Retinal Microvasculature in Alzheimer’s Disease

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Abstract. Although cerebral small vessel disease has been implicated in the development of Alzheimer’s disease (AD), the cerebral microcirculation is difficult to visualize directly in vivo. As the retina and the brain share similar embryological origin, anatomical features and physiological properties with the cerebral small vessels, the retinal vessels thus offer a unique and easily accessible “window” to study the correlates and consequences of cerebral small vessel diseases in vivo. Retinal microvasculature can now be visualized, quantified and monitored non-invasively using state-of-the-art retinal imaging technology. Recent clinic- and population-based studies have demonstrated a link between retinal vascular changes and dementia, in particular AD, and cerebral small vessel disease. In this review, we summarize the current findings on retinal vascular changes such as retinopathy signs and changes in novel retinal vascular network parameters and retinal vascular caliber with dementia, cognitive dysfunction and cerebral small vessel disease, and discuss possible future research to further evaluate whether retinal vascular imaging might help to elucidate vascular mechanisms contributing to the development of AD and provide additional value in predicting who may be at risk of developing AD.

Keywords: Alzheimer’s disease, microcirculation, retina, retinal vascular changes, retinal vasculature, small vessel disease

INTRODUCTION

Alzheimer’s disease (AD) is the most common subtype of dementia and is a major global medical, social, and economic public health issue [1, 2]. AD is characterized pathologically by neurofibrillary tangle aggregation, amyloid plaque deposition, and subsequent neuronal degeneration, with neurotoxicity of amyloid-β forming a major component of the prevailing amyloid cascade hypothesis.

There has been a long-standing interest in determining whether vascular mechanisms contribute to the development and progression of AD [3, 4]. Cerebrovascular disorders often coexist with AD in the elderly. Over the last few decades, studies have increasingly shown that systemic vascular factors such as hypertension and diabetes are associated with increased risk of developing AD. Furthermore, with the advent of neuroimaging technologies such as MRI, it has been shown that presence of cerebrovascular lesions such as infarcts, white matter lesions, and cerebral microbleeds contribute to the development of cognitive decline, [5] suggesting that vascular factors, especially those affecting the cerebral