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Retinal Imaging

Choroidal thinning: Alzheimer's disease and aging

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Abstract

Purpose: To measure and to compare macular choroidal thickness (CT) between patients with mild Alzheimer's disease (AD), patients without AD, and elderly patients.

Methods: CT was measured manually in 13 locations at 500-μm intervals of a horizontal and a vertical section from the fovea. Linear regression models were used to analyze the data.

Results: Fifty patients with a diagnosis of mild AD (73.1 years), 152 patients without AD (71.03 years), and 50 elderly without AD (82.14 years) were included. In the AD patients, CT was significantly thinner in all 13 locations ($P < .001$—comparing with age-match group), and comparing with the elderly group, a more pronounced difference was found in two locations temporal to the fovea.

Conclusions: Patients with AD showed a significant choroidal thinning even when compared with elderly subjects. The reduction of CT may aid in the diagnoses of AD, probably reflecting the importance of vascular factors in their pathogenesis.

Keywords: Alzheimer's disease; Aging; Choroidal thickness; Enhanced depth imaging; Spectral-domain optical coherence tomography; Alzheimer's choroidopathy

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]. There has been a long-standing interest in determining whether vascular mechanisms contribute to the development of AD [2,3]. The earliest AD pathological change in the brain is the accumulation of amyloid β (Aβ) [4,5]. Microvascular amyloid deposition (amyloid angiopathy) [6], granulovacuolar degeneration, loss of neurons and white matter, synapse loss, gliosis [7], inflammation, and oxidative damage are other pathological changes present in AD [4,8].

Accumulating evidence suggests that vascular factors, especially those affecting the cerebral microcirculation (e.g., hypertension, diabetes), play an important role in the pathogenesis of AD [9].

The retinal and cerebral small blood vessels share similar properties (embryological, anatomical, and physiological) such as blood brain and blood-retina barrier and nonanastomotic end arteries [10]. To our knowledge, the first study to demonstrate abnormalities in the retinal circulation of patients with AD was published by Berisha et al., where retinal hemodynamic data obtained in patients with mild or moderate AD showed a marked narrowing of the retinal venous blood column diameter, and a reduction in retinal blood flow rate compared with age-matched controls subjects [11].

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The choroid is affected in many retinal diseases. Changes in choroidal homeostasis have been documented in early macular degeneration and in advanced aging [12,13]. Decreased choroidal vasculature thickness has been described in age-related macular degeneration [14], although it has not been observed universally. Some choroidal thinning occurs during normal aging and is seen specially in some patients in a condition referred to as age-related choroidal atrophy [15]. It has been demonstrated in mice and in transgenic mouse models of AD an age-dependent amyloid accumulation in the choroid vasculature. The atrophy of the choroid capillaries has been shown to occur with normal aging [16].

Historically, imaging of the choroid in patients was possible with indocyanine green angiography, where injection of this fluorescent dye and subsequent imaging of fluorescence allowed two-dimensional imaging of the choroid pattern and the existence of leakage and vessel wall abnormalities [17]. Since the first study of Spaide et al., measuring choroid by enhanced depth imaging (EDI) optical coherence tomography (OCT) [18], it took about 5 years for the firsts studies to be published using this technique to assess choroidal thickness (CT) in patients with AD. Choroidal thickness has shown to be reduced in patients with AD comparing with controls [19–21] as review by Cunha et al. [22].

The present study aimed to identify factors that could explain the differences between CT of patients with mild AD and patients without AD, after controlling for age. Knowing that this factor is highly associated with CT thinning, a third group of elderly subjects without AD was also considered with the purpose of comparing their CT with those of AD patients. To our knowledge, this is the first study to compare CT with spectral-domain OCT (SD-OCT) of AD patients with very old normal subjects.

2. Materials and methods

2.1. Subject groups

This cross-sectional observational study was conducted at the Ophthalmology and Neurology Departments of the Central Lisbon Hospital Center, between October 2014 and April 2016. Consecutive AD patients sent by the Neurology Department for ophthalmological screening were observed for inclusion/exclusion criteria. AD patients with age between 65 and 78 years old with normotensive eyes and with ability to understand the study were included.

The exclusion criteria were as follows: refractive error >5 diopters (D) and/or axial length >25 mm in the studied eye; known diagnosis of diabetic retinopathy or other retinal diseases; glaucoma or ocular hypertension; uveitis; neurodegenerative disease; significant media opacities that precluded fundus imaging. In addition, patients with another relevant known neurological pathology, such as neurodegenerative diseases, other types of dementia, previous stroke, or uncertain/indeterminate diagnosis, were excluded.

Informed consent was obtained for all the patients and the study was approved by our Institutional Ethics Committee. The principles of the Declaration of Helsinki were respected.

Ultimately, 50 patients were recruited for the AD group (ADG) and 202 subjects for the two groups without AD: 152 age-matched patients for the first control group (CG1) and 50 subjects older than 78 years for the second control group (CG2). Subjects without AD were recruited from the Neurology department.

2.2. Study procedures

After a prescreening visit where demographic, background history, full ophthalmological examination with visual acuity, anterior segment examination, Goldmann applanation tonometry, indirect ophthalmoscopy, and ultrasonic biometry were recorded, patients were assigned to a specific study visit. In this study visit, the SD-OCT scan was performed. Randomly, one eye of each subject was used in this study.

2.2.1. Visual acuity

Best corrected distance visual acuity (BCVA) for each eye was measured using Snellen charts and converted to the logarithm of the minimum angle of resolution.

2.2.2. Intraocular pressure

Intraocular pressure (IOP) was measured before pupillary dilation with Goldmann applanation tonometry and taken the mean of 3 measurements.

2.2.3. Spectral-domain optical coherence tomography imaging

All eyes were examined with SD-OCT (*Spectralis Heidelberg Engineering*, Germany). OCT imaging technique consists in obtaining a macular square (20-20°) composed of 25 horizontal B-scans. All scans were performed in EDI mode to improve the quality of choroidal imaging according to the previously reported method [23]. The choroid was imaged by positioning the SD-OCT device close enough to the eye to obtain an inverted image. The profile scans were saved for analysis after automatic averaging 100 frames using the eye-tracking feature embedded in the device. All OCT examinations were performed at the same time of the day from 2 to 4 PM. The OCT images were obtained by one ophthalmologist (A.S.) and were assessed by another ophthalmologist (J.P.C.) independently of each other, masked to the patients' diagnosis. The CT was measured from the outer portion of the hyperreflective line corresponding to the retinal pigment epithelium to the hyporeflective line or margin corresponding to the sclerochoroidal interface. These measurements were made in the subfoveal choroid and at 500-μm intervals from the fovea to 1500 μm nasal, 1500 μm