cmich.edu

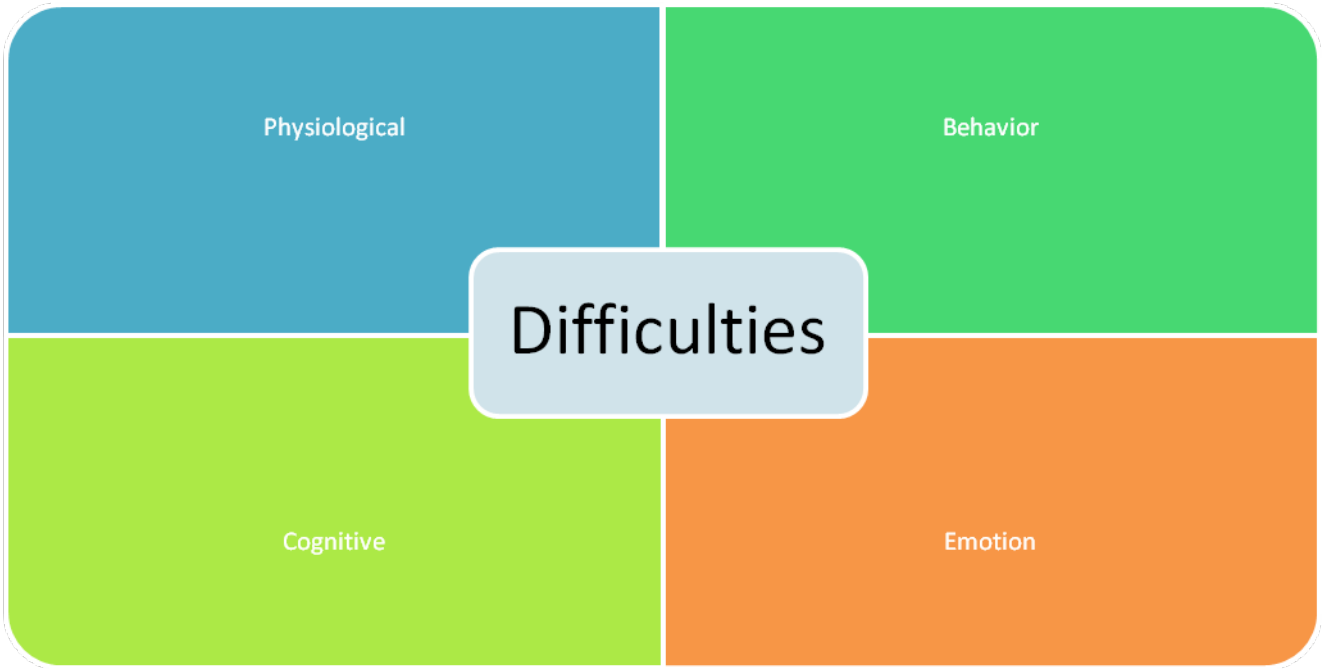
Identifying Regulatory Strengths and Difficulties in ME





Identifying Regulatory Strengths and Difficulties in MY CHILD





Category: Medical/Genetics

Thursday
4:35-5:00
Palomino 1 - 3

More clinical overlap between 22q11.2 deletion syndrome and CHARGE syndrome than often anticipated

Nicole Corsten-Janssen, MD
Dept. of Genetics, University Medical Center Groningen, Groningen, The Netherlands

Presenter Information:

Nicole Corsten-Janssen studied medicine at the University of Groningen in the Netherlands. She has been working in clinical genetics in the University Medical Center Groningen since 2008 and is currently in training to become a clinical geneticist. In 2009 she started her PhD project that focuses on CHARGE syndrome, CHD7 and heart defects for which she has studied among other heart defects in patients with *CHD7* mutation, the overlap between CHARGE syndrome and 22q11.2 deletion syndrome and made an online database for *CHD7* mutations (www.CHD7.org). She also participates in the Dutch multidisciplinary CHARGE outpatient clinic and is actively involved in the Dutch CHARGE parent support group.

Presentation Abstract:

CHARGE and 22q11.2 deletion syndrome are both variable, multiple congenital malformation syndromes that show considerable phenotypic overlap. In our presentation we'll demonstrate this overlap and show that it may hamper their differential diagnosis: patients with clinical CHARGE syndrome may have a 22q11.2 deletion and patients with clinically 22q11.2 syndrome may have a *CHD7* mutation. This overlap also has consequences for the clinical follow-up of thus far not well recognized clinical features in CHARGE syndrome, like T-cell dysfunction and hypocalcaemia.

The clinical overlap between CHARGE syndrome and 22q11.2 deletion syndrome

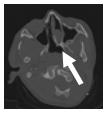
Nicole Corsten-Janssen
Clinical geneticist in training
University Medical Center Groningen
The Netherlands

It started with a patient…

C 3 years old
H > Coloboma of iris and retina
A > Pulmonal stenosis
R > Unilateral choanal stenosis
G > IQ 91
E > Height -1,3 SD
> Simple ears
> Mixed hearing loss
> Abnormal semicircular canals

CHARGE syndrome

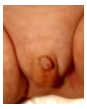
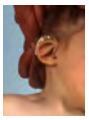




Birth incidence 6-7:100,000

Coloboma
Heart malformation
Atresia of choanae
Retardation
(growth and development)
Genital hypoplasia
Ear abnormality
(including deafness)

Other features

Diagnosis of CHARGE syndrome

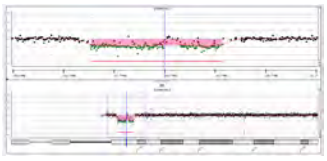
	Verloes:	Blake:
Clinical criteria	> Major criteria > Coloboma > Choanal atresia > Hypoplastic semicircular canals (3 major or 2 major + 2 minor)	> Major criteria > Coloboma > Choanal atresia > Cranial nerve dysfunction > Characteristic ear abnormalities (4 major or 3 major + 3 minor)
DNA analysis	CHD7 gene	

Blake *et al* Clin Pediatric 1998
Verloes AJMG 2005

CHD7 mutation?

> Sequencing and MLPA of CHD7:
no mutations or deletion

> 180 k oligo whole genome array



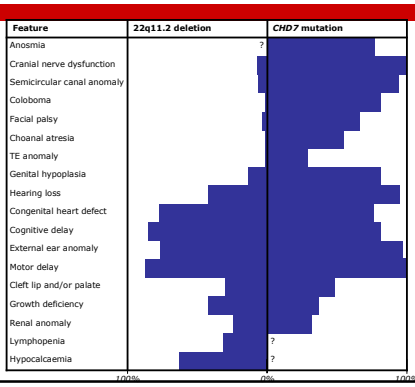
Classical 3Mb 22q11.2 deletion

22q11.2 deletion syndrome

Birth incidence 10-50:100,000

>Congenital heart defect
>Velar insufficiency, cleft palate
>Hypocalceamia
>Learning difficulty, speech delay
>Behavioural problems
>Hypoplastic alae nasi, simple ears
>Thymic abnormalities, T-cel dysfunction

>Problem with TBX1 gene



CHARGE patients with 22q11.2 deletions

> 4 other patients from literature and our own patients

Patients	Features															
	C	H	A	GR	DD	G	E	SCC	C(L)P	HL	FD	VII	TE	Ca	I	T	Other
Emanuel	u	u	u	u	u	u	u	u	u	u	u	u	u	u	u	u	CHARGE association, no further information
Digilio	+	+	+	u	u	+	+	u	-	u	u	u	-	+	+	-	unilateral absent radius and hypoplastic ulna
Devriendt	+	+	+	+	+	-	+	u	-	+	u	u	u	-	u	-	pre-auricular tags, pit left cheek
Pt1	+	+	+	-	+	-	-	+	-	+	+	-	-	-	-	u	bronchotracheomalacia,GERD
Pt2	-	+	+	-	+	-	+	-	-		+	-	-	-	-	-	pharyngomalacia

22q11.2 features in CHARGE patients

> Database
> 802 patients with *CHD7* mutations
> Clinical features
- Hypocalceamia
- T-cel dysfunction
- Severe immunological problems
- Thymus anomalies
- "DiGeorge phenotype"
- "22q11.2 deletion syndrome phenotype"

→ 30 patients (3.7%) *CHD7* positive patients with 22q11.2 deletion features

CHD7 mutations in patients with clinical 22q11.2 deletion syndrome

> 20 patients with clinical 22q11.2 deletion syndrome
> No problems with *TBX1*
> 5 with *CHD7* mutations

Patients	*CHD7* mutations		Clinical features
CH95-172	c.493_496delinsGG	p.Pro165fs	22q11.2 deletion syndrome phenotype
CH95-218	c.2440C>T	p.Gln814X	ADHD; speech therapy; dysmorphia; sensorineural/ conductive hearing loss
CH94-143	c.3024T>G	p.Tyr1008X	thymic hypoplasia, cleft lip and palate; hypocalcemia; normal cardiac ultrasound; auricular dysplasia
CH96-184	c.4357C>T	p.Gln1453X	low PTH; low Ca; low T-cells; small thymus; ASD; dysmorphia
CH99-214F	c.4424del	p.Glu1475fs	22q11.2 deletion syndrome phenotype

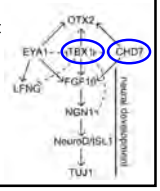
> Important for follow-up CHARGE patients

Explanation clinical overlap?

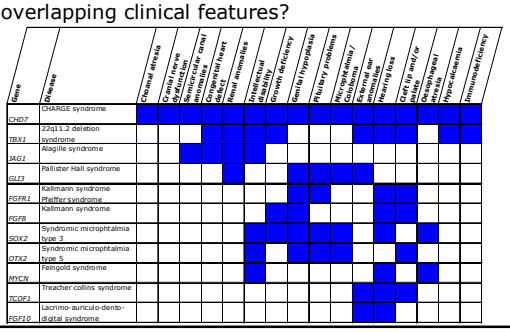
TBX1 is a transcription factor
CHD7 influences gene expression by binding chromatine
→ TBX1 and CHD7 influence other genes

>Hurd et al (2010): neurogenesis inner ear
>Randal et al (2009): great vessel development

>Shared molecular pathway
>Overlap in target genes



Are CHD7 and TBX1 the only genes with overlapping clinical features?



Conclusions

> 22q11.2 deletion syndrome and CHARGE syndrome are more alike than often anticipated

> Challenging differential diagnosis
- CHD7 analysis in clinical 22q11.2 deletion patients
- Whole genome array in CHD7 negative CHARGE patients

> Immunological investigation in CHARGE patients

> Further research on the molecular link

Acknowledgement

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Questions??

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Category: Medical, Behavior

Thursday
5:00-5:25
Palomino 1 - 3

"How to Identify Pain Non-Vocally and the Relationship of Pain to Challenging Behavior"

Kasee Stratton, Ph.D.
Kennedy Krieger Institute/Johns Hopkins University School of Medicine

Presenter Information:

Dr. Kasee Stratton has been researching and working with children and young adults who have CHARGE for the past 7 years. She is a previous student of Dr. Timothy Hartshorne. Dr. Stratton's primary research and clinical interests include: reducing challenging behaviors, teaching appropriate adaptive skills, identifying non-vocal pain behaviors, and reducing the pain experience for individuals with CHARGE. Kasee is currently finishing her Post-Doctoral Fellowship at the Johns Hopkins University School of Medicine and the Kennedy Krieger Institute. She plans to continue her work with CHARGE following completion of her fellowship and hopes to open a CHARGE clinic in the near future.

Presentation Abstract:

This presentation is designed to highlight the importance of pain for individuals with CHARGE and how to identify pain non-vocally. The presentation will emphasize results from two pain studies that are the first of their kind for individuals with CHARGE. Results are presented in a manner appropriate for parents, caregivers, educators, and physicians.

Specific highlights include: the variety of pain experiences (both acute and chronic), how to identify and track pain for your child, how pain impacts behavior, and strategies for reducing the pain experience.

HOW TO IDENTIFY PAIN AND THE RELATIONSHIP OF PAIN TO CHALLENGING BEHAVIOR

11th International CHARGE Syndrome Conference

Kasee Stratton, Ph.D.

Thank you!

- CHARGE Syndrome Foundation
  - Research funding support
  - Supporting our participant lists
- Families of children with CHARGE
- Central Michigan University
  - Funding support

CHARGE and Pain Overview

- Pain in developmental disabilities
- CHARGE syndrome and pain
- Are we identifying pain?
- How pain is related to challenging behavior
- Areas of future research

A Parent's Story…

"Since my son was born almost 29 years ago, every aspect of his care has been a challenge. Being a single parent has been hard, but never harder than when my son is in pain and I can't help him. As a parent, it is my job to make sure his needs are met and that he is loved. I feel like I have let him down when he is having pain and I can't make it better. Unless it is something obvious, I have to play the guessing game of what hurts and why.

…continued

…My son is non-vocal and cannot tell me what is wrong. One of the biggest barriers to our children is others (e.g. doctors) understanding children with disabilities can have chronic pain too. And they don't understand that pain contributes to behavior issues, such as SIB, that can be life-threatening. My son has had two subdural hematomas from SIB. It took me 6 months to get a CT scan of his head. In that 6 months he was in such excruciating pain. There is a fight everyday to get him what he needs."

Pain and Developmental Disabilities

- "Higher" threshold for pain
  - Has been suggested in CHARGE (Davenport, 2002)
  - Limitations with Communication: Changes expression of pain
- No evidence
- Higher risk for experiencing more frequent pain
- High Pain Threshold vs. High Pain Tolerance

Sources of pain related to CHARGE

- Surgery
  - 1 to 63 procedures
  - Average 13
- Procedures
- Doctor visits
- CHARGE Characteristics

Does your child experience pain from?

Pain Experience	(N= 61)	Percentage of Participants
Ear Infections	41	67.2
Sinus Infections	27	44.3
Gastroesophageal Reflux	26	42.6
Constipation	26	42.6
Surgery	23	37.7
Tactile Defensiveness	21	34.4
Migraine	15	24.6
Stoma Pain	12	19.7
Abdominal Migraine	12	19.7
Muscle Pain	12	19.7
Back Pain	8	13.1
Hip Pain	6	9.8
Jaw Pain	5	8.2
Pain During Sleep	5	8.6

Migraines

- Trigeminal nerve (CN V)
  - Sensation and function to your jaws, face, tongue, sinus, palate, eyes, teeth, and lips.
  - Also has a role with chewing and swallowing
  - CN dysfunction in CHARGE

Blake, K.D., Hartshorne, T. S., Lawand, C., Dailor, A. N., & Thelin, J. W. (2008). Cranial nerve manifestations in CHARGE syndrome. *American Journal of Medical Genetics, 146A*, 585-592.

Migraines

- Most intense pain for children with CHARGE
- Range of 2-40 days/year
  - *M*= 14
- Average Rating: 2.67 (Range: 2-4)

Abdominal Migraine

- Typically children ages 5 to 9
- Linked to adult migraines
- Lasts 1 to 72 hours
- Acute stomach pain with
  - Nausea
  - Vomiting
  - Light sensitivity
  - Diarrhea
  - Loss of appetite

Abdominal Migraine

- Range from 2-365 days/year (*M* = 97)
- Average Rating: 2.45 (Range 1-4)

Constipation

- Painful bowel movements
- Dry or hard stool
- Nausea
- Cramps, abdominal pain
- Average pain for 52 days/year (1-203)
- Hurts more rating (2.38) (1-4)
- Fecal impaction
  - Abdominal cramping
  - Rectum discomfort

Otitis Media

- Range from 1 to 160 days a year; *M*=26 days
- Average rating 2.24 (Range 0-4)

Gastroesophageal reflux disease

- Heartburn
  - Involves a burning pain in the chest (under the breastbone)
  - Increased by bending, stooping, lying down, or eating
  - More frequent or worse at night
  - Relieved by antacids
- Nausea and vomiting
- Regurgitation of food
- Sore throat
- 10-365 days/year (*M* = 169)
  - Average rating 2 (hurts more)

Tactile Defensiveness

- textured materials/items
- "messy" things
- vibrating toys
- a hug or kiss
- certain clothing textures
- rough or bumpy bed sheets
- seams on socks
- tags on shirts
- tags on shirts
- light touch
- hands or face being dirty
- shoes and/or sandals
- wind blowing on bare skin
- bare feet touching grass or sand

Most Intense Pain and Average Duration

	Pain Intensity			Days per Year in Pain	
Characteristic	***M***	***SD***	**Range**	***M***	***SD***
Migraine	2.67	.87	2-4	13.50	13.51
Abdominal Migraine	2.45	1.10	1-4	97.47	128.95
Constipation	2.38	.80	1-4	52.25	58.38
Surgery Pain	2.34	.97	1-4	9.52	9.40
Chronic Recurrent Otitis Media	2.24	.99	0-4	22.88	32.18
Sinusitis	2.17	.82	1-4	35.13	41.51
Gastroesophageal Reflux	2.06	1.14	0-4	169.29	133.70
Breathing	2.00	1.03	1-4	108.67	131.82
Hip/Back Pain	1.86	.95	1-4	98.09	144.14
Muscle Pain	1.82	.87	1-3	95.70	136.07
Coughing	1.61	.80	1-3	66.48	99.42
Jaw Discomfort	1.56	.88	1-3	13.22	11.17
Difficulty Swallowing	1.50	.83	1-4	129.00	154.04

Identifying Pain in CHARGE

- Are you able to determine when your child is experiencing pain?
  - 75% -Yes
  - Did not vary significantly by age of child
- What about educators, therapists, & doctors?
- Zero parents could identify chronic pain and no child could indicate chronic pain

What behaviors indicate pain?

- Vocal
  - Crying, screaming, moaning
- Social
  - Irritable, withdrawn, doesn't follow directions
- Facial
  - Grinds teeth, changes in eyes (glassy), furrowed brow
- Activity
  - Lethargic, inconsolable, decreased movement/activity
- Body and Limb Movement
  - Rubbing area of pain, holding body in unusual posture
- Physiological
  - Fever, splotchy appearance, bowel movements, congestion
- Eating/Sleeping
  - Tired, changes in sleep

What behaviors indicate pain?

- Behavioral Challenges
- Self-Injurious Behavior (SIB)
- Dangerous Behaviors
- Aggressive, bites, hits head, throws objects, punches, pulls out g-tube

Amount of Pain

Why is it difficult to measure pain in CHARGE?

- Limited or no communication strategies
  - Cannot use the gold-standard
- Possible social-communicative deficits
  - (Craig, 2006)
- Possible social referencing deficit
  - (Recchia, 1997)

Measuring Pain

- Facial Reactions to Pain
  - Limited research
  - Facial palsy in CHARGE
- Rating Pain
  - Numerical ratings with pictures
  - Multidimensional pain tools

SCALES

- Non-Communicating Children's Pain Checklist-Revised (NCCPC-R)
  - 30 items; 7 subscales
    - vocal, social, facial, activity, body and limbs, physiological, and eating/sleeping

II. Social

Not cooperating, cranky, irritable, unhappy..... 0 1 2 3 NA

Less interaction with others, withdrawn..... 0 1 2 3 NA

PPP

- Pediatric Pain Profile (PPP)
  - 20 items
  - Rate: 0-3
    - Not at all, a little, quite a lot, and a great deal
- Examples:
- Grinds teeth or makes mouthing movements
- Is restless/agitated or distressed
- Tenses/stiffens or spasms

Measuring Pain

- Baseline:
  - Complete NCCPC-R and PPP on a good day
- NCCPC-R and PPP day of pain
- A significant difference was found

Common Pain Behaviors

NCCPC-R

- not moving, less active, quiet
- tears
- not cooperating, cranky, irritable, unhappy
- crying
- moaning, whining, whimpering
- less interaction w/others, withdrawn
- not smiling
- being difficult to distract, unable to satisfy
- furrowed brow

PPP

- not cheerful
- crying, moaning
- not socially responsive
- grimaces, screws up eyes and face
- frowns/furrowed brow
- hard to console/comfort

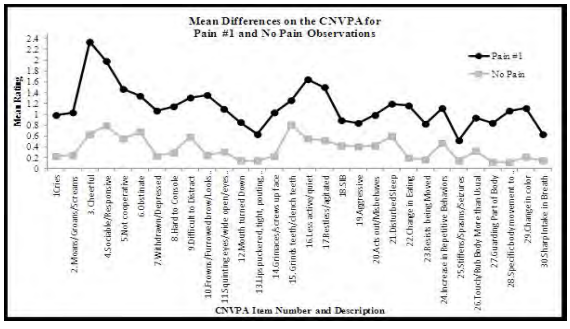
Not entirely useful for CHARGE

- Did not display a meaningful difference:
  - Flexing inward/drawing legs up (PPP #15)
  - Stereotypical movements/jumping/seizures (PPP #20)
  - Flopping (NCCPC-R #16)
  - Shivering (NCCPC-R #22)
  - Jumping around/agitation/fidgety (NCCPC-R #15)

CNVPA

- Items from parental input and previous study
- Significant difference between no pain and pain ratings; strong reliability
- For 36% of our sample, physicians were able to confirm a diagnosis that is known to produce pain (e.g. sinus infection)

CNVPA



CNVPA

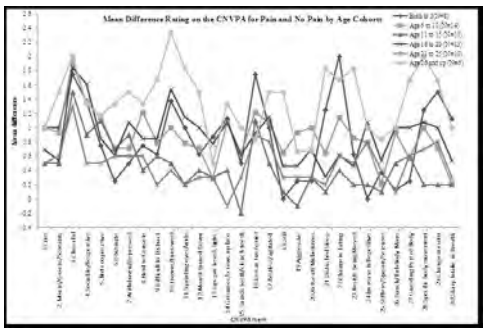
At least 1 point difference:

- Not Cheerful
- Aggressive
- Not Sociable
- Frowns/furrowed brow/looks worried
- Less active/quiet

.9 difference

- Restless/Agitated
- Change in Eating
- Specific movement to indicate pain
- Not cooperative
- Change in color

Differ by age?



Differ by Age?

- 1 month to 5 years
  - Fewer challenging behaviors
  - Change in eating
  - Less active/quiet
  - Change in color
- 11 to 15 years
  - Lower mean difference
    - aggressive behaviors
    - Grinding teeth/clenching teeth
- Age 26 and +
  - Squinting eyes/eyes wide open/eyes frowning
  - Mouth turned down
  - SIB
  - Disturbed sleep
  - Resist being moved
  - Specific body part held

CNVPA: Is it helpful?

Do parents find the CNVPA to be relevant to identify their child's pain (non-vocally)?

- Approximately 85% endorsed the CNVPA to be a relevant assessment to identify pain

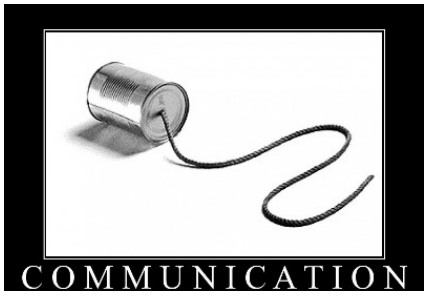
CNVPA helpful?

- Why might this instrument not be relevant?
  - Child can verbalize pain vocally (12)
  - "Never complains of pain and seems to tolerate it well."
  - "I've already developed ways to identify pain for my child" (3)
  - "After 24 years, I am in tune to my child's health"

Functions of Behaviors

- Attention
- To gain access to preferred items/activities
- To escape/avoid demands or less preferred items/activities
- Stimulatory

All Behavior is…



Challenging Behavior in CHARGE

- Common challenging behaviors
  - Preference for certain items
  - Restricted range of interests
  - Difficulty with social relationships
  - Repetitive behaviors; increase under stress
  - High levels of sensation seeking; may include self injurious behavior
  - Executive Dysfunction
  - Regulatory Disorder

Does pain affect behavior?

- Evidence that pain is associated with behavior problems in typical-developing children
  - De Lissovoy (1962) head banging and otitis media
  - Hart, Box, & Jenkins (1984) tantrums and upper respiratory infection
- Evidence that pain is associated with behavior problems in children with disabilities
  - O'Reilly (1997) self-injury and otitis media
  - Carr & Owen-DeSchryver (2007) sick days
  - Lekkas & Lentino (1978) constipation
  - Kennedy & Meyer (1996) allergies

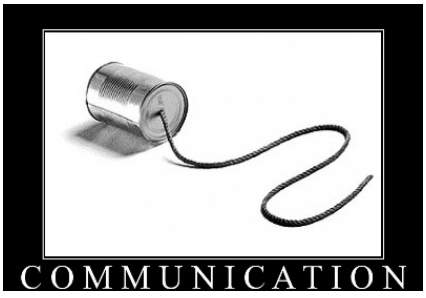
Does pain affect behavior?

- Aggressive behavior, destructive behavior, and self-injury (Kennedy and O'Reilly, 2006)
- Elevated pain → elevated self-injury (Symons and Danov, 2005)
  - We found similar results
- Attachment and Adaptive Functioning
  - Withdrawing and decreased communication
- Quality of life may be compromised (Oberlander & Symons, 2006)

Understanding Pain

- Unknown what children with CHARGE know about pain
  - How to predict when and how it will be resolved
  - Increase the intensity of the experience and also increase challenging behaviors
  - Individuals with CHARGE may need to be explicitly taught coping strategies to help identify pain and how to control these events in their lives

Challenging behavior as…



Reducing the pain experience

- Use CNVPA to track progress over time
- Mitigation
  - Analgesics
  - Dietary change
- Redesigning the environment
  - Reducing the demands
- Teaching coping skills
  - Self advocacy
  - Functional communication alternatives
- Parental Interaction with Physicians

Conclusion

- Children with CHARGE experience considerable amounts of pain and often exhibit problem behavior
- Problem behavior may have many causes, but one of them can be pain
- Pain can be managed when we know the child is experiencing pain, but not all children with CHARGE can easily communicate this
  - CNVPA may be a useful alternative

Future Pain Research

- Relationship between behavior and duration of pain
  - Impact adaptive, academic, and overall functioning
- Relationship between challenging behavior, pain, and communication (adaptive behaviors)
- Analgesics, neurological development, and the treatment of pain
- Controlled validity studies (e.g. surgery)
- Further investigation of age and sex differences

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