

Development of a Conceptual Model to Inform a Clinical Outcome Assessment Strategy in Adolescents and Young Adults with Fragile X Syndrome

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Background

- Fragile X syndrome (FXS) is a rare neurodevelopmental disorder caused by a genetic mutation and is associated with intellectual disability, anxiety disorders, behavioral and learning challenges, and various physical disabilities (Chevreul, 2015).
- Significant heterogeneity exists in the extent of behavioral and cognitive deficits across individuals with FXS, which includes mild to severe learning difficulties and autistic behaviors (Chaste et al., 2012).
- Heterogeneity in symptomology poses a significant challenge when developing a clinical outcome assessment strategy to measure treatment benefit, and to support drug development for future trials in FXS.
- A conceptual model is a visual representation of the concepts considered to be important and relevant to a specific condition (e.g. symptoms, impacts, treatment, and caregiver-related concepts), and can be used for the development of a clinical outcome assessment strategy.

Objective: To conduct a review of qualitative literature in FXS to identify key symptoms and associated impact concepts relevant to individuals with FXS aged 13-30 years in order to inform the development of a conceptual model.

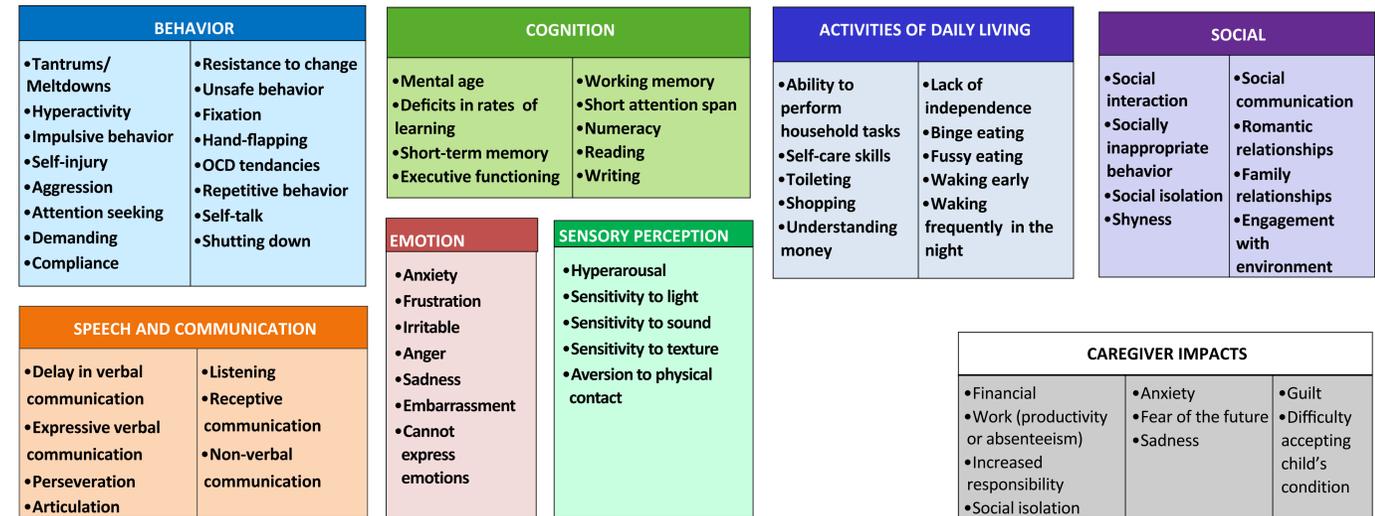
Method

Identification of relevant source material

- Peer-reviewed literature:** A search strategy using database subject headings and keyword searches to combine disease-specific and research method search strings was developed to identify articles reporting the qualitative experience of individuals with FXS and their parents/caregivers (Medline®, Embase® and PsycINFO electronic databases). 418 abstracts pertaining to the qualitative experience of individuals with FXS and their parents/caregivers were returned, with five articles (Abbeduto, 2014; Fourie, 2012; Medved 2004; Weber 2016; Woodcock, 2009) then fully reviewed based on the following inclusion criteria
- Inclusion criteria for peer-reviewed articles:
 - Journal article
 - Title and/or abstract includes relevant disease-specific term
 - Abstract includes symptoms or impacts relevant to FXS
 - Abstract reports data relating to those aged 13-30 years
 - Abstract reports qualitative data documenting patient/caregiver experience of FXS
- Caregiver interviews:** Interview and focus group transcripts (non-verbatim) from a previous qualitative research study that was designed to explore the caregiver experience of FXS were included in this review. Although the study focused on behavior, decision making, and treatment options, any information regarding the key symptom and impact concepts relevant to individuals with FXS was extracted.
- Online blogs/forums:** Considering the limited qualitative literature pertaining to FXS, publicly available online blogs and forums used by patients with FXS were reviewed to provide a rich source of qualitative data relating to the real world experience of patients.
- Additional sources:** A search of key conference proceedings, a Google Scholar review, and a review of key reference lists of selected articles were also completed to identify relevant information.

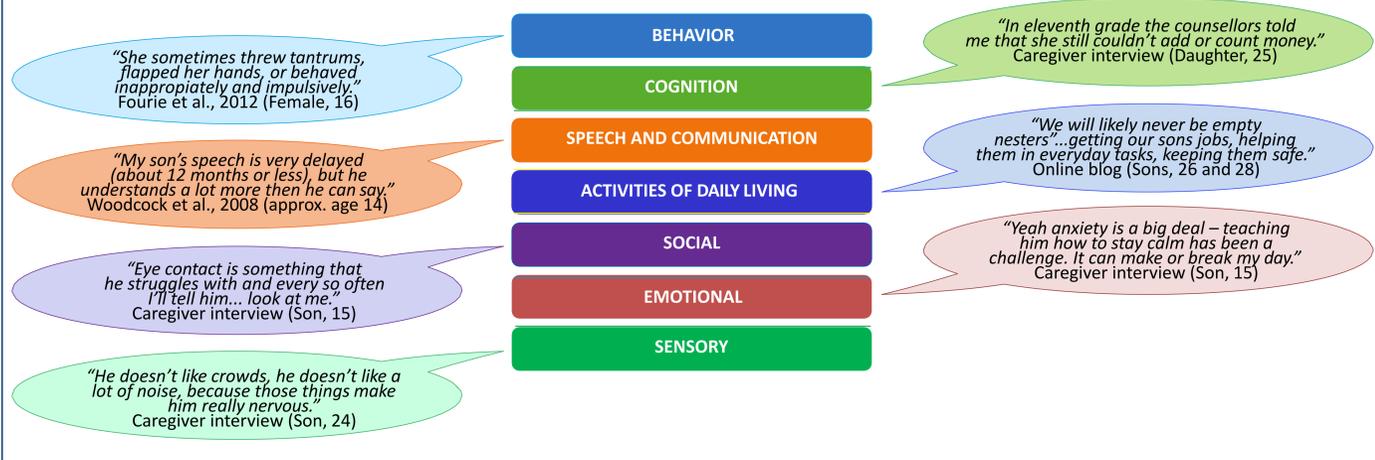
Results

Conceptual Model of Symptoms and Impacts Related to the Experience of Fragile X Syndrome



- Based on the concepts elicited, seven domains with a total of 62 concepts related to the experience of individuals with FXS were developed. These included Behavior (16 concepts), Cognition (9 concepts), Speech and Communication (7 concepts), Activities of Daily Living impacts (10 concepts), Social impacts (8 concepts), Emotional impacts (7 concepts), and Sensory Perception (5 concepts).
- Key symptom concepts included developmental delays in both learning and verbal communication, hyperactivity and impulsive behavior, and issues with short-term and working memory.
- The impact of FXS associated symptoms on the individual with FXS included a lack of independence when completing activities of daily living, social behavior issues (e.g. behaving inappropriately in public) and emotional reactions such as anxiety and frustration.
- An additional nine concepts were identified for inclusion in the conceptual model that related to the impact of caring for someone with FXS. This included concepts such as financial burden, work (productivity or absenteeism), feeling socially isolated, and fear of the future.

Example quotes from caregiver interviews, focus groups and literature



Conclusion

- Findings from the literature review, online materials and caregiver interviews were largely consistent and supported the development of the first known FXS conceptual model.
- The conceptual model provides a valuable resource to inform a clinical outcome assessment strategy and identify key outcome measures for potential use in FXS clinical trials
- Concept elicitation interviews with caregivers of individuals with FXS and clinicians are recommended to further support the concepts identified in this review

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