Microstructural and metabolic alterations in the zebrafish brain induced by toll-like receptor 2 deficiency: insights from ultra-high field magnetic resonance imaging and spectroscopy

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Propositions for the thesis

‘Microstructural and Metabolic Alterations in the Zebrafish Brain Induced by Toll-Like Receptor 2 Deficiency’

i) Toll-like receptor 2 deficiency induces widespread alterations in cerebral microstructure and metabolism in zebrafish. (Chapter 3 and 5).

ii) Non-invasive visualization of cerebral white matter structures in intact zebrafish can be accomplished through diffusion MRI tractography at UHFs by stTDI msmt CSD (Chapter 2).

iii) Integrity changes in white-matter structures of Toll-like receptor 2 deficient zebrafish are in line with behavioral changes observed in tlr2-/- models (chapter 3)

iv) Studying key cerebral metabolites non-invasively in targeted zebrafish brain regions is facilitated by localized MRS at UHFs (Chapter 4 and 5).

v) Localized MRS at the strongest commercially available magnetic field shows great potential for cerebral analysis in vertebrates; however, pronounced field-dependent artifacts must be considered at ultra-high field during method development (Chapter 4).

vi) Diffusion-weighted anatomical imaging significantly enhances MRI contrast in the zebrafish brain, compared to multi spin-echo sequences (Chapter 2).

vii) The Netherlands holds a uniquely advantageous position in the field of micro-MRI at UHF strengths, distinguished by its exceptional combination of diverse field strengths, state-of-the-art hardware, advanced infrastructure, and a strong network of research groups. However, this position is not yet fully taken advantage of, leaving significant opportunities for further development, collaboration, and innovation in the field.

viii) Utilization of animals in clinical research must eventually be phased out. However, this cannot be achieved overnight due to the lack of good alternatives. In this regard, organoids represent a promising and transformative solution.

ix) Increased effort is needed to make clinical MRI systems cheaper, easier to handle, and more available worldwide.

x) International collaboration should be actively stimulated at universities. However, it is crucial these efforts become more inclusive to avoid scientific tunnel vision and the risk of exploitation.

xi) For the well-being of society, it may be preferable we never fully comprehend the complete workings of the human brain.

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