



# Brain Responses Can Serve as Biomarkers of Cognition in Angelman Syndrome

## A Research Report for Families

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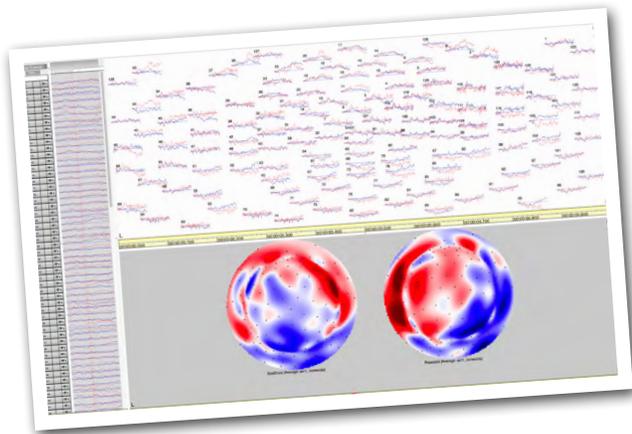
### Introduction

It has long been accepted that not all of our thoughts and abilities are reflected in observable behavior or performance on standardized tests. This idea is particularly relevant for persons with neurodevelopmental disabilities who may not be able to speak or to provide reliable nonverbal responses.

Angelman syndrome is a rare genetic disorder that causes developmental delay, absence or near absence of speech, and difficulties with coordinated movements. Individuals with Angelman syndrome are not able to complete conventional cognitive assessments, which limits the ability of parents, clinicians, and educators to capture accurately their full range of functioning. This lack of sensitive measures also poses a problem for evaluating progress related to development and/or the effects of interventions or treatments.

To date, most available data about cognitive processes in Angelman syndrome have come from observations and reports by parents and other caregivers. In this pilot study, our aim was to test whether brain responses recorded directly from a participant could be used to obtain more objective new insights into the thought process of children and adults with Angelman syndrome.





## What the Study Involved

This study focused on auditory processing, which refers to the natural way that sound is heard through the ear and then travels to the brain to be interpreted. The study targeted auditory processing because researchers have not yet examined it in great detail in Angelman syndrome, even though most daily activities involve processing of spoken language. Another advantage of using sound is that sustained attention and specific task instructions are not required, making auditory stimuli suitable for participants of various ages and abilities.

We used EEG (electroencephalography) to measure brain responses called auditory event-related potentials. An event-related potential (ERP) is the change in brain electrical activity in response to a specific sensory, cognitive, or motor event. Wearing a soft sensor net with many sponges, your son or daughter listened to one or two sets of spoken sounds. The first set included nonsense words, one of which was randomly chosen and presented repeatedly, while the rest of the words were played only once. The second set consisted of familiar names (their own name and close other name) and unknown names.

Our previous work in infants, toddlers, and children with typical development and with various neurodevelopmental disabilities established these tasks as possible measures of auditory-based learning (how we learn through hearing) as well as of more complex social-emotional processing (how we recognize personally relevant events, understand their meaning, and respond to them).

## The Study's Three Questions

The study addressed three main questions:

- Will children and adults with Angelman syndrome tolerate the sensors placed on their heads?
- Will their brain responses reflect the expected learning and social recognition responses?
- Will the observed brain responses be related to parent reports of daily social and communicative functioning?

## Study Design

You and your daughter or son were a part of a study sample of 16 families. All participants had the deletion subtype of Angelman syndrome and were between 4 and 45 years of age (mean age was 14 years). We recorded auditory brain responses during a single research visit. Our measure of communicative and social functioning came from the questionnaire about the behaviors you had observed in your son or daughter over time. By relying on your extensive knowledge and experiences, we learned about what your daughter or son can do not just at the time of our research visit, but on a day-to-day basis at home and other settings.

## Findings

All participants tolerated the sensors on their head for at least 6 minutes, which was long enough to record one set of brain responses. Fifteen participants (94%) provided enough artifact-free brain data to examine spontaneous auditory learning. Eleven of 13 participants (85%) successfully completed the longer, 12-minute name recognition set.

The brain responses demonstrated the expected evidence of memory traces following repeated exposure to previously unknown nonsense words. Greater difference between brain responses to repeated words compared to the novel stimuli heard only once was associated with parent reports of higher adaptive communication functioning.

Brain responses to the familiar and unknown spoken names were more variable across individuals, and overall, did not show clear evidence of spontaneous attention to and recognition of own or close other's name. These results are similar to the findings we previously observed in individuals with Rett syndrome, who share many characteristics with Angelman syndrome, including autism features. At the individual level, larger brain responses to own name in participants with Angelman syndrome were associated with parent reports of more adaptive interpersonal skills.

Together, our results demonstrate that measuring brain responses associated with cognition in children and adults with Angelman syndrome is possible and can provide objective information complementary to the caregiver reports. Without the requirement of behavioral responses, the use of auditory stimuli during brief test sessions placed minimal demands on participants' attention, making the procedures suitable for all ages and ability levels.

With your help, this study provided the first evidence that brain indices of spontaneous learning or social-emotional processing could be a promising new marker for documenting cognitive processes in Angelman syndrome and therefore could be useful for evaluating treatment effects in future clinical trials.

## Heartfelt Thanks

We are grateful to the families who participated in this pilot study. You are our partners in discovery. Without families taking part in research, we could not advance our understanding of how children with and without developmental disabilities grow and learn.

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