

Development of the pupillary light reflex from 9- to 24-months: association with later Autism diagnosis.

1. Background

Autism is **heritable**¹, though the mechanisms through which genes contribute to symptoms remain unclear. Prospectively measuring the development of **early intermediate phenotypes** may reveal these early mechanisms. The **pupillary light reflex** (PLR; the reflexual pupil constriction in response to a bright change in light; Fig 1) is a candidate early intermediate phenotype. **At 9-months, larger PLR constriction Amplitude, but not PLR constriction onset (i.e. Latency), is associated with later Autism**².

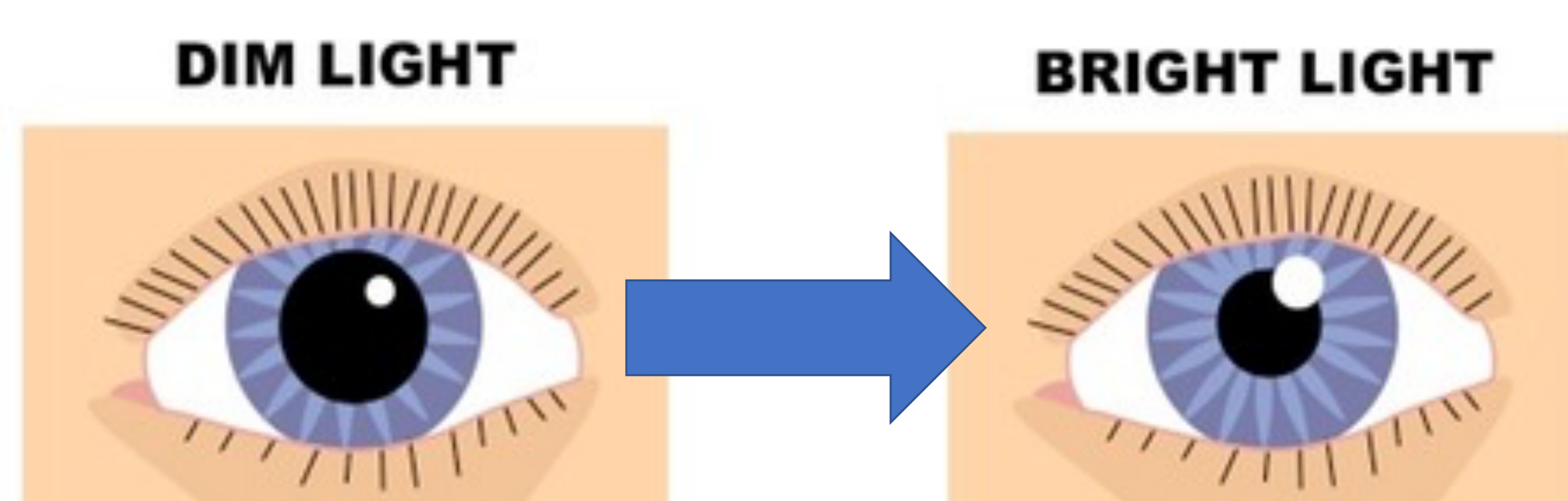


Fig 3. illustration of the PLR

2. Study Aim

Explore whether the **9- to 24-month development of infant PLR Amplitude** (relative to baseline pupil size [%]) and **Latency (ms) associates with Autism diagnosis at 3-years.**

3. Methods

Participants: 69 infants with no family history of Autism (*Typical Likelihood; TL*); 195 with an older sibling with a clinical Autism diagnosis (*Elevated Likelihood; EL*).

At 3-years a team of clinical researchers ascertained a DSM-5 Autism diagnosis:

- 27 EL infants received *Autism diagnosis*
- 50 EL infants scored highly (atypical) on developmental assessments but did not have Autism based on DSM-5 criterion and were classed as *Other*.
- 164 infants had *Typical Development*.
- 23 infants did not attend assessment

Measures:

PLR induced by bright flash of white light on a monitor; Fig 2) measured longitudinally at 9-, 14-, and 24-month using Tobii eye-tracker.

Analysis: Two linear multilevel models (random intercepts for participant): *Dependent Variables:* PLR Amplitude (%) or PLR Latency (ms); *Fixed Effect:* Interaction of Visit*3-year Autism outcome.

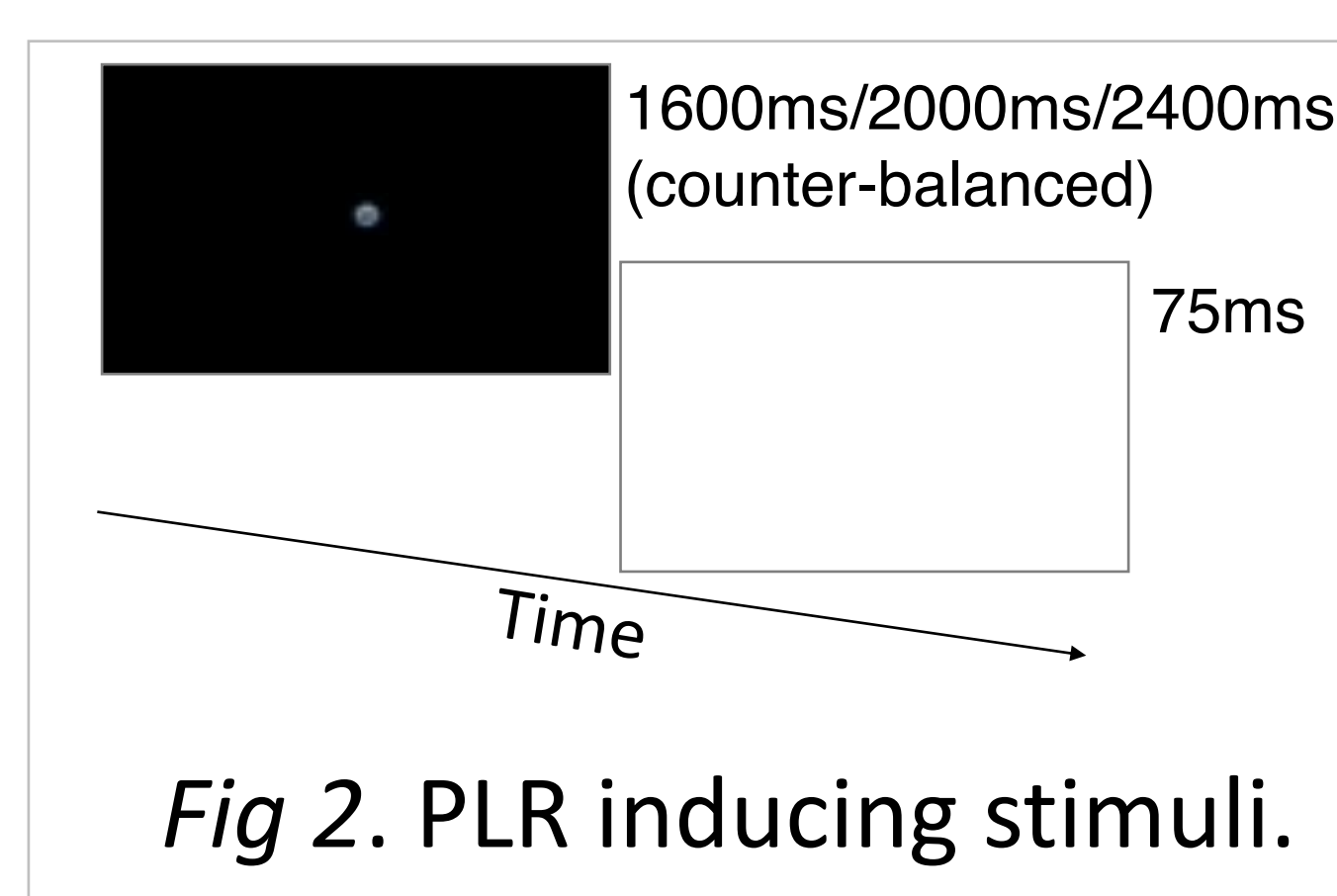
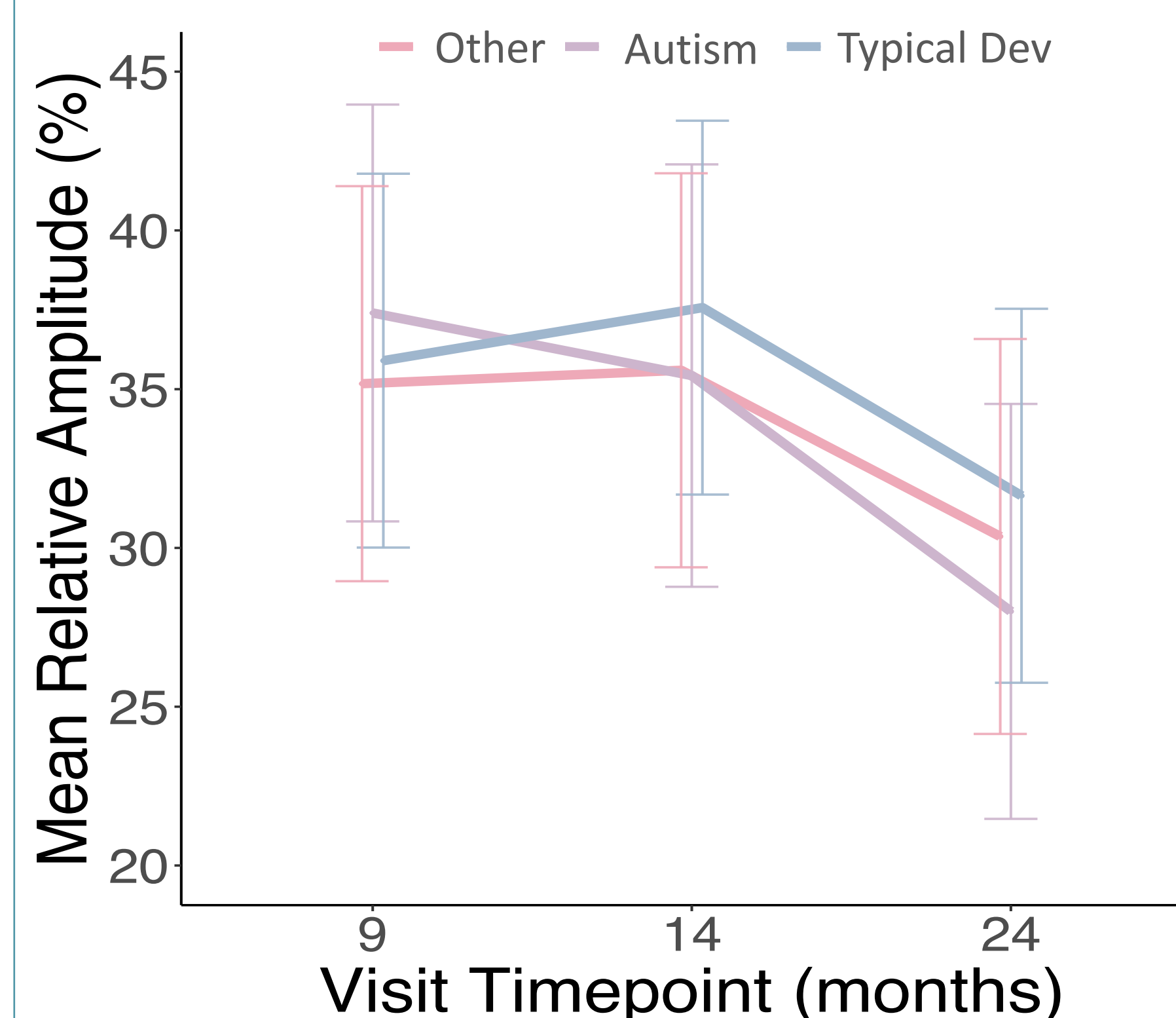


Fig 2. PLR inducing stimuli.

4. Results

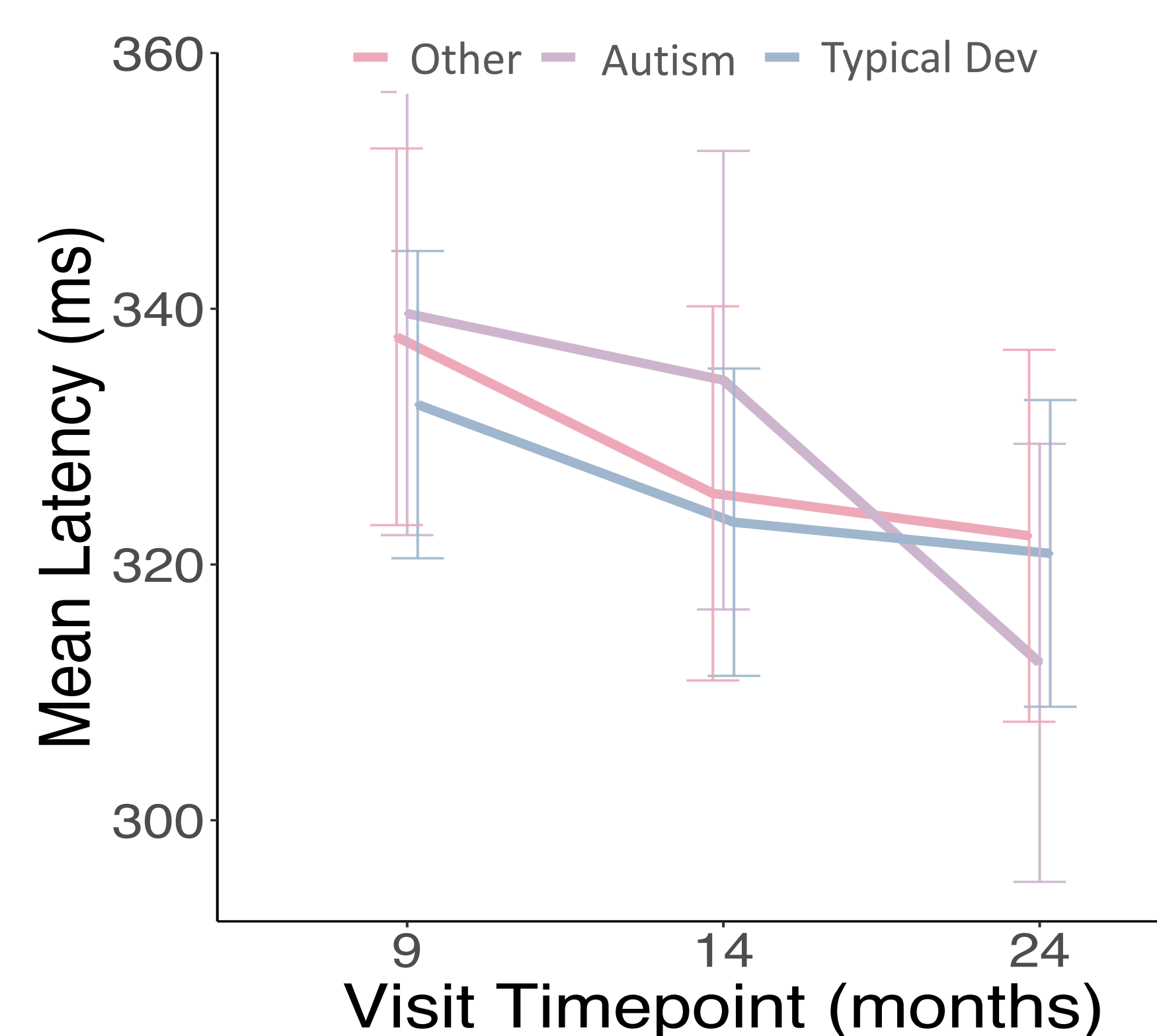
Model 1: Fixed effect of Visit (9-, 14-, 24-months)*3-year Autism outcome (Autism, Other, Typically Developing) on PLR Amplitude (%; Fig 3)



Compared to those with a 3-year **Autism diagnosis**, PLR Amplitude change from 9- to 14-months and from 14- to 24-months did **not significantly differ** from the *Other* group (9-14: $\beta = -2.39$, $CI^{95\%} = -6.71, 1.94$; 14-24: $\beta = 2.19$, $95\% CI^{95\%} = -2.16, 6.54$) or **Typical Development group** (9-14: $\beta = -3.64$, $CI^{95\%} = -7.44, 0.71$; 14-24: $\beta = 1.50$, $CI^{95\%} = -2.31, 5.32$).

Fig 3. Mean Amplitude (%) over visit by outcome.

Model 2: Fixed effect of Visit (9-, 14-, 24-months)*3-year Autism outcome (Autism, Other, Typically Developing) on PLR Latency (ms; Fig 4)



Compared to those with a 3-year **Autism diagnosis**, Latency change from 9- to 14-months did **not significantly differ** for infants in the *Other* group ($\beta = 7.03$, $95\% CI = -11.21, 25.37$) or **Typical Development group** ($\beta = 3.98$, $95\% CI = -12.02, 20.21$)

Latency change from 14- to 24-months for those with a 3-year **Autism diagnosis was significantly steeper** than those in the *Other* group ($\beta = 18.79$, $95\% CI = 0.57, 37.07$) or **Typical Development group** ($\beta = 19.66$, $95\% CI = 3.55, 35.88$)

Fig 4. Mean Latency (ms) over visit by outcome.

6. Discussion

- Early PLR development seems to be altered during the emergence of Autism, particularly PLR Latency.
- These results potentially highlighting implicated neural developmental mechanisms in the emergence of Autism.
- Future work should incorporate alternative measures (e.g. domain analysis of symptoms) to specify neural mechanisms.

7. References

- ¹Tick, B., Bolton, P., Happé, F., Rutter, M., & Rijdsdijk, F. (2016). Heritability of autism spectrum disorders: A meta-analysis of twin studies. *Journal of Child Psychology and Psychiatry and Allied Disciplines*.
- ²Nyström, P., Gliga, T., Jobs, E. N., Gredebäck, G., Charman, T., Johnson, M. H., Bölte, S., et al. (2018). Enhanced pupillary light reflex in infancy is associated with autism diagnosis in toddlerhood. *Nature Communications*, 9(1), 6–10.