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Pupillometry and MRI findings of hippocampus in Alzheimer's disease

Irene Kalliolia*, Dimitrios Fotiou, Dimitrios Tsiptsios, Maria Nakou, Vasilios Stergiou, Evangelia Giza, Evangelia Theodoridou, Catherine Brozou and Charalambos Giantselidis

Address: Laboratory of Clinical Neurophysiology, Aristotle University of Thessaloniki, Greece

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Background

Alzheimer's Disease (AD) is the leading cause of dementia, accounting for 70% of all dementias in old age. In clinical practice the diagnosis is based on typical features of the disease and exclusion of other conditions causing dementia or cognitive dysfunction. So far the diagnosis of definite AD can be confirmed only by brain biopsy or at autopsy. Therefore, a reliable non- invasive diagnostic method is mainly needed at this stage. In recent years, scientists based on the cholinergic hypothesis of the Alzheimer's disease1 developed systems of recording and measuring the pupil size (pupillometry) finding out that the pupil light reflex (PLR) responded in a particular way in Alzheimer's disease patients. Today imaging methods are an integral part of the diagnostic work-up of patients with suspected dementia. MRI provides data of in vivo tissue and enables evaluation of brain structures such as the hippocampus.

To evaluate the pupillometry as an easy, non invasive and efficient tool in AD diagnosis as well as the hippocampal involvement in probable AD.

Materials and methods

Twenty three (23) healthy control subjects (10 males and 13 females) aged 71.87 ± 8.51 years and 23 probable Alzheimer's disease patients, according to NINCDS-ADRDA criteria, that matched age and sex entered the study. The PLR was recorded with a fast video digital camera (262 frames/sec). All subjects were free of any neurological or ophthalmological diseases, underwent standard blood tests, and were free of any medication for at least 2 weeks prior to the testing. Patients with pathological Vis-

ual Evoked Potentials, Electroretinogram and MRI with brain tumors or multifocal angiopathy were excluded. Tc-99m-HMPAO SPECT study of the regional cerebral blood flow (rCBF) was compatible with Alzheimer's disease. All patients had a follow-up of minimum 2 years. The (PLR) parameters that were studied are initial pupil radius (R1), reaction time, minimum pupil radius (R2), amplitude (Amp), maximum constriction velocity (VC max), maximum constriction acceleration (AC max). Hippocampal pathology was evaluated by volumetric measurements using thin, contiguous, optimally oriented image slices.

Results

A statistical significant reduction of initial pupil radius (R1), Amplitude (Amp), maximum constriction velocity (VC max) and maximum constriction acceleration (AC max) was observed in the probable AD patient group when compared to the control group. Difference concerning the minimum pupil radius (R2) was not statistically significant. Although the volume of the hippocampus, evaluated by MRI, was not significantly affected by normal aging, it correlated significantly with clinical severity assessed by MMSE, and with tests assessing delayed recall.

Discussion

The results from the pupillometry study suggest that a cholinergic deficit, may be the main reason of the parameter differentiation between the two groups2. Given that both AC max and VC max are significantly reduced in the AD patients confirms the cholinergic deficit of AD since Ach is considered the main neurotransmitter for the movement we study (pupil light reflex). Although the volume of the hippocampus is not significantly affected by

^{*} Corresponding author

normal aging, bilateral volumetric hippocampal atrophy in early AD. Concerning the findings, their reliability is certain because of the number of subjects used, their strict selection and the confirmation of AD diagnosis throughout the follow-up period which had a mean time of 2 years.

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