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Original article

Ageing effects on flash visual evoked potentials (FVEP) recorded from parietal and occipital electrodes

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Summary – The effects of ageing on flash visual evoked potentials (FVEP) recorded from 6 posterior parietal and occipital sites were studied in a sample of 73 healthy subjects of between 20 and 86 years of age. Latencies of components P1, N1 and P2, and amplitudes of components P1 and P3 increased linearly with age at all emplacements. The results obtained from occipital electrodes are in line with previous reports and additionally show that *i*) the effects of age constantly increase over time, and *ii*) age affects not only the early but also the later components (> 150 ms) of the FVEP. The overall pattern of results suggests that elderly subjects show slower transmission of visual information and deficiencies in the inhibitory regulation of activity generated during the arrival of repetitive non-attended visual stimulation. The findings with parietal electrodes show that ageing effects are more marked at these emplacements than at occipital electrodes. Furthermore, this raises the question of a possible differential involvement of primary and nonprimary visual cortex by age, but this hypothesis can only be explored with high-intensity multichannel recordings and dipolar modelling. © 1998 Elsevier, Paris

ageing / FVEP / parietal electrodes / occipital electrodes / inhibitory deficits

Résumé – Effets de l'âge sur les potentiels évoqués visuels au flash (PEVfs) enregistrés sur les régions pariétales postérieures et occipitales. *L'effet de l'âge sur les potentiels évoqués visuels au flash (PEVfs) enregistrés sur les régions pariétales postérieures et occipitales a été étudié chez 73 sujets âgés de 20 à 86 ans. Les temps de latence des composantes P1, N1 et P2, ainsi que les amplitudes de P1 et P3, montraient une augmentation linéaire en fonction de l'âge. Les résultats obtenus pour les électrodes occipitales sont en accord avec les données rapportées dans la littérature ; par ailleurs, ils montrent que les effets de l'âge augmentent régulièrement, et que l'âge modifie non seulement les composantes précoces mais aussi les composantes tardives des PEVfs. Les effets de l'âge semblent plus marqués quand on considère les électrodes pariétales plutôt que les électrodes occipitales. L'ensemble des données suggère un ralentissement de la transmission de l'information visuelle chez l'adulte âgé, ainsi qu'une diminution des mécanismes d'inhibition de l'activité générée pendant l'arrivée des stimulations visuelles répétitives. © 1998 Elsevier, Paris*

âge / PEVfs / emplacements pariétaux / emplacements occipitaux / déficits inhibitoires

INTRODUCTION

Flash visual evoked potentials (FVEP) represent the electrical activity generated in primary and secondary visual cortical areas when the subject is stimulated with dif-

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fuse flashes [1, 3, 9, 16, 33]. The typical waveform is composed of five waves commonly designated P1, N1, P2, N2 and P3. Since the first report by Straumanis et al [32], FVEP have proved to be useful in the study of ageing. These authors observed that the pre-100-ms FVEP of healthy elderly subjects showed longer latencies and larger amplitudes than those of young subjects. The authors interpreted their results in terms of diminished inhibitory activity in the group of elderly subjects.

Dustman and Beck [10] published the first cross-sectional study, with a sample of 215 subjects aged between 1 month and 81 years. They found that the amplitudes of all FVEP increased between 1 month and 6 years of age, decreased between 7 and 16 years of age, and then remained stable up to the age of 60 years. In the two oldest groups (mean ages 62.8 and 70.2 years) the amplitudes of pre-100-ms waves were larger than in younger subjects.

Since their first study, Dustman and coworkers have published several reports on FVEP in a sample of 220 subjects aged between 4 and 90 years. The results of these studies confirm their previous findings [2, 11]. Furthermore, they found that in elderly subjects, *i*) FVEP recorded from occipital and anterior parietal areas were more homogeneous than in young subjects [11], *ii*) the waveforms of unpatterned and patterned FVEP were more similar than in young subjects [14], and *iii*) there were more "augmenters" (subjects who tend to increase FVEP amplitudes in response to increasing intensity of visual stimulation) than among younger subjects [12, 13]. These results led the authors to suggest that central inhibitory activity is weaker in the elderly, as manifested by slower habituation of electrical activity in visual cortical areas to repetitive stimulation, less differentiation between activity in visual and association cortical areas, less efficient detection of edges and contours, and deficient modulation of stimulus-induced arousal levels.

Mankovskii et al [22] assessed 116 subjects between the ages of 18 and 101 years and found longer latencies of all FVEP components and larger P1 amplitudes in subjects older than 60 years. The authors suggested that the larger P1 amplitude in older subjects is a consequence of a decrease in the numbers of inhibitory interneurons in the visual cortex. Cosi et al [6] observed longer latencies and greater amplitudes of all FVEP components in a group of elderly subjects than in a group of young subjects, although they did not put forward possible explanations for these results.

The principal aim of these studies was to investigate ageing-related changes in FVEP recorded from occipital electrodes to shed light on ageing-related changes in visual processing. Dustman and Beck [11] also compared activity in occipital scalp areas with that in anterior parietal scalp areas, to investigate differences in processing between the visual and association cortices. However, it may be more appropriate to record FVEP from occipital and posterior parietal electrodes to obtain results on ageing-related changes in FVEP more specifically related to visual processing.

The objectives of the present study were to investigate the age dependence of FVEP recorded from occipital and posterior parietal electrodes, and age-related changes in FVEP amplitudes indicative of the existence of inhibitory deficits in the elderly.

METHOD

Design and subjects

The design consisted of the between-subjects factors of age group (six groups from 20 to 86 years divided in decades, as shown in *table I*) and sex; and the within-subjects factors of scalp region (two levels: occipital, parietal) and electrode position (three levels: left, midline, right).

Table I. Descriptive statistics of the sample. MEC = Mini Examen Cognoscitivo.

Age group	*Sex*	*N*	*Age mean (SD)*	*Education (years) mean (SD)*	*MEC score mean (SD)*
1 (20-29 years)	Women	5	26.0 (3.8)	10.0 (4.8)	34.4 (0.5)
	Men	5	25.2 (1.4)	9.7 (4.8)	33.8 (2.1)
2 (30-39 years)	Women	5	36.6 (3.5)	8.2 (4.0)	33.8 (1.6)
	Men	5	35.6 (3.5)	10.3 (4.6)	32.4 (2.0)
3 (40-49 years)	Women	5	43.8 (3.0)	7.0 (1.8)	32.6 (1.8)
	Men	5	44.4 (3.2)	10.3 (4.6)	33.0 (1.5)
4 (50-59 years)	Women	5	56.2 (3.4)	7.2 (3.2)	32.4 (1.6)
	Men	5	56.0 (2.4)	11.7 (6.1)	33.4 (1.3)
5 (60-69 years)	Women	8	64.1 (1.6)	9.6 (4.4)	31.8 (1.4)
	Men	6	66.5 (2.5)	9.3 (5.0)	31.6 (2.3)
6 (70-86 years)	Women	11	75.8 (2.8)	8.5 (4.8)	31.2 (1.9)
	Men	8	76.8 (4.2)	8.3 (4.0)	31.1 (1.9)

One hundred and six healthy volunteers were recruited from retirement homes, day care centres for retired people, departments and schools of the University of Santiago de Compostela, cultural centres and employment agencies. From this initial sample, 33 subjects were excluded because they presented some of the following problems: cardiovascular diseases and/or hypertension ($n = 9$), cataracts and/or glaucoma ($n = 4$), alcohol consumption ($n = 2$), pulmonary problems ($n = 3$), cranioencephalic traumatisms in their childhood ($n = 3$), audiological problems ($n = 7$), antidepressive medication ($n = 1$) and MEC scores lower than 28 ($n = 4$) (Mini Examen Cognoscitivo, (MEC [21], Spanish adapted version of the Mini Mental State Examination, MMS [15]). The final sample was composed of seventy-three healthy subjects (39 women, 34 men) distributed in six age groups (*table I*). There were no significant differences in the number of years of formal education either among age groups ($F(5.61) = 1.33$, $P < 0.3$) or between sexes ($F(1.61) = 2.27$, $P < 0.2$). The cognitive faculties of elderly subjects were in a generally satisfactory condition, as shown by scores on the MEC (*table I*). All subjects were without visual complaints, and corrected visual acuity was 20/30 or better using a Snellen near card. Subjects with refractive errors wore their correction lenses during the recording session.

Stimuli

Diffuse flashes generated by a Grass photic stimulator (model PS22) were presented binocularly. Photostimulator setting 1 was used, corresponding with an intensity of about 93 750 candle power (Grass Instruments, Quincy, MA, USA, 1985). Flash duration was 10 ms and the rate of presentation was 1/s.

Data acquisition and recording

Recordings were made with subjects comfortably seated in an armchair in a semi-darkened room with constant illumination intensity. FVEP were recorded after a 30-min period of adaptation to the illumination level. Subjects were instructed to remain with their eyes open while receiving flashes. The photostimulator was situated 1 m from the subject's eyes. All subjects wore earphones (Telephonics TDH-39-P, Furmingdale, New York, USA) to prevent perception of the clicks generated with each flash by the photostimulator.

The electroencephalogram (EEG) was recorded via an Electrocap (Electrocap International Inc Eaton, OH, USA) from six active electrodes positioned on P3, Pz, P4, O1, Oz and O2,

according to the 10-20 International System and referred to Fz with Cz connected to ground. Vertical and horizontal electro-oculogram (EOG) activity was recorded bipolarly from above and below the left eye, and from the outer canthi of both eyes. Acquisition, amplification, filtering and averaging were performed using a Neuro Scan system (Scan module) connected to a Grass Neurodata Acquisition System (model 12). EEG was segmented into epochs of 500 ms (50 ms for prestimulus baseline and 450 ms for poststimulus epoch), digitized with a 512 Hz rate (256 samples per epoch), amplified (20 K) and filtered with a band-pass filter of 0.1–100 Hz. Signals with an amplitude greater than ± 50 μV were automatically excluded from the average. A total of 100 epochs were averaged on-line.

Peak latencies and amplitudes of the P1, N1, P2, N2 and P3 components were automatically measured on individual waveforms. Amplitudes of each component were measured from baseline to peak using latency windows of 40–100 (P1), 55–120 (N1), 90–180 (P2), 125–200 (N2) and 145–320 (P3) ms. These latency windows were established in grand mean waveforms of each age group and subsequently adapted to individual waveforms.

Statistical analyses

Latency and amplitude values were subjected to mixed-model analyses of variance in a 6 x 2 x 2 x 3 design (see Design and subjects). When describing the effects of electrode position, Greenhouse-Geisser ε values and the corresponding adjustment to degrees of freedom are reported. The age dependence of variables exhibiting significant mean effects of age was further investigated by regression analysis using linear, quadratic and cubic models for the effect of subject age on the dependent variable (a FVEP latency or amplitude) at each electrode. The fit of each model was assessed by means of analysis of variance (ANOVA) F values.

RESULTS

Sex and age group mean effects

Sex had significant effects on P1 amplitude ($F(1.56) = 5.45$, $P < 0.03$). One-way analyses of variance showed that these differences were mainly due to the existence of larger P1 amplitudes in women than in men in the 30–39 ($F(1.6) = 9.54$, $P < 0.03$) and 60–69-year ($F(1.12) = 5.71$, $P < 0.04$) age groups.

The age group had significant effects on latencies of P1 ($F(5.56) = 6.00$, $P < 0.0001$), N1 ($F(5.57) = 11.14$, $P < 0.0001$) and P2 ($F(5.57) = 7.69$, $P < 0.0001$), and on amplitudes of P1 ($F(5.56) = 6.08$, $P < 0.0001$) and P3 ($F(5.60) = 5.91$, $P < 0.0001$). A less significant effect of age was observed on N1 amplitude ($F(5.57) = 2.5$, $P < 0.05$), and Scheffé post-hoc comparison of means showed that the only significant pairwise differences in this variable were between the 60–69-year age group and the 20–29, 30–39 and 40–49-year age groups. As can be seen in *tables II* and *III* and *figure 1*, the effects of age on P1, N1, P2 and P3 appear to reflect increases in peak latencies and amplitudes with advancing age.

Figure 1 shows grand mean FVEP in each age group across electrodes. Here we see that some waves with small amplitude and relatively high intersubject variability (ie, P1) can reduce their amplitudes until disappearing in the grand mean for some age groups and at some electrodes. As the grand mean waveform can distort the results due to these reported causes, *figure 2* represents the individual waveforms superimposed at central electrodes and for each age group. P1 was the most variable wave at all electrodes, mainly in the two youngest groups, and P2 was more variable at parietal than at occipital electrodes in all age groups (*table IV*).

Table II. Mean latency values (standard deviation) (ms) of flash visual evoked potential (FVEP) components for each age group at each electrode position.

Electrode	*component*	*Age group (years)* 20–29	30–39	40–49	50–59	60–69	70–86
Oz	P1	62.87 (7.75)	63.28 (15.23)	72.22 (12.00)	68.66 (11.01)	74.46 (6.69)	73.23 (8.51)
	N1	76.09 (7.45)	78.43 (16.69)	83.90 (20.57)	82.18 (12.66)	98.20 (7.21)	97.76 (10.27)
	P2	112.65 (5.19)	115.36 (13.89)	117.79 (10.69)	126.47 (14.55)	129.11 (7.27)	133.68 (15.15)
	N2	144.37 (12.62)	157.34 (21.02)	151.64 (16.12)	159.76 (30.22)	162.77 (16.81)	171.82 (24.36)
	P3	179.76 (21.37)	190.01 (17.92)	183.42 (23.67)	199.13 (49.79)	198.24 (13.14)	202.08 (30.56)
O1	P1	61.25 (5.37)	62.23 (15.64)	70.15 (11.02)	69.44 (11.33)	74.41 (6.50)	72.72 (8.42)
	N1	75.78 (7.17)	78.51 (17.41)	88.01 (12.03)	82.81 (12.87)	98.73 (6.51)	98.29 (9.77)
	P2	103.34 (32.47)	116.17 (13.04)	120.31 (11.78)	126.71 (13.82)	129.83 (7.10)	135.63 (14.45)
	N2	144.84 (12.85)	156.71 (19.01)	151.87 (16.33)	160.86 (29.67)	162.91 (16.42)	172.63 (24.89)
	P3	180.00 (21.37)	190.71 (17.22)	182.57 (21.37)	199.91 (49.88)	197.52 (13.68)	202.36 (30.56)
O2	P1	62.73 (7.85)	64.84 (17.89)	71.95 (10.33)	66.60 (9.02)	74.11 (6.78)	73.40 (8.36)
	N1	76.56 (7.37)	79.92 (18.07)	88.9 (10.22)	82.96 (13.06)	98.76 (7.21)	98.75 (9.52)
	P2	112.42 (6.41)	116.66 (14.24)	120.62 (11.00)	127.16 (14.57)	130.43 (7.20)	135.27 (15.55)
	N2	144.6 (12.77)	158.83 (19.75)	151.71 (16.56)	159.76 (29.91)	166.27 (16.30)	172.90 (24.10)
	P3	179.14 (22.13)	192.88 (17.54)	184.68 (21.91)	200.00 (50.88)	199.48 (12.97)	203.43 (30.09)
Pz	P1	64.21 (12.70)	72.65 (6.70)	75.85 (10.14)	72.50 (4.75)	74.79 (3.65)	73.81 (4.34)
	N1	83.28 (11.19)	90.93 (9.66)	102.51 (9.55)	99.84 (7.05)	105.06 (4.98)	104.83 (8.55)
	P2	109.68 (8.45)	117.18 (15.45)	128.90 (15.24)	130.99 (22.29)	133.86 (9.82)	141.88 (21.20)
	N2	138.82 (15.96)	157.03 (22.43)	155.66 (22.52)	157.98 (32.90)	157.42 (15.04)	169.31 (35.25)
	P3	182.26 (20.97)	197.96 (15.36)	199.90 (21.00)	206.59 (35.19)	203.14 (10.30)	204.43 (30.70)
P3	P1	61.95 (4.66)	70.22 (4.49)	73.12 (5.49)	69.27 (3.82)	72.41 (4.67)	71.67 (4.43)
	N1	81.17 (7.90)	91.40 (12.48)	92.49 (7.34)	93.40 (8.06)	102.21 (3.91)	98.98 (8.12)
	P2	114.14 (7.86)	116.87 (13.20)	124.76 (15.32)	130.46 (20.89)	131.38 (8.33)	133.31 (14.81)
	N2	144.53 (13.17)	155.46 (19.79)	155.85 (11.37)	161.63 (30.81)	157.72 (14.28	165.52 (33.82)
	P3	184.37 (21.53)	201.91 (16.21)	195.07 (14.81)	201.30 (38.91)	200.54 (12.4)	200.82 (32.19)
P4	P1	62.34 (6.28)	69.26 (6.86)	73.04 (5.03)	69.92 (4.07)	71.99 (4.32)	73.72 (9.61)
	N1	81.17 (10.03)	87.93 (14.37)	90.80 (8.13)	95.54 (7.20)	100.15 (4.98)	101.22 (11.39)
	P2	111.95 (6.00)	117.27 (13.77)	125.07 (10.72)	130.70 (20.87)	129.77 (7.11)	136.53 (17.72)
	N2	144.84 (13.46)	159.81 (22.73)	156.32 (10.57)	159.45 (30.56)	162.64 (13.41)	167.80 (32.45)
	P3	183.90 (22.59)	200.17 (18.35)	198.35 (16.68)	201.71 (35.18)	201.20 (9.31)	200.70 (33.32)

Effects of scalp region and electrode position

Scalp region had significant effects on P1 amplitude ($F(1.56) = 5.11$, $P < 0.03$), N1 amplitude ($F(1.57) = 10.99$, $P < 0.002$), N1 latency ($F(1.57) = 61.34$, $P < 0.0001$), P2 amplitude ($F(1.57) = 94.58$, $P < 0.0001$), P2 latency ($F(1.57) = 8.86$, $P < 0.004$), N2 amplitude ($F(1.57) = 29.37$, $P < 0.0001$) and P3 latency ($F(1.60) = 21.67$, $P < 0.0001$). As can be seen in *tables II* and *III* and in *figures 1* and *2*, these effects may be attributed to the fact that P1, N1 and N2 amplitudes, and N1, P2 and P3 latencies were maximal at parietal electrodes, whereas P2 amplitudes were maximal at occipital electrodes.

Significant interactions between age group and scalp region were observed for N1 latency ($F(5.57) = 2.46$, $P < 0.05$) and P3 latency ($F(5.60) = 2.91$, $P < 0.03$), probably due to N1 and P3 latencies being maximal at parietal electrodes in subjects between 30 and 59 years of age.

Electrode position had significant effects on P1 amplitude ($F(2.112) = 20.70$, $P < 0.0001$, $\varepsilon = 0.71$), P1 latency ($F(2.112) = 5.17$, $P < 0.007$, $\varepsilon = 0.92$), N1 latency ($F(2.114) = 5.86$, $P < 0.004$, $\varepsilon = 0.98$), N1 amplitude ($F(2.114) = 5.6$, $P < 0.006$, $\varepsilon = 0.93$), P2 amplitude ($F(2.114) = 3.47$, $P < 0.035$, $\varepsilon = 0.99$), N2 latency ($F(2.114) = 5.15$, $P < 0.01$), N2 amplitude ($F(2.114) = 38.17$, $P < 0.0001$, $\varepsilon = 0.71$) and P3 amplitude ($F(2.120) = 45.05$, $P < 0.0001$, $\varepsilon = 0.72$). These effects may be

Table III. Mean amplitude values (standard deviation), in μV, of flash visual evoked potential (FVEP) components for each age group at each electrode position.

Electrode	*component*	*20–29*	*30–39*	*40–49*	*50–59*	*60–69*	*70–86*
				Age group (years)			
Oz	P1	0.94 (3.32)	3.49 (4.58)	4.25 (3.66)	1.91 (6.20)	10.60 (10.64)	6.34 (4.03)
	N1	−1.04 (3.35)	1.10 (4.85)	0.84 (3.29)	−1.51 (4.87)	−1.43 (9.19)	−.87 (4.45)
	P2	9.88 (3.15)	13.24 (5.13)	8.72 (3.35)	11.42 (5.16)	14.85 (6.15)	13.08 (7.26)
	N2	1.61 (5.09)	−1.93 (4.95)	1.31 (6.36)	−.42 (6.80)	4.39 (4.70)	2.70 (3.64)
	P3	6.48 (2.87)	2.82 (4.45)	6.6 (4.59)	4.85 (3.56)	11.01 (6.21)	7.77 (4.47)
O1	P1	1.24 (3.00)	3.22 (4.49)	4.37 (3.25)	1.27 (4.90)	9.98 (9.57)	5.9 (3.86)
	N1	−1.04 (2.89)	0.52 (4.35)	0.74 (2.83)	−2.43 (4.55)	−2.13 (8.39)	−3.14 (4.25)
	P2	8.69 (2.99)	11.95 (5.16)	8.80 (4.02)	10.99 (5.04)	13.15 (5.05)	11.51 (5.18)
	N2	0.67 (4.61)	−2.42 (5.87)	0.68 (5.53)	−1.90 (5.95)	3.43 (4.73)	1.33 (3.24)
	P3	5.38 (2.67)	2.59 (4.51)	5.81 (4.50)	3.78 (3.06)	10.43 (4.66)	6.36 (3.48)
O2	P1	0.90 (3.16)	3.40 (3.74)	4.12 (3.18)	1.48 (5.49)	9.48 (8.78)	5.91 (4.35)
	N1	−1.44 (3.29)	0.90 (4.20)	1.31 (2.67)	−2.44 (4.17)	−2.05 (9.65)	−3.58 (5.14)
	P2	9.22 (3.11)	11.62 (4.54)	10.04 (3.70)	11.11 (4.20)	15.61 (7.16)	11.79 (6.05)
	N2	0.93 (5.10)	−2.36 (5.53)	0.63 (5.80)	−1.11 (6.46)	3.43 (4.70)	1.23 (3.30)
	P3	5.48 (2.36)	2.05 (4.62)	5.94 (4.30)	4.96 (3.30)	10.02 (6.24)	6.80 (3.72)
Pz	P1	1.48 (3.17)	4.08 (4.34)	4.59 (4.59)	6.10 (5.18)	19.68 (16.76)	13.46 (9.70)
	N1	−.81 (3.76)	−.07 (3.73)	−.74 (2.67)	−3.79 (7.84)	−5.87 (5.62)	−2.45 (5.29)
	P2	4.45 (4.05)	5.53 (4.61)	4.35 (4.33)	7.37 (5.48)	5.91 (7.13)	7.37 (3.70)
	N2	−.27 (4.78)	−1.09 (4.94)	0.14 (4.92)	−1.13 (4.23)	0.24 (7.54)	2.43 (4.03)
	P3	6.12 (2.73)	4.89 (4.46)	6.40 (5.24)	6.73 (2.41)	14.08 (6.66)	8.70 (3.01)
P3	P1	1.16 (2.13)	2.46 (2.76)	4.13 (2.89)	2.62 (3.44)	12.94 (10.51)	8.22 (7.19)
	N1	−.68 (2.24)	−1.65 (3.67)	−.46 (2.34)	−5.79 (6.20)	−7.98 (6.26)	−5.75 (3.74)
	P2	4.44 (3.18)	4.58 (4.42)	4.57 (3.48)	6.00 (3.94)	5.29 (5.77)	6.25 (4.45)
	N2	−1.77 (3.99)	−4.53 (3.59)	−1.54 (3.92)	−3.67 (5.06)	−2.70 (5.22)	−1.28 (4.13)
	P3	3.18 (2.80)	1.8 (3.7)	3.73 (2.98)	2.46 (3.24)	9.43 (4.75)	4.53 (2.70)
P4	P1	.78 (2.31)	2.87 (3.16)	3.42 (2.44)	2.36 (3.44)	10.37 (8.93)	9.68 (5.66)
	N1	−1.20 (2.48)	−.10 (3.13)	0.02 (2.77)	−5.24 (6.01)	−7.48 (7.93)	−5.12 (3.30)
	P2	4.91 (4.05)	6.31 (4.94)	5.04 (3.62)	6.39 (4.59)	9.62 (7.35)	6.91 (4.51)
	N2	−2.14 (3.51)	−4.55 (3.55)	−1.97 (3.86)	−2.56 (5.30)	−1.68 (5.13)	−1.02 (3.43)
	P3	2.54 (2.60)	1.13 (4.18)	4.59 (3.08)	7.45 (9.48)	8.72 (5.58)	5.37 (3.24)

attributed to the fact that P1 latency was maximal at midline electrodes, especially at Pz; to that, N1 latency was also maximal at Pz and P1 and P3 amplitudes were maximal at midline electrodes. However, N1 and N2 amplitudes were maximal at lateral electrodes (left and right), and P2 amplitude was minimal at left electrodes.

Significant interactions between age group and electrode position were observed for P1 amplitude ($F(10.112) = 4.25$, $P < 0.0001$, $\varepsilon = 0.71$), N1 amplitude ($F(10.114) = 3.33$, $P < 0.001$, $\varepsilon = 0.93$) and P2 amplitude ($F(10.114) = 2.68$, $P < 0.006$, $\varepsilon = 0.99$). These interactions appear to be attributable to maximal values of P1 amplitudes at midline electrodes in subjects older than 50 years of age, to maximal N1 amplitudes at lateral electrodes in subjects older than 60 years of age, and to maximal P2 amplitudes at right electrodes in the 60–69-year age group.

Regression functions

Table V and *figure 3* show the results of regression of FVEP latencies and amplitudes on age, for those variables shown to be significantly affected. All these parameters were adjusted to linear functions, indicating monotonic increases with advancing age. Inspection of *figure 3* and *table V* reveals that *i*) P2 latency shows, with

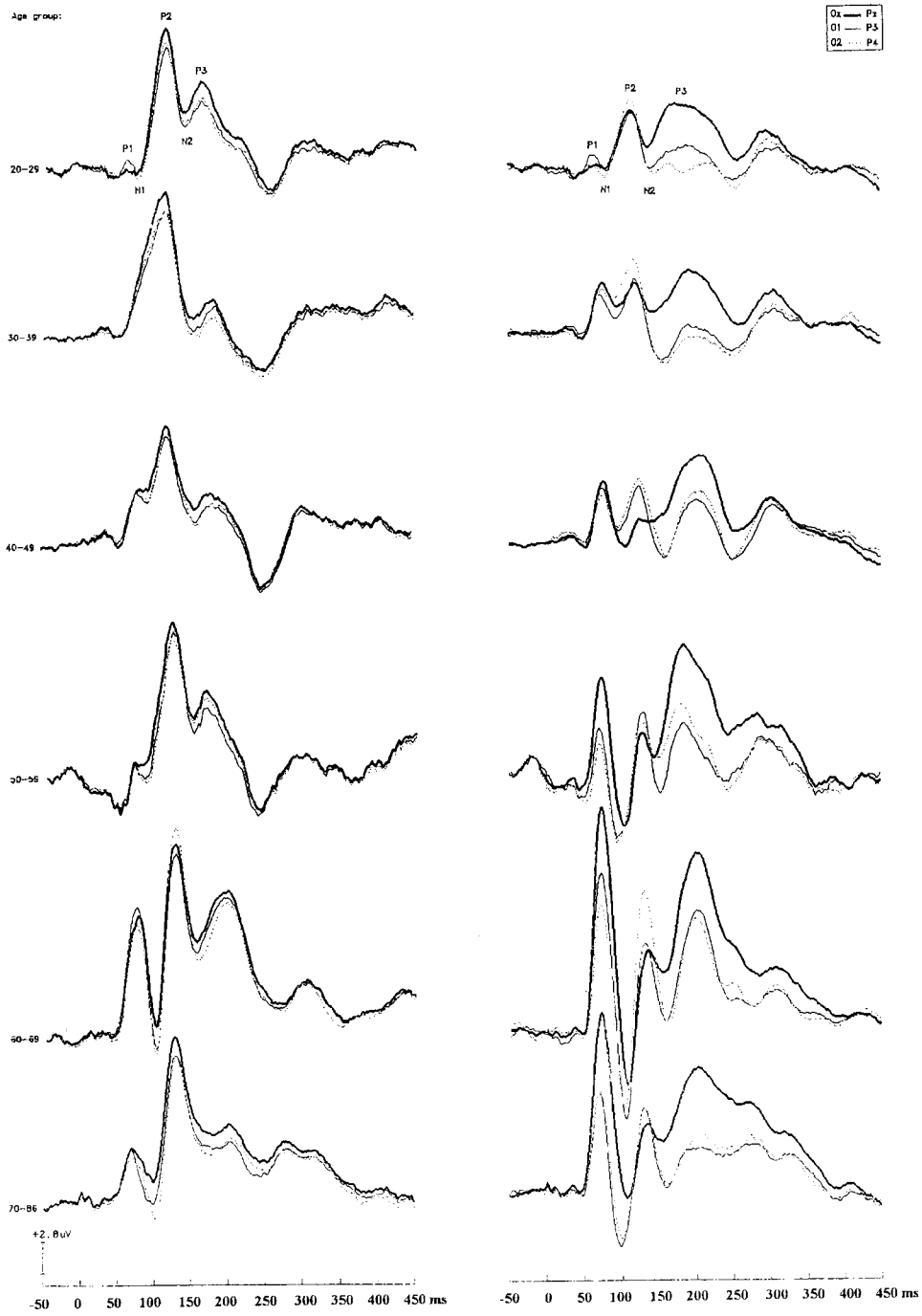

Fig 1. Grand mean flash visual evoked potentials (FVEP) for each age group. Left: occipital electrodes. Right: parietal electrodes.

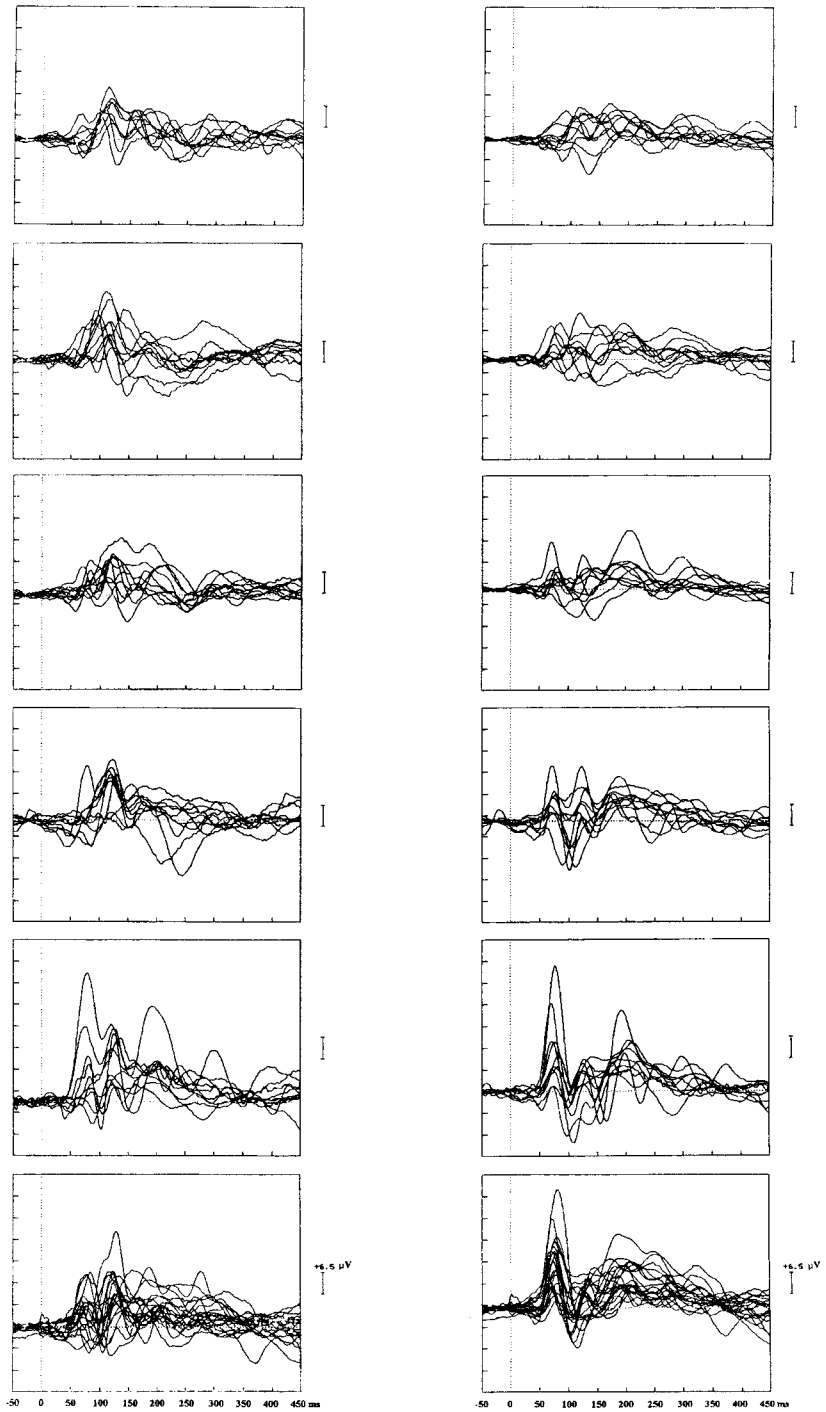

Fig 2. Individual flash visual evoked potential (FVEP) waveforms for each age group. Left: Oz. Right: Pz. From top to bottom: age groups 20–29, 30–39, 40–49, 50–59, 60–69 and 70–86 years. Amplitudes are in μV.

Table IV. Percentages of presence of each peak at central electrodes in each age group.

Age Group	*Electrode*	*P1*	*N1*	*P2*	*N2*	*P3*
20-29	Oz	70	100	100	100	100
	Pz	80	100	80	100	100
30-39	Oz	80	100	100	100	80
	Pz	90	90	90	100	80
40-49	Oz	90	100	100	100	100
	Pz	100	90	60	90	100
50-59	Oz	60	100	100	100	90
	Pz	90	100	90	90	100
60-69	Oz	93	100	100	100	93
	Pz	100	100	79	100	100
70-86	Oz	95	100	100	95	95
	Pz	100	100	90	95	95

Table V. Results of regression of FVEP parameters on age.

Electrode	*Parameter*	*F(d.f.), P*	*Regression function*
Oz	P1 latency	$F(1.68) = 11.53$, $P < 0.001$	Y = 57.82 + 0.22x
	P1 amplitude	$F(1.68) = 6.82$, $P < 0.01$	Y = –1.02 + 0.11x
	N1 latency	$F(1.71) = 34.03$, $P < 0.0001$	Y = 62.14 + 0.47x
	P2 latency	$F(1.71) = 42.55$, $P < 0.0001$	Y = 98.83 + 0.47x
	P3 amplitude	$F(1.70) = 5.73$, $P < 0.02$	Y = 2.77 + 0.07x
O1	P1 latency	$F(1.69) = 15.10$, $P < 0.001$	Y = 55.87 + 0.24x
	P1 amplitude	$F(1.69) = 6.20$, $P < 0.02$	Y = –0.48 + 0.09x
	N1 latency	$F(1.71) = 41.50$, $P < 0.0001$	Y = 63.36 + 0.47x
	P2 latency	$F(1.71) = 34.54$, $P < 0.0001$	Y = 91.33 + 0.60x
	P3 amplitude	$F(1.79) = 5.66$, $P < 0.02$	Y = 2.37 + 0.06x
O2	P1 latency	$F(1.69) = 10.02$, $P < 0.002$	Y = 58.50 + 0.20x
	P1 amplitude	$F(1.69) = 7.75$, $P < 0.006$	Y = –0.89 + 0.10x
	N1 latency	$F(1.71) = 39.73$, $P < 0.0001$	Y = 64.64 + 0.45x
	P2 latency	$F(1.71) = 45.43$, $P < 0.0001$	Y = 98.60 + 0.49x
	P3 amplitude	$F(1.70) = 5.98$, $P < 0.02$	Y = 2.17 + 0.07x
Pz	P1 latency	$F(1.71) = 6.10$, $P < 0.02$	Y = 66.05 + 0.12x
	P1 amplitude	$F(1.71) = 19.38$, $P < 0.0001$	Y = –5.44 + 0.27x
	N1 latency	$F(1.69) = 44.44$, $P < 0.0001$	Y = 77.70 + 0.39x
	P2 latency	$F(1.67) = 34.50$, $P < 0.0001$	Y = 95.74 + 0.61x
	P3 amplitude	$F(1.70) = 9.52$, $P < 0.003$	Y = 2.95 + 0.09x
P3	P1 latency	$F(1.69) = 16.07$, $P < 0.001$	Y = 62.81 + 0.13x
	P1 amplitude	$F(1.69) = 13.67$, $P < 0.001$	Y = –2.82 + 0.16x
	N1 latency	$F(1.69) = 40.12$, $P < 0.0001$	Y = 76.09 + 0.33x
	P2 latency	$F(1.70) = 22.59$, $P < 0.0001$	Y = 103.83 + 0.41x
	P3 amplitude	$F(1.71) = 7.10$, $P < 0.01$	Y = 0.73 + 0.06x
P4	P1 latency	$F(1.70) = 14.04$, $P < 0.001$	Y = 61.46 + 0.16x
	P1 amplitude	$F(1.70) = 20.29$, $P < 0.0001$	Y = –3.46 + 0.16x
	N1 latency	$F(1.70) = 41.89$, $P < 0.0001$	Y = 72.72 + 0.39x
	P2 latency	$F(1.70) = 33.67$, $P < 0.0001$	Y = 99.41 + 0.50x
	P3 amplitude	$F(1.70) = 6.70$, $P < 0.01$	Y = 0.36 + 0.08x

respect to the other latencies considered, the steepest slopes with age (between 0.47 at Oz and 0.61 at Pz); *ii*) the slope of P1 amplitude was steeper at parietal compared with occipital emplacements; and *iii*) the slopes of P1 and N1 latencies were steeper at occipital than at parietal emplacements.

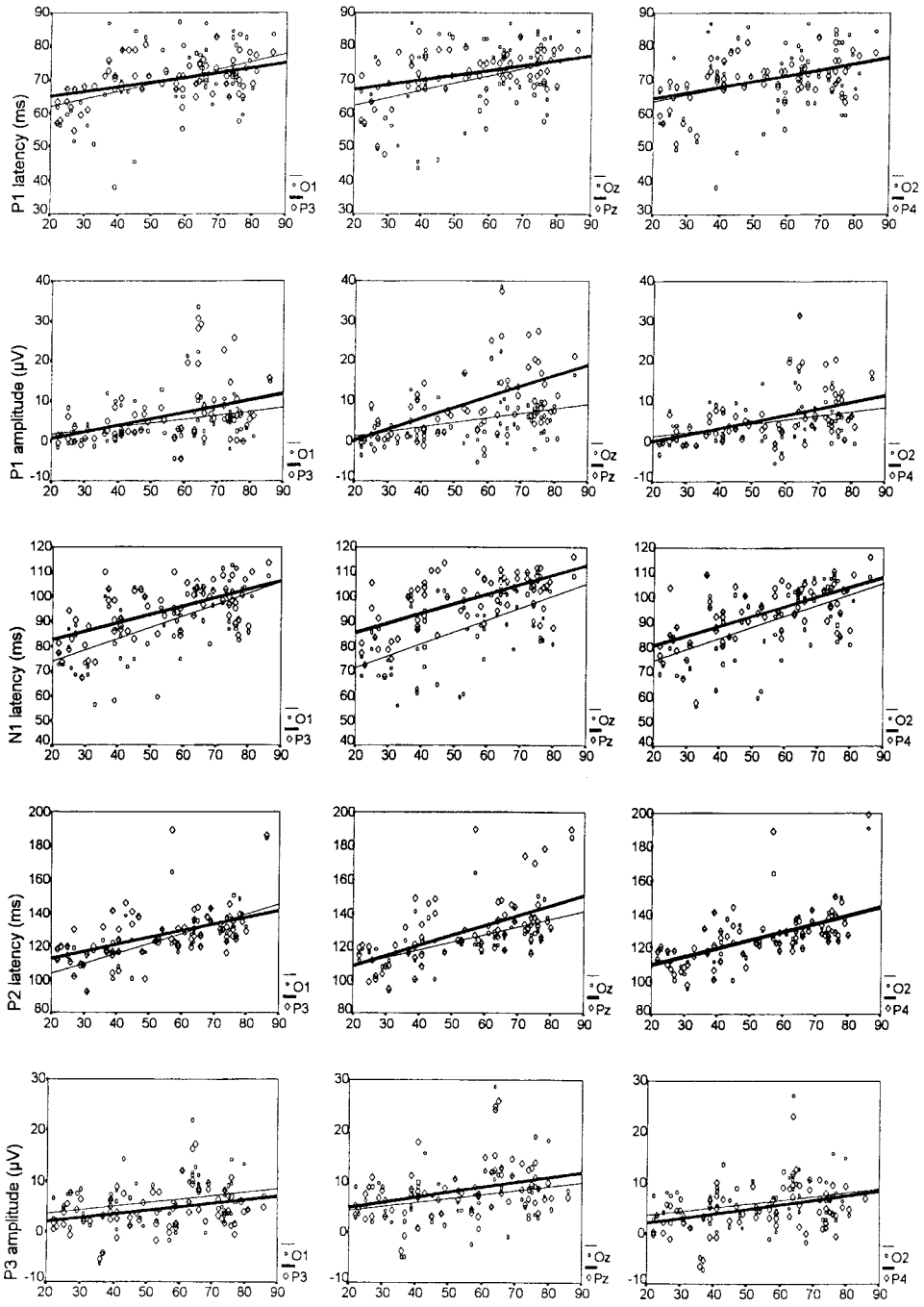

Fig 3. Scatterplots of flash visual evoked potential (FVEP) parameters (*Y* axis) against age (*X* axis), showing the best-fitting regression lines for data obtained at occipital electrodes (circles, thin lines) and at parietal electrodes (diamonds, thick lines).

DISCUSSION

Effects of sex

In this study significantly larger P1 amplitudes were found in women than in men, but the effects of sex were due to the differences in only two age groups. Several studies have found similar between-sex differences in the P100 component of pattern-reversal visual evoked potentials [4, 20], and it has been suggested that these differences may be attributable to hormonal changes in women during adolescence and menopause. The results of the present study do not give support to that hypothesis, as they show that the sex effect was due to the differences between sexes for P1 amplitude in the 30–39 and 60–69-year age groups, and consequently, not in the age groups in which menopause occurs.

Effects of age

The results in this study show that P1, N1 and P2 latencies increase linearly from 20 to 86 years of age. These results are in agreement with those of previous studies [6, 22, 32].

Several studies have concluded that FVEP represent the activity of two complementary visual pathways. Specifically, P1 and N1 are considered to reflect visual processing by the striate cortex at the end of the geniculostriate pathway, while P2, N2 and P3 appear to reflect activity in the parastriate cortex, indicating the arrival of information transmitted by a secondary "retinotectal" pathway [1, 9, 16, 33]. Although factors such as lenticular opacity and myosis, which are common in persons older than 50 years of age, may have influenced the latency findings [5, 18, 25], the present observation that P1, N1 and P2 latencies increase with age may be related to age-related changes in the visual system, such as a decrease in acetylcholine (ACh) levels in the visual cortex with age [7, 23] and/or demyelination of optic radiations and loss of dendritic mass in primary and association cortical areas [5, 19, 28].

The linear increases in P1 amplitude with age observed in this study are in agreement with those of previous reports [2, 6, 10, 12–14, 22, 32]. In contrast, an increase in P3 amplitude with age has only been reported previously by Cosi et al [6]. The observed increase in P3 amplitude may indicate reduced habituation in response to repetitive stimulation, with the consequent maintenance of high levels of cortical electrical activity.

Ageing-related changes in P1 amplitudes have generally been attributed to the existence of inhibitory deficits in old age, supposedly caused by loss of inhibitory interneurons in the primary visual cortex, by alterations in the frontal lobes and by loss of monoaminergic neurotransmitters [2, 13, 14, 32]. Such explanations are of course plausible; however, other putative factors may also explain the observed effects. Firstly, the surface component P1 may be the product of two or more physically separate generators that overlap in time. In young people, the surface components could possibly partially cancel out, yielding lower amplitudes, while in older people one generator could be inhibited or otherwise diminished, resulting in less cancellation and a larger surface potential (see *figures 1* and *2*). Further studies using a larger electrode array are needed to verify this hypothesis.

Most notably, the increase in P1 amplitude may also be related to reduced cholinergic activity in the visual cortex. Although it is generally considered that the specific neural input to the primary visual cortex is not cholinergic [31], it has been suggested that ACh may function as the synaptic transmitter for reticular input to the visual cortex [34]. Moreover, cholinergic activity has been associated with a general

mechanism which improves signal-to-noise ratio in the electrophysiological response to sensory stimulation [24, 27]. ACh levels in the visual cortex decline with age [7, 23], and it would seem reasonable to suppose that this may lead to reduced control of electrical activity in response to repeated and unattended stimuli. The age-related losses of dendritic spines and neurons in the visual cortex [5, 19, 28] may have similar effects.

Effects of scalp region and electrode position

ANOVA showed *i*) that all FVEP latencies, and significantly those of N1, P2 and P3, were longer at parietal than at occipital electrodes. For N1 and P3 latencies, this effect was due to maximal values in age groups between 30 and 59 years; and *ii*) that P1 latency was longer at midline than at lateral electrodes. In contrast, N2 latency was longer at right electrodes. Regression functions show that the slopes were maximal at occipital electrodes only for P1 and N1 latencies. These changes with age give way to a greater similarity in N1 latency among scalp regions from 60 years of age.

ANOVA also showed that P1, N1 and N2 amplitudes were maximal at parietal electrodes. Regression analyses revealed that the slope of the increase in P1 amplitude with age was steeper at parietal than at occipital emplacements. Furthermore, P1 and P3 amplitudes were maximal at midline electrodes, contrary to N1 and N2 amplitudes. The interactions between age and electrode position observed for P1 amplitude were probably due to maximum values at midline electrodes in subjects older than 50 years. However, P2 amplitude was largest at occipital electrodes in all age groups, and shortest at left electrodes in subjects older than 50 years.

These data confirm the widespread distribution of FVEP in parietal and occipital electrodes and in left, midline and right emplacements, and are in agreement with the data of Hobley and Harding [17], who found that P1 had a more widespread distribution than P2: P1 was detectable at both parietal and occipital electrodes, but P2 was more detectable at occipital electrodes, as in the present study.

Origins of FVEP within the first 100 ms are less well known than those of pattern visual evoked potentials (PVEP). Although subcortical origins were initially proposed for these waves [8, 26, 29], more recent findings have led to the conclusion that they are originated in the calcarine fissure [9]. Considering these data, the present age-related changes in P1 amplitude may indicate a change in the location of the dipole involved in its generation towards an upper region of the calcarine fissure, which would generate a more parietal and widespread distribution.

The data referring to FVEP amplitude (and particularly that of interactions between age and electrode position) allow for hypothesis of a possible change in the topographical distribution of FVEP with age. Cortical folding changes with age, and this along with some degree of cortical atrophy and biochemical changes in the visual pathway and centres, may well alter the orientation of cortical sources, giving rise to scalp potential differences. Specific studies are therefore necessary to verify this hypothesis.

In conclusion, the overall pattern of results in this study suggests that ageing is associated with a slower transmission of visual information in visual pathways and centres, and with deficiencies in the inhibitory regulation of cortical activity generated during the arrival of repetitive meaningless stimulation. The fact that ageing changes were more marked at parietal than at occipital electrodes raises the hypothesis that the non-primary visual cortex might be more affected than the primary visual cortex. However, this hypothesis can only be explored with the use of multichannel recordings and topographic mapping studies with modelling of intracranial generators.

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