Autism
The Faroese study

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Faroe Islands

- 18 islands
- 48,424 inhabitants
- Self governing region of Denmark
- Originate from Norwegian Vikings and Celts
- 91% Faroese origin
- Own language
Faroe Islands

- Genetic isolate with a relative homogenous genetic background

- Genetic Bio bank - genealogical registry with records dating 400 years back
Autism

• Characteristic triad of symptoms
  - impairments in social interaction
  - impairments in communication
  - restricted, repetitive or stereotyped behavior

• Most strongly inheritable of all developmental and psychiatric disorders
Population study - 2002

• **Aim**: Screen all children in elementary schools for autism spectrum disorders

• All children born between 1985 and 1994

7,689 children - (3,895 boys-3,794 girls)
Screening process

Screening in elementary schools

• Two clinical psychologist visited and lectured on autism spectrum disorders for teachers in all schools

• Teachers were asked to contact the parents of pupils who raised suspicion of suffering from an autism spectrum disorder regarding participation in the study
Screening process

Special schools
• Pupils with autism disorder symptoms and already known cases

Lectures in radio and television describing autism symptoms
• Encouraging parents to take contact

Children targeted in screening were further examined
Results

Rates of clinical diagnoses of autism spectrum disorders in the Faroe Islands

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>Boys n</th>
<th>Boys population prevalence</th>
<th>Girls n</th>
<th>Girls population prevalence</th>
<th>Total n</th>
<th>Total population prevalence</th>
<th>95% ci</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childhood autism</td>
<td>9</td>
<td>0.23%</td>
<td>3</td>
<td>0.08%</td>
<td>12</td>
<td>0.16%</td>
<td>0.07% 0.25%</td>
</tr>
<tr>
<td>Asperger syndrome</td>
<td>17</td>
<td>0.44%</td>
<td>3</td>
<td>0.08%</td>
<td>20</td>
<td>0.26%</td>
<td>0.14% 0.38%</td>
</tr>
<tr>
<td>Atypical autism</td>
<td>9</td>
<td>0.23%</td>
<td>0</td>
<td>0.0%</td>
<td>9</td>
<td>0.12%</td>
<td>0.04% 0.20%</td>
</tr>
<tr>
<td>Autism spectrum disorder total</td>
<td>35</td>
<td>0.90%</td>
<td>6</td>
<td>0.16%</td>
<td>41</td>
<td>0.53%</td>
<td>0.36% 0.70%</td>
</tr>
</tbody>
</table>

95% confidence interval (ci) calculated from exact Poisson distributions

Follow up study in 2009

Screening the same group as in 2002

2002 - 7,689 (3,895 boys-3,794 girls)
2009 - 7,128 (3,590 boys-3,538 girls)

• Public lectures/information about autism symptoms

• Hospital doctors, GPs, teachers and psychologists were encouraged to refer any cases, diagnosed with autism or undiagnosed but raising some suspicion of suffering from autism

• All 41 cases from former study were invited to participate
Comparison of rates of clinical diagnoses of ASDs and gender ratios in the Faroe Islands in the original (2002) and the follow-up (2009) studies

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Original study 2002 ( n = 43 ) (ratio 5:1)</th>
<th>Follow-up study 2009 ( n = 24 ) (ratio 1.2:1)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>Childhood autism</td>
<td>9*</td>
<td>4</td>
</tr>
<tr>
<td>Asperger’s syndrome</td>
<td>18</td>
<td>3*</td>
</tr>
<tr>
<td>Atypical autism</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Total (( n = 67 ))</td>
<td>36</td>
<td>7 (16.3%)</td>
</tr>
<tr>
<td></td>
<td>(83.7%)</td>
<td></td>
</tr>
</tbody>
</table>

* Five individuals within these groups did not receive their clinical diagnoses from the research team

Results

- The total prevalence of autism in the Faroe Islands in 2009: **0.94% (CI: 0.73%, 1.19%)**
Genetic study

Blood or saliva samples from

- Cases participating in 2002 and new diagnosed cases (2009)
- Parents
- Siblings
- Control group (age and gender matched - 4 for each case)
### Population stratification

<table>
<thead>
<tr>
<th>Sample</th>
<th>Total</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>209</td>
<td>130</td>
<td>79</td>
</tr>
<tr>
<td>Mothers</td>
<td>24</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>Fathers</td>
<td>26</td>
<td>0</td>
<td>26</td>
</tr>
<tr>
<td><strong>Proband</strong></td>
<td>33</td>
<td>6</td>
<td>27</td>
</tr>
<tr>
<td>Grand parents and relatives</td>
<td>6</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Unaffected sibs</td>
<td>41</td>
<td>20</td>
<td>21</td>
</tr>
<tr>
<td>Control sibs</td>
<td>10</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>349</td>
<td>190</td>
<td>159</td>
</tr>
</tbody>
</table>
Inferred genealogy of the cohort
de novo CNVs

de novo NRXN1 deletion

de novo 22q11 deletion
Inherited autosomal CNVs

Intragenic duplication of *NLGN1*

Intragenic duplication of *IQSEC3*
Inferred genealogy of the cohort

**NLGN1**  **IQSEC3**  **NRXN1**  **22q11**
Gene – Environment interactions

• Methyl mercury – prenatal exposure
• D-vitamin - prenatal levels

- measured from blood spots on filter paper
Ackowlegdement

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