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# Cortical morphometry and cognition in very preterm and term-born children at early school age

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ABSTRACT

Very preterm birth influences brain development and may result in alterations of cortical morphometry. These structural alterations may interact with cognitive development. The aim of the present study was to investigate the structure-function relationship in school-aged very preterm and term-born control children. A comprehensive neuropsychological test battery was administered to 41 very preterm (< 32 weeks of gestation) and 30 term-born control children aged seven to twelve years. The automated method FreeSurfer was used to obtain cortical thickness and cortical surface area measures from T1-weighted MRI images. Regional cortical thickness differed between groups but differences disappeared when controlling for age. Global cortical thickness differed between groups in the right hemisphere (very preterm children > controls). No group differences occurred for cortical surface area. The relationship between cortical morphometry and cognition differed between very preterm and control children. In very preterm children, some cognitive domains correlated positively and others negatively with regional cortical thickness and cortical surface area. Our findings contribute to the understanding of the structure-function relationship in very preterm children and their term-born peers. They add to the notion that this relationship varies depending on the brain region and the cognitive function in question and suggest developmental differences between very preterm and term-born children.

## 1. Introduction

Very preterm-born children may show structural brain alterations, including smaller total brain volume [1,2], alterations in gray and white matter volume [3,4] and reduced volumes of corpora callosa, hippocampi, cerebellum and nuclei caudati [2,5–8]. In addition to differences in gray and white matter volume, more recent methods have detected alterations in cortical thickness and cortical surface area in very preterm-born children (< 32 weeks of gestation) [9–14]. While cortical morphometry has been suggested to parallel cognitive functioning in typically developing children [10,15–17], morphometric alterations in the preterm brain may likewise interact with cognitive functioning. Indeed, children born very preterm are at increased risk of a range of cognitive difficulties concerning memory, language, attention, processing speed, reading, spelling and arithmetic [18]. Defining how cognitive performance relates to cortical thickness and cortical surface area in very preterm and term-born children will help to understand the structure-function relationship in the atypically and typically developing child's brain.

Neuroimaging offers the possibility of non-invasively examining cortical characteristics at a large-scale brain level. The formation of cortical thickness and cortical surface area seems to be driven by different neurodevelopmental processes and is thought to be influenced by different genes [19,20]. As the developmental trajectories of those measures differ across the brain, it is important to include both measures - cortical thickness and cortical surface area - in studies of the cortical structure-function relationship [21].

Cortical thickness is thought to be an indicator of the number of neurons per cortical column (groups of neurons that connect the six horizontal layers of the neocortex vertically) and relates to glial support and dendritic arborization [22]. Normal development in childhood is accompanied by an increase in cortical thickness during early childhood followed by a progressive cortical thinning during middle childhood and adolescence. This decrease of cortical thickness co-occurs with the pruning of dispensable neurons and synapses [23]. Because pruning is accompanied by increasing cognitive performance during development, it is suggested that higher cognitive performance might be associated with a thinner cortex [24]. Indeed, in healthy term-born children cortical thickness was negatively related to language abilities [15], verbal learning and memory, visuospatial functioning, problem

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**Table 1**
Literature on cortical morphology (cortical thickness and surface area) and cognitive functioning in very preterm children.

| Authors | Morpho-logical measures | Cognitive measures | Sample | Sample size | Cohort | Age (years) | Main findings |
|---|---|---|---|---|---|---|---|
| Østgård et al. [38] | CTh and CSA | Attention, EF | VLBW | VLBW: 46<br>TB: 61 | 1986–88<br>University Hospital Trondheim | 19–20 | - EF and antero-medial frontal and temporal CSA in VLBW (positive).<br>- No correlations cognition and CTh. |
| Nam et al. [32][a] | CTh | Global IQ Memory, Verbal Learning, EF | VPT (< 33 gestational weeks) | VPT: 160 and 67<br>TB: 88 and 42 | 1979–82<br>1983–84<br>University College London Hospital | 15, 20 | - EF and temporal CTh in TB (positive; non-significantly in VPT).<br>- EF and occipito-temporal CTh in VPT (positive)<br>- EF and parietal CTh in VPT (negative). |
| Sripada et al. [31] | CTh and CSA | Global IQ | VLBW | VLBW: 47<br>TB: 56 | 1986–88<br>University Hospital Trondheim | 18–22 | - Visuomotor performance and widespread CSA in VLBW (positive).<br>- Visual performance and occipito-temporo-parietal junction, superior temporal and parietal CTh in VLBW (positive).<br>- No sig. correlations in TB. |
| Sølsnes et al. [33] | CTh and CSA | Global IQ | VLBW | VLBW: 37<br>TB: 104 | 2003–2007<br>University Hospital Trondheim | 5–10 | - IQ and widespread CTh in VLBW (negative, non-sig. trend).<br>- IQ and temporal, parietal CTh in VLBW (positive).<br>- IQ and CSA only sig. in the larger group of TB (positive). |
| Skranes et al. [37] | CSA | Global IQ | VLBW | VLBW: 38<br>TB: 59 | 1986–88<br>University Hospital Trondheim | 19 | - IQ and frontal, temporal, occipital CSA in VLBW (positive). |
| Bjuland et al. [30] | CTh | Global IQ | VLBW | VLBW: 47<br>TB: 61 | 1986–88<br>University Hospital Trondheim | 18–21 | - IQ and ventrolateral frontal, temporal, parietal CTh in VLBW (positive).<br>- No sig. correlations in TB. |
| Skranes et al. [29] | CTh (entorhinal cortex) | Global IQ, Visual motor integration, EF | VLBW | VLBW: 49<br>TB: 58 | 1986–88<br>University Hospital Trondheim | 15 | - Motor coordination, EF, IQ and right entorhinal CTh in VLBW (positive). |

VLBW = very preterm with very low birth weight (< 1500 g), TB = term-born, VPT = very preterm, CTh = cortical thickness, CSA = cortical surface area, sig. = significant, EF = executive function.
[a] Longitudinal study.