

## Preeclampsia is Associated with Increased Likelihood of Autism Spectrum Disorder in Offspring

### Executive Summary

• **We** conducted the largest epidemiological study on preeclampsia and autism spectrum disorder (ASD) to date, and in doing so, we addressed key limitations of existing literature.

Results indicate that preeclampsia is associated with an increase in the likelihood of ASD, while there is a stronger association between preeclampsia and small for gestational age (SGA) combined (i.e. SGA baby exposed to preeclampsia) and ASD.

The stronger association between preeclampsia/SGA combined and ASD suggests that placental pathology may be a common factor increasing the likelihood of ASD.

Further research is needed to investigate the role that maternal inflammation may play, as well as the potential impact of antihypertensive medication in the development of ASD

### Introduction

• **A**utism spectrum disorder (ASD) is characterised by persistent impairments in interpersonal interaction and restricted or repetitive patterns of behaviour. The prevalence of ASD is approximately 1-1.5%, and while genetics play a major role in the development of ASD, the environmental contribution is estimated to be between 17-50%. This highlights the importance of investigating factors contributing to the likelihood of its onset, and potentially facilitate the development of appropriate interventions.

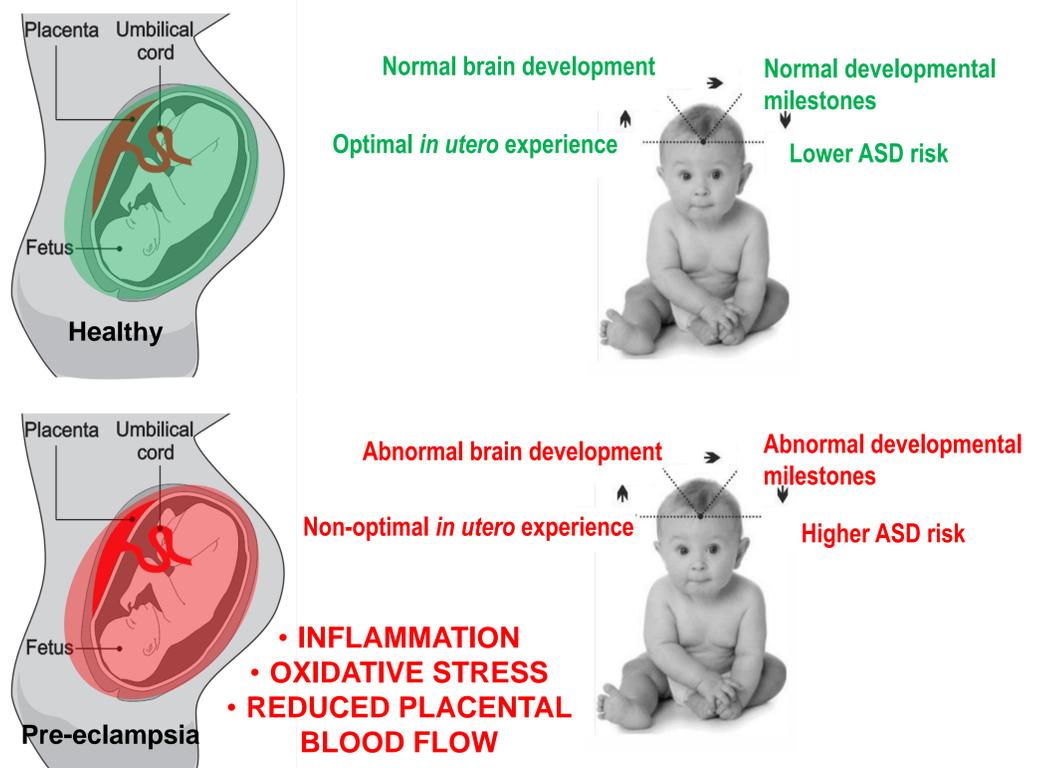
Preeclampsia is one of the leading causes of maternal morbidity and mortality, affecting approximately 5% of all pregnancies. Results of a comprehensive systematic review and meta-analysis suggest that preeclampsia is associated with an increased likelihood of ASD. However, several limitations of the literature were identified that needed to be addressed before we could reach more definitive conclusions.

Therefore, the objective of our research was to conduct the largest epidemiological study on preeclampsia-ASD to date, while addressing key limitations uncovered in the systematic review.

### Methods

• **We** conducted a population-based cohort study including all singleton live births in Sweden from 1982-2010 using data from Swedish National Registers. The cohort consisted of 2,842,230 children, with 54,071 cases of ASD.

Multivariate Cox proportional hazards regression analysis allowed us to adjust for several perinatal and sociodemographic factors, while sibling-matched analysis allowed us to further controlled for shared genetic and familial confounding.



Potential biological mechanisms contributing to a preeclampsia-ASD relationship.

## Results

- **P**reeclampsia was associated with a 32% increase in the likelihood of ASD with intellectual disability, while those exposed to preeclampsia and SGA (i.e SGA babies exposed to preeclampsia) were over 3 times more likely to have ASD with intellectual disability. (See Table 1).

## Conclusion

- **E**xposure to preeclampsia or preeclampsia/SGA was associated with ASD. The stronger association with preeclampsia/SGA than preeclampsia alone suggests that placental pathology may be a mechanism for the increased likelihood of ASD.

## Recommendations

It is important to investigate factors that may contribute to the development of ASD, and potentially facilitate the development of appropriate interventions .

Our study has found that exposure to preeclampsia and preeclampsia/SGA is associated with an increased likelihood of ASD in offspring.

The stronger association between preeclampsia/SGA combined and ASD suggests that placental pathology may be a common factor increasing the likelihood of ASD.

However, future research should investigate the role that maternal inflammation may play, as well as the potential impact of antihypertensive medication in the development of ASD.



## Reference

The full text of this research is available at:

<https://onlinelibrary.wiley.com/doi/epdf/10.1111/jcpp.13127>

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**Table 1:** Association between Preeclampsia and Autism Spectrum Disorder Among Singleton Live Births in Sweden between 1982 and 2010

	ASD with Intellectual Disability			Sibling pairs
	Exposed cases	Model 1 HR (95% CI) <sup>a</sup>	Model 2 HR (95% CI) <sup>b</sup>	Model 3 HR (95% CI) <sup>c</sup>
ASD+ID (n=8981)				
Preeclampsia	388	1.59 (1.44, 1.76)	1.56 (1.41, 1.73)	<b>1.32 (1.07, 1.62)</b>
Preeclampsia and SGA	90	3.11 (2.52, 3.82)	2.95 (2.40, 3.64)	<b>3.07 (1.97, 4.79)</b>

Abbreviations: HR, hazard ratio; 95% CI, 95% confidence interval; ASD, autism spectrum disorder; ID, intellectual disability; SGA, small for gestational age.

<sup>a</sup>Adjusted for year of birth.

<sup>b</sup>Adjusted for year of birth, infant sex, maternal age, maternal and paternal country of birth, birth order, parental mental health, family income, maternal smoking status, BMI at first antenatal visit, gestational weight gain and parental level of education.

<sup>c</sup>Adjusted for same potential confounders as 'b' above with the exception of maternal country of birth.

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