

Head Circumference Trajectories in Autism and Psychotic Experiences

Sarah A. Ashley¹, Kate Merritt¹, Francesca Solmi¹, Pedro L. Laguna², Abraham Reichenberg³, Anthony S. David¹

¹ Division of Psychiatry, University College London; ² CUBRIC, Cardiff University; ³ Department of Psychiatry and Seaver Center for Autism Research and Treatment, Icahn School of Medicine, Mount Sinai

Introduction

- Head circumference is a strong proxy for brain size and clue to neurodevelopment.
- Evidence suggests that **autism** is associated with early brain overgrowth and enlarged head size.
 - When does this increase occur?
 - Does it persist? and
 - Does it manifest across the whole ASD spectrum.
- Similarly, **psychotic disorders** (e.g. schizophrenia) are associated with reduced brain volume however little is known about how the brain develops prior to clinical onset.
- Samples at risk for psychosis may help identify biomarkers for psychotic disorder.
- **Aim:** To investigate how head circumference trajectories differ among individuals on the autism and psychosis spectrums to controls.

Method

- We charted head circumference from birth to 15 years using data from a longitudinal birth cohort (the Avon Longitudinal Study of Parents and Children [ALSPAC]).
- Linear mixed regressions compared trajectories in children with a clinical ASD diagnosis (N = 78), elevated autistic traits (N = 639), psychotic experiences (339), and psychotic disorder (n = 62) to controls (~N = 6,404).
- We fitted a series of univariable and multivariable models, adjusting for confounders.
- ASD cases were identified via parent-report when children were aged 9 years.
- Elevated autistic traits were assessed using the Social Communication Disorder Checklist (scoring > 7) at age 7.5 years.
- Psychotic experiences and 'psychotic disorder' (i.e., severe psychotic experiences plus help-seeking and/or social impairment) were assessed using Psychosis-like Symptoms Interview (PLIKSi) at age 18 years.

Results - Autistic Traits & ASD

- **ASD diagnosis** was associated with **larger head circumference from birth through to adolescence** compared to controls (Univariable: B = 0.69, 95% confidence interval [CI]: 0.28 – 1.09, p = 0.001; fully adjusted multivariable model: B=0.38, 95% CI: 0.003 – 0.75, p=0.048).
- There was no evidence of a group by age interaction, however post-hoc t-tests suggest that differences become more notable at **2 months** of age. There was no interaction with sex (p = 0.89).
- Elevated **autistic traits** were associated with **smaller head circumference** compared to controls following adjustment for confounders (Univariable: B = -0.08, 95% CI: -0.22–0.06, p=0.28; multivariable: B=-0.16, CI: -0.28–0.03, p = 0.016)

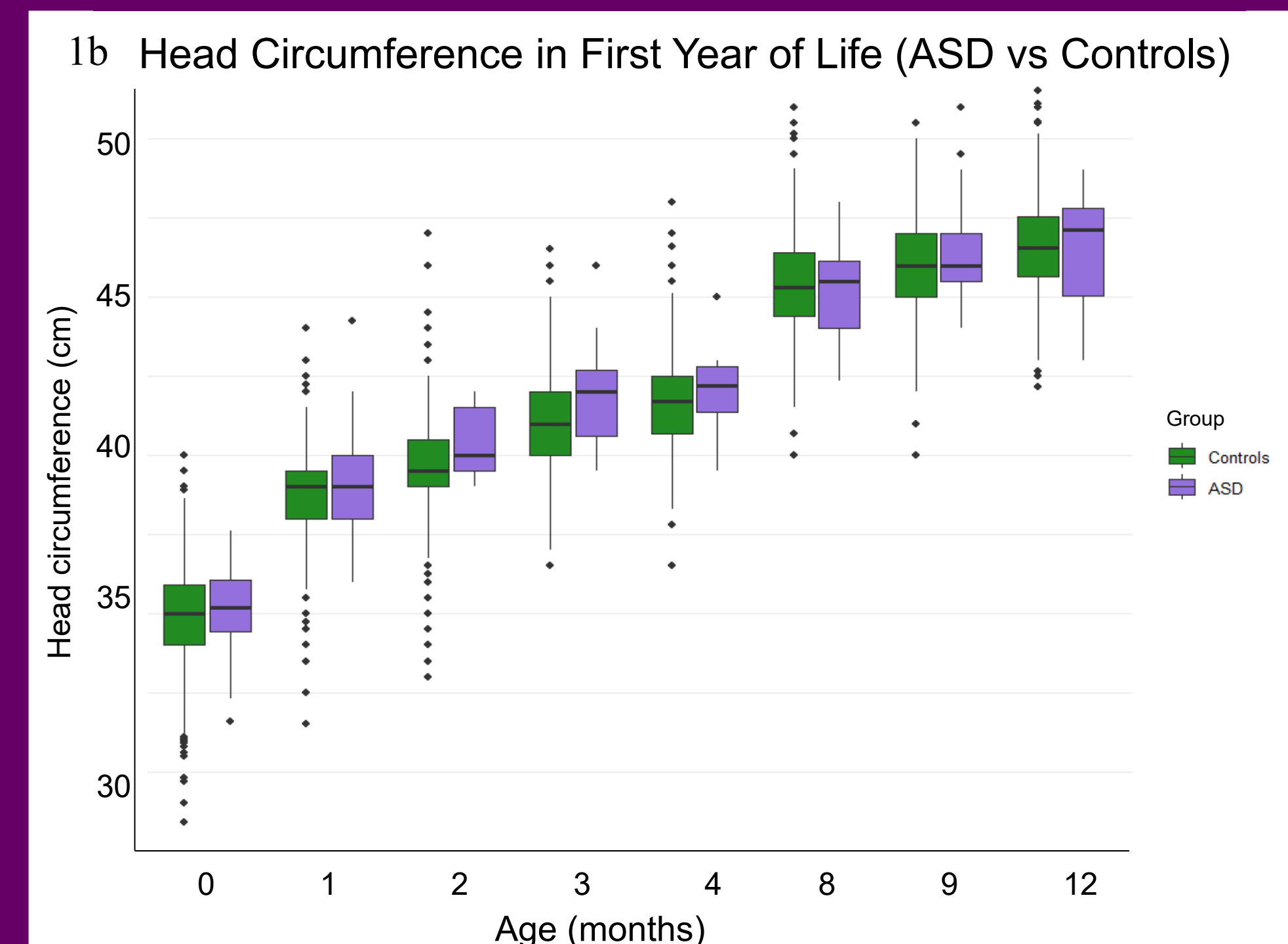
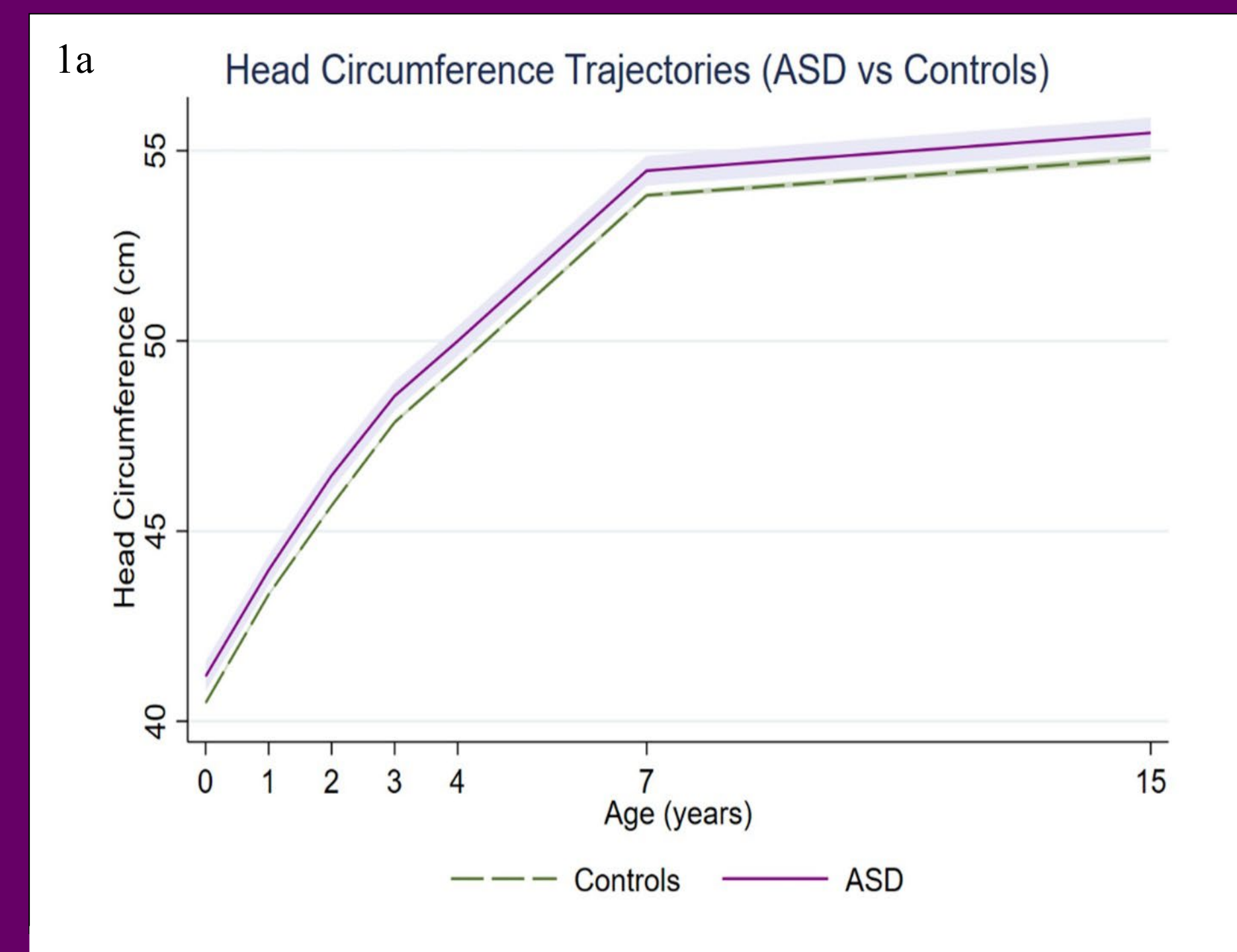


Figure 1a shows modelled head circumference (cm) values in ASD vs controls with 95% confidence intervals; Figure 1b shows head circumference across the first 12 months of life in ASD vs controls.

Results - Psychotic Experiences & Psychotic Disorder

- Young people with **psychotic disorder** had **smaller head circumference** across birth to adolescence compared to controls, with no interactions with age or sex.
- For **psychotic experiences**, results were modulated by sex. **Females** with psychotic experiences displayed **smaller** head circumference compared to female controls, whereas head circumference was **larger in males** with psychotic experiences compared to male controls.

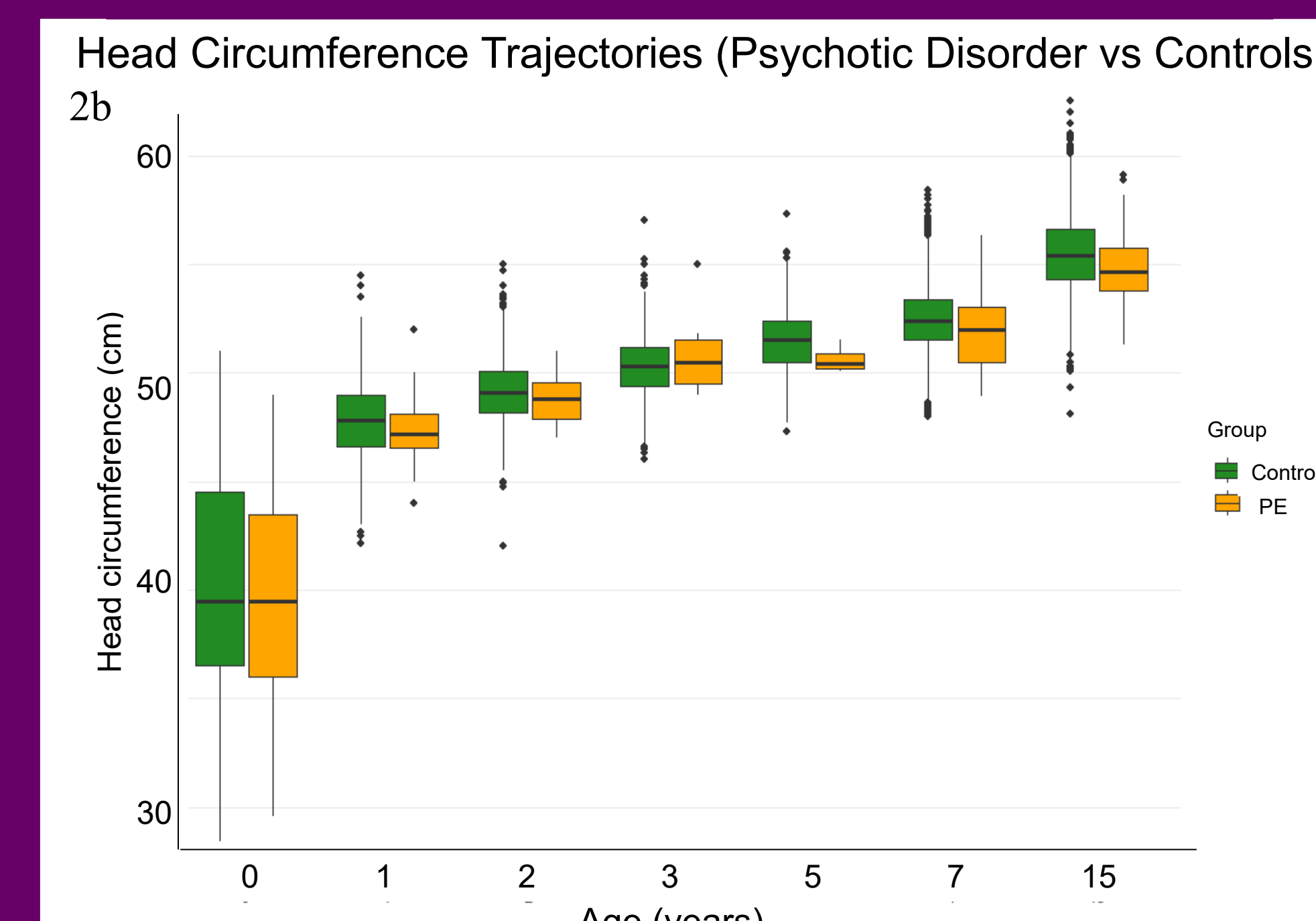
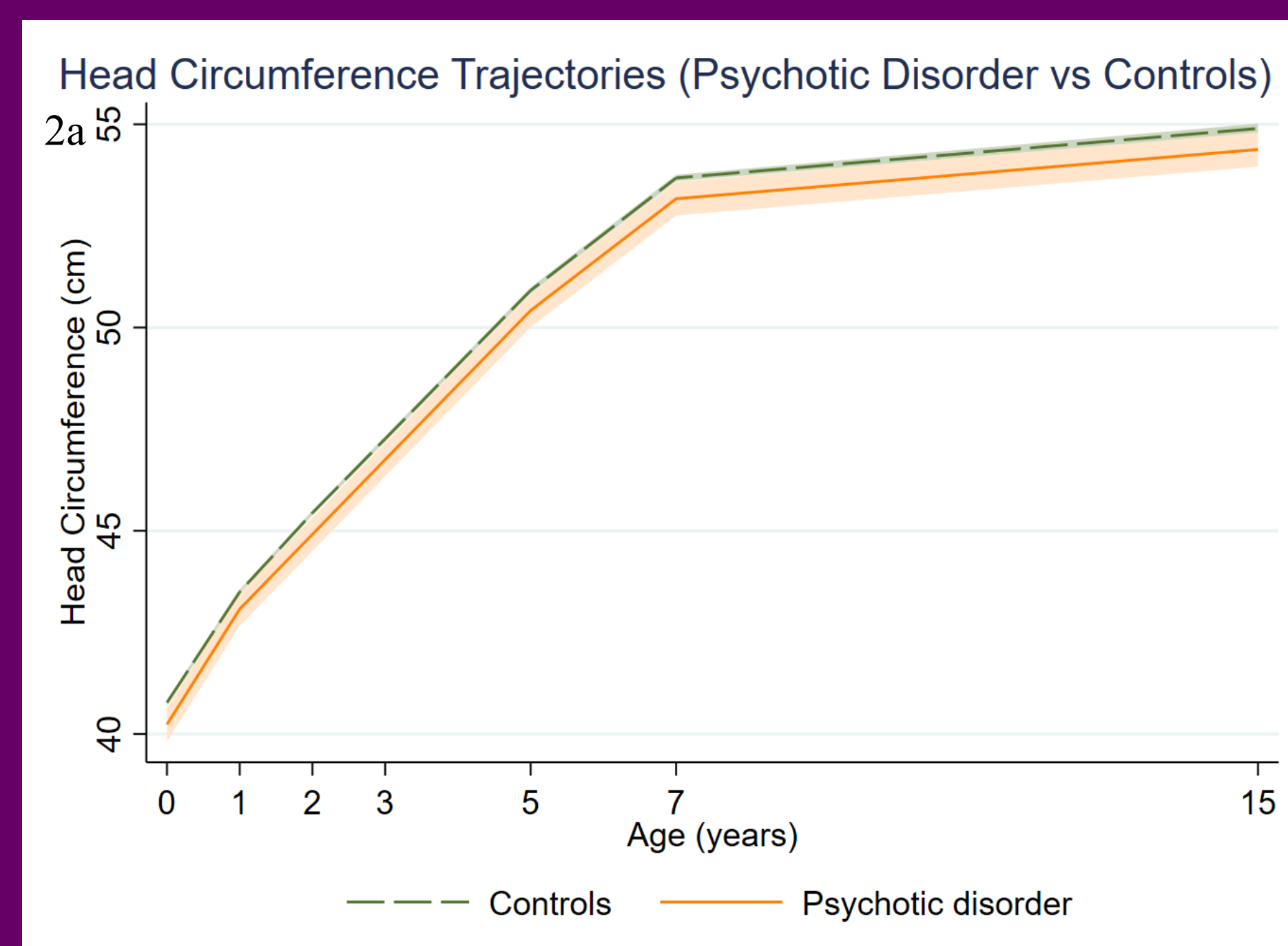


Figure 2a shows modelled head circumference (cm) values in individuals with psychotic disorder vs controls with 95% confidence intervals; Figure 2b is an alternative boxplot illustration of figure 2a, displaying head circumference trajectories from birth to 15 years.

Conclusion

- Head circumference is atypical from an early age in individuals across ASD and psychosis spectra.
- Our findings go against the idea of a pathophysiological continuum of autistic traits and ASD, highlighting distinct aetiological differences that may separate clinical versus non-clinical cases.
- Psychotic experiences and psychotic disorder were associated with smaller head circumference trajectories (especially in females). These results compliment observations of brain volume reductions in adults with psychosis and provide support for the neurodevelopmental model for psychosis.
- Future studies should continue to monitor HC across the full extent of the developmental trajectory and combine with MRI measures of brain structure.

Acknowledgements & Contact Details

Thank you to the ALSPAC participants who took part in this study, and to our funders: Beatrice and Samuel Seaver Foundation; and the MRC (MR/S003436/1).

✉ sarah.ashley.20@ucl.ac.uk

✉ @psych_ashley

