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Diffusion magnetic resonance imaging for investigating alterations in brain organization after injury during early development, with specific reference to the motor and visual system

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ABSTRACT

Disturbances or injuries to the brain during early development cause different types of structural abnormalities, depending mainly on the stage of maturation of the brain at the time of the insult. These are, herein, collectively referred to as early brain lesions. Early brain lesions can cause a wide range of clinical symptoms including disturbances to motor or sensory functions, perception, cognition, communication and behaviour; epilepsy is common. There is a large variation in outcomes and severity of impairments, contributed to by the superior compensatory mechanisms in the young brain compared to the adult brain.

The overall aim of this thesis was to study the organization of the motor and visual system in early brain lesions by using diffusion-weighted magnetic resonance imaging (MRI) and white matter fibre tractography. The specific aims of the studies on the motor system (Study I & II) were to investigate the microstructural changes in motor and sensory tracts in individuals with early brain lesions causing unilateral cerebral palsy (CP), and to explore associations with hand motor function. The specific aims of the studies on the visual system (Study III & IV) were to seek evidence of a relationship between damage to the immature optic radiation (OR) and subsequent development of the retinal ganglion cell layers, and associated visual field function, in individuals with early brain lesions caused by with white matter damage of immaturity (WMDI).

The results from Study I showed that diffusion parameters in central cortico-fugal fibres, distant from the primary lesions, were sensitive markers for injury and correlated with hand function in the non-dominant hand in children with unilateral CP. Study II used an improved fibre tractography method in the same cohort, to study the cortico-spinal tract (CST) and adjacent thalamic projections to the primary sensory cortex (TRS1). The results showed dissimilarities in both the structural and the parametric changes seen in CST compared to TRS1 on the lesion-side, indicating that the tracts are affected differently by the injury; however, reactive changes in TRS1 is a possible alternative explanation.

The results from Study III show that injuries to the immature OR are associated with reduced thickness of the retinal nerve fibre layer, causing predictable visual field defects. Study IV showed, by including visual field mapping with functional MRI, a strict topographical and correlating relationship between injury to the superior portion of the OR, the part of OR that projected to the visual field map below the horizontal meridian, and the secondary thinning of the macular ganglion cell layer, and corresponding visual field defects. The results from both studies provide convincing evidence of retrograde trans-synaptic degeneration in WMDI. The structural changes to the OR may suggest re-organisation to the tract upon injury.

The overall conclusion from this thesis is that diffusion-weighted MRI is more sensitive in detecting and assessing the extent of early brain lesions than conventional MRI, and provides a sensitive marker for studying relevant changes to structural entities of fibre tracts that have a direct effect on the clinical function.