SPECIFIC AIMS

Although language abilities vary across the autism spectrum,[5] the majority of children with Autism Spectrum Disorder (ASD) have language deficits that emerge early in development and have long lasting negative impacts on other domains of functioning.[6-8] While we do not know what causes these language deficits, previous work using functional magnetic resonance imaging (fMRI) has suggested that reduced activation in left-lateralized frontal and temporal regions of the brain, as well as reduced inter- and intra-hemispheric functional connectivity, may contribute to the development of language deficits in ASD. However, only a handful of fMRI studies have explored the functional brain systems associated with language processing in preschool-aged children with ASD.[9-11] Furthermore, in all of these studies, children listened to recorded stories while they were asleep and socially-isolated in the fMRI scanner; this is *not* how children are exposed to language in everyday life. Functional near-infrared spectroscopy (fNIRS) is a sensory-friendly neuroimaging method that is more tolerant of motion artifacts than fMRI, and thus well-suited for measuring brain function while children are awake and interacting with a social partner. Despite the promise of this neuroimaging method, *no* studies have used fNIRS to measure how the brains of preschool-aged children function during live social interactions. It is particularly important to study brain function during the preschool years, as this is a sensitive developmental period during which children learn language by interacting with others. **Therefore, the overall goal of the proposed research project is to use fNIRS to investigate the neural bases of language processing during a live social interaction in preschool-aged children with and without ASD.** To meet this goal, we will enroll 50 children with ASD and 50 TD controls, 36- to 60-months-old. We will use fNIRS to measure children's brain function during two conditions – a live condition and a recorded condition. During the *live condition*, a live experimenter will interact with the child by reading him/her a scripted story from an illustrated book. During the *recorded condition*, the child will listen to a recording of a scripted story while viewing illustrations on a screen.

AIM 1: Determine how live social interaction modulates brain response to language in preschool-aged children with and without ASD.

Approach: We will compare oxyHb concentration values (i.e., "brain response") across groups (ASD, TD control), conditions (live, recorded), brain regions of interest (superior temporal gyrus, middle temporal gyrus, inferior frontal gyrus, middle frontal gyrus, temporal parietal junction), and brain hemispheres (left, right). ***Hypothesis:*** Based on findings of previous work,[12-17] we predict that in all regions of interest, TD controls will have greater brain response during the live condition compared to the recorded condition, while children with ASD will have similar brain response across both conditions. Brain response in left-lateralized regions of interest will be lower in the ASD group compared to the TD group across both conditions.[9-11]

AIM 2: Examine functional connectivity (FC) in preschool-aged children with and without ASD during a live social interaction.

Approach: We will assess group differences in inter- and intra-hemispheric FC during the live condition (i.e., live social interaction). ***Hypothesis:*** Compared to the TD control group, the ASD group will demonstrate reduced inter- and intra-hemispheric FC.[18-22]

AIM 3: Investigate the relation between brain function during a live social interaction and language abilities, communication skills, and autism severity in preschool-aged children with and without ASD.

Approach: Within both groups, we will examine correlations between measures of brain function (brain response and FC) during the live condition and standard scores on the Preschool Language Scales (PLS-5),[23] a measure of language abilities, and the communication domain of the Vineland Adaptive Behavior Scales (Vineland-3),[24] a measure of communication skills. Within the ASD group, we will also explore the relation between measures of brain function and autism severity, as measured by Autism Diagnostic Observation Schedule (ADOS-2)[25] calibrated severity scores.[26] ***Hypothesis:*** Within both groups, greater brain response and FC will be related to better language abilities and communication skills.[10,11,22,27] In the ASD group, greater brain response and FC will be related to lower autism severity.[17,28-30]

Findings from the proposed project will begin to **fill the gap** in research on the neural bases of language processing by demonstrating how the brains of preschoolers with and without ASD, an understudied age group, function during real-world social interactions. Clinically, findings will elucidate the neural mechanisms underlying the development of language deficits in children with ASD, and may provide insights into how the brain functions during different types of language interventions.