BRAIN STRUCTURE AND FUNCTION IN CHILDREN BORN SMALL FOR GESTATIONAL AGE

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SUMMARY

Brain structure and function in children born small for gestational age

An optimal intrauterine environment is vital for normal brain development. Adverse prenatal circumstances such as uteroplacental insufficiency can interfere with normal development and may result in underdevelopment of both the body and the brain. When the birth weight of a child is too low for its gestational age, the child is considered small-for-gestational-age (SGA). Postnatally, the majority of the SGA children exhibit postnatal catch-up growth, only 10% remain short-statured.

Being born SGA is associated with cardiovascular and metabolic disease such as obesity and insulin resistance in adulthood. Also, decreased levels of intelligence and cognition have been described (Chapter 3). Interestingly, postnatal catch-up growth of both head circumference and body height is associated with better cognitive outcome. In this thesis, structural and functional MRI and neuropsychological testing were used to investigate brain structure and function, intelligence and cognition in 4-7 year old children born SGA in a group of children with (SGA+) and without (SGA-) postnatal catch-up growth compared to children born appropriate for gestational age (AGA).

In this study, children were prepared in a mock scanner according to a newly developed protocol (Chapter 4) because the design and dimensions of an MRI scanner can be intimidating (huge machine, narrow bore, loud noise) especially for young children. Children underwent the actual MRI investigation only after successful completion of the training session. We demonstrated that preparation according to our mock scanner training protocol results in a high proportion of good quality MRI scans for both research and clinical purposes.

Results of the structural MRI study (chapter 5) showed that children born SGA have smaller brains in which white matter volume is predominantly affected. Regional differences in thickness of the cortical mantle, mainly in the prefrontal cortex, were observed between SGA and AGA children.

Resting state functional connectivity MRI was performed (chapter 6) to identify and characterize resting-state networks. In 5-8 year old children in an awake state, almost all networks previously identified in adults, are present, yet in an immature state. For this study, only AGA ans SGA+ children were included. Subgroup comparison between AGA and SGA did not reveal differences but may be due to small group size. In the task related functional MRI study, children had to memorize pictures (picture encoding task, Chapter 7). Our results showed that the neural substrate of picture encoding in SGA children is comparable to AGA although SGA children showed slightly lower activation in the left parahippocampal region.

The IQ of SGA children is within the normal range but lower than of AGA children (Chapter 7&8). SGA children have lower scores than AGA controls on practically all

measures of cognition and behaviour, although not statistically different. Already in the earliest stages of their academic career, twice as many SGA children repeated a grade at school, and needed more extra educational services or special education.

The influence of postnatal catch-up growth on brain structure, function and cognitive outcome was investigated by studying a subgroup of SGA+ and SGA- children (Chapter 5,7,8). We found that SGA+ children constitute an intermediate between SGA- and AGA with respect to most brain parameters, but most obvious in the structural MRI study. Moreover, SGA+ children were an intermediate with respect to intelligence and working memory. For the other cognitive domains, SGA- and SGA+ children differ with respect to the precise nature of cognitive vulnerabilities and disadvantages. In SGA+ children, disadvantages mainly concern imperfections of self-regulation and behavioural performance, whereas SGA- children had lower scores on measures of learning and retention.

It can be concluded that, catch-up growth of height in children born SGA does not implicate full catch-up growth of the brain structure, function and neuropsychological functioning. Therefore, careful observation of the SGA children, both SGA+ and SGA-, during schoolage is warranted.