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CHANGES IN MUSCLE MORPHOLOGY, STRENGTH AND ENZYMES IN A 4–5-YEAR FOLLOW-UP OF SUBJECTS WITH POLIOMYELITIS SEQUELAE

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ABSTRACT. Twenty subjects with polio sequelae were studied on two occasions 4–5 years apart by means of dynamometer measurements of knee-extension and flexion strength and muscle biopsy for histochemical and enzymatic analyses. The subjects were divided into those who reported (unstable, $n = 12$) and did not report (stable, $n = 8$) new or increased muscle weakness in the tested leg between the two examinations. Muscle strength decreased significantly in the unstable subjects, but only for knee-flexion in the stable subjects. However, the endurance test comprising 50 consecutive knee-extensions at 180°/sec showed increased fatigability at the second examination only in the stable subjects. Most subjects had markedly increased muscle fiber areas, which in some subjects increased further, but in those already with very extreme hypertrophy the fiber size decreased. Capillarization and activity of citrate-synthase were decreased at the initial examination, but no significant further reduction was observed at the second examination. The results demonstrate individual patterns in the compensatory process for the presumed loss of motor units.

Key words: post-polio syndrome, muscle strength, muscle morphology, capillarization, muscle enzymes, adaptive processes.

Subjects with poliomyelitis sequelae (late polio) are characterized by structural and functional muscular changes, which are main factors in the development of new symptoms such as joint pain, muscle weakness, and fatigue, defined as the post-polio syndrome (15).

In the literature, however, there are only few long-term data on the post-polio syndrome. Dalakas et al. (8) reported a follow-up in 27 patients after an average of 8.2 years, with biopsy data in 8 of the patients and without any systematic comparison of the repeated biopsies. They summarized their findings as presence of reinnervation of both type I and II fibers, new active denervation, indicated by isolated atrophic angular fibers, but no group atrophy. The rate of decline in muscle strength was 1% per year, but that estimate was based on "points" from manual muscle testing and not on a linear scale using quantitative measurements. Agre et al. (2) recently reported that symptomatic post-polio subjects do not lose neuromuscular function to any significant extent in one year. Munin and coworkers (21) found no change in strength in 7 patients with late polio followed for 3 years. Munsat et al. (22) reported that the muscle strength of 6 post-polio patients with complaints of progressive loss of neuromuscular function varied greatly as shown by dynamometer measurements during a period of 400–2,100 days, but without a systemic change with time.

We have previously reported functional compensation in patients with late polio showing a combination of very large motor units (10) and muscle fiber hypertrophy (12). In the present study, we were able to demonstrate different individual patterns in muscle strength and morphological changes over a 4–5-year period and further elucidate the extreme muscle fiber hypertrophy previously described. As preliminarily reported (13) there was also evidence of on-going denervation/reinnervation, resulting in still larger motor-units in most polio subjects.

MATERIAL AND METHODS

Study group

Of the original groups of 39 subjects with poliomyelitis sequelae studied previously (11,12), 20 subjects (10 men and 10 women) could be re-examined with muscle biopsies 4–5 years later. Of the remaining subjects, one had died, one had developed a non-polio-related serious disease, one had moved and 9 did not agree to a new biopsy. The biopsy did not provide adequate material for histochemical analysis in 7 of the subjects, especially in some subjects with severe atrophic muscles.

patterns, as demonstrated in the present study, and depend both on muscle fiber hypertrophy and reinnervation by collateral sprouting. In a subsequent paper (preliminarily reported in ref. [13]) it will be demonstrated that most subjects, unstable as well as stable, show signs of an ongoing reinnervation/denervation with an increase in number of muscle fibers within the motor units. However, there is also indirect evidence of quite a large reduction in the number of motor units during the observation period. Why certain subjects can still use compensatory processes fully and others cannot is still unclear, but there may be some upper limits for muscle fiber hypertrophy as well as reinnervation. The upper limit for hypertrophy may well be reached before that of reinnervation.

The hypertrophic fibers have been interpreted to be the result of extreme use of remaining motor units in weight-bearing activities (12), which is also evident in the anterior tibialis muscle in still mobile subjects with motor unit overuse (4). In the present study the subjects being reexamined after 4–5 years, those with the largest muscle fibers in the vastus lateralis muscle showed a reduction in muscle fibre area, although those areas remained far beyond the normal range in several cases. The question then arises whether they had reached an optimal size for maintained fiber hypertrophy, a suggestion already made on the basis of a high-resistance training study in post-polio subjects, in which the 2 subjects with the highest fiber areas showed a reduction (9). It might be that muscle fibers which hypertrophy, when exposed to a high degree of resistance, either split or start to hypotrophy after reaching a certain size. However, splitting was only seen in a few fibers in half of the subjects. There may also in a few subjects have been major changes in the physical activity pattern with reduced resistance load, which caused the decrease in fiber size exemplified below. Reduction in fiber size could be seen as well as type I as in type II fibers. Other subjects, on the other hand, showed an increase in fiber size during the follow-up period. This finding can be interpreted as on-going compensation, although no functionally complete, for the continuous loss of muscle fibers, which is assumed from electrophysiological and histopathological data (10,13). The on-going process of denervation and reinnervation in the muscles affected by polio is indicated by increased jitter, blocking, high fiber density and further increase in the large macro motor unit potentials (13), which already initially were 7.5 times larger than in the reference population (10). It might then have been assumed that an increasing frequency of atrophic muscle fibers would be noted in the biopsies. This was not the case, the main explanation being the relatively slow process and the fact that some atrophic fibers had already been recorded in the previous examination. It should be pointed out that a large variation in fiber size was noted both at the first and at the second examination, as illustrated in the case reports with large recorded quartile ranges (Fig. 4).

As has been previously reported (7,10), it has not yet been possible to distinguish between stable patients with prior poliomyelitis and those with new weakness from electromyographic or muscle biopsy findings. No clear distinctions were brought out in the present study either, since subjects with new or increased muscle weakness and those without new symptoms could not be clearly separated with respect to changes in fiber areas (Figs. 3 and 5). However, if functional deterioration causes a subject to change his activity pattern markedly, such as changing from walking to using a wheelchair, further loss of strength and fiber areas can be assumed, since the daily resistance training in weight-bearing activities ceases. In the present study, this is illustrated in the subject with the largest decrease in the area of type I fibers (from a median value of 12.7 to 3.4 $\mu m^2 \times 10^3$) and also in type II fibers (from 7.9 to 6.4 $\mu m^2 \times 10^3$) (patient no. 1018 in Fig. 4D, see also Fig. 5B). It should also be noted that the variation coefficients for fiber areas were very large, specially at the first examination (type I 61%, type II 72%, compared to an average of 38% and 47% respectively, for the whole group), probably indicating on-going changes in fiber size. This patient's muscle strength was reduced by 30–40% during the same period, as evident from the dynamometer readings, and he had used his wheelchair more or less constantly during the last 2 years.

Some evidence of reduced capillarization was noted at the first examination, a finding similar to that reported from the anterior tibial muscle (5) and an overall reduction in the concentration of an oxidative enzyme, citrate synthase (12), was also seen. Some subjects with rather normal values showed reduction in the enzymatic activity values during the observation period, which might be due to some reduced level of physical activity during that

period. Several factors may contribute to the complaints of muscle fatigue; reduced capillarization and oxidative enzyme activities are possible explanations. The increased fatigability in the endurance test in the stable, but not in the unstable, subjects points to divergent patterns for the increase in muscle weakness and in fatigue. Unfortunately, the number of subjects with biopsies for enzyme measurements was too low to allow separate analyses to be made for unstable and stable patients, and measurements of capillarization gave no conclusive evidence of changes over time.

Further studies, including long-term follow-up, will elucidate positive and negative effects of the functional compensatory processes in the post-polio state. Such information will also be of interest for other conditions in which there is a successive reduction in the number of motor units, such as motor neuron disease and ageing, and will provide basic knowledge of biological processes in primary non-myopathic muscle fibres subjected to stress.

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