Characterizing the Anxiety Phenotype in Triple X Syndrome

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BACKGROUND
- Triple X syndrome occurs in approximately 1 in 1000 female births.
- It can be associated with developmental delays and psychological difficulties.
- The behavioral phenotype of Triple X includes anxiety and shyness.
- In a 2014 study by London et al., that included 35 participants with Triple X syndrome (age 5-24 yo), 83% reported symptoms of anxiety and 40% met DSM-IV criteria for an anxiety disorder using K-SADS standardized interview. (Ref: PMC424157)

STUDY AIMS
- In this project we aimed to characterize the anxiety phenotype associated with Triple X syndrome by evaluating profiles of anxiety-related behaviors and symptoms at different stages of development.

METHODS
- Females with nonmosaic Triple X were recruited for an ongoing IRB-approved study on health and development in sex chromosome disorders.
- Participants included 74 individuals with Triple X syndrome (age 5-24 yo), including psychological evaluation. These medical records were reviewed and clinical findings summarized.
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RESULTS: Behavioral Symptoms in Anxiety Group (n=51)

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Anxiety Group Diagnosis</th>
<th>% of Diagnosis</th>
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<tbody>
<tr>
<td>2-6</td>
<td>Generalized Anxiety Disorder 2/12</td>
<td>75%</td>
</tr>
<tr>
<td>7-11</td>
<td>Generalized Anxiety Disorder 2/7</td>
<td>57%</td>
</tr>
<tr>
<td>12-24</td>
<td>Generalized Anxiety Disorder 7/11</td>
<td>45%</td>
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CONCLUSIONS
- Anxiety symptoms and anxiety-related behaviors were very common in Triple X syndrome across age groups in this cross-sectional sample.
- Within the subset who received clinical evaluation, multiple different anxiety disorders were confirmed, along with other comorbid cognitive/learning, attentional and psychological diagnoses known to be associated with Triple X.
- Selective mutism was identified in 3 young girls of the 30 (10%) who received a clinical evaluation, a diagnosis previously unreported in Triple X syndrome.
- There were no differences in VIQ, PIQ, or FSIQ scores when comparing those with and without an anxiety disorder, however there was a trend toward lower adaptive scores when an anxiety disorder was present.
- Clinically significant anxiety disorders were present in at similar rates in girls with both a prenatal and postnatal Triple X diagnosis.
- There were no differences in the BASC-2 Anxiety Scale between those with and without clinical anxiety disorders, and the mean overall score was not different in either group. Further, the BASC-2 Withdrawal scale was higher in the group with confirmed anxiety disorder, and may be a better scale for identifying anxiety symptoms in Triple X. This finding may relate to less verbal expression of anxiety and more of a behavioral profile of anxious reactions.
- Some behaviors typically assumed to diminish with age increased in this cross-sectional study, most notably tanntrums, aggression, poor eye contact and lying among other concerns that were more prominent in the older age group.
- Further research is needed to evaluate:
  - the interplay between anxiety and other features including cognitive and language deficits
  - prospective evolution of anxiety symptoms in a longitudinal cohort
  - the role of family mental health history and SES on anxiety symptoms
  - medical and psychological interventions