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CORRESPONDENCE

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Using the Blink Reflex as Measured by Electromyogram to Assess Cranial Nerve Involvement in People Affected by Leprosy[1]

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ABSTRACT

Damage to the peripheral nervous system is particularly frequent in leprosy patients. Trigeminal and facial nerves are among the most commonly affected. The aim of our study was to evaluate the efficacy of the blink reflex as a method for diagnosis of cranial nerve involvement in people affected by leprosy. We studied 37 affected people (mean age: 38 yrs, 20 female and 17 male) and 35 age-matched healthy subjects (mean age: 34 yrs, 20 female and 15 male). Blink reflexes were obtained after unilateral electrical stimulation of the supraorbital nerve for quantitative analysis of 3 responses, early ipsilateral phasic component (R1), late ipsilateral tonic component (R2i), and late contralateral tonic component (R2c). Nerve conduction parameters were studied in all subjects.

The latencies of both the ipsilateral early phasic component (R1) and bilateral late tonic components (R2i and R2c) in people affected by leprosy were significantly prolonged compared with the controls. Out of 37 people affected by leprosy, 22 (59%) showed abnormalities R1 latency, 28 (75%) R2i latency and 31 (83%) R2c latency. No correlation was observed between prolonged latencies and duration of the disease. We conclude that blink reflex testing, which can be easily and rapidly performed in an EMG laboratory using standard equipment, can provide useful and objective information for the diagnosis of cranial nerve lesions and for the determination of the degree thereof.

RÉSUMÉ

Les atteintes du système nerveux périphérique sont particulièrement fréquentes chez les patients lépreux. Les nerfs trijumeaux et faciaux sont parmi les nerfs les plus souvent affectés. Le but de cette étude était d'évaluer l'efficacité du réflexe de clignement comme méthode de diagnostic d'atteinte des nerfs crâniens chez les personnes affectées par la lèpre. Nous avons étudié 37 personnes affectées (âge moyen : 38 ans, 20 femmes et 17 hommes)

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et 35 personnes saines d'âge similaire (âge moyen : 34 ans, 20 femmes et 15 hommes). Les réflexes de clignement furent obtenus après stimulation électrique unilatérale du nerf supra-orbital afin de procéder à l'analyse quantitative de 3 types de réponse : la composante de la phase précoce ipsilatérale (R1), la composante tonique tardive ipsilatérale (R2i) et la composante tonique tardive controlatérale (R2c). Les paramètres de conduction nerveuse furent étudiés chez tous les sujets.

Les latences d'à la fois la composante de la phase précoce ipsilatérale (R1) et des composantes toniques tardives bilatérales (R2i et R2c) des personnes af fectées par la lèpre étaient significativement prolongées lorsque comparées aux personnes témoins. Parmi 37 personnes souffrant de lèpre, 22 (59%) montrèrent des latences anormales de R1, 28 (75%), des latences anormales de R2i et 31 (83%) de R2c. La prolongation des latences n'était pas corrélée à la durée de la maladie. En conclusion, le réflexe de clignement, qui peut être facilement et rapidement réalisé dans un laboratoire d'électromyographie utilisant des équipements standards, peut apporter des informations utiles et objectives au diagnostic des lésions des nerfs crâniens et à la détermination du degré de celles-ci.

RESUMEN

El daño al sistema nervioso periférico es particularmente frecuente entre los pacientes con lepra. Los nervios trigémino y facial están entre los más frecuentemente afectados. El objetivo del estudio fue evaluar la eficacia del parpadeo reflejo como un método de diagnóstico de afección del nervio craneal en pacientes con lepra. Se estudiaron 37 pacientes (edad promedio: 38 años, 20 mujeres y 17 hombres) y 35 sujetos sanos apareados por edad (edad promedio 34 años, 20 mujeres y 15 hombres). Los reflejos de parpadeo se indujeron por estimulación eléctrica unilateral del nervio supraorbital y se evaluaron cuantitativamente 3 respuestas: el componente fásico ipsilateral temprano (R1), el componente tónico ipsilateral tardío (R2i), y el componente tónico contralateral (R2c). En todos los sujetos también se estudiaron los parámetros de conducción nerviosa. En comparación con los controles sanos, las latencias tanto del componente fásico ipsilateral temprano (R1) como de los componentes tónicos bilaterales tardíos (R2i y R2c) en los pacientes con lepra estuvieron significativamente prolongados. De 37 personas afectadas por la lepra, 22 (59%) mostraron anormalidades en la latencia R1, 28 (75%) en la latencia R2i, y 31 (83%) en la latencia R2c. No se observó correlación entre las latencias prolongadas y la duración de la enfermedad. Concluimos que la prueba de reflejos de parpadeo, la cual puede hacerse fácil- y rápidamente en un laboratorio de EMG usando equipo estándar, puede proporcionar información útil y objetiva para el diagnóstico de las lesiones en el nervio craneal y para determinar su grado de afección.

TO THE EDITOR:

Leprosy remains an important health problem worldwide. Leprosy was once widely distributed in Europe and Asia but now occurs mainly in resource-poor countries in tropical and warm temperate regions ([3]). According to the World Health Organization (WHO), at the beginning of 2003, the number of leprosy patients in the world was around 534,000, as reported by 1 10 countries. About 621,000 new cases were detected during 2002 ([22]). It is a very serious and mutilating disease in many parts of the world and diagnosis and therapy is the most important strategy for its control ([12]). All patients with leprosy have some degree of nerve involvement, making leprous neuritis undoubtedly the most common cause of treatable neuropathy in the world. Deformities from involvement of facial structures, eyes, nerves, bone, and skin can result in stigmatization and social ostracism. The diagnosis of leprosy is often missed by physicians in the United States, leading to delay of treatment during which progressive neuropathy, visual loss and deformity may occur ([13]). Diagnostic delay in leprosy can have serious neurological consequences for the patient. Lockwood, *et al*. ([8]) demonstrated that the median time from symptom onset to diagnosis was 1.8 yrs (0.2 to 15.2) and delayed in diagnosis occurred in 82% of cases in the United Kingdom. They also demonstrated that misdiagnosis as other dermatological and neurological conditions were important causes of delay 68% of patients in the UK were found to have nerve damage resulting in disability . Increased awareness among general practitioners and hospital specialists would lead to more rapid diagnosis, thus minimizing damage

TABLE 1. *The demographic characteristics of patients and control subjects.*

Sex	Patients		Control group	
	Number	Age (yrs)	Number	Age (yrs)
Female	20	35	20	32
Male	17	41	15	36
Total	37	38	35	34

and disability. When detected and treated early, primary impairments may be reversible ([21]). For this reason, early recognition of leprosy is very important.

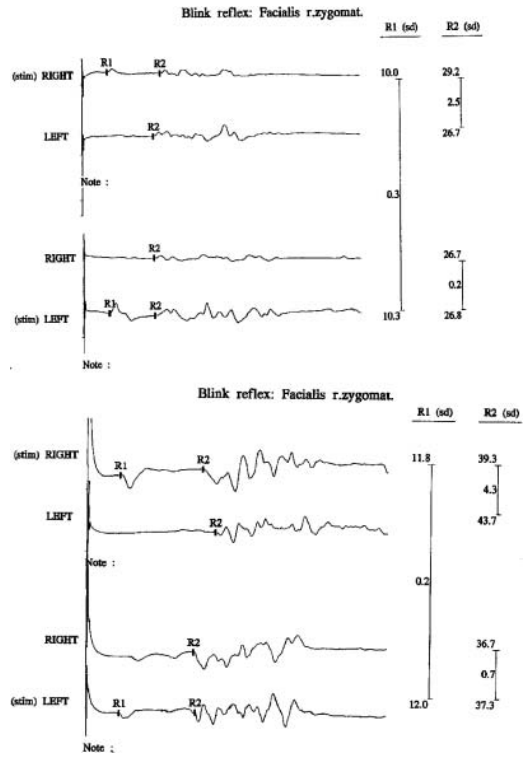
Trigeminal and facial nerves are among the most commonly affected in leprosy patients ([11]). Electrophysiological studies such as the blink reflex have been shown to be an effective method for revealing subclinical involvement of cranial nerves in generalised neuropathies ([4, 5, 9, 11]). The aim of our study was to evaluate the efficacy of the blink reflex as a method for diagnosis of cranial nerve involvement in people affected by leprosy.

METHODS

We studied 37 patients who had been treated for lepromatous leprosy (LL) with a mean age of 38 ± 17 yrs (range 23 yrs to 62 yrs; 20 female and 17 male), and 35 age-matched healthy volunteer subjects (control) with a mean age of 34 ± 12 yrs (range 24 yrs to 48 yrs; 20 female and 15 male). The demographic characteristics of patients and control subjects are presented in Table 1. Patients were hospitalized in Elazığ Leprosy Hospital for treatment and rehabilitation. The patients involved in this study had completed treatment and were cured of leprosy The period between diagnosis of leprosy and study was 16.73 yrs. The patients and controls were carefully examined. All subjects in the study had a negative history and negative physical examination for central nervous system disease.

Exclusion Criteria:

- alcohol abuse
- cigarette consumption of over 10 cigarettes/day
- the presence of disease of the peripheral nervous system not related to leprosy
- tuberculoid and borderline leprosy (according to the Ridley-Jopling classification) ([23])



THE FIGURE. Examples of blink reflex in an adult control subject (upper) and a patient of similar age with leprosy (lower).

Informed consent was obtained from all patients and controls before the investigations were carried out. Routine blood analysis was performed.

All subjects were studied using electromyogram (EMG) equipment (KEYPOINT, DANTEC, DENMARK). Following the standardized protocol proposed by Kimura, *et al.* ([6]) the supraorbital nerve in the supraorbital foramen was stimulated and the evoked responses from both *orbiculares oculi* muscles were recorded. Subjects were awake, in dorsal *decubitus* position, with room temperatures between 22 and 27 °C, in a semi-darkened room. Surface platinum disc electrodes of 0.5 cm diameter were positioned as follows: channel 1, active electrode G1 was placed on the belly of the left *orbicularis oculi* muscle, 1 cm below the left lateral epicanthal point; reference electrode G2 was placed on the lateral surface of the nose; channel 2 was symmetrically positioned in relation to the channel 1 electrodes, on the right side. Fil-

TABLE 2. *Mean values of some parameters in the leprosy patients and the control group.*

	Leprosy patients	Control group	p
Left eye R1 mean latency (msec)	12.68 ± 3.43	11.28 ± 2.32	<0.05
Right eye R1 mean latency (msec)	13.01 ± 2.07	11.14 ± 2.18	<0.05
Left eye R2i mean latency (msec)	37.4 ± 6.55	32.51 ± 6.65	<0.05
Right eye R2i mean latency (msec)	38.25 ± 4.72	30.23 ± 3.6	<0.05
Left eye R2c mean latency (msec)	38.01 ± 9.76	32.91 ± 4.75	<0.05
Right eye R2c mean latency (msec)	39.76 ± 3.48	31.67 ± 5.9	<0.05
Median nerve motor distal latency (msec)	4.1 ± 0.58	3.4 ± 0.56	<0.05
Ulnar nerve motor distal latency (msec)	4.6 ± 0.84	3.2 ± 0.54	<0.05

ter band-pass was set to 20–3000 Hz, sensibility to 200 μV/cm, and the sweep velocity was 10 msec per division. Stimulation was performed with the cathode over the supraorbital foramen, with single stimuli on each side, consisting of square-wave pulses of 0.2 msec duration and 25 mA intensity. The ground electrode was positioned comfortably around the neck. Two recordings were obtained from both sides for each subject, with ten seconds or more between stimuli. Blink reflexes were obtained after unilateral electric stimulation of the supraorbital nerve for quantitative analysis of 3 responses, early ipsilateral phasic component (R1), late ipsilateral tonic component (R2i) and late contralateral tonic component (R2c). Latency was measured from the stimulus onset to the shortest initial deflection of the height R1 or R2 components. Amplitude was not important. Examples of blink reflex in a control subject and a patient are presented in Fig. 1.

Statistical methods. Data are expressed as mean ± standard deviation (mean ± S.D.). Differences between the means of groups were determined using the unpaired *t*-test. The correlation of two parameters was tested using a linear regression analysis. Values of $p < 0.05$ were accepted as statistically significant.

RESULTS

The data from each group studied are summarized in Table 2. The latencies of both the ipsilateral early phasic component (R1) and bilateral late tonic components (R2i and R2c) in people affected by leprosy were significantly prolonged compared with the controls (Fig. 1). In general, abnormal R1 latency was less than that of R2. Out of 37 people affected by leprosy, 22 (59%) showed abnormalities R1 latency, 28 (75%) R2i latency and 31 (83%) R2c latency. No correlation was observed between prolonged latencies and the duration of disease.

DISCUSSION

Trigeminal and facial nerves are among the most commonly affected in people affected by leprosy ([11]). Diagnostic delay in leprosy can have serious neurological consequences for the patient. The diagnosis of leprosy is often missed by physicians, leading to delay of treatment during which progressive neuropathy, visual loss, and deformity may occur ([8, 13]). It is a very serious, mutilating and stigmatizing disease in many parts of the world and early diagnosis and therapy is the most important strategy for its control ([3, 8, 13]). There is evidence that nerve damage in leprosy occurs before clinical manifestations become apparent ([16, 17, 20]). When the clinical signs are apparent, extensive and often-permanent nerve damage has already taken place. A method to detect asymptomatic neuropathy of trigeminal and facial nerves electrophysiologically could be valuable to identify patients at high risk for symptomatic cranial neuropathy. One opportunity for this is the measurement of damage to trigeminal and facial nerves using the blink reflex in standard EMG equipment.

The blink reflex is a very practical, reproducible electrical response, which can be used in comparative clinical studies and experimental models ([6, 18]). It is an electrically induced glabellar response that has long been used in clinical neurology and is known to be a polisinaptic reflex with an afferent arc through sensory fibers of the trigeminal nerve and with an efferent arc through the motor fibers of the facial nerve ([6, 7, 14]). It has been most useful in the evaluation of lesions affecting the trigeminal

nerve and facial nerve ([1, 2]). For the detection of a lesion in the first division of trigeminal nerve, the blink reflex is the only physiological test available at this time. The classic findings indicative of such a lesion are an afferent defect, a prolonged latency of R1, R2i and R2c ([2]). In facial nerve lesions, there is a delay in the reflex latency only on the affected side, regardless of the side of the stimulation ([6, 9]).

In our study, latency of R1, R2i and R2c were significantly prolonged in the people affected by leprosy compared to the control subjects, similar to the findings in previous studies ([5, 11]). These results, together with previous studies, demonstrate that some degree of cranial neuropathy may be present in the people affected by leprosy with neuropathy. The blink reflex study may indicate an effective diagnosis of cranial nerve involvement.

Shetty, *et al.* ([17]) reported that subclinical neuropathy may take place before clinical manifestations become apparent. Indeed, histopathological and immunocytochemical studies have demonstrated that nerve damage progresses from small unmyelinated to small myelinated and finally to large myelinated fibers ([15]). The authors suggest that this electrophysiological study may well indicate subclinical neuropathy in these patients, since a significantly prolonged latency was not seen in the normal control subjects.

Ramachandran, *et al.* ([10]) reported an association between the severity of autonomic neuropathy and a longer duration of leprosy. In this study, no significant correlation between duration of leprosy and positive test results was found. This was probably due to a longer duration of the effects of leprosy after treatment in our patients. The period between diagnosis of leprosy and study was 16.73 yrs.

In conclusion, we have observed markedly abnormal patterns of blink reflex in leprosy. The use of blink reflex testing which can be easily and rapidly performed in an EMG laboratory using standard equipment can provide useful, objective information for diagnosis and in determining the degree of cranial nerve lesions. However, future electrophysiological trials in active leprosy will provide further information for the use of this test in the early diagnosis of cranial nerve involvement in leprosy patients.

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