POSTER Session

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INSIGHT ON ALZHEIMER DISEASE FROM VISUAL SYSTEM ELECTROPHYSIOLOGY.

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Background and Rationale: Visuo-spatial troubles are common in Alzheimer's disease (AD) patients (pts); moreover, the neurosensory retina emerges as a prominent site of AD pathology. The post-receptoral visual pathways of primates contain two major parallel streams specific for colour contrast/form discrimination and luminance contrast/movement discrimination. The magnocellular (M) pathways has anatomo - physiological characteristic which make it more suitable for detecting form, motion and depth compared with parvocellular (P) one. In this study, we aimed to evaluate electrophysiologically each visual subsystem involvement in a group of AD pts, using both Luminance and equiluminant Chromatic Pattern Electroretinograms (ChPERGs) and Chromatic Pattern Visual Evoked Potentials (ChVEPs) in attempt to detect differential involvement of M, P, and K visual subsystem focussing on M deficit as specific pathognomonic markers of disease (Fig. 1).

Materials and Methods: Data were obtained from 15 AD pts (9 females and 6 males, mean age ± 1SD 77.6 ± 4.01 yrs) not yet undergoing any treatment, and from 10 age- and sex-matched healthy controls (5 females and 5 males, mean age ± 1SD 71.3 ± 7.2).
ChPERGs were recorded monocularly in response to equiluminant red-green (R-G) and blue-yellow (B-Y) stimuli, known to emphasize the contribution of parvo- (P) and konio- (K)-cellular streams respectively, and achromatic luminance (Lum, magnocellular stream, M) yellow-black (Y-Bk) horizontal square gratings of 0.3 c/deg and 90% contrast (K), reversed at 1Hz, displayed on a TV monitor at a viewing distance of 24 cm (59.2*59 deg field). ChVEPs were recorded to onset (300 ms) and offset (700ms) equiluminant chromatic sinusoidal gratings of different K (90 and 25%) (see bottom inset in fig. 1). Diagnosis was clinically and neuro-radiologically established, after having excluded other possible causes of dementia.

Results: all data were retrieved in terms of peak-amplitude and latency (for both ChPERGs and ChVEPs) and the obtained values were assessed using the Student's t-test for paired data (Table 1). As expected, temporal features of ChPERGs, as well as ChVEPs, in AD patients differed from those of luminance Y-Bk grating in AD group ($p<0.01$). Individual transient waveforms and grand average of PERGs and VEPs, obtained in in both controls and AD patients are summarized in Figures 2 and 3. Compared to controls, Lum PRGs in patients resulted in an altered grand-average waveform with reduced amplitude and delayed latency, suggesting the existence of a specific magnocellular or M-pathway deficit between controls and AD pts. Chromatic PERGs did not show obvious difference. To asses retinal vs post-retinal defects, Retino-cortical times (RCT) analysis was performed and did not reveal a retino-carlcarine pathway involvement associated with AD.

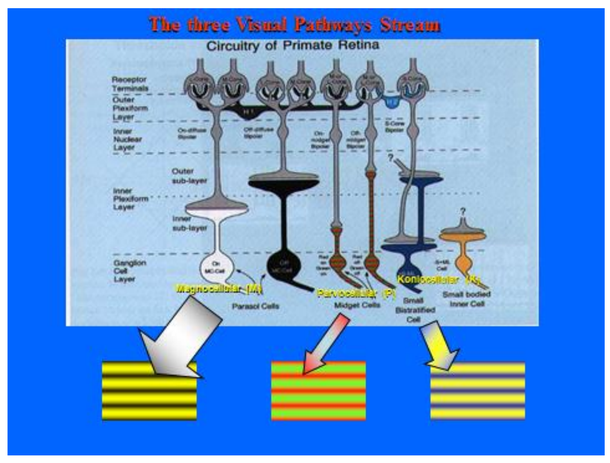

Fig. 1. The three different streams (M, P and K) of the post-receptoral visual pathways of primates and the specific stimuli to selective activate them, used in this study.

	Y-Bk P1 (± 2 DS)	Y-Bk N1 (± 2 DS)	R-G P1 (± 2 DS)	R-G N1 (± 2 DS)	B-Y P1 (± 2 DS)	B-Y N1 (± 2 DS)
PERGs						
Cts latency (ms)	38.1 ± 2.4	73.4 ± 8.6	65.5 ± 5.7	126.9 ± 6.8	65.0 ± 5.6	133.3 ± 5.8
AD-latency (ms)	60.0 ± 4.8**	95.6 ± 5.7*	62.5 ± 7.3	130.3 ± 7.5	64.0 ± 6.2	135.3 ± 9.0
Cts amplitude (µV)	0.3 ± 0.2	1.5 ± 0.9	0.50 ± 0.3	1.16 ± 0.93	0.1 ± 0.3	3.31 ± 1.55
AD-amplitude (µV)	0.15 ± 0.1*	0.31 ± 0.49*	0.2 ± 0.33*	0.42 ± 0.56	0.25 ± 0.4**	1.29 ± 0.45*
VEPs						
	Y-Bk N-wave (± 2 DS)		R-G N-wave (± 2 DS)		B-Y N-wave (± 2 DS)	
Cts latency (ms)	166.6 ± 6.8		175.1 ± 6.7		180.4 ± 8.8	
AD-latency (ms)	186.9 ± 8.5*		175.2 ± 11.1		175.9 ± 7.7	
Cts amplitude (µV)	3.60 ± 1.20		2.1 ± 1.34		4.19 ± 1.34	
AD-amplitude (µV)	0.23 ± 0.45*		2.6 ± 1.68		3.61 ± 1.66	

** = p ≤ 0.01
* = p ≤ 0.05

Latency and amplitude of Lum (Y-Bk) and Ch (R-G, B-Y) PERGs and PEVs, both in controls (Cts) and AD patients (±SD)

Table 1: PERGs and VEPs latency and amplitude both in controls and AD patients (1 SD). Surrounded in red are significant different findings.

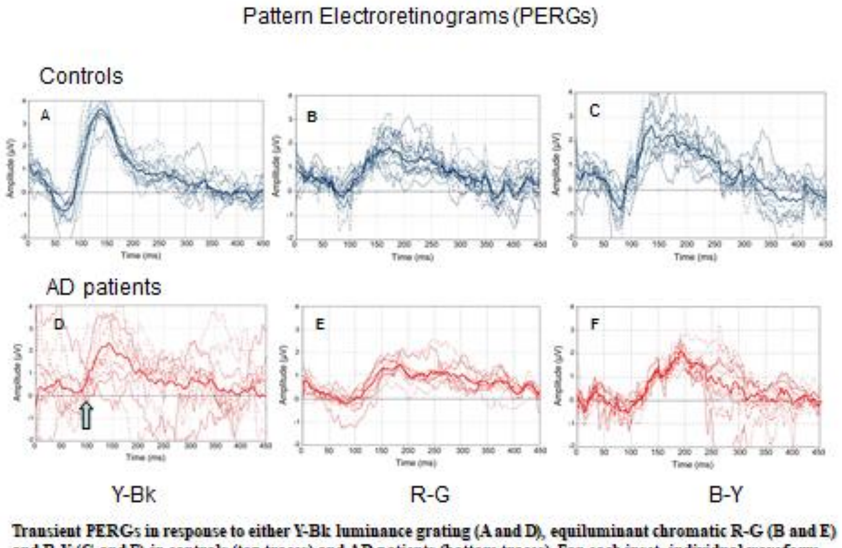

Fig. 3 Transient PERGs in response to either Y-Bk luminance grating (A and D), equiluminant chromatic R-G (B and E) and B-Y (C and F) in controls (top traces) and AD patients (bottom traces). For each inset, individual waveform are represented by dotted line, the grand mean by bold line. Note the evident amplitude loss and latency delay for Y-Bk stimuli (A and D), insignificant for R-G (B and E) and B-Y (C and F) stimuli.

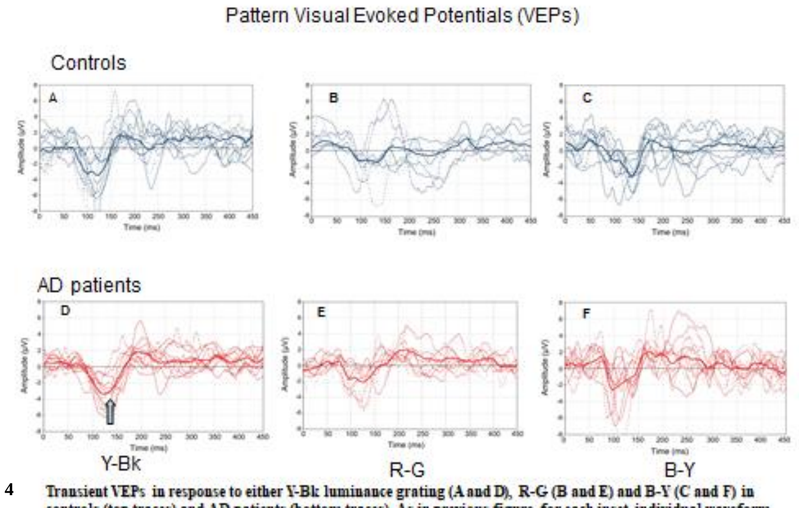

Fig. 4 Transient VEPs in response to either Y-Bk luminance grating (A and D), R-G (B and E) and B-Y (C and F) in controls (top traces) and AD patients (bottom traces). As in previous figure, for each inset, individual waveform are represented by dotted line, the grand mean by bold line. Note the latency delay for Y-Bk, whereas R-G and B-Y stimuli are relatively spared.

Discussion: Our data show evident abnormalities both in latency and amplitude of Lum PERGs, and irrelevant of ChPERGs, in AD patients compared with controls. Ageing instead causes an unspecific decline of the response of the visual system to luminance and colour contrast arising at a peripheral level promoted by regionally-specific Aβ proteins aggregation (miosis, increased intraocular light scatter, decreased blood flow, opacification of ocular media). VEPs and RCT analysis did not revealed a retino-calcarine pathway involvement associated with AD, suggesting the existence of a specific Magnocellular or M-Pathway deficit.
The involvement of Magnocellular stream in AD could be demonstrated by both retinal and cortico-subcortical evidences: the largest retinal cells seemed to be selectively affected by neural degeneration; amplitude of ERG responses driven by the Magnocellular stream is reduced; a high concentration of neurofibrillary tangles in area V5.
Thus, in summary our findings suggest: i) a deficit in primary visual processing and a selective deficit in secondary visual processing in cases of dementia. The shift is most prominent for black-yellow gratings; ii) that M-stream activation primarily involves extra-geniculate pathways.
The deficits of the responses arising from the M streams of visual processing pointed out in this study could be related or indicate a primary dysfunction of the M-pathways in Alzheimer's disease. Indeed the M pathway has anatomo-physiological characteristic which make it more suitable for detecting form, motion and depth, compared with P one, functions impaired in AD patients.

Bibliography:

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