Cognitive and behavioral development of children with 47,XXX: first results of the TRIXY study

Sophie van Rijn, PhD | AXYS 2019 Atlanta, USA
TRIXY Center of Expertise
Trisomy of the X and Y Chromosomes
75% of research focused on physical/medical issues (Pieters et al, 2011)
A review of neurocognitive functioning and risk for psychopathology in sex chromosome trisomy (47,XXY, 47,XXX, 47, XYY)

Sophie van Rijn

<table>
<thead>
<tr>
<th>diagnosis</th>
<th>general</th>
<th>47,XXX</th>
<th>range</th>
<th>symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD</td>
<td>0.6 %</td>
<td>15 %</td>
<td>10-20 %</td>
<td>10-20 %</td>
</tr>
<tr>
<td>ADHD</td>
<td>7 %</td>
<td>30 %</td>
<td>25-35 %</td>
<td>49 %</td>
</tr>
<tr>
<td>Anxiety</td>
<td>7 %</td>
<td>20 %</td>
<td>-</td>
<td>27-30 %</td>
</tr>
<tr>
<td>Depression</td>
<td>13 %</td>
<td>36 %</td>
<td>18-54 %</td>
<td>27-30 %</td>
</tr>
</tbody>
</table>

- Language, executive functioning, social cognition, emotion regulation
The TRIXY study

• 800,000 euro funding in 2016
• XXX, XYY, XXY
• 1 to 6 years
• Longitudinal study
• Based at Leiden University
• Collaboration with all academic medical centers in The Netherlands and Belgium
• TRIXY Partner site: XtraordinarY kids clinic, Denver CO
Discover the world at Leiden University
Behavior

• Questionnaires
• Systematic observations
Cognitive tests
Social perception: Eyetracking
Emotion regulation: Arousal markers in heart rate
TRIXY study – update on 47,XXX

SCT group: 71 children
Control group: 74 children (41 girls, 33 boys)

SCT variations:
23 children with XXX
36 children with XXY
12 children with XYY

Recruitment XXX group:
• 44 % active follow-up/monitoring after prenatal diagnosis
• 30 % interested in research (study flyer / supportgroups)
• 13 % in clinical care because of physical/medical issues
• 13 % in clinical care because of neurobehavioral issues

Time of diagnosis XXX group: 57 % prenatal diagnosis
43 % postnatal diagnosis
Top 10 behavior observations of parents of children with 47,XXX

Does your child currently have, or had in the past, any of the following behaviors on a regular basis?

60 % Tamper tantrums
43 % Short attention span/distractable
43 % Bothered by things touching him / her
40 % Cries often
40 % Poor coordination
39 % Immature
39 % Shy
34 % Nail-biting
30 % Resistance to change in routines
30 % Anxiety
22 % Moodiness
Cognitive and behavioral risks
# DSM scales in girls with 47,XXX

<table>
<thead>
<tr>
<th>CBCL</th>
<th>Average (T&lt;65)</th>
<th>Borderline (65&lt;T&lt;70)</th>
<th>Clinical (T&gt;70)</th>
<th>Different from control group?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pervasive developmental problems</td>
<td>69 %</td>
<td>10 %</td>
<td>21 %</td>
<td>yes</td>
</tr>
<tr>
<td>Anxiety problems</td>
<td>79 %</td>
<td>-</td>
<td>21 %</td>
<td>yes</td>
</tr>
<tr>
<td>Affective problems</td>
<td>90 %</td>
<td>10 %</td>
<td>-</td>
<td>yes</td>
</tr>
<tr>
<td>Oppositional defiant problems</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention problems</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Autism and social anxiety in children with sex chromosome trisomies: an observational study

5 to 16 years

Alexander C. Wilson¹, Judith King², Dorothy V.M. Bishop¹

¹Department of Experimental Psychology, University of Oxford, Oxford, OX2 6GG, UK
²Department of Psychiatry, University of Oxford, Oxford, UK

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Low Bias</th>
<th></th>
<th></th>
<th></th>
<th>High Bias</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>XXX</td>
<td>XXY</td>
<td>XYY</td>
<td>XXX</td>
<td>XXY</td>
<td>XYY</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>25</td>
<td>14</td>
<td>15</td>
<td>4</td>
<td>14</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neither</td>
<td>20 (80%)</td>
<td>9 (64.3%)</td>
<td>10 (66.7%)</td>
<td>2 (50%)</td>
<td>7 (50%)</td>
<td>4 (23.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDDNOS</td>
<td>3 (12%)</td>
<td>1 (7.1%)</td>
<td>1 (6.7%)</td>
<td>1 (25%)</td>
<td>1 (7.1%)</td>
<td>3 (17.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autism</td>
<td>2 (8%)</td>
<td>1 (7.1%)</td>
<td>4 (26.7%)</td>
<td>1 (25%)</td>
<td>2 (14.3%)</td>
<td>9 (52.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social Phobia only</td>
<td>0 (0%)</td>
<td>2 (14.3%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social Phobia+PDDNOS</td>
<td>0 (0%)</td>
<td>1 (7.1%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social Phobia+Autism</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>4 (28.6%)</td>
<td>1 (5.9%)</td>
<td></td>
<td></td>
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</tbody>
</table>
### Social behavior/cognition in girls with 47,XXX

<table>
<thead>
<tr>
<th>Social Responsiveness Scale</th>
<th>Average (T&lt;65)</th>
<th>Mild range (65&lt;T&lt;70)</th>
<th>Clinical range (T&gt;70)</th>
<th>Different from control group?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social awareness</td>
<td>67 %</td>
<td>22 %</td>
<td>11 %</td>
<td>yes</td>
</tr>
<tr>
<td>Social cognition</td>
<td>50 %</td>
<td>12 %</td>
<td>38 %</td>
<td>yes</td>
</tr>
<tr>
<td>Social communication</td>
<td>72 %</td>
<td>6 %</td>
<td>22 %</td>
<td>yes</td>
</tr>
<tr>
<td>Social motivation</td>
<td>67 %</td>
<td>11 %</td>
<td>22 %</td>
<td>yes</td>
</tr>
<tr>
<td>Restricted interests and repetitive behaviors</td>
<td>83 %</td>
<td>11 %</td>
<td>6 %</td>
<td>yes</td>
</tr>
</tbody>
</table>
Neurocognitive functioning in girls with 47,XXX

Global intelligence (WPPSI)

<table>
<thead>
<tr>
<th></th>
<th>FSIQ</th>
<th>VIQ</th>
<th>PIQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>105</td>
<td>106</td>
<td>103</td>
</tr>
<tr>
<td>SCT</td>
<td>94</td>
<td>92</td>
<td>91</td>
</tr>
</tbody>
</table>

Executive functioning (BRIEF):
More problems in emotional control and shifting (flexibility)
Similar scores as controls on organizing, inhibiting, working memory

Language (NEPSY, PPVT):
Similar scores as controls on receptive/expressive language and phonological processing
What’s next?

Mechanisms of emotion regulation:
- Executive function tests
- Arousal regulation, based on heart rate
  - unexpected events
  - in response to (emotions of) others
  - when frustrated

Mechanisms of social behavior:
• Recognizing and understanding emotional expressions of others
• Empathy (emotional sharing)
• Coordinating social gaze (including joint attention)
• Attention to social cues: Eyetracking
• Perspective taking (theory of mind)
Prediction over time

Early cognitive functioning → Behavioral outcome

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We thank all participating families!

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