Holotomography for preclinical investigation in neurodegenerative diseases

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As research in neurodegenerative diseases progresses, many similarities appear that relate these diseases to one another at *cellular and molecular levels*. One of the unmet needs common to neurodegenerative diseases of the central nervous system (CNS) is the possibility to assess and monitor the fine neuropathology, like tissue inflammation and damage, throughout the disease course and upon treatment. The lack of a suitable technology able to perform this monitoring makes it therefore difficult to assess the efficacy of new therapies at the cellular level at the site of injury. X-ray phase contrast tomography (XPCT) and Holotomography allow the 3D visualization of disease-relevant networks within the CNS and to monitor inherent and infiltrating cells involved in the pathogenesis and that are of crucial importance in surveying disease progression at its earliest physiological changes, as well as in monitoring therapies.

Alzheimer's disease (AD), the most common form of dementia, is a progressive neurodegenerative disorder associated with aberrant production of beta-amyloid (Aβ) peptide depositing in brain as amyloid plaques. While animal models allow investigation of disease progression and therapeutic efficacy, technology to fully dissect the pathological mechanisms of this complex disease at cellular and vascular levels is lacking. We exploit XPCT and Holotomography to simultaneously analyse disease-relevant vascular and neuronal networks in AD mouse brain. Our findings clearly show the different typologies and internal structures of Aβ plaques, together with their interaction with patho/physiological cellular and neuro-vascular microenvironment. We detect, for the first time, amyloid-angiopathy at capillary level, which is impossible to achieve with other approaches.

The degenerative effects of **Multiple Sclerosis** at the level of the vascular and neuronal networks in the central nervous system are currently the object of intensive investigation. Preclinical studies have demonstrated the efficacy of mesenchymal stem cell (MSC) therapy in experimental autoimmune encephalomyelitis (EAE), the animal model for multiple sclerosis, but the neuropathology of specific lesions in EAE and the effects of MSC treatment are under debate. X-ray phase-contrast tomography and Holotomography enable an unprecedented direct 3D characterization of EAE lesions at micro-to-nano scales, with simultaneous imaging of the vascular and neuronal networks. We reveal EAE-mediated alterations down to the capillary network and how the disease and MSC treatment affect the tissues.

References

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