P1-101 FEASIBILITY STUDY OF SYNCHROTRON-BASED MICROTOMOGRAPHY TO IDENTIFY α-SYNUCLEIN OLIGOMERS IN POSTMORTEM TISSUE

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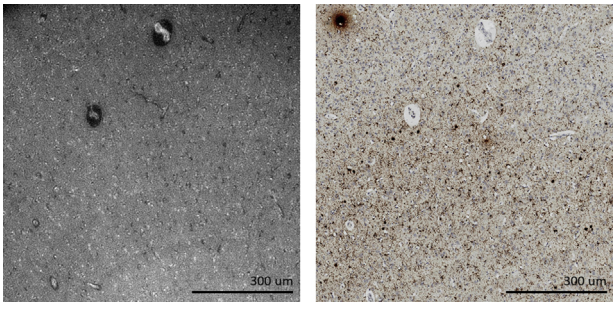
Background: Lewy body disease (LBD) is the second most common cause of neurodegenerative dementia after Alzheimer's disease and presents a challenge to healthcare services in an ageing society because current therapeutic approaches do not halt the disease's progress. It has been suggested that aggregation of the protein α-synuclein plays a critical role in LBD. One pathway for aggregation involves the creation of low molecular weight α-synuclein oligomers, which have been observed to induce cell death. Precise location of Lewy bodies and their precursors could allow researchers to better relate their presence to clinical symptoms as well as infer their physiological effects. While conventional light microscopy of histological slices can visualize Lewy bodies and larger protein aggregates, it provides only two-dimensional information and diffraction-limited resolution prevents visualization of the smaller (approximately 50 nanometer) protein bundles. For this reason, we propose hard X-ray micro- and nano-tomography modalities for complementary, non-destructive, three-dimensional visualization of brain tissues taking advantage of developments at synchrotron radiation facilities. **Methods:** As a proof-of-concept, we imaged paraffin-embedded fusiform gyrus tissue (provided by Newcastle Brain Tissue Resource) from a DLB case at the European Synchrotron Radiation Facility (ESRF Grenoble, France provided beamtime at ID19 from proposal MD-1055) using single-distance inline phase-contrast X-ray tomography with pixel size of 1.6 micrometers. A H&E stained histology slice of the same sample was also taken. **Results:** A correspondence between the micro computed tomography and histology datasets could be made by tracking the orientation of vessels in the specimen. The micro computed tomography demonstrated as shown in figure (left) sufficient contrast and resolution for identification of the lower cortical layer as well as visualization of cells in three-dimensional manner, with confirmation from the annotated histology slice. **Conclusions:** The present work serves as a proof-of-concept for the complementary use of phase contrast X-ray tomography and histology in the investigation of neurodegenerative diseases down to the cellular level. These results open the door for further nanometer resolution studies.



Nearby slices from phase-contrast microcomputed tomography (μ-CT) (left) and H&E stained histology (right) of diseased human brain tissue. The modalities can be used in complement, with the non-destructive μ-CT directing cutting planes for histological sectioning and extending histology into the third dimension.

P1-102 THE NEUROPROTECTIVE ROLE OF VDAC1 IN ALZHEIMER'S DISEASE

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Background: Alzheimer's disease is the most frequent form of dementia, accounting for 70 to 80% of all cases. The greatest risk factor for AD is aging with an estimated 30 million people living with AD worldwide. The pathology of AD consists primarily of amyloid-beta plaques and neurofibrillary tangles composed of microtubule-associated protein tau. Mitochondrial dysfunction has been implicated in the pathogenesis of AD. Voltage dependent anion channel one (VDAC1) functions as the main mitochondrial membrane conduit for ions, ATP and other metabolites as well as acting as a sentinel between the cytoplasm and mitochondria. Proteomic analysis describes an increase in VDAC1 expression associated with the progression of AD. In AD, VDAC1 accumulates in plaques, dystrophic neurites, and in the neuronal soma, which may suggest that mitochondrial transport is impaired. In addition, two-month-old VDAC1 (+/-) heterozygous mice have been shown to have reduced mRNA levels of amyloid precursor protein (APP), presenilin 1 (PSEN1), presenilin 2 (PSEN2), and microtubule-associated protein tau. In order to investigate the role a reduction in VDAC1 plays in AD, we crossed VDAC1(+/-) and VDAC1 (-/-) in an APP/PSEN1 background. We hypothesize that reduction of VDAC1 in an APP/PSEN1 background will reduce plaque deposition. **Methods:** Mice: APP/PSEN1(APPswe/PSEN1DE9, Jackson: 34832) were crossed to VDAC(-/-)(provided by William Craigen) to produce VDAC1(+/+)/APP/PSEN1, VDAC1(+/-)/APP/PSEN1, and VDAC1(-/-) /APP/PSEN1. Plaques were analyzed using immunofluorescence staining with anti-Ab (CST) to determine differences in plaque count and size. Primary neuronal cultures expressing VDAC1(+/+), VDAC1(+/-), and VDAC1(-/-) were evaluated for sensitivity to Ab toxicity and changes in mitochondrial bioenergetics. **Results:** We observe some changes in mitochondrial bioenergetics, which suggests a role of VDAC1 in AD. In 8-month old mice expressing reduced levels of VDAC1 in an APP/PSEN1 background there is an increase in plaque area in the hippocampus and cortex. **Conclusions:** With no decrease in plaque deposition associated with VDAC1 expression levels and only marginal changes in bioenergetics, the role of VDAC1 in AD needs further evaluation.

P1-103 DOT BLOT ASSAY FOR QUANTITATIVE MEASUREMENT OF AMYLOID BETA OLIGOMER

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Background: Soluble amyloid beta oligomers (AβOs) are believed to cause synaptic failure in Alzheimer's disease. Because the AβO has