Short report

VEP changes in Parkinson's disease are stimulus dependent

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SUMMARY Two stimulus configurations (gratings and checkerboards) have been presented to a series of consecutive patients with the aim of exploring VEP changes in Parkinson's disease. The outcome turned out to be quite different according to the stimulus employed. Specifically, grating pattern produced a high diagnostic yield as opposite to checkerboard, which did not reveal substantial modifications of the latency of the VEP major positive peak with respect to a control group. This finding raises problems as to the characteristics of visual changes associated with Parkinson's disease.

Bodis-Wollner and Yahr,¹ using a 2 c/degree grating stimulus, subtending 4° of visual angle, found that in 60% of their sample of Parkinsonians the main positive component of VEP (P100) was significantly delayed with respect to that of an age-matched control group. This finding has been subsequently confirmed using the same stimulus configuration,²⁻⁴ whereas contradictory results have been obtained with the checkerboard stimulus⁵⁻⁷ unless checks 50' or 55' wide were used,⁸⁻⁹ as commonly employed in clinical practice.¹⁰⁻¹² With the latter technique, in contrast to the results obtained with the grating stimulus, VEPs did not reveal changes in the latency of P100 in Parkinsonians. However, different stimuli, such as gratings and checks, presented to unmatched samples of patients might lead to contradictory results, independent of the stimulus configuration. In fact the causes of any VEP changes in Parkinson's disease are unknown.

We have compared VEPs evoked by different stimuli in the same patients. Specifically, we selected patterns closely matching those used respectively by Bodis-Wollner and Yahr¹ and by Hansch *et al.*,⁸ to find out whether the latency of P100 in Parkinson's disease might change as a function of the stimulus configuration. The possible relevance of other parameters such as the dimension of the stimulus elements, the angular subtense of the field and the

overall luminous flux will be considered in a further investigation.

Methods

Our sample consisted of 13 patients with Parkinson's disease and 13 control patients (reversible ischaemic attacks (five), brain tumour (two), motor neuron disease (one), cervical spondylosis with myelopathy (one), subacute combined degeneration of the spinal cord unassociated with pernicious anemia (one), psychoneurosis (two)), whose ages ranged from 49 to 74 years (Parkinsonians: mean 61.3 ± 8.5 yrs; controls: mean 60.8 ± 7.1 yrs). Duration of illness varied from 6 months to 24 years (mean 7.8 ± 7.4 yrs). All the Parkinsonian patients were under treatment with different combinations of levodopa, dopa decarboxylase inhibitors, anticholinergic drugs and bromocriptine. Since visual acuity had to be not less than 20/25, in six out of 13 Parkinsonians only one eye could be tested. In all the cases pupil reactivity was normal. Checkerboards (subtending 10° of visual angle with single checks of 55' aperture at a distance of 171 cm from the observer's eye) and sinewave gratings (subtending 4° of visual angle at the same distance with spatial frequency of 2c/degree) were generated by a standard system (MPS LACE 01) on a TV-screen. The average luminance of the two patterns was identical, the dark elements presenting a luminance of 0.6 cd/mq and the light ones 30 cd/mq. Neither stimulus had a luminance surround. VEPs were evoked by pattern-reversal at a temporal frequency of 2 reversals/second. The patients were requested to fixate a black bar in the centre of the screen and for each stimulus condition no less than 256 reversals were presented. The signal was picked up by the usual derivation (mid-occiput—mid-frontal) through needle-electrodes. The latency under investigation (that is, the time interval between the onset of the pattern reversal and

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the peak of VEP major positive component¹³) was measured both on the plot and with a cursor on the computer oscilloscope.

Results

Table 1 presents the individual latencies of the main positive peak (P100) of potentials evoked by either stimulus in patients with Parkinson's disease, as well as the respective transformed scores, the latter being defined as $(A - \bar{X}_c)/SD_c$ where A is the individual latency of Parkinsonian patients, $\bar{X}_c$ the mean latency of the control group for the same stimulus condition and SD_c the corresponding standard deviation of the control group. The abnormal values are the ones exceeding 95% (that is, transformed scores $> +1.645$) or 99% (that is, transformed scores $> +2.333$) of the estimated normal range, adopting a one-tailed criterion. Therefore the negative scores are considered within the normal limits irrespective of their absolute value. Only one Parkinsonian patient showed an abnormal increase in latency of P100 to the checkerboard stimulus, while nine out of 13 presented a remarkable shift of P100 to the grating stimulus in one or both eyes.

Statistical analysis of data (table 2) was performed using a two-way analysis of variance with a one-between factor that is group (controls vs. Parkinsonians) and one-within factor that is stimulus

Table 2 Analysis of VEP latency (ms) changes in Parkinson's disease

(A) Mean latencies of P100 (13 eyes)			
	Checks	Gratings	
Controls	108.46 $\pm$ 4.27	109.38 $\pm$ 6.43	
Parkinsonians	110.15 $\pm$ 6.41	123.07 $\pm$ 6.35	
(B) Summary of analysis of variance			
	SS	df	F
A (group)	776.94	1	13.94*
Subj. w. groups	1337.30	24	
B (stimulus)	630.01	1	27.51*
A $\times$ B	462.01	1	20.18*
B $\times$ Subj. w. groups	549.46	24	

* = $p < 0.01$

(checks vs. gratings). Each subject entered the analysis with one eye, namely the one characterised by the longer latency for the checkerboard stimulus; when both eyes had equal latencies of the P100 to checkerboard stimulation, the one related to the longest latency with gratings was used for the statistics. It was found that the control and Parkinsonian groups differed with respect to the outcome of the two stimulus conditions, as shown by the significant interaction between main factors (table 2, upper half). The individual comparison indicated that the latency of P100 to presentation of gratings in Parkinsonians was longer than under all the other conditions. Changes in amplitude of both N50-P100

Table 1 VEP latency (ms) changes in Parkinson's disease

(A) Control group (13 subjects; 26 eyes)					Checks		Gratings	
Mean latency					107.46		109.07	
Standard deviation					5.33		6.59	
(B) Parkinsonians (13 subjects; 20 eyes)					Checks		Gratings	
Case n°	Sex	Age (yr)	Eye					
					Latency	Transformed score	Latency	Transformed score
1	M	49	OD	108	0.100	112	0.443	
			OS	108	0.100	108	-0.163	
2	M	70	OD	113	1.037	113	0.595	
3	M	53	OD	108	0.100	119	1.505	
			OS	108	0.100	106	-0.466	
4	F	69	OD	107	-0.086	119	1.505	
			OS	108	0.100	120	1.657	
5	F	52	OS	108	0.100	118	1.353	
			OD	114	1.224	121	1.809	
6	M	55	OS	114	1.224	124	2.264	
			OD	107	-0.086	131	3.326	
7	F	68	OS	107	-0.086	127	2.719	
			OD	117	1.786	125	2.416	
8	M	68	OS	122	2.723	127	2.719	
			OD	114	1.224	132	3.477	
9	M	69	OS	112	0.850	135	3.933	
10	M	71	OD	113	1.037	121	1.809	
11	F	70	OS	107	-0.086	127	2.719	
12	M	61	OS	95	-2.334	127	2.719	
13	F	65	OD	116	1.599	128	2.871	
Mean latency					110.3		122.0	
Standard deviation					5.53		7.85	

and P100–N150 VEP components were evaluated by the same design. It was found that controls and Parkinsonian patients showed a greater amplitude of both components to checkerboard presentations (N50–P100: $F = 8.1$; $df\ 1, 24$; $p < 0.01$ and P100–N150: $F = 76.98$; $df\ 1, 24$; $p < 0.001$) in the absence of any difference between groups (N50–P100: $F = 0.966$; $df\ 1, 24$; ns and P100–N150: $F = 1.344$; $df\ 1, 24$; ns).

Discussion

This study was undertaken to overcome some of the existing confusion as to the occurrence of changes of VEP latency in Parkinson's disease. It is possible to obtain both abnormal and normal responses in the same patient according to the stimulus employed. Sixty-nine per cent of our sample showed an increase of latency of P100 when compared to an age-matched control group, provided that 2 c/degree gratings presented in a small central area were used. Thus Bodis-Wollner and Yahr's¹ data have been confirmed, though the latency shift was smaller in our patients and the interocular difference not significant. Only one patient with clear VEP change could be picked up from the same sample when the large checkerboard with 55' wide elements was employed. Hence the data of Hansch *et al.*⁸ and Halliday⁹ also have been confirmed. It has been recently shown¹⁴ that gratings and checkerboards have a different diagnostic yield in multiple sclerosis, the former increasing the efficiency of the test by approximately 25%. Although our data do not presume to answer the general question as to whether gratings are more effective than checkerboard stimuli, there is little doubt that in Parkinson's disease the large checkerboard pattern, which has been successfully employed in other conditions, can be misleading.

A possible explanation of such a behaviour might be that the processing of visual information related to checks and gratings corresponds to different functional organisation, possibly depending on their unequal Fourier spectrum.¹⁵ Thus, one would expect the processing of grating to be more easily disrupted, being made up of a single spatial frequency, whereas the more composite spectrum of checkerboard would compensate for the possible loss of single frequency-specific channels. If this is the case, the different outcome of the two stimuli ought to be more general, applying to other pathological conditions, as some data suggest.¹⁴ Alternatively, the dopamine deficiency of Parkinson's disease might affect a specific retinal function, for instance the foveal rather than peripheral vision. This would explain why the grating presented in a small, mainly foveal, region of the field is more likely than the large checkerboard to reveal functional abnormalities of the visual system.

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