Microvascular network alterations in the retina of patients with Alzheimer’s disease

Carol Yim-lui Cheung a,b,c,*, Yi Ting Ong a,b,d, M. Kamran Ikram a,b,c,e,f, Shin Yeu Ong a,c, Xiang Li a,b, Saima Hilal e, Joseree-Ann S. Catindig e, Narayanaswamy Venketasubramanian e, Philip Yap g, Dennis Seow h, Christopher P. Chen e,i, Tien Yin Wong a,b

aSingapore Eye Research Institute, Singapore National Eye Centre, Singapore
bDepartment of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
cCentre for Quantitative Medicine, Office of Clinical Sciences, Duke-NUS Graduate Medical School, Singapore
dNUS Graduate School for Integrative Sciences and Engineering, National University of Singapore, Singapore
eMemory Aging and Cognition Centre, National University Health System, Singapore
fDepartment of Ophthalmology, Erasmus Medical Center, Rotterdam, The Netherlands
gDepartment of Geriatric Medicine, Khoo Teck Puat Hospital, Singapore
hiDepartment of Pharmacology, National University of Singapore, Singapore

Abstract

Background: 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. Because the retina provides a noninvasive window to assess the microcirculation, we determined whether quantitatively measured retinal microvascular parameters are associated with AD.

Methods: We conducted a case-control study (case:control matching 1:2). Retinal photographs were analyzed using a computer program, and a spectrum of quantitative retinal microvascular parameters (caliber, fractal dimension, tortuosity, and bifurcation) were measured. Logistic regression models were used to compute the odds ratio (OR) and 95% confidence interval for AD adjusting for age, gender, ethnicity, smoking, hypertension, diabetes, hypercholesterolemia, and history of myocardial infarction.

Results: We included 136 demented patients with AD and 290 age-gender-race-matched controls. Persons with narrower venular caliber (OR per standard deviation [SD] decrease, 2.01 [1.27–3.19]), decreased arteriolar and venular fractal dimension (OR per SD decrease 1.35 [1.08–1.68], 1.47 [1.17–1.84], respectively) and increased arteriolar and venular tortuosity (OR per SD increase, 1.84 [1.40–2.31], 1.94 [1.48–2.53], respectively) were more likely to have AD. These associations still persisted when only AD cases without a history of cerebrovascular disease were included.

Conclusions: Patients with AD have altered microvascular network in the retina (narrower retinal venules and a sparser and more tortuous retinal vessels) compared with matched nondemented controls. These changes in retinal microvasculature may reflect similar pathophysiological processes in cerebral microvasculature in the brains of patients with AD.

Keywords: Retina; Retinal vasculature; Alzheimer’s disease; Microcirculation; Small-vessel disease

1. Introduction

Alzheimer’s disease (AD) is the most common form of dementia and is a major global medical, social, and economic public health issue [1,2]. There has been a