

## Abnormal fetal growth and placental size and risk of neurodevelopmental disorders

Larsen ML, Pihl K, Rackauskaite G, Greisen G, Krebs L, Høi-Hansen CE, Petersen OB

Center of Fetal Medicine, Department of Obstetrics, Copenhagen University Hospital - Rigshospitalet, Copenhagen, Denmark

### Objective

Neurodevelopmental disorders are assumed to be mostly caused by impaired development during pregnancy. Therefore, we aimed to investigate associations between abnormal fetal growth in the first and second halves of pregnancy, placental size, and the risk of neurodevelopmental disorders in childhood.

### Methods

A population-based registry study using data from the Danish Fetal Medicine Database, including all singleton liveborn children in Denmark from 2008 to 2013 who had undergone routine first- (gestational weeks 11<sup>+0</sup>–13<sup>+6</sup>) and second-trimester (18<sup>+0</sup> to 21<sup>+6</sup>) screening and were alive after the first year of life. All were followed in the first six years of life for the diagnosis of cerebral palsy (CP), epilepsy, intellectual disability and autism spectrum disorders (ASD). We evaluated the growth of the biparietal diameter (BPD) between the first and second trimesters, calculated as the difference in BPD divided by the number of days between measurements; growth in fetal size between the second trimester and birth, calculated as the difference in estimated fetal weight at the second-trimester scan; birthweight divided by the number of days between measurements; and placental size. We compared the mean Z-scores and proportions <10<sup>th</sup> and >90<sup>th</sup> centiles in cases and controls, estimated by linear regressions adjusted for sex and gestational age at measurements.

### Results

We included 249,130 children and found 78 with ASD, 130 with intellectual disability, 381 with CP, and 1515 with epilepsy. Some children had more than one diagnosis. The mean growth of BPD between the first- and second-trimester scans was 0.51 mm/day (SD 0.05). The mean growth in fetal size between the second trimester and birth was 22.8 grams/day (SD 3.3), and mean placental size was 674 grams (150). All included neurodevelopmental disorders were associated with a lower mean fetal growth rate between the second trimester and birth ( $p < 0.01$  for all) and, therefore, all had higher proportions of fetal growth rate <10<sup>th</sup> percentile ( $p < 0.01$  for all). In addition, children who developed epilepsy in childhood had significantly higher mean BPD growth than controls ( $p = 0.02$ ). Furthermore, children with CP and ASD had significantly lower mean placental weights ( $p < 0.01$  and  $p = 0.04$ ) and higher proportions of placental size <10<sup>th</sup> percentile (16.3% vs. 9.3%,  $p < 0.01$  and 23% vs. 9.3%,  $p < 0.01$ ).

### Conclusion

Abnormal fetal growth and small placental size are associated with the diagnosis of neurodevelopmental disorders in childhood.