Electrophysiological investigations in cranial hyperkinetic syndromes
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Citation for published version (APA):

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Chapter 4

Orbicularis oculi and orbicularis oris reflexes in blepharospasm and torticollis spasmodica during spasm free intervals.

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Abstract.

To investigate possible abnormalities of the blink reflex pathways, we analyzed latencies and amplitudes of the blink reflex responses in the orbicularis oculi (Ooculi) muscle, following the supraorbital nerve stimulation, in 19 patients with blepharospasm, in 16 patients with torticollis spasmodica and in 22 control subjects. Furthermore, in order to examine the suprasegmental control upon the responses, the reflex responses were also evoked in the orbicularis oris (OOris) muscle after stimulation of the ipsilateral supraorbital nerve. The responses were recorded only when subjects had no contractions of the eyelid muscles, either involuntarily, voluntarily or spontaneously, which could be controlled by the sound signal. The metrics of the reflex responses in the OOoculi and OOoris muscles in patient groups were comparable to those in controls. Our data indicate that the afferent and efferent pathways of the reflex arc and the suprasegmental control of the reflex are intact in patients with blepharospasm and torticollis spasmodica at least during the spasm free intervals. Alterations of responses may occur during spasms due to either segmental or suprasegmental changes. Keywords: blink reflexes, blepharospasm, torticollis spasmodica. Eur Neurol, accepted.
Introduction.

By electrical stimulation of the supraorbital nerve, two reflex responses can be elicited in orbicularis oculi muscle (OOculi)\textsuperscript{79,110} an early ipsilateral response, R1, mediated by an oligosynaptic pathway in the pons, and a late bilateral response, R2, mediated by a polysynaptic pathway. Afferents for R2 response descend through the spinal trigeminal tract to the caudal spinal trigeminal nucleus. Bilateral polysynaptic pathways, located in the medial part of the lateral tegmental field, ascend from this region to both facial nuclei.\textsuperscript{8,110} The facial nerve is the common efferent route for both R1 and R2.

One earlier study showed abnormalities of latency, amplitude and duration of blink reflex responses in patients with blepharospasm,\textsuperscript{16} while others could not confirm these findings.\textsuperscript{114} Abnormal blink reflexes have also been demonstrated in patients with torticollis spasmodica.\textsuperscript{103}

Furthermore, after stimulation of the supraorbital nerve, reflex responses can also be recorded in the orbicularis oris (OOris) muscle.\textsuperscript{57,86} It seems that perioral muscles are under more stringent cortical control than periocular muscles.\textsuperscript{76} However, these responses have not yet been examined in patients with focal dystonia.

In the present study, in order to examine the integrity of the reflex arc, we analyzed the blink reflex responses in patients with blepharospasm and torticollis spasmodica. The responses were evoked and recorded during the spasm free intervals and when there was no voluntary or spontaneous closure of the eyelids in order to exclude the possible suprasegmental influences upon the responses. As the influence of cortical structures is more obvious upon the perioral muscles than upon the periocular muscles, under the same condition we recorded the reflex responses in the OOris muscle to investigate the possible role of suprasegmental, especially cortical, structures on the reflex responses in patients with focal dystonia.

Material and Method.

The blepharospasm group consisted of 19 patients, seven male and 12 female, with a mean age of 64 years (range 44-80). Spasms were bilateral in all patients. For inclusion, patients were required to have frequent involuntary eyelid contractions in combination with frequent short electromyographic (EMG) discharges lasting from 50 msec to seconds.\textsuperscript{5,16} The torticollis spasmodica group consisted of 16 subjects, four male and 12 female, with a mean age of 49 years (range 22-67). The patients had predominantly a rotational type of torticollis, rather than lateroflexion or retroflexion. The chin was rotated to the left in eight patients and to the right in eight patients. Inclusion criteria required involuntary contractions of neck muscles and involuntary EMG discharges in at least one sternocleidomastoid muscle.\textsuperscript{39} The
control group consisted of 22 healthy subjects, 17 male and five female, with a mean age of 54 years (range 19-80).

Examinations were performed using a Nicolet Viking EMG apparatus. The supraorbital nerve was stimulated supramaximally with a 20 mA, 0.2 msec square-wave pulse. Stimuli were only given in the absence of spasms in patients with blepharospasm and voluntary or spontaneous eyelid closure in all subjects, which could be controlled by EMG sound signal. Responses contaminated with spontaneous muscle activity were rejected. Reflex responses from the OOculi were recorded bilaterally with surface electrodes placed on the middle of the inferior orbital rim and lateral to the eye. Reflex responses in the OOris were recorded with the active electrode placed about half way medially to the nasolabial fold and the reference electrode at the corner of the mouth. Amplifications ranged from 20 to 500 μV/cm.

The R1 and R2 latencies and amplitudes were determined from three superimposed trials. Latency was measured from the stimulus artefact to the deflection of the EMG response from the baseline. Amplitudes were measured from the largest positive peak to maximal negative peak values.

The mean values of latencies and amplitudes of responses in OOculi and OOris, whenever present, were calculated in each group. An amplitude ratio OOris/OOculi was also calculated for R1 and R2. For both patient groups, responses from both sides were compared with controls. The side contralateral to the direction of chin rotation in patients with torticollis was considered as the most affected side and the ipsilateral side, defined as unaffected, was also compared to controls. Differences between groups were examined by unpaired t-tests (BMDP 3D). The number of subjects with responses in OOris were compared in groups with a χ²- square test. In view of the explorative nature of this study, no statistical adjustments for multiple comparisons were made. However, we are aware of amount of associations studied. Therefore, we set our p-value arbitrarily at p < 0.01.

Results.

Latency and amplitude of the R1 and R2 responses in the OOculi were not statistically different between the patients and controls. Patients with torticollis spasmodica did not differ significantly from the controls, neither when responses on the left and right sides nor when the affected and unaffected sides were compared. One subject in the blepharospasm group and one control subject showed a bilateral R1 response in the OOculi muscle.

Reflex responses in the OOris muscle could be evoked in 16 of the 19 blepharospasm patients, seven of the 16 torticollis patients and in 14 of the 22 control subjects. The amplitudes of these responses were much lower than those in the OOculi muscle (a tenfold difference for R1 and threefold for R2). R1 and R2 responses
were seen more frequently on the side ipsilateral to the stimulation than on the contralateral side. Synchronous EMG recording from the OOculi and OOris muscles showed responses with different latencies and configurations in both muscles.

There was no significant difference in number of elicited R1 and R2 responses between the controls and patients with blepharospasm. The mean amplitudes and OOris/OOculi amplitude ratios in blepharospasm were higher than in controls, but the difference was not statistically significant.

In patients with TS, the R2 amplitude in the OOris on the unaffected side after stimulation of the supraorbital nerve on the affected side was higher in torticollis patients than in controls (p < 0.01), which was the only significant difference between the patients and controls as far as the metrics of the responses in the OOris are concerned.

Discussion.

Neck torsion to one side predominates in most patients with torticollis spasmodica, although neck muscles are affected bilaterally. The right and left sides and affected and unaffected sides were examined in all patients with torticollis spasmodica, which appeared to have no influence on the OOculi blink reflex responses. We found no significant differences in latency or amplitude of R1 and R2 between patients and controls. One study[6] found abnormal blink reflexes in patients with torticollis only when they had more general dystonia. Thus, besides this possible exception, the blink reflexes in the OOculi muscle in patients with torticollis spasmodica appear to be normal.

Normal amplitudes and latencies of the OOculi responses were previously described in patients with blepharospasm. One important study, however, found increased amplitudes of R1 and R2 and longer duration of R2 responses. In another study, R1 and R2 latencies and amplitudes were normal, but duration of bilateral R2 was increased. It is possible that these differences are due to the effect of muscle contraction on the recorded responses.

We studied latencies and amplitudes, but not the duration, of blink reflex responses. However, in a previous study we demonstrated that the values of amplitudes and areas of rectified and averaged R1 and R2 responses, measured during time windows of respectively 10-25 and 32-90 ms, show no differences between control subjects and patients with blepharospasm or torticollis.

Bilateral R1 responses in the OOculi muscle have been considered as pathological in patients with blepharospasm and hemifacial spasm. In this study one patient with blepharospasm and one control subject showed a bilateral R1 response. Willer
reported bilateral R1 responses in control subjects after subliminal facilitation. It can be concluded from our results that spasms may also cause such facilitation.

The R1 or R2 responses can be recorded in the OOris muscle because of volume conduction of the reflex response elicited in the OOoculi muscle. However, synchronous recordings from both muscles in several subjects disclosed clearly different latencies and wave configurations in both muscles. This indicates that responses in the OOoculi and OOris muscle are elicited through separate pathways and after excitation of distinct facial subnuclei. Anatomical evidence for this phenomenon has been shown in the cat.

In this study we first examined systematically whether reflex responses can be evoked in the OOris muscle in control subjects after stimulation of the supraorbital nerve. Kugelberg found that these responses could easily be elicited, especially after mechanical stimulation, but Gandiglio and Fra demonstrated them in only one of their twenty control subjects. Previous authors, who studied these responses in patients believed that they are not present in control subjects. However, improvements in the recording techniques make the accurate demonstration of low-voltage responses much easier.

We found either R1 or R2 responses, or both, in the OOris muscle in 14 of 22 control subjects, although their amplitudes were three to tenfold lower than the amplitudes of these responses in the OOoculi muscle. There were no differences in latency between the controls and patient groups and there was no significant difference between patients and controls in the number of responses in the OOris muscle.

Topka and Hallett demonstrated an increased incidence of the OOris R2 responses and increased rectified and integrated R2 amplitudes in a group of patients with orofacial dyskinesia after stimulation of the infraorbital and mental nerves. In our group of 19 patients, only two patients had dyskinesia of perioral muscles. Methods and patients differ too much for valid comparison of these different results.

We examined blink reflex responses in perioral muscles in order to study the possibility of an altered cortical control on the reflex responses in patients with blepharospasm and torticollis spasmodica. In cats, a larger sensorimotor cortical influence has been demonstrated on perioral than on periocular muscles in the spinal trigeminal tract and nucleus, structures which are involved in the blink reflex generation. This influence was predominantly inhibitory. When an abnormal sensorimotor inhibitory cortical influence is present in blepharospasm and torticollis spasmodica, changes in amplitude and latency of the blink reflex responses would be expected. Our results did not demonstrate such an alteration, at least at times when there are no signs of involuntary contractions of the facial muscles.

Our data indicate that the afferent and efferent pathways of the blink reflex arc are intact in blepharospasm and torticollis spasmodica at least during the spasm free
intervals. Alterations in metrics of the responses, such as latency and amplitude, may occur during spasms due to either segmental or suprasegmental changes, but an altered cortical influence seems not to play a relevant role.

Additional studies on blink reflex responses during spasms of the eyelids and during spasm free intervals in the same subject are required to provide more insight in pathophysiological mechanisms involved. It may be that opposing input in the basal ganglia from direct and indirect pathways on activity in the globus pallidus internus determines a "gating" inhibitory effect on premotor systems like brainstem interneurons. Fluctuations in this activity could lead to intermittent interneuron hyperactivity, without disturbing the blink reflex pathway.²⁸