

## **Early sex differences in attention to the articulating mouth as a female protective candidate mechanism in Autism Spectrum Disorder**

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that starts early in life. Individuals with autism show difficulties in social interaction and communication and present repetitive behaviours. Females are four times less likely to be affected by ASD than males. Females are also less likely to present the language difficulties associated with the disorder, which are more common in males. One current theory (the *female protective effect hypothesis*) explains that the reason behind this female resilience is that females need to accumulate more risk factors than males to develop ASD or the associated language difficulties. Females may also carry more protective factors than males, making them less vulnerable to the disorder and the linked language atypicalities. However, what these factors are is still unclear.

In the general population, sex differences in language development are observable from early in life until adulthood, with females showing better overall skills than males. For example, females tend to show better vocabulary and build more complex sentences than males. One of the factors explaining these sex differences is that females scan with their eyes the human talking faces in a different way than males. We recently found that as early as 5.5 months of age, female infants pay more attention to the articulating mouth of a speaker than males while still being capable of paying attention to the talker's eyes. This particular way of looking at the faces gave females an advantage relative to males in their vocabulary skills at age two years. These results suggest that increased looking at the mouth during infancy may be a female-specific protective factor of later language development.

Since developing ASD highly depends on genetic factors, it is frequent that first-degree relatives of the affected individuals also show the disorder and the language difficulties associated to it. Infants at elevated likelihood of ASD (who have an older sibling with ASD) are more likely to show the disorder and difficulties in language development themselves. Conducting studies with infants at elevated likelihood of ASD brings the opportunity to explore potential protective factors specific to each sex before the disorder and the language difficulties emerge. In this project, I propose to study whether, as we observed in typically developing infants, increased attention to the articulating mouth is also an early female-specific protective factor of later language acquisition in infants with an elevated likelihood for autism. If this is the case, then we may target a protective candidate factor underlying the *female protective effect hypothesis*.

To explore this research question, I will track sex differences in mouth-looking in infants at elevated and low likelihood for autism during the first year of life. These looking patterns will be related to the measures of their later language skills in toddlerhood. I expect that both females (at elevated and low likelihood of ASD) look more at the mouth than both males (at elevated and low likelihood for ASD). Further, I expect that only in females (at elevated and low likelihood of ASD) increased mouth-looking is related to better language skills in toddlerhood.

I will analyze already collected longitudinal data across several time-points of infants at elevated and low likelihood of ASD (N=463) from three European labs (UK, Sweden, and Italy). Infants' looking patterns to the mouth of talking faces will be extracted across two contexts: traditional screen-based eye-tracking tasks and during 'live' interaction with real people. This approach will allow exploring in a large-scale sample how generalizable mouth-looking is as a potential female protective factor across time-points of life, countries, and tasks.

This project has important implications for understanding to what extent sex-specific protective factors may compensate the genetic risk factors affecting infants at elevated likelihood for ASD. It may also have several practical implications for the clinicians and speech therapists working with this population. The findings of this project may help them to target a key attentional skill that could need intervention early in life to prevent future language difficulties, especially in male infants. This project may also provide some preliminary insights into how we can detect with 'live'-eye trackers in real-time a deviation from the expected trajectory of looking and support these infants to learn how to more efficiently attend to talking faces so that they reach their best language development.