Scand J Rehab Med, Suppl 30: 33-44, 1994

DYNAMIC CHANGES IN MUSCLE STRUCTURE AND ELECTROPHYSIOLOGY IN LATE POLIO WITH ASPECTS ON MUSCULAR TRAINABILITY

Gunnar Grimby, M.D.[1] and Erik Stålberg, M.D.[2]

From the [1]Department of Rehabilitation Medicine, Göteborg University and [2]Department of Clinical Neurophysiology, University of Uppsala, Sweden

INTRODUCTION

The muscular impairment in patients with a history of polio varies from none to severe. The relationship between the degree of initial involvement and the effect of various compensatory mechanisms determines the clinical picture that changes dynamically. Early and late recovery after *poliomyelitis* is due to a number of factors. Clinical improvement that appears within a *few weeks* after the acute phase is probably due to recovery in the excitability of functionally, but not degenerated, motor neurons. Degeneration of neurons, causing peripheral denervation is compensated by collateral sprouting, i.e. by nerve twigs branching off from surviving motor units overlapping with the denervated ones. This is most likely the main factor explaining recovery within the first *6-12 months*. Another late compensatory process is the increase in size of the muscle fibres. As a result of these processes, normal muscle strength and presumably normal muscle volume can be seen in spite of a calculated loss exceeding 50% of the number of motor neurons.

Besides the need for a certain muscle volume and, thus, potential for force development, the metabolic adaptation to endurance activity is also a key issue. It is well-known that capillarization and the activity of mitochondrial enzymes adapt to a level dependent on the physical activity (3, 15). With immobilization or reduced physical activity, these factors, of basic importance for aerobic capacity and, thus, performance in endurance activities, are reduced. Polio patients with low general physical activity, may have reduced aerobic muscle capacity in combination with marked muscle fibre hypertrophy, demonstrating different adaptation patterns for endurance and resistance activities.

In this paper, we will first describe the basic morphological and electrophysiological adaptation with respect to muscle function and then review the changes, which can be seen over time in persons with polio sequelae. By combining data on muscle

strength, muscle structure and electrophysiological recordings of the size of the motor units, further insight will be obtained on these compensatory processes. Aspects will also be given on the trainability of muscle function.

MUSCLE STRENGTH

For strength measurements, the reader should be reminded of the need for objective measurements of muscle strength in polio patients, either by special dynamometers, such as Cybex (11), Kin-Com (12) and Lido (l), or by hand-held manual measuring devices, such as Myometer (10). Good reliability of repeated dynamometer measurements of knee-muscles has been reported by Kilfoil & St. Pierre (16) and Grimby et al. (12). Manual muscle testing will not give reliable information in muscles with strength levels of fair (being able to move the extremity against gravity) or above, as shown already in the 1960s by Beasly (4). Isometric measurements are usually quite adequate, as isometeric and isokinetic strength values correlate significantly (9) and change in parallel over time (13).

Muscle strength can be reduced by various degrees and obviously quite differently in different muscle groups depending on the distribution of the original polio involvement. Whether the dynamics of the compensatory processes differ between muscle groups has, however, not been studied. The stimulus for muscle fibre hypertrophy may vary between muscle groups depending on their activity pattern.

It is possible to demonstrate a relationship between perception of new or increased muscle weakness and measurements of reduction in muscle strength. In follow-up studies of subjects with poliomyelitis sequelae, it has been possible to demonstrate significant reduction in muscle strength in those who acknowledge new weakness but not in those who did not acknowledge new muscular weakness (10, 11). Thus, in a group of 44 Swedish subjects (13) a 9% ($p < 0.01$) reduction in strength for knee-extension at 60°/s angular velocity during a four to five year period was demonstrated. When the material was divided into two groups, the strength reduction was significant (16%, $p < 0.01$) only among those that reported new muscle weakness. As a comparison, the normal age-dependent reduction in muscle strength in the age-ranges of 30-70 years (mean age 53) can be estimated to be around 2-5% during a similar time period, thus not more than about 1% per year (6, 17).

In the following presentation we will use the terms unstable and stable muscle function for those who acknowledge and do not acknowledge, respectively, new or increased muscle weakness in the tested extremity. Such a division is better than

using the postpolio syndrome classification in studies comparing various muscle parameters.

MUSCLE STRUCTURE

Markedly increased muscle fibre areas are seen in the polio-affected muscles (5, 11), providing muscle strength is only slightly reduced and the muscle not severely atrophic. According to the report by Grimby and coworkers (11) on the vastus lateralis muscle, mean fibre area was 8 $\mu m^2 \times 10^3$ in the post-polio muscles compared to 4.4 and 4.1 $\mu m^2 \times 10^3$ for men and women respectively in the control groups. There was an increase in type I as well as type 11 fibres, but a somewhat lesser increase in type IIB fibres. Similar results were found by Borg and coworkers (5) in the tibialis anterior muscle in polio subjects who were excessive users as defined from EMG.

In a four- to five-year follow-up study, no systematic changes in mean muscle fibre area could be seen, but when analysing the changes in individual polio subjects certain patterns were noted (12). Subjects who acknowledged increased muscle weakness (unstable) did not, as a group, show a significant reduction in muscle fibre area. However, some subjects who had average fibre areas close to three times the control values at the first study showed a reduction in size during the follow-up period usually combined with a decrease in muscle strength, but proportionally less. Other subjects, on the other hand (stable as well as unstable), showed further increase in fibre size during the follow-up period. These findings illustrate the dynamic process, where increased use of remaining motor unit due to the parallel loss of motor neurons can be a stimulus for fibre hypertrophy, but also indicate that an optimal size for fibre hypertrophy may be reached. The reduction in size of these very large muscle fibres may be caused by several factors, such as basic biological mechanisms leading to reduced capacity to maintain fibre hypertrophy or fibre size reduction due to disuse.

NEUROPHYSIOLOGICAL METHODS

Single fibre EMG (SFEMG)

The method is described in detail elsewhere (22). Two parameters are usually measured. One is *fibre density,* a measure of the number of muscle fibres of a motor unit within a hemisphere with a radius of about 300 μm from the small recording electrode. This measure increases with changes in the topography of muscle fibres within the motor unit, typically in cases of reinnervation.

The other parameter is *neuromuscular jitter*, an indicator of neuromuscular transmission. When neuromuscular transmission is disturbed, e.g. in myasthenia gravis, the jitter is increased. With more pronounced disturbance, there is also occasional impulse blockings due to impulse failure. Jitter, however, is also increased in conditions with on-going reinnervation. This is usually due to immaturity of nerve endings and neuromuscular junctions. There may be both pre- and postsynaptic reasons. Increased jitter and intermittent neuromuscular blocking are seen in some of the recordings from polio patients, but blocking to such a low degree that neuromuscular failure could only explain part of the muscular symptoms.

Concentric or monopolar electrode EMG (conventional EMG)

This is the most commonly used EMG technique. In the normal muscle no activity should be recorded. Denervated muscle fibres, not yet reinnervated, usually discharge spontaneously, and so- called fibrillation potentials and positive waves are recorded. These are often signs of recent denervation.

Motor unit potentials (MUPs) obtained during weak voluntary activation are studied regarding various shape parameters. Long duration and high amplitude MUPs reflect reinnervation and are typical of a neurogenic disease. In cases of a neurogenic condition with loss of some motor units and reinnervation of others, the pattern during maximal contraction will show higher amplitudes of the peaks and over-all a less dense signal than in the normal muscle.

In every patient with polio, at least some muscles show neurogenic changes on EMG, i.e. MUPs with long duration and high amplitudes. If no neurogenic changes are seen in any muscles in a patient with a history of polio, the diagnosis should be questioned. It should be noted that such changes are often found even in muscles that are clinically normal regarding strength and volume. By complete reinnervation a full functional restoration can be achieved.

In some muscles denervation activity is seen, usually as fibrillation potentials. This is often due to denervation after recent loss of neurons as an effect of age. Sometimes this finding may be due to local reasons such as radiculopathy or nerve entrapment unrelated to polio (not uncommon in non-polio patients) or is due to unfavourable situations related to sequelae of polio.

Macro EMG

Macro EMG is a method described in detail elsewhere (19, 22). A modified SFEMG electrode is used to study the total electrical strength of a motor unit. The amplitude of the obtained signal comprises the number and size of muscle fibres in one motor unit.

ELECTROMYOGRAPHIC FINDINGS

In a recent study (20) of 18 patients with two examinations 4 years apart, Macro EMG from the vastus lateralis muscle was used to quantify muscle changes. Muscle biopsies were taken in this muscle and maximal isokinetic and isometric torque measurements of knee extension were performed. The results are briefly summarised as follows: At the initial evaluation, the Macro MUP amplitudes were increased, compared to age-matched controls, at first investigation by 10 times in the stable group and by 16 times in the unstable group, an intergroup difference which is significant ($p < 0.01$). There was no correlation between EMG findings and strength values during the initial examination. Four years later, the strength was unchanged in the stable, but decreased in the unstable as described above, while the Macro MUP amplitude had increased by 67% and 35% in the stable and unstable group, respectively. This increase could not be explained by a change in fibre area, which on an average was unchanged.

In two other Macro EMG studies, no increase over time was demonstrated. In one of them (24), this conclusion was based on the lack of correlation between Macro EMG size and time from acute polio, although the possibility of changes with time was not excluded. In the other study (18), the two examinations were performed only one year apart with no consistent change in Macro MUP.

MUSCLE TRAINING

With the background of the very marked compensatory changes, the question arises whether muscle training can further improve muscle function. Two training studies in post-polio subjects have been performed in our research group.

In the first study (8), 12 post-polio subjects (age 43-63 years) participated. All were walkers, most of them used a cane either regularly or occasionally. The average quadriceps strength was 50% of control values before training. Their average muscle fibre area in the vastus lateralis muscle was about 2 times control values. Nine of the subjects reported a post-polio syndrome with reduced function 2-15 years before the study. The high resistance training programme for knee-extension, consisting of 12 x

8 maximal isokinetic contractions at 180°/sec and 12 x 4 sec maximal isometric contractions, was performed 3 times per week for 6 weeks. Knee-extension muscle strength increased significantly (24-29%), whereas there was no increase of the strength of the untrained knee-flexors. The strength increase was maintained 6-12 months after training. Muscle biopsy from the vastus lateralis did not show any significant further increase in the area of the already large muscle fibres. No new histopathological changes, to indicate deleterious effects of the training, could be noted.

In the second training study (10), a more comprehensive programme was used with resistance as well as endurance activities and performed as group activity. The resistance training was submaximal using body or extremity gravity as resistance. Twelve polio subjects (age 39-50 years) participated, 8 of them reporting post-polio syndrome decline in function. Training took part two times a week for approximately 6 months. It consisted of warming-up light exercises, walking (running), bicycling, submaximal resistance exercises with different muscle groups and stretching exercises. Some home-programmes were also given. Muscle strength increased in some but not all muscle groups. There was also an increase in the maximal work load on a bicycle ergometer and lower heart rate at a submaximal work load after training as an indication of an increased endurance. Also endurance for repetitive knee-extensions increased. However, muscle fibre area or the total cross-sectional area of the thigh muscle did not change significantly with training in the total group.

When combining the results from both these studies it was possible to demonstrate an increase in the muscle fibre area with training. A significant correlation was found between the percentage changes in muscle strength and in mean fibre area with training ($r=0.62$, $p<0.05$), with two subjects demonstrating reduction in strength as well as in fibre area after training. A proportionately larger increase was noted in average mean fibre area than in strength and could be due to several factors, such as reduced contractile properties in the large reinnervated muscle fibres, simultaneous loss of muscle fibres without sufficient reinnervation, and uneven distribution of the size of the muscle fibres.

Training may, thus, be advantageous, except in situations where the muscle already has been overused. There may also be muscles within a synergistic group, which are less trained than other muscles in that group, that will particularly benefit from a training programme. The experiences gained in the post-polio studies are to a large extent relevant also for other neurogenic lesions of the motor unit and where the interaction between the spontaneous compensatory process and any effect of a training programme should be taken into consideration.

The adaptation for endurance muscle activities is probably reduced in many polio survivors, as indicated from low values for muscle oxidative enzymes (5, 11, 12) and capillarization (5, 12) and also from indications of limitations in aerobic capacity due to "peripheral" (muscular) factors (19). One reason behind a relatively reduced capacity for endurance muscle activity could be that due to the reduced muscle strength, activities are often performed near its maximal limit and only for a very short period, as standing up from a chair or climbing stairs. This will allow for enough force development to stimulate synthesis of muscle contractile proteins and muscle fibre hypertrophy, but does not give enough stimulus for an increased mitochondrial activity or capillarization. By a training programme including endurance activities, it was possible to demonstrate an increased performance for repeated knee-extension with maximal voluntary effort (10). Further studies are needed to analyze the trainability and optimal muscle endurance adaptation in polio subjects with different type and degree of muscle impairment and various types of training programmes. There is also need for pacing daily activities by using appropriate exercise duration and intensity and to utilize the benefit of short pauses (2).

GENERAL DISCUSSION

The dynamics of *late changes* after polio will be summarized briefly.

Fibre size

Muscle fibre hypertrophy seems to be a characteristic feature of the muscles in these patients. The upper limit for this compensatory factor is probably reached earlier than that for reinnervation. This is indicated by the fact that during the four-year follow-up period there was no further average increase in muscle fibre area in the studied group, while the size of the motor unit due to reinnervation continued to increase. Muscle fibre size depends on muscle activity as already discussed, but also influences muscle strength. Thus, increased activity of motor units as a consequence of the reduction in number in motor units may be a stimulus for muscle fibre hypertrophy. In that way, muscle strength will be better maintained than it would have been without utilization of this compensatory process. It seems possible to further increase the muscle fibre size by resistance training. However, there is an upper limit also for the fibre hypertrophy, where fibres do not react with protein synthesis or start to split.

Reinnervation

As seen from our Macro EMG studies, there is an on-going denervation/reinnervation years after the acute stage. The motor units will successively contain increasing numbers of muscle fibres, to a great extent reflecting the degree of reinnervation. Collateral sprouting is highly effective as a compensatory mechanism after denervation. In patients with acute polio more than 20 years ago, the motor unit size due to reinnervation is often 10-15 times the normal size. Even after this time reinnervation takes place as a compensation for continuous loss of motor neurons.

There was no correlation between strength and Macro MUP amplitudes in our study (20). Such a correlation was reported, however, in another study of 10 patients with L5 rhizopathy or history of polio (23). Lack of these correlations is, however, not surprising. Strength depends on the varying combinations of the number of motor units, fibre size, and the number of muscle fibres. Furthermore, the contractile properties of reinnervating motor units may be abnormal with less mechanical output for a given electrical signal (7). Extramuscular factors, such as joints and connective tissue, may also play a functional role influencing, for example, the degree of maximal muscle activation and force output. The disturbed neuromuscular transmission, typical of reinnervation, could influence the functional output, as earlier reported (24), although this was not an important factor in our study.

Decompensation

Decompensation of the muscle changes in late polio occurs during life due to two phenomena. One is the reversion of the factors discussed above. With decreased daily activity and less training, decompensation related to muscle fibre size and oxidative metabolism will occur. The other factor is the continuous loss of motor neurones indicated by the increase in Macro EMG. When this compensatory mechanism is utilised more or less completely, further neuronal loss leads to a functional impairment that is proportional to reduction in neurones.

The reinnervation is limited both by central and peripheral factors. The peripheral factors set the limit when a denervated motor unit is no longer overlapping with other motor units, i.e. when all muscle fibres within certain fascicles belong to one motor unit due to previous reinnervation cycles. Overlapping with another motor unit is a prerequisite for reinnervation.

The central factors are related to the status of the motor neuron. In post polio subjects the number of muscle fibres losing their innervation with the degeneration of each anterior horn cell is much larger than typically occurs with normal aging where

the motor units usually are only slightly increased in size. This implies a greater strain on reinnervation mechanisms when patients with earlier enlarged motor units suffer additional loss of neurons. Furthermore, the physiological aging process may be exaggerated due to increased demands on the remaining reduced motor neuron pool. For every movement involving weak muscles, a larger portion of the motor neuron pool is utilised to produce the necessary force. In addition, mechanical strains occurring with reduced muscle mass may damage the muscle at myofibrillar level. Negative effects of training in polio subjects have been discussed, but have not been clearly demonstrated. In our training studies we noticed only in a few cases lack of positive training effects (8), which could be due to overexertion of polio-affected muscles.

Combination of factors

Although some statistical characteristics could be found to separate the stable and unstable group, none of the measured morphological parameters, strength or neurophysiological findings could be used to predict post polio syndrome (PPS as defined by Halstead & Rossi) (14) in the individual patient. Most EMG studies have failed to depict EMG changes that may be used to diagnose or predict PPS (9, 24). Even in studies where functional tests concern individual muscles, the EMG changes may be similar in patients with unstable and stable muscle function.

Thus, muscle strength in post polio patients reflects the dynamic changes in degeneration, compensation, and decompensation. The progressive enlargement of Macro EMG signals, as a compensatory response to loss of neurones, is only one factor in the dynamic change in muscular strength, since the change in strength is the combined effect of the number of available motor neurones, number and size of muscle fibres in each motor unit, neuromuscular transmission and the mechanical properties of reinnervated muscle fibres. There are a number of possible combinations of denervation-reinnervation and strength that make interpretation of their relationship difficult. (a) If there is a loss of functioning motor units, not leading to axonal degeneration and therefore not reinnervation, the Macro EMG will not change while strength decreases. This stage of inexcitable neurones may be seen in the acute phase of polio but probably not later in life. (b) If reinnervation is successful, but the strength developed by each individual motor unit is decreased compared to normal motor units, Macro MUP amplitude increases but strength will still be maintained. It has been demonstrated that reinnervated motor units in ALS are weaker than expected from their electrical size as measured with Macro EMG (7), and our patients may show a similar situation. (d) Finally, and probably most importantly, reinnervation may compensate

for new denervation until a maximal capacity for reinnervation is reached. After this stage, additional loss of motor units cannot be compensated. A continued loss of motor units will then present clinically as a new or accelerating decrease in strength and activity level over time and may, as a result, also be combined with reduced stimulus to maintain the marked fibre hypertrophy. Individual assessments are necessary to evaluate whether such muscles may benefit from resistance and/or endurance type of training programme. It seems sometimes appropriate to try resistance training with moderate to heavy intensities for a short period and with careful monitoring of muscle function in order to evaluate the trainability and, if possible, achieve improved ability to participate in endurance activities. We summarize in Table I our present suggestions concerning use of muscle training in polio subjects with different levels of muscular impairments.

Table I. *Schematic aspects on trainability in poliomyelitis sequelae*

Polio category	Muscle strength	Muscle endurance	Motor unit size	Muscle fibre size	Training
Stable	Normal	Normal or -	+	(+)	Strength and endurance training witbhout restrictions
Stable	-	-	++	+	Short period of strength training, regular endurance training
Unstable	-	-	+++	++	Submaximal resistance and endurance training with careful monitoring
Unstable	--	--	+++	+++	As above with low intensity. Pacing at daily activities
Severe atrophy	---	Not measurable	+++	-	No training

ACKNOWLEDGEMENT

Three studies were supported by grants from the Swedish Medical Research Council (project no 3888, GG, and no 135 ES) and the King Gustaf Vth 80th Birthday Foundation.

REFERENCES

1. Agre, J.C. & Rodriguez, A.A.: Neuromuscular function in polio survivors at one-year follow-up. Arch Phys Med Rehabil 72: 7-10, 1991.
2. Agre, J.C., Rodriquez, A.A. & Tafel, J.A.: Late effects of polio: critical review on neuromuscular function. Arch Phys Med Rehabil 72: 923-931, 1991.
3. Andersen, P. & Henriksson, J.: Capillary supply of the quadriceps femoris muscle of man: adaptive response to exercise. J Physiol (Lond) 270: 677-690, 1977.
4. Beasley, W.C.: Quantitative muscle testing: principles and applications for research and clinical services. Arch Phys Med Rehabil 42: 398-425, 1961.
5. Borg, K., Borg, J., Edström, L. & Grimby, L.: Effects of excessive use of remaining muscle fibers in prior polio and LV lesion. Muscle Nerve 11: 1219-1230, 1988.
6. Borges, O.: Isometric and isokinetic knee-extension and flexion torque in men and women aged 20-70. Scand J Rehab Med 16: 45-53, 1989.
7. Dengler, R., Konstanzer, A., et al.: Amyotrophic lateral sclerosis: macro-EMG and twitch forces of single motor units. Muscle Nerve 13: 545-550, 1990.
8. Einarsson, G.: Muscle conditioning in late poliomyelitis. Arch Phys Med Rehabil 72: 11-14, 1991.
9. Einarsson, G., Grimby, G. & Stålberg, E.: Electromyographic and morphological functional compensation in late poliomyelitis. Muscle Nerve 13: 165-171, 1990.
10. Ernstoff, B., Wetterqvist, H., Kvist, H. & Grimby, G.: The effects of endurance training on individuals with post-poliomyelitis. Arch Phys Med Rehabil, submitted.
11. Grimby, G., Einarsson, G., Hedberg, M. & Aniansson, A.: Muscle adaptive changes in post-polio subjects. Scand J Rehab Med 21: 19-26, 1989.
12. Grimby, G., Hedberg, M. & Henning, G.-B.: Changes in muscle morphology, strength and enzymes in a 4–5-year follow-up of subjects with poliomyelitis sequelae. Scand J Rehab Med 26: 121-130, 1994.
13. Grimby, G. & Thoren-Jönsson, A.-L.: Disability in poliomyelitis sequelae. Phys Ther 74: 415-424, 1994.
14. Halstead, L.S. & Rossi, C.D.: Post-polio syndrome: clinical experience with 132 consecutive outpatients. In: Research and clinical aspects of the late effects of poliomyelitis. Birth Defects: Original series, vol 27, no 4, pp. 13-16. March of Dimes, White Plains, NY, 1987.

15. Henriksson, J. & Reitman, J.S.: Time course of changes in human skeletal muscle succinate dehydrogenase and cytochrome oxidase activities and maximal oxygen uptake with physical activity and inactivity. Acta Physiol Scand 99: 91-97, 1977.

16. Kilfoil, M. & St. Pierre, D.M.M.: Reliability of Cybex II isokinetic evaluations of torque in post-poliomyelitis syndrome. Arch Phys Med Rehabil 74: 730-735, 1993.

17. Larsson, L., Grimby, G. & Karlsson, J.: Muscle strength and speed of movement in relation to age and muscle morphology. J Appl Physiol 46: 271-281, 1979.

18. Ravits, J., Hallet, M., et al.: Clinical and electromyographic studies of postpoliomyelitis muscular atrophy. Muscle Nerve 13: 667-674, 1990.

19. Stanghelle, J.K,, Festvåg, L. & Aksnes, A.K.: Pulmonary function and symptom-limited exercise stress testing in subjects with late sequelae of poliomyelitis. Scand J Rehab Med 25: 125-129, 1993.

20. Stålberg, E.: MACRO EMG, a new recording technique. JNNP 43: 475-482, 1980.

21. Stålberg, E. & Grimby, G.: Dynamic electromyography and biopsy changes in a 4-year follow-up study of patients with a history of polio. Muscle Nerve, in press 1994.

22. Stålberg, E. & Trontelj, J.V.: *Single Fiber Electromyography.* Studies in Healthy and Diseased Muscles, pp 1-336. Raven Press, New York, 1979.

23. Tollbäck, A., Borg, J. & Knutsson, E.: Isokinetic strength, Macro EMG and muscle biopsy of paretic foot dorsiflexors in chronic neurogenic paresis. Scand J Rehab Med 25: 183-187, 1993.

24. Wiechers, D.O. & Hubbel, S.L.: Late changes in the motor unit after acute poliomyelitis. Muscle Nerve 4: 524-528, 1981.

Address:

Gunnar Grimby, M.D.

Department of Rehabilitation Medicine

Sahlgrenska University Hospital

S-413 45 Göteborg, Sweden