Social-Emotional Development in 22q11.2 Deletion Syndrome: Psychiatric Risk Factors

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Presentation Outline

• Behavioral, temperament and psychiatric features

• Autistic Spectrum Disorders in 22qDS?

• Cognitive and brain differences

• Our new UCLA study and some (very) preliminary findings

• Early warning signs for psychosis and importance of early intervention
Cognitive Function

Cerebral Structure

Gross Anatomy
Microscopic
Chemical
Molecular

Genes
Environment

Something happens

Neurodevelopmental Disorder
ADHD
Autism
22q11.2 microdeletion
Neural Features
- Decreased frontal Gray Matter
- Anomalous myelination
- Dopamine Neurotransmission
Neurocognitive deficits
Difficulties with Time and Space
- Response Inhibition/Planning
- Social Cognition
Clinical Symptoms
Psychosis
Anxiety Disorders
OCD
Autism
DSM-V-TR
Psychiatric Findings in 22q11.2 Deletion Syndrome

- Risk of schizophrenia ~ 25x the general population risk (Bassett et al. 1998; Murphy et al. 1999; Shprintzen et al. 1992)
- 6.4% of child-onset schizophrenics had a 22q11 deletion (Nicolson et al. 1999)
- Elevated rates of ADHD (35-55%), Bipolar Disorder (~30%), OCD (33%) and Autistic Spectrum Disorder (14-50%) in childhood
“Schizotypy” in 22qDS

- Bassett et al. (2003) – Adults with 22qDS, with and without-SZ; no differences in severity of core positive or negative symptom scores.
  - “Excitement” factor scores higher in 22qDS-SZ group (Poor impulse control, uncooperativeness, and hostility)

- Feinstein et al. (2002) - children & adolescents, age 6-19 yo:
  22qDS vs. developmentally delayed controls
  - Rates of anxiety disorder (esp. phobia) & ADHD similar in both groups (~50%)
  - Evidence of delusions /hallucinations in 14% of 22qDS vs. 7% of controls

- Arnold et al. (2001)- 12/20 pts (60%) diagnosed w/ a psychiatric dx, vs. 3/11 sibs (27%)
- 2/3 22qDS pts with schizotypal traits later developed schizophrenia

- Baker & Skuse (2005) - adolescent 22qDS, age 13-25 yo vs. IQ-matched controls
  - CAPA interview & Junior Schizotypy Schedule (Diduca & Joseph, 1999)
  - Higher rates of ADHD, anxiety & mood disorder in 22qDS
  - Higher schizotypy scores in 22qDS vs. controls; 48% reported psychosis-like phenomena
5/16 had received a diagnosis of PDD /autistic spectrum, 10/16 diagnosed with SZ/other psychosis, 5/16 with mood disorder
• What do we know about Autistic Spectrum Disorders (ASD) in 22qDS?


• Children with 22qDS + autism scored similarly to idiopathic autism on ADI-R - less make believe play, more rituals, motor stereotypies and repetitive use of objects (Kates, et al, 2007).

• Is ASD a risk factor for future psychiatric difficulties in kids with 22qDS?
Psychosocial Profile of Children with 22q11.2 DS (N=31)

Child Behavior Checklist Scale: Mean Scores for 31 patients

Woodin et al. Gen in Medicine 2001
Why the debate about whether 22qDS kids have ASD?
Symptoms of PDD

Social
- Poor regulation of social interaction through eye contact, facial expression, gesture, posture, intonation
- Failure to develop age-appropriate peer relationships
- Limited social-emotional reciprocity

Communication
- Repetitive or idiosyncratic language (echolalia, neologisms, pedantic language)
- Poor conversational abilities (limited reciprocity)

Repetitive Behavior
- Preoccupations/ restricted interests
- Insistence on sameness/routine, ritualistic behavior
- Stereotyped body movements
- Preoccupation with parts or sensory aspects of objects
Spatial attentional shifting is impaired in:

- Parietal lesion pts *(Posner et al. 1984; Petersen et al. 1989)*
- Autism *(Palmen & van Egeland 2004)*
- Schizophrenia *(Posner 1988; Maruff et al., 1995; Gold et al. 1992)*
Cueing Task: Performance of children with 22qDS (N=38) and Controls (N=35)

Simon, Bearden & Bish; Dev & Psych, 2005
Cortical Thickness Maps
Cortical thickness deficit in 22q11DS

Significance
Gray Matter Thinning in:
- anterior cingulate and medial frontal cortex (attention/motivation)
- occipito-parietal cortex (visuospatial navigation)
Gyrification differences in 22q11.2DS

Scatterplot of Cognitive Outcome Variables With Gray Matter Volume: For 22qDS patients, gray matter volume was a robust predictor of FSIQ.
New Study at UCLA: Neural Basis of Autistic Spectrum Disorders in 22q11.2DS
Study Procedures

Neurocognitive Assessment
Autism Diagnostic Interview (ADI)/Autism Observation Schedule (ADOS)
C-DISC (parent interview)
Magnetic Resonance Imaging (3D Structural Scan and Diffusion Tensor Imaging)
Dimensional Self/Parent Report Measures:
  Child Behavior Checklist (CBCL)
  Behavior Rating Inventory of Executive Functions (Gioia 2000)
  Social Reciprocity Scale (SRS; Constantino et al. 2000)
  Disruptive Behavior Disorder Scale
  Short Sensory Profile
  Bodfish Repetitive Behaviors Scale
  Junior Schizotypy Scale
DNA/RNA samples
Theory of Mind

• The ability to represent others' mental states and use social cues to interpret behavior (Kasari & Rotheram-Fuller, 2005)

• Capacity to understand and manipulate mental states of others and to thereby alter their behavior (Frith & Frith, 1999)

• The ability to reflect on the contents of one's own and other's minds (Baron-Cohen, 2000)
Some Early Findings: Common Themes
Withdrawn / Social Problems / Rather be alone

Difficulty making friends

Sensory symptoms: hypersensitivity to sound

Restricted interests: Gets ‘stuck’ on 1 topic

Difficulty with transitions

Oppositional behavior at home: argues with adults

Attentional: loses things, forgetful, interrupts

Phobias
## What Factors Might Predict Future Psychiatric Problems?

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Genetic Risk with ↓ Function</th>
<th>Unusual Thought Content (&gt;3)</th>
<th>Suspicion-Paranoia (&gt;2)</th>
<th>Social Functioning (&lt;7)</th>
<th>Any Drug Abuse</th>
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<td>52</td>
<td>48</td>
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Cannon et al. *Arch Gen Psychiatry* 2008;65:28-37.
What to Look For: Red Flags/ Early Warning Signs

Suspiciousness
- Are people talking about me in a negative way?
- Sometimes I think people might be watching me.

• Unusual Thinking
  - Confusion about what is real and what is imaginary
    ❖ Sometimes I can't tell if something that happened was real or if it was from a dream.

• Ideas of Reference
  ❖ I think the billboard is hinting at a special message to me.

• Preoccupation with the supernatural (telepathy, ghosts, UFOs)
  ❖ Sometimes I think that I can read other peoples’ thoughts.
Red Flags (continued)

• **Perceptual Disturbances**
  
  • Increased sensitivity to light and sound; trouble filtering out irrelevant stimuli (e.g. background noise)

• Hearing things that other people don’t hear
  
   Did someone call my name?

• Seeing things that others don’t see
  
   Sometimes I see something out of the corner of my eye, but when I look, there’s nothing there.

• Smelling, tasting, or feeling unusual sensations that other people don’t (e.g. numbness or tingling on parts of the body)

• Assess **frequency of symptoms and effect on behavior**!
What Can You Do?

- Careful, frequent monitoring!
- Psychosocial treatments (social skills groups, etc.)
- Use medications with caution
- Stress reduction/ supportive family environment
Importance of Early Intervention

• Screening of at risk groups for early signs of illness
  - E.g., mammography, liver function tests, EKG

• Invasiveness of intervention scales with stage of illness

![Invasiveness Scale]

- Early: diet, exercise
- Advanced: drug therapy, surgery
Summary and Implications

- Children with 22qDS are at increased risk for a variety of psychiatric symptoms

- Mechanisms are not well understood but likely involves a cascade of neurodevelopmental events caused by deletion – affects brain development, cognition, socio-emotional development

- Poor social function very common in 22qDS - developmental trajectory not clear

- Early intervention can help!
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And most importantly.. THANK YOU!!
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