Why we monitor the cognitive development of children and adolescents with 22q11DS

A study by the International 22q11.2 Deletion Syndrome Brain Behavior Consortium (IBBC 22q11DS)

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The average child with 22q11DS
Schizophrenia
Cognitive development & schizophrenia
IBBC study
Recommendations
The average child with 22q11DS ......

DOES NOT EXIST!!!!
...yet there are similarities...
(Common) personality characteristics in 22q11DS

- Sweet
- Creative
- Determined
- Loyal and focussed
- Pleasant
- Musical
- Love to chat
(Common) personality characteristics of parents with a child with 22q11DS

- Committed
- Patient
- Determined
- Loving
- Powerful
- Creative
(Common) cognitive characteristics in 22q11DS

- Nearly 100% learning difficulties
- Difficulties with comprehension
- Word finding difficulties
- Difficulties with perceptual organization
- Relatively strong short term memory
- Relatively strong processing speed
- Verbally strong impression

Confusing profile for parents, teacher & child

22q11DS is an invisible handicap
(Common) behavioral characteristics in 22q11DS

- Fearful at a young age
- Social behavior:
  - prefer older or younger children
  - few friends, socially isolated
- Social clumsiness
- Attention and thought problems
- Strong moodswings
- Increased risk for psychiatric problems:
  ADHD/ ASD/ schizophrenia
Schizophrenia

- Affects 25-30% of adolescents with 22q11DS
- One of the major concerns of parents, therefore focus of attention by researchers

Schizophrenia
- Is not a split-brain condition
- Has nothing to do with multiple personalities
A. Characteristic symptoms:
   Two (or more) of the following (at least 1 of these should include 1-3)
   1. Delusions
   2. Hallucinations
   3. Disorganized speech
   4. Catatonia
   5. Negative symptoms, i.e. restricted affect or avolition/asociality

B. Social/occupational dysfunction

C. Duration: continuous signs of the disturbance persist for at least 6 months.
PSYCHOSIS

Schizoaffective
Affective disorders
Schizophrenia
PSYCHOSIS
Delirium
Drug abuse
Borderline
PTSD
Schizophrenia trajectory

- Premorbid phase
- Prodromal phase
- Psychotic phase
- Stable phase

Global function level

Childhood > Adolescence > Adulthood
22q11DS
Summary findings so far

Based on previous cognitive research:

- Overall intelligence level does not appear to be strongly associated with global childhood psychopathology (ASD/ADHD) in 22q11DS

- Individuals with psychotic disorders appear to have lower (verbal) IQ

- All cross-sectional data; what about cognitive development?
Cognitive development & schizophrenia in 22q11DS

- 5.5 years WPSSI-R / SON
- 7.5 years WISC-III
- 9.5 years WISC-III

Duijff et al.
Br J Psychiatry, 2012
• International Brain Behavior Consortium on 22q11.2 Deletion Syndrome (IBBC)
• 22 sites worldwide participating
• 12 sites for this study

• JAMA Psychiatry, 2015 Apr; 72(4):377-85
- N=829
- IQ (Wechsler) data

- N=388
  > 2 IQ measurements, AND psychiatric assessment

- Without psychotic disorder (n=341)
- With psychotic disorder (n=47)
Overall cumulative IQ decline (FSIQ, VIQ, PIQ) in 388 individuals with 22q11DS
Verbal IQ normative chart for 22q11DS

Psychiatric assessment

Psychiatric assessment
Our finding is not novel

**COMT** genotype predicts longitudinal cognitive decline and psychosis in 22q11.2 deletion syndrome

Doron Gothelf\(^1,2\), Stephan Eliez\(^3\), Tracy Thompson\(^1\), Christine Hinard\(^4\), Lauren Penniman\(^1\), Carl Feinstein\(^1\), Hower Kwon\(^5\), Shuting Jin\(^1\), Booil Jo\(^1\), Stylianos E Antonarakis\(^6\), Michael A Morris\(^4\) & Allan I. Reiss\(^1\)

**NATURE NEUROSCIENCE**

Risk Factors and the Evolution of Psychosis in 22q11.2 Deletion Syndrome: A Longitudinal 2-Site Study

Neuroanatomic Predictors to Prodromal Psychosis in Velocardiofacial Syndrome (22q11.2 Deletion Syndrome): A Longitudinal Study

Wendy R. Kates, Kevin M. Antshel, Stephen V. Faraone, Wanda P. Fremont, Anne Marie Higgins, Robert J. Shprintzen, Jo-Anna Botti, Lauren Kelchner. and Christopher McCarthy

**BIOL PSYCHIATRY** 2011;69:945–952
Conclusions IBBC data

• The *average* IQ trajectory in 22q11DS is characterized by a modest downward slope.

• In a subgroup: a more prominent decline starts in early childhood (<10 yrs)

• A negative deviation from the (V)IQ 22q11DS normative chart is a risk factor for schizophrenia
Finding & maintaining balance

Invisible handicap
  +
Strong verbal impression (but have poor comprehension)
  +
Cognitive decline
  -/-

balance
Recommendations

• Regular IQ testing

• Watch out for overdemanding/ overestimation as a result of:
  – Strong verbal impression
  – Strong short term memory
  – Relatively high processing speed

• Regard behavior as a thermometer
  - internalizing behavior
  - school vs home

• Make use of your child’s strengths!
Recommendations

- Your child is unique, follow your heart…

- …but, make use of the knowledge that is available by regularly consulting the 22q11 professionals. That is what we are here for.
“Alone we can do so little; together we can do so much”

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<th>22q11 psychiatric lab UMC Utrecht:</th>
<th>22q11 multidisciplinary clinic UMC Utrecht:</th>
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<tr>
<td>Jacob Vorstman</td>
<td>Aebele Mink van der Molen</td>
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<td>Elemi Breetvelt</td>
<td>Michiel Houben</td>
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<td>&amp; 22q11DS BBC</td>
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<td>&amp; Dutch parent association:</td>
<td>Sarah Haverkamp</td>
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<td><a href="http://www.steun22q11.nl">www.steun22q11.nl</a></td>
<td>Marise van der Heul</td>
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Thank you!