NEONATAL EXPOSURE TO INVASIVE PROCEDURES IN RELATION TO HIPPOCAMPUS, AMYGDALA AND THALAMUS VOLUMES IN VERY PRETERM CHILDREN AT SCHOOL AGE

Manon Ranger, Ph.D.
University of British Columbia

Student/Trainee

INTRODUCTION / AIM

Altered hippocampal morphology and reduced volumes have been found in children born preterm compared to full-term. Stress inhibits neurogenesis in the hippocampus, and in rodent pups neonatal stress and noxious stimulation are associated with long-term alterations in hippocampal volumes. We have shown reduced cortical thickness and cerebellar volumes in relation to more exposure to neonatal invasive procedures in children born very preterm. Targeted gene-by-pain environment interactions have been shown to contribute to long-term brain development and outcomes in this population. Determine whether exposure to neonatal invasive procedures (adjusted for clinical factors and genotype) differentially impact subcortical brain volumes, and investigate relationships with outcomes in very preterm children.

METHODS

57 children born very preterm (<32 weeks GA) followed longitudinally from birth, underwent 3D T1 MRI neuroimaging at mean age 7.9 yrs. Hippocampal subfields and white matter tracts, thalamus and amygdala were automatically segmented using the MAGeT Brain algorithm. The relation between volumes (adjusted for total brain volume) and neonatal invasive procedures, GA, illness severity, postnatal infection, mechanical ventilation, surgeries, morphine exposure, and genotype (COMT, SLC6A4, BDNF) was examined using constrained principal component analysis.

RESULTS

Neonatal clinical predictors and genotypes accounted for 46% of the overall variance in volumes of hippocampal subregions, tracts, thalamus and amygdala. After controlling for clinical risk factors, greater neonatal invasive procedures was associated with lower volumes in amygdala and thalamus (p=0.0001) and in interaction with COMT genotype predicted smaller right hippocampal subregional volume (p=0.0001). More days of ventilation, surgeries and lower GA were also related to smaller volumes (p<0.002). These reduced volumes were related to poorer cognitive, motor and behavioral outcomes.

DISCUSSION / CONCLUSIONS

In very preterm children, exposure to neonatal invasive procedures, as well as additional neonatal risk factors were associated with reduced volumes in hippocampal subregions, amygdala and thalamus which were related to poorer outcomes at school age.

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OTHER AUTHORS

Cecil MY Chau
Min TM Park
Robert SC Amaral
M. Mallar Chakravarty
Hannah S McNeill
Bruce H Bjornson
Anne R Synnes
Steven P Miller
Ruth E Grunau