Angelman Syndrome Natural History Study – What have we learnt and what more can we learn?

Wen-Hann Tan\textsuperscript{1}, Lynne M. Bird\textsuperscript{2}

\textsuperscript{1}Boston Children’s Hospital, Boston, MA
\textsuperscript{2}Rady Children’s Hospital San Diego and University of California, San Diego, San Diego, CA

Although Angelman syndrome (AS) was first described in 1965 and is now a well-recognized neurodevelopmental disorder, many aspects of the natural history of AS remain poorly characterized. Until recently, most clinical descriptions of AS have been in children and relied on cross-sectional observations. The developmental trajectory of individuals with AS and the long-term complications in the older adults remain unclear, which has hampered the development of effective therapeutic interventions for AS.

To address these unanswered questions on AS, a longitudinal natural history study of AS was conducted from 2006 to 2014 under the auspices of the NIH Rare Diseases Clinical Research Network (RDCRN), during which 302 participants with a molecular diagnosis of AS were evaluated between one and nine times annually at one of six study sites in the United States. Structured developmental assessments were performed, growth data were obtained, and specific medical complications were assessed at each visit. Following a hiatus in funding, a revised longitudinal natural history study sponsored by the FDA was launched in 2018. This new study was designed specifically to evaluate outcome measures that can potentially be adopted in future clinical trials in AS, and to obtain longitudinal pre-treatment data for the outcome measures that are likely to be used in the forthcoming clinical trials in AS.

We will present the lessons that we learned through the previous RDCRN-supported natural history study, as well as the rationale, design, and value of this new FDA-sponsored natural history study, including its direct relevance to future therapeutic trials in AS.