AUCD Research Topics of Interest (RTOI) Webinar

September 26, 2007

Presented by AUCD and supported by Cooperative Agreement U59/CCU321285-01 from the National Center on Birth Defects and Developmental Disabilities (NCBDDD) at Center for Disease Control and Prevention (CDC)



Webinar Agenda

- I. Welcome & Introduction Sue Lin, MS Project Director, AUCD-NCBDDD Cooperative Agreement
- **II.** Presentation
- Prevalence of Autism Spectrum Disorder in Children with Down Syndrome- Is There an Association? – Susan Hyman, MD & Steve Sulkes, MD (Strong Center for Developmental Disabilities, NY UCEDD); Cordelia Robinson, PhD, Susan Hepburn, PhD, & Deborah Fidler, PhD (JFK Partners, CO UCEDD)

III. Discussant

- Diana Schendel, PhD, NCBDDD, CDC
- **IV.** Question and Answer

NCBDDD-AUCD Cooperative Agreement

- Strengthen the nation's capacity to carry out public health and disability activities
- Foster collaborations among AUCD, its members, and NCBDDD
- Facilitate a wide range of research, education, and dissemination activities.



Research Topics of Interests (RTOI)

- RTOI are specific research area of significance identified by scientists at NCBDDD, CDC. Past RTOI projects have focused on the following areas:
- Health Communication and Education
- Prevention of Secondary Conditions
- Healthcare Cost Analysis
- Quality of Life Studies
- Developmental Factors and Outcomes
- Health Promotion Interventions
- Co-Morbidity Prevalence Studies



Specific disabilities areas include: autism, Down syndrome, Duchenne muscular dystrophy, hearing loss, fetal alcohol syndrome, spina bifida, and Tourette syndrome.

Presenters and Discussant











Susan Hyman, MD Steve Sulkes, MD Strong Center for Developmental Disabilities University of Rochester Medical Center

Cordelia Robinson, PhD Susan Hepburn, PhD JFK Partners University of Colorado at Denver Health Sciences Center Diana Schendel, PhD NCBDDD, CDC

Webinar Guidelines

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Sample webinar screen

Down syndrome and Autism: Is there an association?



AUCD/CDC RTOI Projects University of Colorado and University of Rochester



Medical and Behavioral Characteristics of Children with Down Syndrome in New York State





Prevalence of Autism Spectrum Disorders in Down Syndrome



Cordelia Robinson Susan Hepburn **JFK Partners**



HEALTH SCIENCES CENTER TOWN DENVER CAMPUS

University of Colorado at Denver and Health Sciences Center



Down syndrome (DS)

Epidemiology of Down syndrome

- 1-3/1,000 (10-30/10,000) births in European countries 1995-9 (Dolk et al, 2005)
- 1/800 (12.5/10,000) live births in US 1996-2000 National Birth Defects Prevention Network
- Survival rate to 1 year is 93% and to 10 years is 88.6% (Rasmussen et al, 2006)

Autism Spectrum Disorders (ASD)



Modern Epidemiologic Studies of ASD

Author	Location	Prevalence	Comment
Ca Dept Dev Svc, 1999	California, 1987-97	300 x increase	Not an epi study
Bertrand, 2001	Brick Twp, New Jersey	AD 40/10,000 PDD 60	No different from rest of NJ
Chakrabarti & Fombonne, 2001	Staffordshire	AD 17/10,000 PDD 45.8	26% MR, <6 yrs.
Yeargin- Allsopp, 2003	Metro Atlanta	34/10,000	3-10 yrs. 68% MR
Barbaresi, 2005	Olmstead Cty	4.5/10,000	Increase definitional
MMWR, 2006	US - survey	55-57/10,000	No difference with age
MMWR, 2007	US-multiple source, ADDM	66/10,000 ave	AL 3.3/1000 NJ10.6/1000

Genetic Disorders at Increased Risk for Autism

Down syndrome?

- Fragile X Syndrome
 Smith Lemli Opitz
 Tuberous Sclerosis
 15 q 11 duplication
 MECP2 related disorders
- PKU
- Smith-Magenis
- Angelman Syndrome

Why is it important to determine risk for comorbidity?

- Potential for understanding the neurobiology of autism, phenotypic symptoms of autism, phenotypic symptoms of the comorbid disorder
- Provision of appropriate services to children with both diagnoses
- Determine need for screening
- Better understanding of child and access to appropriate support mechanisms for families



Down syndrome + Autism Spectrum Disorder

???/10,000

Comorbid Down syndrome and ASD

Author	Location	Prevalence	Comment
Kent et al, 1999	UK, 2-16 yrs multiple source	33/58 screened 4 ASD, 7%	11/29 rituals, obsessions ASSQ, CARS
Rasmussen et al, 2001	Sweden Clinic sample	25 cases over 15 years	5 had + FHx 5 IS
Starr et al 2005	UK,test validation	3/13 ADI-R+ 2 ADOS+	Not the same subjects!
Capone et al 2006	US, clinic sample n=127	64 ASD, 19 + SMD, 18+DB, 26 DS alone	ABC + Aut Behav C, 13.6% min., type of stereotypy
Kraijer	Holland, multiple source n=254		Different pattern of scores, high stereotypy

Comorbid Intellectual Disability and ASD

Author	Location	Prevalence	Comment
Kraijer, 1997	Holland	38.3% residential (718), 22.6% home (297)	40% PMR/SMR, 20% Mod MR, 17.3% Mild
de Bildt et al, 2003	Holland	16.7% total, 9.3% mild, 26.1% Mod- PMR	DSM IV TR, ADI-R, ADOS
La Malfa et al 2004	Italy	39.2% of 166 residential care	PDD-MRS
de Bildt et al 2005	Holland N=825	Range 7.8-19.8% DSM IV TR 16.7%	Depends on instrument used

Screening and Diagnosis of ASD

Modified Checklist for Autism in Toddlers (M-CHAT) Social Communication Questionnaire (SCQ) Pervasive Developmental Disorder-Mental Retardation Scale (PDD-MRS) Autism Diagnostic Interview-Revised (ADI-R) Autism Diagnostic Observation Schedule (ADOS) Child Behavior Checklist (CBCL) Social Responsiveness Scale (SRS)

All are used to inform DSM IV diagnostic criteria

Epidemiologic Approaches to Investigation of Comorbidity

- Birth Registry to ascertain regional cohort
 - New York Congenital Malformation Registry
 - Colorado Dept. of Public Health and Environment (CDPHE)
- Multiple source recruitment to increase ascertainment
 - Parent support groups e.g. Flower City Down Syndrome Network, Mile High Down Syndrome Association
 - Recruitment from medical sources of specialized care

Differences in Design in the two RTOI Projects

Rochester, New York

- Tiered assessment
- Level 1: Large number screened from total sample
- Level 2: ADI on sample of screen
 + and screen -
- Level 3: Geographic sample (within 2 hours of Rochester)
 ADOS on sample of ADI + and ADI -



Denver, Colorado

- Population study
- Study entrance with screening
- All screen positive complete evaluation
- Two thirds of screen negative go on to complete evaluation



Specific Aims of the NY RTOI

- Determine the comorbidity of Autism Spectrum Disorders and Down syndrome in New York State (outside of NYC)
- Examine tools currently used for screening and diagnosis of ASD
- Examine medical comorbidities of behavior
- Investigate nature of repetitive behaviors in children with Down syndrome with/without ASD

NY: Stepwise Evaluation

Level 1 Screening:

Paper-based (M-CHAT, SCQ, & Medical History Questionnaire specific for DS)

Telephone Screening (PDD-MRS)

All screen + Next screen -

Level 2 Parent Report:

Paper-based (Vineland-II, RBS-R)

Telephone Interview (ADI-R)

All ADI-R +

Level 3 Direct Assessment:

Paper-based (CBCL & SRS)

Direct Assessment (ADOS, Leiter-R, EOWPVT, PPVT)



NY Demographics to date

Average Age	94 months (36-167)
Gender	Male 54%
	Female 46%
Average Maternal Age at Child's Birth	33.36 years (16-45)
Average Paternal Age at Child's Birth	34.97 years (18-59)
Race	Caucasian 92.5%
	African American 4.4%
	Asian 0.3%
	Native American 0.9%
	Other 1.9%

Consenting participants (to date) Compared to Refusals/no answer (NYCMR)

	Consenting participants	Refusals/no answer
Race	Caucasian 95.8%	Caucasian 88.9%
	African American 2.8%	African American 7.5%
	Asian 0.4%	Asian 2.3%
	Other 1.1%	Other 1.3%
Parental Age at child's birth	Maternal 33.3 years (6.3SD)	Maternal 32.8 (6.8SD)
	Paternal 35.2 years (6.1SD)	Paternal 35.0 (7.3SD)
Maternal	12 years 22.4%	12 years 32.0%
Education	16 years 21.7%	16 years 14.4%
	16+ years 22.4%	16+ years 10.3%
Child's Gender	Male 51.8%	Male 55.7%
Child's Age	7.4 (3.2SD)	8.0 (3.2SD)

Interim Report as of September 2007 – New York...What do Screen positives look like?





Interim Report as of September 2007 – New York...What do Screen Negatives look like?

> Screen Negative (MCHAT AND SCQ) 149 (n= 318)





53% of respondents screened positive on either the MCHAT or SCQ So far, 1/3 of participants evaluated through Level 3 have been discordant between the ADI-R and ADOS. This is similar to the observation of de Bildt et al in people with **Intellectual Disability**

Summary (continued)

The "gold standard" screening and diagnostic tests used for research and clinical assessment of autism require additional evaluation for validity in children with Down syndrome/Intellectual Disability There is currently no substitute for Clinical **Diagnosis using DSM IV criteria** These data are preliminary, reflecting only a portion of the projected study population

Future Directions

- Complete recruitment and testing
- Evaluate association of medical characteristics and behavioral diagnosis
- Evaluate characteristics of repetitive behavior and diagnosis in children with DS
- Examine PDD-MRS as a screening instrument for people with intellectual disability in the US
- Collaborate with Colorado RTOI in interpretation of data

Prevalence of Autism Symptoms in Children with Down Syndrome: Preliminary Findings from Colorado

Based on data verified by 9/1/07



Conduct a population-based epidemiological study of the prevalence of ASD in children with Down syndrome

Recruitment Process

- Mile High Down Syndrome Society publicizes the study and sends out 228 letters to member families
- Colorado Dept. of Public Health and Environment (CDPHE) utilizes their birth registry monitoring program to invite families of children with DS who were:
 - Born between Jan.1, 1996-Dec.31, 2003
 - While mother resided in 1 of 10 north-central Colorado counties
- Families who respond are offered a screening for social, communication, and behavioral difficulties – and possibly a follow-up diagnostic evaluation



* INCLUDES 20 OBTAINED AFTER WORKSHOPS/ALSO GOT LE34TER





HAS THE AUTISM SCREENING BEEN COMPLETED?







Participant Characteristics: (n= 124)	Screening Sample
Chronological age (in mos.)	
Mean (SD)	69.76 (23.45)
Range	36 – 129
Gender (% Male)	59.3% male
Maternal Age: Mean (SD)	41.20 (7.5)
Paternal Age: Mean (SD)	39.89 (11.5)
	Hispanic: 11.5%
Race/ethnicity	Caucasian: 82.7%
	African-American: 7.7%
	Other: 9.6%

Very preliminary rates of co-occurring ASD and DS in this small but thoroughly studied sample...

After completing 58 full evaluations:

- 10 (17%) received a clinical diagnosis of PDD-NOS
- 4 (7%) meet criteria for Autism
- 44 (76%) do not meet criteria for a cooccurring ASD



Evaluate the appropriateness of screening tools for autism (M-CHAT, SCQ) with children with DS by examining sensitivity, specificity and convergence with clinical diagnosis

Pooled Sample (n=58)

CLINICAL DIAGNOSIS

		NO ASD	PDD-NOS	AUT
RISK IDENTIFIED IN SCREENING	Negative for ASD (N = 35)	32 (91% of negative screens)	3 (9% of negative screens)	0 (0% of negative screens)
	Positive for ASD (N = 23)	12 (52% of positive screens)	7 (30% of positive screens)	4 (17% of positive screens)

M-CHAT SAMPLE (N = 48)

CLINICAL DIAGNOSIS

		NO	PDD-NOS	AUT
		ASD		
Z				
IED	Negative	27	1	0
	for ASD	(96% of	(4% of	(0% of
<pre>C IDE SCRE</pre>	(N = 28)	negative screens)	negative screens)	negative screens)
RISK	Positive	11	7	2
	for ASD	(55% of	(35% of	(10% of
	(N = 20)	positive screens)	positive screens)	positive screens)

SCQ SAMPLE (N=10)

Ζ

RISK IDENTIFIED

CLINICAL DIAGNOSIS

		NO ASD	PDD-NOS	AUT
SCREENING	Negative for ASD (N = 7)	5 (71% of negative screens)	2 (29% of negative screens)	0 (0% of negative screens)
	Positive for ASD (N = 3)	1 (33% of positive screens)	0 (0% of positive screens)	2 (67% of positive screens)

Sensitivity and Specificity So far... (remember, n=58– small sample)

- M-CHAT: Children under 7 years
 - Sensitivity is 96% for spectrum and 100% for full autism
 - Specificity is 45%, with a 55% false positive rate

SCQ: Children 7 years and older

- Sensitivity is 71.4% for spectrum and 100% for full autism
- Specificity is 67%, with a 33% false positive rate

Aim 3

Examine child characteristics associated with social and communication impairments in children with DS

Cognitive functioning
Temperament
Executive function

Question	<u>Consider</u>
Could co-occurrence be related to low developmental level?	Perhaps an ASD becomes relevant only when social development is below expectations for overall developmental level
Could co-occurrence be related to difficult temperament or other problem behaviors?	Perhaps a child presents with social difficulties because of temperamental factors, and not difficulties with core social relatedness
Could co-occurrence be related to difficulties with executive functioning (i.e., shifting set)?	Perhaps a child who has significant issues in attention (e.g., shifting, sustaining, organizing) demonstrates some poor social relating skills due to poor flexibility, not problems in core social relatedness

Measures

- <u>Cognitive/Developmental functioning</u>
 Mullen Scales of Early Learning
 - Differential Ability Scales
- Adaptive functioning
 - Vineland Scales of Adaptive Behavior

Temperament, Attention, and Behavior

- Carey Temperament Scales
- Behavior Rating Inventory of Executive Function (BRIEF)
- Developmental Behavior Checklist (DBC)
- Short Sensory Profile

Intellectual Disability and Autism Symptoms

Preliminary Findings

Pooled Sample (n=58)

Severity of Cognitive Impairments by Screening Status



Pooled Sample (n=58)

Severity of Cognitive Impairments by Clinical Diagnosis



On/off spectrum by cognitive status: X^2 (2,58) = 4.24, p = .11

Video examples

Temperament, Attention, and Autism Symptoms

Preliminary Findings

In our sample, 68% of children with Down syndrome and a difficult temperament (n= 22) score above the Autism cutoff on Social section of the Autism Diagnostic Interview, but do not have autism.

Children with difficult temperaments were often able to coordinate nonverbal and verbal behaviors to flexibly initiate interactions, and share affect and enjoyment, but were often rated more poorly on ADOS items tapping social responsivity and attention shifting.

Many children are reported to have poor peer relationships (81%) and to interact with others in a one-sided, "on his/her own terms" kind of social style (74%); however only 24% of children with both of these endorsements presents with an ASD.

Video clip: Temperament issues

Future Directions

More work is needed:

- Analyze symptom profiles associated with co-occurring autism
- Analyze data concerning temperament, sensory-motor responses, and executive function as a function of screening identification and clinical diagnosis
- Examine utility of ADOS and ADI in children with DS
- Collaborate with the Rochester team on drafting applied articles concerning implications for assessment and intervention in clinical and educational settings

In Conclusion

These are the first epidemiologic studies investigating whether there is an increased rate of autism or ASD in children with DS

The phenotype of ASD in children with DS may be unique

Application of screening and diagnostic tests designed for people with idiopathic autism may result in artifactual reporting of symptoms related to skill deficits, developmental level and language.

Clinical application of DSM IV criteria remains important in making an ASD diagnosis in people with DS with critical review of the information provided by the ADI-R and ADOS.

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