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Structural And Functional Changes In The Retina And Optic Nerve In Cases Of Alzheimer's Disease

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INTRODUCTION

Alzheimer's disease (AD) is the most common dementia in the world and its incidence and prevalence are projected to double by 2050. Although conventionally Alzheimer's has been diagnosed clinically using cognitive battery and neuroimaging like MRI and PET, efforts are ongoing to detect Alzheimer's in the preclinical asymptomatic stage so that treatment or preventive strategies could be started at an earlier stage. In this regard, optical coherence tomography (OCT) has been studied over the past decade with some fruitful results. Our study evaluated a group of early stage Alzheimer's patients using ocular tests for structural imaging and electrophysiology to detect changes suggestive of disease.

METHODOLOGY

A total of 15 Alzheimer's patients were included in the study after being referred to our tertiary care centre from the Neurology department where they were screened for dementia using the Mini Mental State

Examination. The inclusion criteria was best corrected visual acuity better than 6/12, intraocular pressure less than 18, wilfulness to participate and cooperation towards tests. The Global Deterioration Scale was used to determine the disease severity. 15 age matched controls were selected randomly from the outpatient department patients and included only after ruling out any ocular, neurological or cardiovascular diseases. All subjects underwent extensive ophthalmological examination including visual acuity, intraocular pressure, colour vision, contrast sensitivity, anterior segment and posterior segment examination. Any subject found to have posterior segment pathology which may result in OCT or electrophysiological changes were excluded. Spectral domain OCT using Cirrus HD-OCT 4000 (Carl Zeiss Meditec, US) was performed to detect the retinal nerve fibre layer (RNFL) thickness with the Optic nerve 200x200 program and the ganglion cell layer (GCL) thickness and macular volume using the Macular 520x128 program. Sensitivity was kept at 50% for the effective data collection. Metrovision Monpack 3 vision monitor system was used to perform multifocal electroretinogram (mfERG) and pattern visual evoked response (pVER) for all patients. mfERG P1, N1 and N2 waves were evaluated. pVER P100 wave was evaluated. Descriptive statistics in the form of Mean ± Standard Deviation was used to analyse normally distributed variables. Pearson's correlation coefficient were used to determine any correlations among variables and the strength of such correlations. Data was considered significant when 2-tailed p value was <0.05.

RESULTS

The study evaluated 60 eyes of 15 patients and 15 controls. The demographic characteristics of the sample population is given in Table 1. The mean age of AD patients was 59.8 ± 6 .24 years (range 45-72). The median MMSE score in AD patients was 16 (range 10-23). The median duration of disease was 2.25 years (range 6 months-3.5 years).

Mean BCVA of patients was 0.183 ± 0.14, which was essentially normal. Mean contrast sensitivity was significantly reduced in the AD cases (1.4 ± 0.16) according to the Pelli-Robson chart. The anterior segment, intraocular pressure, fundus examination and colour vision were within normal limits in all subjects. Visual fieldswere evaluated for all cases and found normal. The RNFL, GCL thicknesses and the Macular volume measured using SD-OCT have been shown in Table 2.

Table 1: Demographic characteristics of AD cases and Healthy control subjects (mean ± SD)			
	AD cases (n=15)	Healthy controls (n=15)	P value
Age	59.8 ± 6.24	60.7 ± 7.96	0.73
Sex (M/F)	8/7	6/9	-
BCVA (logMAR)	0.183 ± 0.14	0.125 ± 0.13	0.25
IOP (mm Hg)	14.67 ± 2.84	14.87 ± 2.6	0.84
Contrast sensitivity	1.4 ± 0.16	1.85 ± 0.1	<0.001
			Median
Disease duration (years)			2.25
Mini Mental State Examination score			16

Table 2: Mean ± SD of SD-OCT parameters of nerve fiber layer, ganglion cell layer and macular volume			
	Cases (n=30)	Controls (n=30)	P value
Average nerve fibre layer thickness (um)	73.43 ± 12.74	86.04 ± 11.42	<0.001
Average ganglion cell layer thickness (um)	63.69 ± 14.77	84.99 ± 7.27	<0.001
Macular volume (cumm)	8.98 ± 0.84	9.75 ± 0.42	0.001

The electrophysiological data analysed in the subjects has been recorded in Table 3. RNFL and GCL thinning was observed in AD patients along with significant electrophysiological abnormalities (p<0.001).

Table 3: Mean ± SD of amplitudes of mfERG and pattern VER waves			
	Cases (n=30)	Controls (n=30)	P value
Average P1 amplitude (nV)	896.26 ± 239.67	1135.33 ± 234.83	<0.001
Average N1 amplitude (nV)	-471.87 ± 119.07	-609.01 ± 108.51	<0.001
Average N2 amplitude (nV)	-705.41 ± 209.66	-1040.57 ± 224.89	<0.001
p100 amplitude (µV)	7.62 ± 2.97	11.04 ± 2.89	0.015
Average P1 implicit time (ms)	48.57 ± 4.3	44.95 ± 2.05	<0.001
Average N1 implicit time (ms)	28.47 ± 4.53	2.44 ± 2.57	<0.001
Average N2 implicit time (ms)	65.28 ± 4.6	63.32 ± 5.2	<0.001
p100 latency (ms)	120.01 ± 6.99	108.36 ± 4.84	<0.001

The structural and functional changes of the retina and optic nerve were correlated with each other (Table 4). RNFL thickness changes significantly correlated directly with mfERG amplitude changes and inversely with implicit time. RGCL had a weaker yet significant correlation with the functional parameters. Pattern VER amplitude correlated directly with RNFL, RGCL changes and mfERG amplitudes

Table 4: Summary of correlation of structural and functional changes in the retina and optic nerve in AD patients		
	r	P value
	Average RNFL thickness	
Average P1 amplitude	0.65	<0.001
Average N1 amplitude	0.54	0.002
Average N2 amplitude	0.534	0.002
Average N2 implicit time	-0.384	0.036
P100 amplitude	0.737	<0.001
P100 latency	-0.368	0.046
	Average RGCL thickness	
Average P1 amplitude	0.374	0.042
Average N1 implicit time	-0.377	0.04
P100 amplitude	0.474	0.008
	P100 amplitude	
Average P1 amplitude	0.48	0.007
Average N1 amplitude	0.495	0.005
Average N2 amplitude	0.426	0.019
Average N2 implicit time	-0.719	<0.001
	P100 latency	
Average P1 amplitude	-0.397	0.03

significantly. Pattern VER latency correlated inversely with RNFL thickness and mfERG amplitude.

DISCUSSION

Several studies have evaluated the RNFL using time domain and spectral domain OCT machines and found global thinning in Alzheimer's patients.[1,2,3] Cheung et al evaluated the GCL separately and found thinning of the average GCL thickness in the macula.[4] Moschos et al evaluated the RNFL along with mfERG changes in AD patients and found a diffuse retinal electrical dysfunction, but they did not study the correlations between the different parameters.[5] Pattern VER has been found to be deranged in early stages of AD and it may represent an impairment in the anterior visual pathway function.[6] No study till date has evaluated the correlation between the structural and functional impairment present in Alzheimer's patients. Our study has observed that there is a conclusive evidence of correlation between the structural degeneration and the functional impairment of the neural component of the eye in AD patients and these tests may help in evaluation of mild cognitive impairment cases in future.

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Idiopathic Orbital Inflammation Of Orbit And Ocular Adnexa: Histopathological Analysis

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INTRODUCTION

Non-specific orbital inflammation affects orbital tissue including fats, lacrimal glands, extraocular muscles etc focally or diffusely.[1,2,3,4] Affection of Tenon's capsule is the least frequent location.[2,3,4] Incidence and prevalence findings of non-specific inflammatory disease of orbitbased on scientific literature was very difficult as it depended on inclusion or not of specific and non-specific inflammatory pathologies.[3,4,5,6,7,8]