Heritability of Sound Processing Deficits in Autism: Neural Insights

By Nina Kraus, PhD, and Trent Nicol, BS

Over the years, my team has published a few studies on auditory processing in autism and I have written about the topic here in Hearing Matters.[1,2] In a new study published in the *Journal of Autism and Developmental Disorders*[3], my colleagues down the hall at the Northwestern University Neurodevelopmental Disabilities Lab, headed by Dr. Molly Losh, teamed up with my Brainvolts Lab to look at sound processing not only in people with autism, but in parents of people with autism.

It is common in autism spectrum disorder (ASD) for the prosody of speech to be atypical. Sometimes patients will speak in an overly sing-song voice or, conversely, with a flat affect. They might speak at an atypical rate, an inappropriate volume, or with excess formality.

Nearly 20 years ago, Dr. Nicole Russo, a then-doctoral student in my lab, reasoned there might be a connection between these outward vocal manifestations of ASD and the processing of vocal prosody in the brain. If the sounds of speech are not being encoded accurately by the central auditory system, the sounds of standard speech production might not be learned. She tested this in children with autism using the frequency following response (FFR) and noted that the brains of children in her study population were less proficient at "tracking" the pitch of speech[4] with a moving fundamental frequency.

If I speak a statement to you, my voice pitch tends to go down at the end. If I ask you a question, my pitch will usually rise. These pitch movements throughout the course of running speech follow a particular course that is learned over time; this aspect of prosody may be atypically processed in persons on the autism spectrum. The FFR can track this by reliably echoing the fundamental frequency–the primary acoustic basis for what we hear as voice pitch–as it changes. We can apply a pitch-tracking algorithm to the voice pitch of an utterance and apply the same algorithm to the FFR and compare the results. If the auditory brain has tracked the fundamental frequency of the evoking speech, the FFR will contain matching frequency components–with the pitch of both speech and the response sweeping upward or downward together. Russo found the FFRs in her young ASD subjects did a poorer job tracking the voice-pitch frequencies in her speech stimuli than those of her typically developing controls. A follow-up study[5] found abnormalities in the FFR evoked by the familiar 40-ms "da" that has featured in many investigations of language-related disabilities, suggesting a broader deficit in the central auditory perception of sound.

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From left: At Northwestern University, **Dr. Nina Kraus** is a professor of auditory neuroscience, investigating the neurobiology underlying speech and music perception and learning-associated brain plasticity (Learn more at www.brainvolts.northwestern.edu), and **Trent Nicol** is a research associate in the Auditory Neuroscience Lab.

GENETICS

One approach to investigate the possibility of genetic causes of autism involves looking for signs, usually subclinical, of ASD-like behaviors in first-degree relatives of people with autism. Indeed, there have been findings of parents exhibiting personality, communicative, and social-behavioral traits that tend to be milder, but qualitatively similar, to their ASD children.[6,7] Findings like these suggest evidence of a broad autism phenotype that is likely heritable.

There is intriguing evidence that some first-degree relatives of people with autism show differences in the realm of prosody. For example, both individuals with autism and their parents produce larger pitch shifts in their voices when they listen to perturbed feedback of their voice[8], suggesting less efficient audio-vocal integration. Differences in speech rate also have been identified in parents of ASD individuals.[9]

NEW RESEARCH

Now, Dr. Shivani Patel and others from our two labs have joined vocal prosody, auditory processing via FFR, and familial connections in ASD by testing 34 individuals with autism and 49 parents of individuals with autism on extensive pragmatics and prosody surveys, and with the FFR to two speech syllables. There were also 24 and 32 controls to match the ASD and parent-of-ASD groups, respectively. The parents were not necessarily parents of the ASD participants. However, among these cohorts, there were 35 mother-child pairs (16 ASD and 19 control) that enabled a deeper exploration of familiality.

The FFR syllables used in the investigation were the 40-ms "da" and a longer (220 ms) "ya" with a rapidly rising voice pitch, as though this utterance was being voiced as a question. In addition to replicating past findings of prolonged latencies, increased noise, and reduced consistency for the "da" and reduced pitch-tracking strength for the "ya" in the ASD participants, we found the ASD-parent group also exhibited some, but not all, of these response outcomes.

Intriguingly, several of these FFR response measures related to the measures of pragmatic language in the combined groups. Briefly, within the ASD plus control group, there were relationships between FFR and pragmatic language violations, particularly those related to discourse management and nonverbal communication, as well as a variety of receptive and expressive prosody metrics. Within the ASD-parent plus control-parent groups, the FFR related to pragmatic language violations, specifically factors contributing to a dominant conversational style and violations of listener expectation, as well as receptive and expressive prosody. [For a full description of these language assessments and the details of the exact FFR correlates, please see the full *JADD* manuscript.]

Upon closer examination of familial FFR relationships in the 35 mother-child pairs, a permutation analysis found that certain FFR metrics—namely wave V timing, F1 amplitude, pitch-tracking error, and pitch-tracking strength—familiality was predictable with a greater than 97% certainty. In other words, there was a much greater similarity between the ASD and ASD-mother FFRs than between the ASD and either the control or control-mother FFRs.

This new study advances our understanding of auditory processing in autism and makes a compelling addition to our understanding of the heritability of pragmatic-language anomalies, including prosody, often accompanying this disorder. It cements the notion that disruptions in neural sound processing occur in ASD and that they may contribute to the complex ASD language profile. Additionally, the close associations we found between both language and neural processing of speech between individuals with ASD and their parents suggest that ASD-related speech processing and language impairments have a heritable mechanism. Finally, it is encouraging news that sound processing may contribute to atypical language in autism, because we have seen evidence that training may engender biological changes in the auditory brain in autism.[10] Taken together, the results of this study provide more evidence for the important role sound plays in a holistic understanding of the brain.[11]

References for this article can be found at http://bit.ly/HJcurrent.