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Fasciculations: clinical, electromyographic, and ultrasonographic assessment

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Abstract Widespread fasciculations are an important clinical sign in, for example, degenerative lower motor neuron diseases (LMND). Usually they are detected by clinical inspection and electromyography. Recently myosonography has been proposed for the detection of fasciculations. This prospective study compares the value of these three modes of examination in patients with degenerative LMND. Seventy healthy control persons and 34 patients (11 women, 23 men; aged 43–78 years; median age 60.5) with LMND were included in the study. All participants were subjected to thorough visual screening for the presence of fasciculations. Fourteen muscles were examined bilaterally by myosonography and a median of 8 muscles were screened electromyographically (only in the patients); the investigators were blinded to the other findings. Clinical inspection and ultrasonography exhibited fasciculations in up to 5 and 8 muscles, respectively, in 8 healthy persons. Ultrasonography demonstrated fasciculations in all patients, clinical inspection in all but 2, and electromyography in 26 of 33 patients (1 patient was not examined electromyographically). Comparing the three methods, clinical observation revealed fasciculations in 42%, electromyography in 39%, and ultrasonography in 67% of all muscles. Thus, ultrasonography was significantly more sensitive than the other techniques ($P < 0.001$). The inter-rater agreement (correlation coefficient) r in respect of the presence or absence of fasciculation was 0.71 for the clinical, 0.85 for the electromyographic and 0.84 for the myosonographic examinations. Ultrasonography and electromyography were more reliable than the clinical examination ($P < 0.001$ and $P < 0.01$, respectively). Our study indicates that ultrasonography is more sensitive than clinical and electromyographic examination in visualizing fasciculations in patients with LMND. Additionally, it is more reliable than clinical examination.

Key words Lower motor neuron disease · Fasciculation · Ultrasonography · Electromyography

Introduction

Fasciculations are brief muscle twitches, usually lasting for 0.2–0.5 s [9] or 500 (SD 110) ms [14]. They are commonly found in amyotrophic lateral sclerosis and degenerative lower motor neuron disease (LMND), but can occur in other diseases of the lower motor neuron at any level from the anterior horn cells to the axon terminals [6]. They are detected, for example, in multifocal motor neuropathy, muscular pain-fasciculation syndrome, radiculopathies, sequelae of poliomyelitis, syringomyelia, tetany, myelopathies, following an overdose of anticholinesterase medication, plexopathies, peripheral nerve in-

juries, polyneuropathies, and rarely even in primary muscle disorders [3–6, 13]. In addition, about 70% of healthy subjects occasionally experience muscle twitches [8]. They can be detected by clinical inspection, and sometimes they can be palpated or even heard by auscultation. Furthermore, they can be depicted by conventional needle electromyography or by surface electromyography [5]. Recently, Reimers et al. [9], Rott et al. [10], and Walker et al. [14] described the possibility of visualizing fasciculations by B- or M-mode ultrasonography. A systematic study on the sensitivity and specificity of ultrasonographic screening for fasciculations has not yet been reported.

The purpose of the present study was to compare the sensitivity and specificity of a clinical, electromyographic, and ultrasonographic assessment of fasciculations. We chose patients with degenerative LMND for the study group because of the high incidence of fasciculations in these patients.

Materials and methods

Control group

Seventy voluntary healthy individuals without signs or symptoms of neuromuscular diseases (35 women and 35 men, aged 21–80 years, median age 42 years) were checked clinically and ultrasonographically for the presence of fasciculations in the same way as the patients.

Patients

Thirty-four consecutive patients (11 women, 23 men, aged 43–78 years, median age 60.5 years) with degenerative LMND, seen between January 1994 and August 1995, were included in the study. All had a history of progressive muscle wasting and weakness without sensory changes. Asymmetrical or multifocal electromyographic signs of motor neuron degeneration, i.e. fibrillation potentials and positive sharp waves and/or motor unit action potentials of increased amplitude and duration in muscles, outside the distribution of a single peripheral nerve or nerve root, were visible in at least three limbs or two limbs and the head [6, 11]. Possible differential diagnoses such as syringomyelia, polyradiculopathies or polyneuropathies were excluded by radiological examination, motor and sensory neurography, and examination of the cerebrospinal fluid. Ten patients additionally revealed involvement of upper motor neurons, documented by obvious spasticity, abnormally brisk tendon reflexes or reflexes of the Babinski group. Three patients started with a progressive bulbar palsy with gradual generalization of their muscle weakness. Twenty-five patients were examined ultrasonographically for the first time during their initial clinic admission. Nine patients were included in the study during follow-up visits.

The study was approved by the local ethical committee.

Methods

Clinical examination

The control subjects and patients were carefully visually screened for the presence and location of fasciculations by a neurologist not involved in the ultrasonographic and electromyographic examinations, first in the sitting, then lying in the supine and finally in the prone position. The duration of the clinical examination was on average 6–8 min.

Electromyography

Electromyography was performed exclusively in order to verify the clinical diagnosis of a degenerative LMND using a Nicolet Viking (Nicolet, Madison, Wis., USA) or Neuropack 2 (Nihon Kohden, Tokyo, Japan) electromyograph. The muscles included in the examination were determined, according to the clinical findings, by an experienced examiner who was not involved in the clinical and ultrasonographic investigations. The muscles were usually examined at only one or two sites with the concentric needle electrode inserted fanwise to register as many motor units as possible. According to our experience, this procedure is sufficiently sensitive for the detection of positive sharp waves and fibrillation potentials and large polyphasic motor unit action potentials, these being electrophysiological hallmarks of degenerative LMND. In each muscle, searching for fasciculations took at least 10 s, that is as long as for ultrasonography (see below). In 1 patient with a diagnosis proven by recent examinations, no follow-up electromyography was performed. In the remaining 33 patients, 3–11 (median: 8) limb muscles were examined. Electromyographic findings in facial, tongue and paravertebral muscles were not considered in the statistical evaluation as relaxation was often not adequate for assessing the presence or absence of fasciculations.

Ultrasonography

A real-time B-mode scanner with a 5-MHz electronic linear array transducer (Philips P700, Philips, Santa Ana, Calif., USA) was employed. The following muscles were regularly investigated bilaterally: when sitting, the deltoid, biceps and triceps brachii muscles; when lying supine the rectus abdominis, rectus femoris, vastus medialis, vastus intermedius, vastus lateralis, sartorius, and tibialis anterior muscles; and while lying prone the lumbar paraspinal, semitendinosus, gastrocnemius and soleus muscles. Undue pressure was not exerted on the imaged tissue. Each muscle was observed for at least 10 s in searching for spontaneous muscle movements. The presence of fasciculations was determined by several irregular movements of small parts of the muscle, lasting for about 0.2–0.5 s [9]. Arterial pulses were easily distinguished by their rhythmic appearance and their close topographical relation to blood vessels [9, 14]. Movements due to poor relaxation could also be differentiated from fasciculations as they – in contrast to fasciculations – result not only in contraction of the small parts of the muscle [14] and have a longer duration. We tried to avoid muscle shivering by ensuring a warm room temperature. If it was nevertheless present, it could be distinguished from fasciculations as it persisted for a longer period, involved several muscles, and was relatively regular. Finally, displacement of the transducer due to the examiner's movements is also more coarse than fasciculations. This could be avoided by propping up the arms.

Frequency of fasciculations

The time intervals between consecutive fasciculations within a single muscle (935 single fasciculations in 13 patients), i.e. the reciprocal of the number of twitchings per second (not necessarily belonging to a single motor unit), visualized on videotapes were analysed by means of a personal computer program, the occurrence of muscle twitchings being marked by pressing a key on a keyboard.

Inter-rater agreement

To assess the inter-rater agreement of the clinical examination, the numbers of fasciculating muscles determined by two investigators in 12 patients (260 muscles; considering only those 22 muscles which were examined both clinically and sonographically) were compared. Analogously, video recordings of the ultrasonographic examination of 13 patients (317 muscles) were judged by two examiners (C.D.R. and A.S.). The electromyographic findings in 9 patients (68 muscles) were assessed simultaneously and independently by two investigators.

Fasciculations are a typical sign in patients suffering with LMND. Our statistical evaluations are based on the assumption that each patient suffering from LMND presents with fasciculations, being aware that, at present, there is no reliable method to verify the absence of fasciculations. Methodological limitations of the current techniques are discussed below.

In order to prevent investigator bias, the examiners changed from patient to patient (clinical and electromyographic examination: C.D.R., P.R., U.Z.; ultrasonographic examination: C.D.R., A.S.).

Statistics

Numerical data were compared using the two-tailed Fisher's exact test. The specificity, sensitivity, accuracy, positive and negative predictive values were calculated according to the algorithms cited by Altman [1] and Metz [7]. The inter-rater agreement r was calculated using the phi/phi$_{max}$ quotient [2]. Comparisons of correlation coefficients were performed using the algorithms given by Bortz [2].

Results

Control group

Ultrasonography revealed fasciculations, probably so-called benign fasciculations, in 1–8 muscles in 3 of 40 subjects (8%) aged 21–49 years, and 7 of 30 subjects (23%) aged 50–80 years. The difference was not significant ($P = 0.09$). There was no significant correlation between age and the number of fasciculations, which were found predominantly in the calf (in 8 subjects) and semitendinosus (in 4 subjects) muscles. Fasciculations were manifest at clinical inspection in up to 5 muscles in the same persons. No fasciculations were detected in the arm, vastus medialis, sartorius and tibialis anterior muscles.

Patients

Fasciculations were detected during the clinical examination in 32 of 34 patients (94%), in 26 of 33 (79%) patients by electromyography, and in all patients by ultrasonography (100%). Thus, ultrasonography proved to be significantly more sensitive than electromyography ($P = 0.01$). The number of muscles showing fasciculations during ultrasonography ranged from 1 to 27 out of 28 muscles (median value: 17 muscles). The specificity, sensitivity, accuracy, positive and negative predictive values of the different methods, assuming that all patients with LMND really exhibit fasciculations, are listed in Table 1. If fasciculations in at least 9 muscles (more than in any control person) were considered as pathological with a specificity of 100%, the sensitivity of ultrasonography was then 28 of 34 (82%), the accuracy 98 of 104 (94%) (Fig. 1).

Table 1 Reliability of the clinical, electromyographic, and ultrasonographic search for fasciculations (70 controls, 34 patients; *PPV* positive predictive value, *NPV* negative predictive value)

Criterion	Methodological approach		Ultrasonography
	Inspection	Electromyography	
Specificity	86%	Not assessed[b]	86%
Sensitivity[a]	94%	79%	100%
Accuracy	88%		90%
PPV	76%		77%
NPV	97%		100%

[a] Assuming that every patient really exhibits fasciculations
[b] The control group was not examined electromyographically

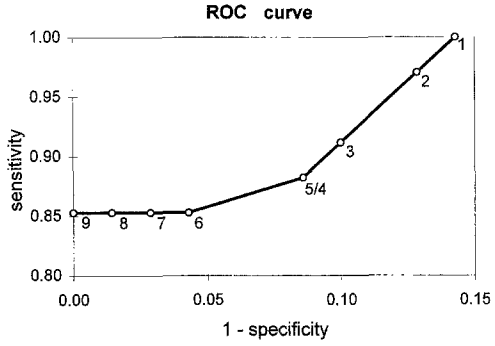

Fig. 1 Receiver operating characteristic (ROC) curve illustrating the dependency of sensitivity on specificity of ultrasonographic detection of fasciculations. Sensitivity and specificity were calculated for 1–9 muscles examined

In large muscles such as the quadriceps and calf muscles, the twitchings could be attributed to different sites of the muscles, indicating different generators.

Detailed muscle analysis

Considering only those muscles examined both clinically and ultrasonographically ($n = 732$), fasciculations were visible in 260 (36%) during clinical and in 446 (61%) muscles during ultrasonographic investigation ($P < 0.001$). Comparing those muscles which were examined clinically, electromyographically and ultrasonographically ($n = 163$), clinical examination revealed fasciculations in 69 (42%), electromyography in 63 (39%), and ultrasonography in 109 (67%) of the muscles under investigation. Vastus intermedius, sartorius and soleus muscles were not in-

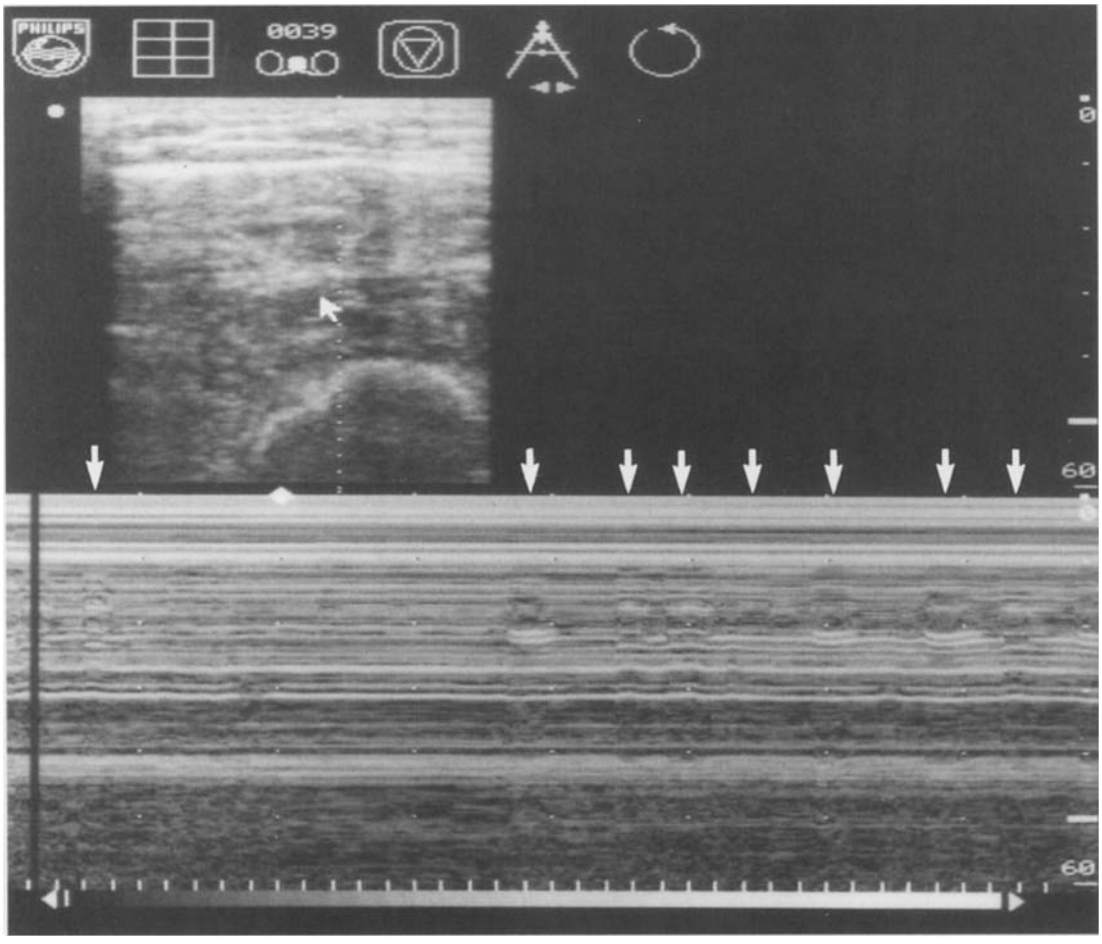

Fig. 2 B-mode (*upper section*) and M-mode ultrasonography of the right rectus femoris and vastus intermedius muscles in a patient with lower motor neuron disease: at least 8 short muscle twitchings (indicated by the *arrows*) within 8 s were recorded

cluded in the clinical assessment, as they cannot be identified by clinical inspection.

Thus ultrasonography was significantly more sensitive than clinical examination and electromyography ($P < 0.001$ each), whereas the sensitivity of the clinical and electromyographic examinations did not differ significantly.

The rectus femoris, vasti and semitendinosus muscles showed fasciculations most frequently in the ultrasonographic examination, at least 50 of 66 examined muscles each. Fasciculations were detected in only 14 rectus abdominis and 23 lumbar paraspinal muscles.

The ultrasonographic examination lasted for about 15 min. Videotapes proved to be the most convenient method for documenting the fasciculations. Another way to demonstrate the muscle twitchings was videoprints of M-mode recordings. This technique provides exact information about the frequency and duration of fasciculations in a small part of the muscle(s) depicted. However, the sites of the fasciculations usually remain obscure, since the discharges of the muscle fibres result in concomitant movements of the surrounding muscle bundles (Fig. 2).

Frequency of fasciculations

In consecutive fasciculations, regardless of their sites within the single muscle, 77% occurred with a frequency of more than 0.5 Hz (Fig. 3). The number of two consecutive fasciculations n (regardless of their origin) occurring within a time interval Δt [seconds] nearly met an exponential curve expressed by the formula $n = 315 * e^{-0.47\Delta t}$ ($r = 0.94$). There was no significant difference in the frequency of fasciculations in the different muscles.

Inter-rater agreement

The inter-rater agreement r was 0.71 for the clinical, 0.85 for the electromyographic and 0.84 for the ultrasonographic assessment of fasciculations. Electromyography and ultrasonography were significantly more reliable than

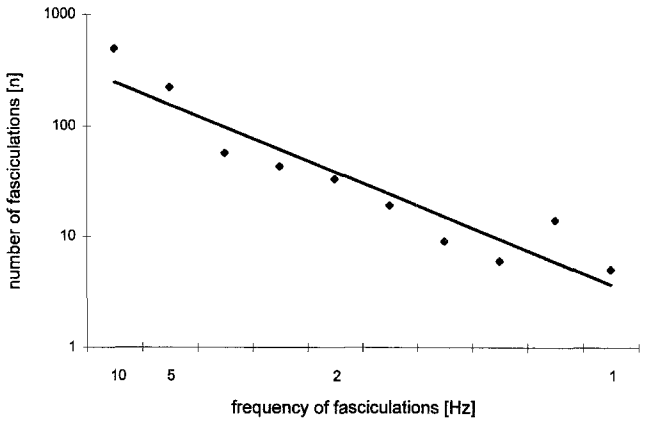

Fig. 3 Scatterplot diagram illustrating the number of consecutive fasciculations within a single muscle relative to the frequency of the discharges (regardless of their origin)

the clinical examination ($P < 0.01$ and $P < 0.001$, respectively).

Discussion

Our study shows that real-time ultrasonography is more sensitive in the detection of fasciculations than clinical examination and electromyography. Ultrasonography revealed fasciculations in 67% of the muscles under investigation, whereas clinical inspection and electromyography detected fasciculations in 42% and 39%, respectively. On the other hand, each of the patients presented with fasciculations that could be detected by ultrasonography in at least one muscle. This fact confirms our belief that fasciculations are an obligatory sign in patients suffering from LMND. Clinical inspection failed to detect fasciculations in 2, electromyography in 7 patients.

Walker et al. [14] reported one patient in whom needle electromyography of the tibialis anterior muscle revealed 6 fasciculations within 3 min, whereas ultrasound examination revealed 103 in the same time period. Probably the sensitivity of electromyography can be improved by additional needle insertions. However, the main purpose of needle electromyography in suspected neurogenic muscle diseases such as LMND is to demonstrate signs of denervation, reinnervation or both. This task can usually be fulfilled by a few and brief needle insertions. Thus, prolonged needle insertions to detect additional fasciculations result in considerable discomfort for the patient and seem unjustified. The sensitivity of clinical assessment is limited when fasciculations occur in deep-seated muscles or under thick layers of subcutaneous fat. The pick-up area of concentric needle electrodes is very small [5, 14]. Thus, muscle fibre twitches remote from the inserted needle may be missed by electromyography. B-mode ultrasonography, however, covers a broad volume of single or several muscles simultaneously. Different sites of twitching within a single muscle indicate different generators; however, fasciculations deriving from adjoining motor units cannot be distinguished. In this respect electromyography with needle and surface electrodes is advantageous, since individual potentials can be identified by their morphology. Ultrasound examination is not limited by subcutaneous fat. Thus its higher sensitivity can easily be explained. On the other hand, the specificity is somewhat lower than that of the clinical examination.

Hjorth et al. [4] found a sensitivity of 62% for clinical inspection and of 96% for surface electromyography, which was not performed in this study. Howard and Murray [5] also showed the superior sensitivity of surface electromyography as compared with clinical examination. However, the sensitivities were much lower than those reported by Hjorth et al. [4], namely 38% and 83%, respectively. The sensitivity of conventional needle electromyography was 42%. Continuous surface electromyography recordings were performed for 20 min. Neither study provided information about the frequency of fasciculations in normal controls.

Fasciculations are typical, but in no way pathognomonic, signs of diseases affecting the lower motor neuron, especially of anterior horn cell damage. Thus with localized muscle weakness and wasting, proof of widespread fasciculations is a strong indicator of a generalized disease. However, additional clinical or electromyographic evidence of widespread denervation is needed in order to be able to make a definite diagnosis. It is generally accepted that the electromyographic diagnosis of a degenerative LMND requires (1) proof of denervation in at least three locations of either limbs or head, (2) a reduced number and an increase in both amplitude and duration of motor unit action potentials, (3) normal electrical excitability of the surviving motor nerve fibres, (4) normal or only slightly reduced motor nerve conduction velocities in nerves of affected muscles, and (5) normal excitability and conduction velocity of sensory nerves [6, 11]. In the present study, 10 of our 70 control persons without symptoms or signs of diseases of the lower motor neuron presented with ultrasonographically visible muscle twitches, probably due to so-called benign fasciculations. Therefore care must be taken that benign fasciculations are not misinterpreted as hints of generalization of the suspected LMND.

The ultrasonographic depiction of fasciculations in at least 9 of 28 muscles (that is more than in any of the control persons) indicated that these muscles twitchings were not benign, but a sign of LMND. Using this cut-off, the sensitivity of ultrasonography was 82%, its specificity 100%, and its accuracy 94%. At this high level of specificity, the sensitivity of the clinical search for fasciculations is not significantly lower (62%). Fasciculations in special muscles such as arm, trunk, sartorius and tibialis anterior are of much higher diagnostic significance than

those detected in the quadriceps, calf and hamstring muscles.

In the present study, muscle twitching visualized by ultrasonography occurred with a wide range between less than 1 and more than 10 s. About three-quarters of the fasciculations occurred with a frequency of 0.5 Hz or more regardless of the origin of the discharges. Screening single muscles for 8 s provides a probability of 95% that no fasciculation is ignored. Trojaborg and Buchthal [12] reported that fasciculations in LMND appeared irregularly with an average interval of 3.5 s. Using surface electromyography, Hjorth et al. [4] reported the median value of the intervals between consecutive fasciculations to range between 4 and 5 s. By ultrasonography, Walker et al. [14] found fasciculations to occur within an interval of 0.5–4.0 s. The higher frequency of fasciculations seen on ultrasonography can be explained by the fact that electromyography covers only few motor units, whereas ultrasound examination depicts fasciculations generated by a much higher number of motor units. The distribution of the interdischarge intervals presented by Hjorth et al. [4] shows a marked similarity to ours (Fig. 2), even though electromyography detects only discharges of single or few motor units. Obviously, the experimental data can best be represented by a graph according to a negative exponential function.

Finally, Howard and Murray [5] reported that surface electromyography revealed discharge intervals of individual units between less than 1 s and more than 1 min. The higher frequency of the twitchings detected by ultrasonography compared with needle electromyography may be explained by the much larger volume of the muscles screened by the former.

In summary, this appears to be the first systematic comparative study of the search for fasciculations using clinical inspection, conventional needle electromyography and ultrasonography. The results indicate that ultrasonography and electromyography have the same interrater reliability, whereas clinical examination is less reliable. Ultrasonography is a rapid as well as a more sensitive technique than clinical examination and electromyography for the visualization of fasciculations, at least in LMND. However, a small number of (benign) fasciculations can also be detected in healthy persons. Eight seconds are sufficient for ultrasonographic screening for fasciculations in every single muscle. Our data do not exclude the possibility that other, non-degenerative diseases of the lower motor neuron result in a similar number of fasciculations detectable by real-time ultrasonography. Thus, the ultrasound findings should be interpreted only in the context of the clinical, electroneurographic, electromyographic, neuroimaging and cerebrospinal fluid findings.

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