Chapter 3

Soleus H-reflex tests in dystonia

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Abstract

Vibratory inhibition, the homonymous recovery curve and the ratio of the maximal H-reflex to direct muscle potential (H/M-ratio) of the soleus H-reflex were assessed in ten patients with leg dystonia and in six patients with arm or neck dystonia. The results were compared with those obtained in 48 healthy control subjects. H-reflex variables most helpful for the discrimination of patients and healthy subjects were identified. In patients with leg dystonia vibratory inhibition was less marked than in control subjects, whereas late facilitation of the recovery curve was increased. In patients with leg dystonia area values of test reflexes in the late facilitatory phase of the recovery curve relatively exceeded peak-peak values, in contrast to findings in control subjects. This finding may be attributable to less synchronisation of enhanced test reflexes in dystonia than in the control condition. In differentiating patients with leg dystonia from control subjects a combination of parameters of vibratory inhibition and the late facilitatory phase of the recovery curve appeared most useful. In patients with arm or neck dystonia and in the unaffected legs of hemidystonic patients, soleus H-reflex test results were in the normal range. Abnormalities in the results of the Soleus H-reflex tests we used appear to be related to the presence of clinical signs in the extremity under examination and not to the severity of features.
Introduction

Dystonia is a syndrome dominated by sustained muscle contractions frequently causing twisting and repetitive movements or abnormal postures (Fahn et al. 1987). In some instances a cause can be identified, however ancillary investigation is often unrewarding. In dystonic movement disorders motoneuron activity evoked with H-reflex tests can be used for studying underlying pathophysiological mechanisms (Panizza et al. 1990; Bour et al. 1991; Berardelli et al. 1987; Nakashima et al. 1989; Artieda et al. 1991). As dystonia is often characterized by simultaneous contraction of antagonistic muscles, in most studies reciprocal inhibitory mechanisms are examined (Panizza et al. 1990; Berardelli et al. 1987; Nakashima et al. 1989; Artieda et al. 1991). However the study of other H-reflex tests such as the homonymous H-reflex recovery curve, inhibition of the H-reflex during vibration, and the ratio between the H-reflex and the direct muscle (M)-response may reveal additional neurophysiological mechanisms that contribute to the origin of dystonia (Panizza et al. 1990; Bour et al. 1991). In this presentation we report our results of the H/M ratio, vibratory effects and recovery curves of the soleus H-reflex in patients with leg dystonia, in patients with arm or neck dystonia without leg involvement and in control subjects. In addition we investigated which H-reflex variables are helpful for the discrimination of dystonic and healthy subjects.

Methods

Subjects

Ten dystonic patients, aged 21 - 66 years (mean 43 years), were selected on the basis of dystonic features in one or both legs with or without dystonic features in other parts of the body. In addition six patients, aged 23 - 48 years (mean 34 years) with arm or neck dystonia with sparing of the legs were examined. Additional features of an upper motoneuron syndrome - such as paresis, extensor plantar responses or evident tendon jerk asymmetry – were not present in any of the patients. Severity of dystonic features in the leg, arm or neck was scored with use of the Fahn-Marsden Scale for primary torsion dystonia (Fahn 1989). Only severity factors for the clinically affected site were used. Grades of severity ranged from 0 (no dystonia present) to 4 (severe...
dystonia). At the time of investigation none of the patients received medical therapy known to influence hypertonia or dystonia. All subjects gave informed consent. The neurophysiological results obtained were compared with those in a control group of 48 healthy subjects 20 - 70 years of age (mean 38). Results of neurophysiological tests of the healthy subjects have been published earlier (Koelman et al. 1993).

Experimental procedure

Recording and stimulation techniques for the soleus H-reflex have been described previously (Ongerboer de Visser et al. 1989; Hugon 1973). During all tests subjects were seated in a reclining chair in a standardized position. H-reflexes were elicited only in the absence of triceps surae EMG activity, which also was monitored aurally during the investigation. Soleus H-reflex responses elicited by 1 ms square current pulses to the posterior tibial nerve in the popliteal fossa were amplified with a bandpass filter of -3 dB at 2 Hz and 10 kHz, and digitally stored with a sample frequency of 10 kHz in a mini-computer (PDP 11/73). The time interval between successive trials during the investigation was at least 30 seconds (Ongerboer de Visser et al. 1989; van Boxtel 1986). For the construction of an H-reflex recruitment curve as a function of stimulus intensity, intensity increments of successive stimuli were chosen small at low intensity levels, and were gradually enlarged at higher intensities. Each recruitment curve consisted of 12 or more H-reflexes at different intensities. Simultaneous with the H-reflex recruitment curve, a recruitment curve of direct soleus M potentials was constructed also as a function of stimulus intensity. Peak-peak (P-P) values of the maximal H-reflex response and maximal M-potential were used for the H/M ratio (Bour et al. 1991).

Vibration of the Achilles tendon with a frequency of 100 Hz and an undamped amplitude of 1 mm was applied continuously by a Brüell and Kjær 4809 vibrator. The cumulative vibratory index (CVI) was used as a quantitative measure for the vibratory effects on the H-reflex (Ongerboer de Visser et al. 1989). This CVI is defined as the ratio between the surface under the recruitment curves obtained during and without vibration at the stimulus intensity up to which integration is carried out. Only the CVI at the stimulus intensity level yielding the maximal H-reflex response was used (Bour et al. 1991).

H-reflex recovery curves were constructed by application of paired pulses of equal intensity. The stimulus intensity level where the H-reflex reached half its maximum
value was used (Bour et al. 1991). Time-intervals between conditioning and test stimulus were 100, 200, 250, 300, 400 and 500 ms and at 1, 3, 10 and 30 seconds. Early facilitation and inhibition were not examined. The recovery curves were plotted as the ratio in percentage between the area values of the test and the conditioning H-reflex response against the time-interval between the two stimuli. Four characteristic values were used for statistical analysis: (a) the local maximum of the test H-reflex occurring in the late facilitatory phase at a stimulus time-interval ranging from 50 to 320 ms; (b) the local minimum of the test H-reflex found in the late inhibitory phase of the recovery curve at a stimulus time-interval ranging from 320 to 1000 ms; (c) the ratio of the difference in P-P and area values of the test and the conditioning H-reflex response at the local maximum of the late facilitatory phase; (d) the ratio of the difference in P-P and area values of the test and the conditioning H-reflex response at the local minimum of the late inhibitory phase.

Statistical analysis

To assess differences in soleus H-reflex test results between the groups, analysis of variance (BMDP statistical software package, 7D) was performed with use of t-tests. To assess the collective value of the variables yielded by the H-reflex recruitment curves, H/M ratios and recovery curves in discriminating the patients with leg dystonia and healthy controls, a stepwise discriminant analysis (BMDP statistical software package, 7M) was performed. F-Statistics were used to determine whether a feature was entered (F > 5.0) into the discrimination. With discriminant analysis a canonical variable was derived to differentiate patients with leg dystonia from healthy subjects. A canonical variable is a linear combination of variables that contribute most significantly to the discrimination. From the canonical variable, a posterior probability score was derived by which each individual case was classified in one of the two groups. Patients with arm or neck dystonia were classified with use of the same canonical variable. Correlation between the severity of dystonic features and the canonical variable was also determined (BMDP statistical software package 2R).
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Results

Clinical features

Table 1 shows the clinical data of the dystonic patients. All patients in the dystonic group with leg involvement showed in the early stage of the disease a slowly progressive form of dystonia. In only one subject an anatomical lesion was demonstrated that consisted of a lacunar infarction in the basal ganglia. In one of the patients, isolated neck dystonia was thought to be secondary to cerebral palsy.

Neurophysiological features

The results of the soleus H-reflex tests in the three groups are presented in figure 1. Comparison of neurophysiological findings obtained in the group of patients with leg dystonia with those in the control group yielded the following results. In patients with leg dystonia H/M ratio (mean 48%, range 18-100%) is similar to the one seen in

Table 1. Clinical features of patients with dystonia

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</table>

| arm and neck dystonia |     |          |          |                     |          |
| 11   | 28  | unknown  | 4        | focal dystonia arm  | 1        |
| 12   | 23  | trauma?  | 3        | focal dystonia arm  | 4        |
| 13   | 27  | unknown  | 1        | focal dystonia arm  | 2        |
| 14   | 38  | unknown  | 4        | focal dystonia arm  | 1        |
| 15   | 39  | cerebral palsy| 39 | torticollis        | 4        |
| 16   | 48  | unknown  | 7        | torticollis        | 3        |

*Components of the Fahn-Marsden scale for primary torsion dystonia are used with respect to the affected site only. Grades of severity range from 0 (no dystonia present) to 4 (severe dystonia) (Fahn 1989)*
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Figure 1. Soleus H-reflex test results in 48 healthy control subjects, 10 patients with leg dystonia (LEG), and six patients with arm or neck dystonia (ARM). Each value represents the group mean ± 1 SE. 

- H/M ratio
- CVI = cumulative vibratory index
- LF = late facilitatory phase in the recovery curve
- LI = late inhibitory phase in the recovery curve
- LF(P-A) = peak-peak (P) minus area (A) value in the late facilitatory phase in the recovery curve
- LI(P-A) = peak-peak minus area value in the late inhibitory phase of the recovery curve

Control subjects (mean 48%, range 6-100%, p>0.1). However, in patients with leg dystonia, vibratory inhibition is markedly more depressed (mean CVI 71%, range 32-114%) than found in the controls (mean 19%, range 0-60%, p<0.001). Furthermore, in the patients with leg dystonia late facilitation of the recovery curve is increased (mean 149%, range 45-335%) to a markedly larger extent than observed in control
Figure 2. Recovery curve of soleus H-reflex response in a dystonic patient. Peak-peak as well as area values are shown. Area value in the late facilitatory phase, is larger than peak-peak value.

In leg dystonia the late facilitatory phase showed in most instances larger potentiation in area values than in P-P values, resulting in lower P-P minus area values in leg dystonia (mean P-P minus area value -9%, range -26% to 3%) than in control subjects (mean P-P minus area value 4%, range -7% to 19%, p<0.01; figure 2). Late inhibition did not differ significantly between patients with leg dystonia (mean 40%, range 3-88%) and control subjects (mean 17%, range 2-44%, p=0.04). Neither did the mean of P-P minus area values in the late inhibitory phase: in leg dystonia 0% (range -7% to 5%), in control subjects 1% (range -7% to 8%, p>0.1).

In patients with arm or neck dystonia soleus H-reflex test results did not differ significantly from the results in the control subjects. The mean H/M ratio was 57%.

Figure 3. Histogram of canonical variable for discrimination of controls subjects (C) and dystonic patients (D).
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(range 38-87%, p>0.1), and the mean CVI was 28% (range 2-67%, p>0.1). The mean late facilitation was 49% (range 14-88%, p>0.1) and the mean late inhibition was 8% (range 2-20%, p=0.02). P-P minus area values were normal both in the late facilitatory phase (mean 2%, range -4% to 11%) and in the inhibitory phase (mean 0.9%, range -3% to 8%).

In three of the four patients with hemidystonia soleus H-reflex tests also were performed on the asymptomatic side. An asymmetry in vibratory and recovery features was found in all three patients. In the patient with dystonia secondary to a lacunar infarction in the basal ganglia, vibratory inhibition was depressed in the dystonic leg (CVI 99%), whereas CVI was normal (23%) in the asymptomatic leg. In the dystonic leg late facilitation was 123% and late inhibition was 69%, whereas in the asymptomatic leg late facilitation (47%) and late inhibition (12%) were normal. In the first of the two patients with idiopathic hemidystonia, in the dystonic leg CVI was 113% and late facilitation was 112%, whereas in the asymptomatic leg vibratory inhibition was normal (CVI 48%) and late facilitation of the recovery curve was near the abnormal range (86%). In the second patient CVI was 110% and late facilitation was 92% on the symptomatic side, whereas test results were normal on the asymptomatic side (CVI 17%, late facilitation 8%).

In differentiating patients with leg dystonia from control subjects by using stepwise discriminant analysis, the most distinctive factor appeared to be vibratory inhibition. Late facilitation and P-P minus area values of the late facilitatory period also contributed to the differentiation. With the help of these parameters, for each individual a canonical variable was derived (Bour et al. 1991). With this canonical variable eight of the ten patients with leg dystonia and all control subjects were classified correctly (figure 3). All patients with arm or neck dystonia as well as the unaffected legs of hemidystonic patients were classified in the control group.

No relationship was found between the degree of abnormality in the soleus H-reflex test results and the severity of leg dystonia. In some patients with only moderate disability, prominent abnormalities in soleus H-reflex tests were observed, but the reverse also occurred. In patients with leg dystonia, we could not establish a significant relationship between the canonical variable and severity of leg dystonia (r = 0.44, p > 0.05).
Discussion

In dystonic patients the H/M-ratio was unaltered compared with control subjects and may indicate that in dystonia excitability of soleus motoneurons is not affected. The normal H/M ratio is in accordance with the fact that enhancement of tendon jerks is not a characteristic feature in dystonia as it is in the upper motoneuron syndrome, in which H/M ratio increases with increase of tendonreflex activity (Koelman et al. 1993, Rothwell et al. 1983).

H-reflex suppression during Achilles tendon vibration, which strongly activates primary muscle spindle endings, is supposed to be predominantly caused by an autogenic axo-axonal presynaptic inhibition of Ia terminals (De Gail et al. 1966; Gillies et al. 1969; Burke and Ashby 1972; Delwaide 1973; Hultborn et al. 1987). However, other mechanisms such as neurotransmitter depletion or post-activation depression have been suggested as well (Hultborn et al. 1987; Nielsen et al. 1993). In spasticity, vibratory inhibition of the H-reflex is markedly decreased (Delwaide 1973; Taylor et al. 1984; Ongerboer de Visser et al. 1989; Koelman et al. 1993). To date, there are few data on vibratory inhibition in dystonia. In an earlier study (Bour et al. 1991) decrease of vibratory inhibition was found in some patients with dystonic features, but most of them had mixed dystonia and upper motoneuron signs. In the present study a similar decrease of vibratory inhibition has been found in purely dystonic patients. Presynaptic inhibition is probably also involved in the second phase of the reciprocal inhibition curve (Berardelli et al. 1987), which is reduced in forearm muscles in dystonia as well as in the upper motoneuron syndrome (Nakashima et al. 1989; Panizza et al. 1990; Artieda et al. 1991). However, it is not known whether vibratory and reciprocal induced presynaptic inhibition are correlated intraindividually.

Enhancement of late facilitation in dystonia is in accordance with findings reported previously (Sax et al. 1976; Panizza et al. 1990). The late facilitatory phase of the homonymous recovery curve occurs at time intervals around 250 ms between the conditioning and the test stimulus (Magladery et al. 1952). The facilitatory period is proposed to be mediated by cutaneous afferents (Gassel 1970; Pierrot-Deseilligny et al. 1973). However, the potentiation of late facilitation in dystonia and in the upper motoneuron syndrome as well as in Parkinsonian rigidity reflects polysynaptic pathways in either spinal cord or supraspinal long-loop pathways or both (Yap 1967; Zander Olsen and Diamatopoulos 1967; Pierrot-Deseilligny et al.
In dystonic patients in the late facilitatory phase area values of the test response were relatively larger than peak-peak values, resulting in lower P-P minus area values. In controls and spastic patients peak-peak values and area values are similarly enlarged even when late facilitation is significantly enhanced (Bour et al. 1991). Therefore, in dystonia additional mechanisms are involved in the late facilitatory potentiation. The finding is a consequence of a more asynchronous H-reflex response to the second, test stimulus than to the first conditioning stimulus. Whereas in spasticity and healthy controls the configuration of the first and second response are more or less the same, in dystonia the configuration of the first and second response are different, which results in a larger facilitation for the area than for the P-P value. The asynchronicity of the second H-reflex response may be explained as follows. It may be that the polysynaptic pathways do not induce excitatory postsynaptic potentials in all motoneurons at exactly the same time. As a result of temporal summation the motoneurons then may fire more asynchronously to the second stimulus. Another explanation may be that through hyperactivity of polysynaptic pathways more oligosynaptic induced motoneuron discharges are elicited by the second stimulus. These oligosynaptic reflex responses will have longer latency times and thus prolong the second H-reflex response. The fact that a similar discrepancy between P-P and area values does not exist in the late inhibitory phase may be due to the longer interstimulus interval and consequently different influences originating from the polysynaptic pathways (Taborikova 1969).

Soleus H-reflex test results in patients with arm or neck dystonia were normal. However, in patients with focal dystonias more generalized neurophysiological abnormalities have been found. The recovery of the blink reflex may be enhanced in patients with spasmodic torticollis and in blepharospams, but not in patients with focal arm dystonia (Nakashima et al. 1990). The recovery curve of the H-reflex in the forearm shows enhancement of late facilitation in patients with spasmodic torticollis, but not in patients with blepharospasm (Panizza et al. 1990). In contrast, reciprocal inhibition of the H-reflex in the forearm may be disturbed both in patients with spasmodic torticollis and in patients with blepharospasm (Panizza et al. 1990; Deuschl et al. 1992). It has been suggested that the extent of abnormal neurophysiological mechanisms relate to the site of maximal dystonic symptoms so that the interneuronal circuits relatively distant from the clinically affected site would be less influenced than those that are closer (Nakashima et al. 1990). As such, abnormalities in the recovery
curve as well as in vibratory inhibition may be more defined to the symptomatic site than abnormalities in reciprocal inhibition. In addition, the results in patients with hemidystonia suggest that abnormalities both in vibratory inhibition and in the recovery curve of the soleus H-reflex may occur unilaterally, even in the absence of a unilateral cerebral lesion.

A clear relationship between the combination of abnormalities in the neurophysiological tests yielding the canonical variable and severity of leg dystonia could not be established. As such, other neurophysiological mechanisms may add to the clinical symptomatology. In healthy subjects a relatively large interindividual variation of neurophysiological test results is present. In addition, the group of patients with leg dystonia is rather small and heterogeneous, which may further obscure a possible relationship between neurophysiological and clinical parameters. Finally, the scale used includes disability items next to impairment items. Neurophysiological correlations, if present, would be expected to occur with impairment rather than with disability parameters.

Eight out of 10 patients with leg dystonia showed a combination of abnormal soleus H-reflex test results that classified them correctly. Two cases were in the borderline region between dystonia and control findings. In contrast, all control subjects had a combination of test results that were clearly distinct from the findings seen in the patients. These observations suggest that the presented tests may be useful in verifying an underlying abnormality in patients with suspected dystonia (Panizza et al. 1989). As in dystonia frequently uncertainty exists whether presented clinical signs have an organic basis (Fahn et al. 1987), soleus H-reflex tests may be helpful in the management of these patients.

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