

Chui's Student Excellence Scheme

Ho King Chun Leadership Fund

Learning Report for Elective on Alzheimer's Disease at University of Cambridge

In Hong Kong and around the world, the prevalence of dementia continues to rise. This means the burden of care and societal impact is also ever-increasing. Much effort is needed to look into ways for earlier detection, better prevention and, hopefully, find a cure.

My elective at the University of Cambridge is truly eye-opening. Through the experience, my desire to continue Alzheimer's disease research is strengthened. I would like to continue on the research I have done in the elective, involving both animal and human research and bridging its gap. I am particularly interested in developing disease modifying treatment and methods to delay and prevent dementia. Through the electives and after speaking with leading professionals in the field, I discovered there are several issues for me to solve before I can develop drugs. In order to develop disease modifying treatments, I believe treatment needs to be administered prior to significant brain changes. I would like to use methods for early detection of pre-Alzheimer's disease found in the Chan Group and bring it further. I also need to develop better outcome measures for the drugs. It may be the case that current drugs are shown not to be effective due to outcome measures being insensitive or inaccurately reflect the needs of patient and families.

As a delay of 5 years of dementia means a 50% reduction in dementia prevalence in the population, I would also like to further strengthen evidence for mid-life activities and cognitive training to improve people's cognitive reserve for the delay and thus prevention of AD. This elective has given me hope on what, I, as a future doctor can do to reduce the prevalence of AD and to improve dementia care.

In Cambridge, I was involved in two aspects of dementia research: methods of early detection of Alzheimer's disease (AD) and prevention of AD with cognitive training.

I was involved in a study that taps into spatial navigation abilities of patients. Spatial navigation is governed by the entorhinal cortex (EC). It is also the first part of the brain to be affected by Alzheimer's pathology. This area is affected earlier than the hippocampus. Conventional screening tests mainly tests hippocampal memory function, rather than the area first affected. I tested patients and healthy controls on the virtual reality task we developed, specifically for testing allocentric spatial navigation. Early results suggest that it can reliably distinguishes between patients on the trajectory to AD (MCI with biomarkers) versus patients with cognitive impairment but not due to early stages of AD (MCI without biomarkers). I also performed neuropsychological testing, segmentations of magnetic resonance imaging (MRI) and data collection of electroencephalography. These were analysed with virtual reality testing data. The MRI segmentations will be put forward as part of a journal paper.

Virtual reality, as a means of testing, was chosen as not only humans can perform tasks in it, so does rodents. It provides a vital platform for the integration of animal and human research to give truly translatable research. Through rats with lesions at the EC and

hippocampus doing virtual reality task, we can predict the changes in performance that will occur in patients with AD in the human version of the same virtual reality task.

I was also involved in cognitive training to improve people's cognitive reserve. Many of the academics I saw in Cambridge present with much milder symptoms with more severe brain changes than people of the same age but different education level. This can be attributable to better cognitive reserve. We looked into modifiable ways, during mid-life (30-60 years old) that people can improve their cognitive reserve to delay development of dementia. I was involved in the testing of a new virtual reality cognitive training task that also includes electromyography. I looked into the main problems of current cognitive training: the lack of transfer to daily life activities that improve the quality of life of patients and the lack of motivation to continue. Virtual reality as an immersive experience allows participants to practice real life quests. I also devised method to promote mid-life activities, which has been suggested to delay cognitive decline seen in dementia. This includes activities like social interactions, traveling and learning new skills, language and music instruments.

I was also delighted to be able to participate in Alzheimer's Research UK Conference learning about the cutting-edge array of research into different aspects of Alzheimer's disease, from solubility equilibrium models for amyloid beta and tau formation to mitochondria's role in AD to the role of inflammation in AD. I also participated in the Cambridge Memory Clinic consultations and case discussions. I was especially inspired by the brain pathology meeting where we discussed the patients' case before they died, and the brain pathology seen in autopsy. Some cases suggest that patients may have numerous underlying neurodegenerative change giving a mix picture, others have the symptoms but no underlying brain pathology at all, emphasising that we should not confine ourselves in the diagnosis of neurodegenerative changes. I also gain better understanding of the dynamics between doctors, nurses, neuropsychiatrists and speech-language pathologist.

I am very thankful for the opportunity to learn and research in the University of Cambridge and hope bring my enthusiasm and passion for research on Alzheimer's disease prevention and treatment back to Hong Kong.