Alzheimer’s disease (AD) is a progressive neurodegenerative disorder characterized by cognitive and memory deterioration, as well as changes in personality, behavioral disturbances and an impaired ability to perform activities of daily living. AD is known to be the most common type of dementia. Despite decades of intensive research, the precise etiology of AD remains elusive. The majority of AD cases are sporadic AD with late onset and seem to result from a complex interaction of multiple genetic and environmental factors. There is a strong age-dependence of the disease. Its prevalence rises exponentially, doubling approximately every 5 years between the ages of 65 and 85. With the rapidly aging population, AD represents one of the most frequent, major public health problems. Principal neuropathological hallmarks of AD include extracellular senile plaques containing β-amyloid derived from β-amyloid precursor protein after sequential cleavage by β-secretase and γ-secretase, and intracellular neurofibrillary tangles caused by abnormally phosphorylated tau protein. Despite major advances in understanding the molecular etiology of the disease, progress in the clinical treatment of AD patients has been extremely limited.

Glaucoma is an important cause of blindness worldwide. Primary open-angle glaucoma (POAG), the most common type, is a progressive optic neuropathy with characteristic structural changes in the optic nerve head and functional changes in the visual field. Although elevated intraocular pressure (IOP) remains one of the most important risk factors for POAG, it was reported that approximately 20% to 50% of patients with POAG have normal IOP measurements, a condition known as normal tension glaucoma (NTG). In addition, many patients, comprising about 40% of POAG, are still undergoing progressive visual field loss and/or optic disc cupping despite normalization of IOP with pressure-lowering treatment strategies. Clearly, factors other than IOP are likely to be involved in the optic neuropathy of POAG. Furthermore, not all subjects with elevated IOP have glaucoma. Patients in whom the optic nerve and visual field show no signs of glaucomatous damage but the IOP is above the normal range are classified as having ocular hypertension. Only a small percentage of such patients may convert to POAG. The precise mechanisms by which elevated IOP may lead to optic nerve damage are still unclear. Mechanical and vascular theories for the pathogenesis of glaucomatous optic neuropathy (GON) have been presented. According to the mechanical theory, GON may be a direct consequence of increased IOP leading to regions of high shear stress and strain in the lamina cribrosa. The lamina cribrosa forms the bottom of the optic cup on the inner surface of the optic nerve head and allows the optic nerve to emerge from the orbit. At this site, increased IOP may result in mechanical forces on retinal ganglion cell (RGC) axons with subsequent cell injury. The vascular theory considers GON as a
consequence of insufficient blood supply due to either elevated IOP or other risk factors reducing ocular blood flow.

There is a growing body of evidence demonstrating a link between AD and glaucoma. It has been reported that patients with AD exhibit optic nerve degeneration and loss of RGCs. In addition, other studies found a significantly high rate of occurrence of glaucoma among patients with AD. In spite of intensive research, the clinical and genetic relationships between AD and glaucoma remain obscure. It is unclear whether the clinical correlation between the two diseases might be due to shared risk factors or the influence of one disorder on the other.

Importantly, lately published cerebrospinal fluid pressure (CSFP) measurement studies in AD patients and patients with glaucoma may provide a clue towards a better understanding of the high rate of comorbidity reported between AD and glaucoma. Recent studies have shown that intracranial pressure (ICP) is lower in patients with POAG and NTG when compared with nonglaucomatous control subjects. It has been suggested that the relationship between IOP and ICP may play a fundamental role in the development of glaucoma. A decreased ICP could result in an increased trans-lamina cribrosa pressure difference (IOP minus ICP) and lead to glaucomatous damage. A higher trans-lamina cribrosa pressure difference may lead to abnormal function and potential optic nerve damage due to changes in axonal transport, deformation of the lamina cribrosa, altered blood flow, or a combination of them all. Interestingly, in AD, a high occurrence of very low ICP has been demonstrated. We recently hypothesised that there may be a causal relationship between AD and glaucoma that may be explained by decreased CSFP in patients with AD. As the etiology for the higher glaucoma prevalence in AD remains still unclear, in the present study we will evaluate whether there is a correlation between CSFP and glaucoma prevalence. Our objective is to compare the CSFP and the trans-lamina cribrosa pressure difference in a group of AD patients with glaucoma versus a group of AD patients without glaucoma. Our hypothesis is that a low CSFP and a high trans-lamina cribrosa pressure difference may be correlated with the presence of glaucoma. The correlation of the two parameters will be investigated in this prospective study.

Selected Publications

