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# SACCADIC EYE MOVEMENT AND VISUAL PATHWAYS FUNCTION IN DIABETIC PATIENTS

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The saccadic or Eye fast Movement System (EMS) is the ocular motor system which allows the eyes to move rapidly in order to fixate an intended target on the fovea (1).

The triggering peripheal stimulus of saccadic eye movement is the central and peripheral etinal input travelling through the visual pathways (2). Reports exist about prolonged reaction time of the saccadic movements in diabetic patients (3), however it is not clear if this is caused by impairment of the afferent or the efferent system.

The functional integrity of the whole afferent visual system can be assessed by recordings of Visual Evoked Potentials (VEPs) that represent a mass response of cortical, and possibly subcortical, visual area to visual stimuli (4).

Impaired VEPs has been observed in diabetic patients (5-7), indicating a dysfunction in the visual pathways.

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In this study we examined both the saccadic eye movements and the visual evoked potentials in insulin-dependent diabetic mellitus (IDDM) patients and normal controls with the aim to evaluate whether a correlation exists between the saccadic eye movement and the visual pathways function.

## MATERIALS AND METHODS

Forty-one subjects were enrolled in the study. They had normal visual field (Goldmann perimetry), normal intraocular pressure (<21 mmHg) and best corrected visual acuity of 10/10, and were free of any labyrinthine and/or neurological signs or symptoms.

The subjects were distributed into two groups: group C, 21 control subjects; group IDDM, 20 insulin-dependent diabetic patients without neurophaty or retinophaty. Diabetic peripheral neuropathy was excluded according to the San Antonio Consensus Conference guidelines (8), namely the absence of signs and sympoms of peripheral neurophaty and normal response to electrophysiological evaluation. Retinopathy was assessed by fluorescein angiographty and, only patients without signs of retinopathy (level 1, according to the Klein levels) (9) were included in the study.

The IDDM patients had not exhibited ketoacidosis or diabetic coma during the 2 months preceeding the study, and only patients with stable metabolic control (HbA1c less than 8%) were included in the study. Clinical population profile is given in Table 1.

TABLE 1

*Clinical population profile*

| Group | n | M/F | Age (yrs) | Disease duration (yrs) | Hba1c (%) |
|---|---|---|---|---|---|
| Controls | 21 | 9/12 | 31.7 ± 4.1 | ---------- | 4.7 ± 0.27 |
| IDDM | 20 | 8/12 | 27.5 ± 8.7 | 9.1 ± 3.4 | 6.8 ± 0.89 |



After informed consent, the following tests were performed in all subjects.

### SACCADIC OR FAST EYE MOVEMENT SYSTEM (EMS)

Examination of the eye movement on the horizontal axis was performed projecting a bright spot onto a horizontal bar 100 cm long placed 100 cm in front of the subject examined.

Electronystagmography (ENG) recording was performed during the examination on the alert and collaborative subject, seated in a semidarkened room on a comfortable chair with his head fixed by an occipital support.

Silver-silverchloride electrodes were fixed with collodium at the outer canthus of each eye, and the reference electrode was located on the forehead. The interelectrode resistance was maintened lower than 8 KOhms. The analog signal was amplified (gain 20.000), digitized and stored in a PC (Compaq 286n) for later analysis. The equipment employed was a three-channel Computerized Electronystagmography package (SITER, Racia, Bordeaux, France) and an automatic light bar visual stimulator (SOMAU, Racia, Bordeaux, France). The calibration of eye movements was peformed at the beginning of each session. The eye movements recorded during calibration were then presented on the computer display to allow the operator to verify the correct calibration. Saccadic movements were induced by a series of lights, generated by LEDs, separated by known angles and moved through a series of stepwise jumps.

The patients followed the light which was switched on at a position of 15 degrees at each side of the primary position. This generated 30° saccades with inter-saccade interval between 1 and 5 s, the analysis time was 40 sec. We assessed at least three records in order to check the repeatability of the waveforms obtained. Examples of ENG layout of EMS are shown in Fig. 1.

The following parameters were analyzed:

—Latency (delay in msec) between the start of the target movement and the start of saccades.

—Peak velocity (Deg/sec): maximum eye velocity during the saccade.

Accuracy (%): defined as the ratio of the saccade amplitude

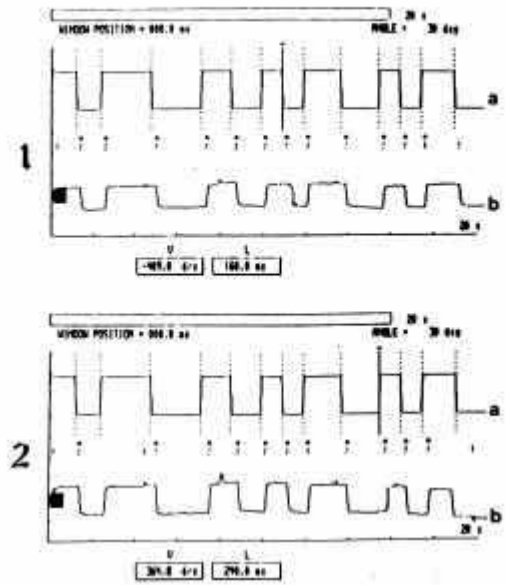


FIG. 1

Examples of EMS recordings from a control subjecty (1) and from an IDDM patient (2). a: target position; b: subject tested layout; V: eye maximum velocity (deg/s); L: latency (ms).

derived from the target displacement amplitude. We considered a saccade amplitude ±15% of the target amplitude inaccurate.

## VISUAL EVOKED POTENTIALS (VEPs)

Details about the method of VEP recordings applied here have previously been published (5-7).

Under examination the subjects were seated in a acoustically isolated room in front of the display that was surrounded by a uniform field luminance of 5 cd/m$^2$.

Prior to the experiment, each subject was adapted to the room light for 10 min and the pupil diameter was about 5 mm. Mydriatic or miotic drugs were never used.



The simulation was monocular, after occlusion of the other eye.

The visual stimuli were checkerboard patterns (contrast 70%, mean luminance 110 cd/m$^2$) generated on a TV monitor and reversed in contrast at the rate of 2 reversals. At the viewing distance of 114 cm the single check size subtended 15 min of visual arc.

The screen of the monitor subtended 18 degrees and in order to maintain stable fixation a small target (0,4°) was placed in the center of the stimulation field.

Cup shaped electrodes of silver-silver-chloride were fixed with collodium in the following positions: active electrode at Oz, reference electrode at Fpz, ground on left arm.

The interelectrode resistance was kept below 3KOhm. The signal was amplified (gain 20.000), filteres (band-pass 1-100 Hz) and averaged with automatic rejection of artifacts over a number of stimulus period using a BM6000 apparatus (Biomedica Mangoni, Pisa, Italy).

In the recording session at least two VEPs were recorded averaging over 100 stimulus periods, excluding the time of artifacts. The analysis time was 500 msec. The resulting waveforms were superimposed to check for the repeatability of the results.

The trasient response was characterized by several waves with three peaks, that in normal subjects appeared after 75, 100 and 145 ms. These peaks had negative (N75), positive (P100) and, negative (N145) polarity, respectively. For all VEPs recorded,

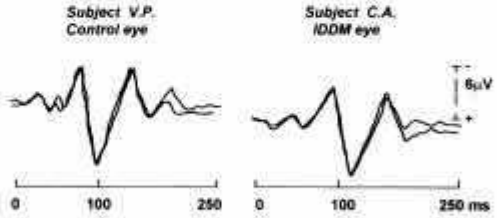


FIG. 2

VEP recording of a control subject (V.P.) and of a IDDM patient (C.A.). In the IDDM patient the recordings show delayed latencies and reduced amplitudes when compared to the control ones.

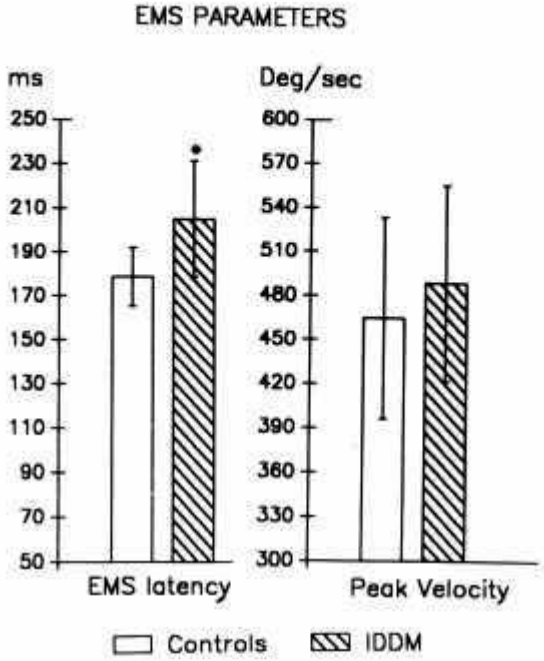


FIG. 3

Graphic representation of mean values of EMS parameters. Error bars represent one standard deviation of the mean. *: P<0.01 vs Controls.

the peak latency and the peak amplitude of each of the waves were measured directly on the displayed records by means of a pair of cursors. Examples of VEPs recordings are show in Fig. 2.

## RESULTS

### SACCADIC OR EYE FAST MOVEMENT SYSTEM (EMS)

The mean data are presented in Fig. 3. In IDDM patients we found EMS latency significally delayed with respect to controls ($F(1,39)=16.49$, $P<0,01$), while peak velocity was similar to con-



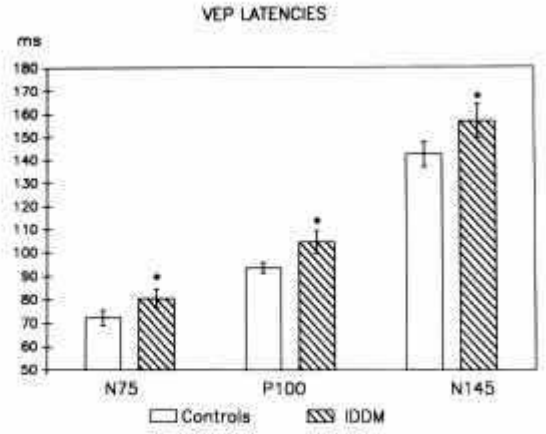


FIG. 4

Graphic representation of mean values. VEP latencies. Error bars represent one standard deviation of the mean. *: P<'.01 vs Controls.

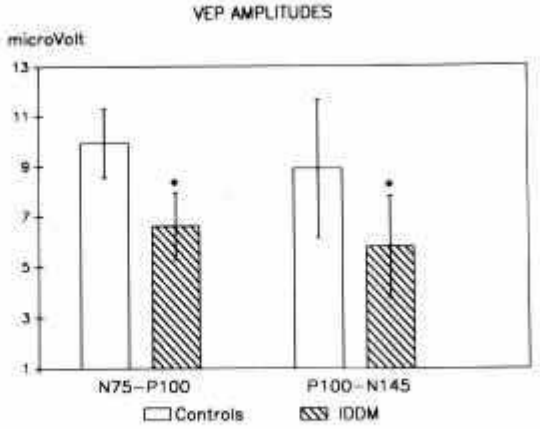


FIG. 5

Graphic representation of mean values. VEP amplitudes. Error bars represent one standard deviation of the mean. *: P<0.01 vs Controls.

trols (F(1,39)=2042, P<0,128). No inaccurate or morphologically abnormal saccades were detectable in Controls and IDDM patients.

### Visual Evoked Potentials (VEPs)

The mean data are reported in Figs. 4 and 5. In control subjects the VEP parameters (N75, P100 and 145 latencies and N75-P100 and P100-N145 amplitudes) were within our normal limits (10) expressed as mean value ±3SD for N745, P100 and N145 latencies and mean value ±1SD for N75-P100 and P100-N145 amplitudes.

In IDDM patients VEP latencies and amplitudes were both impaired when compared with those of controls. N75, P100 and N145 latencies were significantly delayed (respectively: F(1,39)=52.30, P<0.01; F(1,39)=85.59, P<0.01; F(1,39)=52.51, P<0.01) with respect to those of controls. N75-P100 and P100-N145 amplitudes was significantly reduced (respectively: F(1,39)=60.43, P<0.01; F(1,39)=16.78, P<0.01) with respect to control ones.

### EMS vs VEPs

In IDDM patients EMS parameters (EMS latency, EMS velocity) were matched to VEPs parameters (N75, P100 and N145 latencies; N75-P100 and P100-N145 amplitudes): the statistic analysis did not reveal any significant correlation.

## DISCUSSIÓN

Our study indicates that EMS latency is impaired in IDDM patients. This is in agreement with previous studies (3).

Since saccadic eye movement results from sensory input, central nervous system control and motor outputs (2), its impairment might be ascribed to a selective or widespread involvement of the visual pathways, or different CNS areas, or of the oculomotor neuromuscular structures.

EMS parameters can be differently influenced by various brain areas: specifically EMS peak velocity seems to be related to brainstem reticular formation function, while EMS latency seems to depend mainly on higher function (2). However, an increase of EMS latency may be found in the case of reduced transmission velocity of central neural pathways and also in the presence of impaired visual pathways (2, 11).



We focused our attention on the contribution of the visual pathways function to EMS impairment in IDDM patients.

In our IDDM patients with impaired EMS latency, VEPs revealed impaired function of the visual pathways (increased N75, P100, N145 latencies and reduced N75-P100 and P100-N145 amplitudes) in the absence of retinopathy and in the presence of a normal visual acuity.

It is known that VEPs represent a mass response of cortical and possibly subcortical visual area to visual stimuli (4); nevertheless, different structures of the visual system may contribute to the impaired VEP response observed in IDDM patients.

The different visual system structures may be widely evaluated by several electrophysiological methods such as Electroretinographic signals (ERGs) evoked by flash or patterned stimuli that reveal the bioelectric activity of different retinal layers (12), VEPs after photostress that represent an objective way to evaluate the macular function (13), simultaneous recordings of VEP and Pattern-ERG that give an index of neural conduction in the postretinal visual pathways by the evaluation of the retinocortical time (14). Impaired function of the outer, middle and innermost retinal layers (5, 15-18), of the macula (5, 6, 19-21) and of neural conduction in the postretinal visual pathways (22) has been observed in diabetic patients. This leads us to believe that an involvement of the different structures may contribute to the VEP abnormalities observed.

We recently observed that retinal, macular and visual pathways function are differently impaired in IDDM patients with different disease duration and without signs of retinopathy: the impairment starts in the nervous conduction of the visual pathways with an early involvement, goes on in the innermost retinal layers and in the macula and ends in the middle and outer retinal layers (5).

Since we found both EMS and VEP impaired responses in IDDM patients, we performed the regression analysis between

EMS and VEP parameters to evaluate the contribution of the visual pathways dysfunction on prolonged saccadic latencies.

The lack of correlation between the VEPs impairment and the EMS latency delay suggests that the latter cannot be exclusively ascribed to the dysfunction observed in the visual pathways. This suggests that other neural structures may be involved in the delay of EMS latency in IDDM patients.

Our results are in accordance with another analogous study in which the pupillary light reflex was matched with the visual pathways function in IDDM patients: no correlation between pupillary light reflex and VEP were found (23).

In conclusion, in our IDDM patients the delay of saccadic latency could be ascribed to a diffuse neuron problem (24) exceeding the visual pathways dysfunction assessed by VEPs.

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## RÉSUMÉ


SACCADES OCULAIRES ET FONCTIONNEMENT DES VOIES OCULAIRES CHEZ DES DIABÉTIQUES. (TEXTE EN ANGLAIS).

On a evalué les saccades oculaires (SO) et les potentiels visuels évoqués (PVE), dans le but d'éclaircir s'il y a une corrélation entre eux, chez un groupe de malades affectés de diabète mellitus insulino-dépendants (DMID).

Chez les diabétiques on observe un accroissement significatif de la latence de SO, tandis que les PVE montrent l'accroissement significatif de la latence et une importante diminution de l'amplitude.

On n'a pas trouvé aucun rapport entre les paramètres SO et PVE. A cause de cette manque de corrélation on tire la conclusion que chez nos patients DMID le rétard de la latence des saccades peut être occasionné par un problème neuronique.


*Mots-clés:* Mouvements saccadiques. Potentiels evoqués. Voies ophtalmologiques.

## SUMMARY

SACCADIC EYE MOVEMENT AND VISUAL PATHWAYS FUNCTION IN DIABETIC PATIENTS.

We assessed saccadic eye movements (SEM) and the visual evoked potentials (VEP) with the aim to evaluate whether a correlation exist between SEM and visual pathways function, in insulin-dependent diabetes mellitus (IDDM) patients.

In IDDM patients we observed significantly longer SEM latency, while SEM velocity and accuracy were similar to those of the controls; VEP showed a significant delay of the latencies and significant reduction of the amplitudes in IDDM patients no relationship between SEM and VEP parameters were found.

In conclusion SEM latency delay suggest an impairment of the saccadic eye movement system, while impaired VEP may be ascribed to a dysfunction of the visual pathways. The lack of correlation between VEP impairment and SEM latency delay suggests that in our IDDM patients the delay of saccadic latency could be ascribed to a difuse neuronal problem exceedind the visual patways disfunction.


*Keywords:* Saccadic movements. Visual evoked potentials. Visual pathways. Diabetes.


## ZUSAMMENFASSUNG

OKULAR SAKKADEN UND EVOZIERTE VISUELLE POTENTIALE BEI DIABETIKERN. (TEXT IN ENGLISCH).

Wir haben die Okular Sakkaden (OS) und die visuell evozierten Potentiale (VEP) gewertet, mit der Absicht festzustellen, ob eine Wechselwirkung zwischen ihnen bei Patienten mit Diabetes mellitus mit Insulin Abhängigkeit (DMIA) besteht.

Bei den Diabetikern stellt man ein bedeutendes Erhöhen der Latenz und eine bedeutende Verringerung der Ausdehnung fest. Es wurde keine Verbindung zwischen den Parametern OS und VEP gefunden. Wegen dieses Nichtvorhandenseins einer Wechselwirkung schliesst man, dass bei unseren DMIA Patienten die Verzögerung der Latenz der Sakkaden durch ein unbestimmtes Neuronalproblem entstehen kann.


*Schlüsselwörter:* Sakkadiert. Augenbewegungen. Visuelle evozierten Potentiale. Sehbann. Diabetes.

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