

# Vegf effect on the type of amd associated with alzheimer's disease

## Abstract

**Aim:** The aim was to explain the importance of the type of age related macular degeneration (AMD) detected in patients with Alzheimer's Disease (AD). Vascular endothelial growth factor (VEGF) levels are known to decrease in AD which may affect the configuration of the retina.

**Material and Methods:** Retinal images of 50 patients (age range 65- 84) with PET proven AD were observed retrogradely. Macular region and changes in the retinal pigment epithelium (RPE) were inspected in detail with optical coherence tomography (OCT).

**Results:** In 48 patients early dry AMD was detected and in 2 patients neovascularization with edema due to wet type AMD was observed. The ratio of early dry AMD to wet AMD was 48/2:24 in our group. A large Australian epidemiologic study revealed the ratio of early dry AMD to neovascular wet AMD as 13.65% /1,38% : 9,8.

**Conclusion:** We believe that decreased VEGF levels in AD protect against neovascularization in the retina

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## Introduction

Recent evidence suggests that angiogenesis might play a role in the progression of Alzheimer's disease (AD).<sup>1</sup> Among angiogenic cytokines, vascular endothelial growth factor (VEGF) has gained the most attention. VEGF was originally described as a growth factor playing a part in vascular permeability and migration of endothelial cells and its expression may be upregulated by chronic inflammation.<sup>2,3</sup> VEGF has been detected in the walls of intraparenchymal vessels, in diffuse periventricular deposits and in clusters of reactive astrocytes in the brains of patients with AD.<sup>4</sup> The deposition of beta amyloid plaques may be activated by the angiogenic functions of the brain endothelium in AD and the secreted neurotoxic peptides kill the cortical neurons.<sup>4</sup> Thus, the abnormal regulation of VEGF is thought to be involved in the process of cognitive impairment in AD.<sup>5,6</sup> Age-related macular degeneration (AMD) and AD are both neurodegenerative diseases strongly associated with increased age and share environmental risk factors as well as histopathologic features like the deposition of the beta amyloid in retinal drusen and senile plaques.<sup>7</sup> But, the genetic risk factors for AMD and AD were found to be different.<sup>8</sup> Although studies have reported an association between AMD and AD, another epidemiologic report found no significant association between the two diseases.<sup>9</sup> Differences in methodologies and Manuscript number of patients in these studies may explain the different findings. A recent study showed the link between AMD and AD.<sup>10</sup>

## Materials and methods

The files of 50 patients with the diagnosis of both AMD and cranial PET proven AD were reviewed retrospectively by two ophthalmologists in a masked fashion. The age range was between 65 and 84. The macular images detected by optical scanning tomography (OCT) were examined and the ratio of early dry AMD plus geographic atrophy to neovascular (wet) AMD was found. The researches agreed on the diagnosis of the type of AMD. This ratio was compared with the

ratio in a large Australian epidemiologic study result.<sup>11</sup> The findings were interpreted by the investigators.

## Results

The number of patients with early dry AMD plus geographic atrophy was 48 according to the images obtained by OCT (Figure 1) and neovascular (wet) AMD was 2 (Figure 2). The ratio was 48/2:24. The Australian epidemiologic study (Table 1) numbers were 13,65 % and 1,38 % respectively. And the ratio was 13,65/ 1,38:9,8. The difference between these two ratios was found significant. The serum and CSF levels of VEGF were found low in patients with AD.<sup>12</sup> The difference between the two ratios might be explained by the- highly possible-low VEGF levels in the study group AD patients. Low VEGF levels might show protective effects against neovascularization in AD.



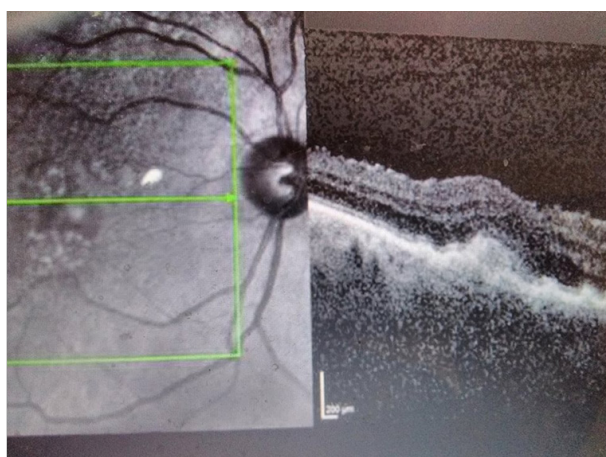
Figure 1 Dry AMD.

**Table 1** Estimated early and late AMD prevalence rates, BMES

Age group	Early AMD		Neovascular AMD		Geographic atrophy	
	Male	Female	Male	Female	Male	Female
50-59	8.5 (1.2)	3.6 (0.4)	0	0	0	0
60-69	11.4 (3.1)	10.1 (3.1)	0.34	0.57	0	0
70-79	20.1 (8.2)	19.1 (8.5)	1.82	1.67	0.78	1.11
80-89	24.2 (11.9)	26.1 (15.0)	4.03	10	2.42	2.78
90+	37.5 (25.0)	31.58 (13.6)	12.5	13.64	12.5	22.73
all ages (50+)	13.9 (4.7)	12.4 (5.0)	0.98	1.69	0.46	0.8
combined (50+)	13.0 (408)		1.38		0.65	

**Source** BMES data based on Mitchell et al, 1995 and later.

Defined ad presence of large drusen (>125 microns) and/or retinal epithelial abnormalities (hyper pigmentation or hypo pigmentation). Values in parentheses represent the prevalence of the more severe BMES early AMD definition (large indistinct soft drusen or large distinct soft drusen with accompanying retinal pigment epithelial abnormalities). Sydney West Area Healthy service.

**Figure 2** Wet AMD.

## Discussion

Recent studies provide evidence that beta amyloid plaques exhibit vascular regression by endothelial cell apoptosis; they also show antagonistic activity against VEGF.<sup>13</sup> These findings may explain the mechanism of vascular destruction in AD. VEGF displays a neurotrophic effect on nerve cells and this activity is also destroyed in neurodegeneration.<sup>14</sup> Both vascular and neuronal protective effects of VEGF are altered in AD. Considering these study results, VEGF- C induced neural stem cell stimulation in mice resulted in the production of new neurons.<sup>15</sup> VEGF- C stimulation may prevent cognitive decline in humans, too. Decreased serum levels of VEGF in AD support the evidence that angiogenesis is a pathogenic mechanism involved in neurodegeneration.<sup>16</sup> Regarding the retina, low VEGF may explain why neovascularization was less common in our study group. Uncontrolled high VEGF results in growth of new blood vessels which may show structural abnormalities leading to exudation and bleeding in the retina.<sup>17</sup> Photoreceptors are damaged and vision may be impaired. AD can cause visual abnormalities by different mechanisms ; retinal nerve fiber layers and macular thickness are affected.<sup>18</sup> But, interestingly by way of decrease in VEGF, it may provide some defence against neovascular membranes. In larger

series, future examinations of the macular degeneration and VEGF levels in different compartments will be beneficial. Our study is the first that combines AMD with AD explaining a possible mechanism for the type of the degeneration in the macula.

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## Conflict of interest

The author declares no conflict of interest.

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