

Neuromuscular Research in Czechoslovakia

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This survey is intended to provide some basic information about the main trends of Czechoslovak neuromuscular research in the last four decades. Further particulars concerning excitation-contraction coupling and muscle mechanics are to be found in the contribution by J. Poledna and about acetylcholine synthesis and release at the neuromuscular junction by S. Tuček of this issue.

A. Neuromuscular Transmission

Extensive work has been done in the field of acetylcholine release at the mammalian neuromuscular junction and its regulation. Work in this field was first initiated by R. Beránek and after his premature death in 1969, had successfully been taken over by Vyskočil, Zemková-Dlouhá and a number of other collaborators. Their contribution includes crucial findings concerning the following main topics:

a) The frequency of quantally released acetylcholine was found to decrease with age (Gutmann *et al.* 1971a), is dramatically reduced in hibernators (Vyskočil *et al.* 1971) and is diminished under the influence of prostaglandins (E_1) (Illés and Vyskočil 1978). On the contrary, it is enhanced in the androgen-dependent levator ani muscle of castrated male rats after administration of testosterone (Vyskočil and Gutmann 1977).

b) A series of important papers concerned the phenomenon of non-quantal release of acetylcholine at the neuromuscular junction of the murine and rat diaphragm. This non-quantal acetylcholine release induces membrane depolarization after cholinesterase blockade, which can be demonstrated as a hyperpolarization following receptor blockade with curare, alpha-bungarotoxin or in the course of postsynaptic receptor desensitization (Vyskočil and Illés 1977). The ionic selectivity of postsynaptic acetylcholine receptors is the same in case of non-quantal and quantal acetylcholine release. Both types of release respond in an analogous manner to vesamicol, quinacrine and tetraphenylborate. Together with other data these findings support the original hypothesis of this group that the non-quantal release is the consequence of incorporation of acetylcholine carriers from the vesicular membrane into the nerve ending membrane during exocytosis (Edwards *et al.* 1985).

c) It is being postulated that the physiological significance of non-quantal release of acetylcholine concerns the activation of membrane Na^+,K^+ -ATPase in mature muscles (Dlouhá *et al.* 1979) and that it may play a role in the depolarization of myotubes thus stabilizing the agglomeration of acetylcholine receptors. It was

also shown that this enzyme regulates non-quantal acetylcholine release and postsynaptic polarization of muscle fibres.

d) Muscle denervation results in extrasynaptic acetylcholine receptor induction and these receptors have a fivefold lower sensitivity to curare. This binding was actually the first evidence that there is a distinct difference between junctional and extrajunctional acetylcholine receptors (Beránek and Vyskočil 1967) and became the basis for the pharmacological and biochemical characterization of "adult" and "immature" (or foetal) receptors not only for acetylcholine but also for many ligand-regulated postsynaptic receptors.

These and other important findings in this field have recently been published in monograph form (Vyskočil 1991).

B. Non-impulse Transfer of Information Between Nerve and Muscle

One of the leading concepts propagated by E. Gutmann and his group was the idea that communication between nerve and muscle cells (and nerve to nerve cells) is not only mediated by impulse transmission. This may not seem as heuristic at the present time as it did in the midfifties.

Gutmann, Vodička and Zelená showed in 1955 that some early denervation changes (reduced glycogen synthesis, degeneration of nerve terminals and loss of indirect muscle excitability) occur earlier in muscles the transected peripheral nerve stump of which is short than in those with a long stump. In the same year, Luco and Eyzaguirre (1955), who used the onset of denervation fibrillations and denervation acetylcholine hypersensitivity as their indicator of early denervation changes, came to the same conclusion. The peripheral nerve stump was assumed to contain a "trophic" substance(s) in the axoplasm which may maintain, for a certain period of time, a normal "eutrophic" state of the muscle, including its motor nerve terminals.

Since then, much work has been done in numerous laboratories in support of the hypothesis that motoneurons supply muscles with some metabolite(s) necessary for maintaining their structure, function and metabolism. The obvious possibility seemed to involve axoplasmic flow. A significant contribution to this field was made by Zelená *et al.* (1968), who showed that axoplasmic flow is bidirectional, implying the possibility of mutual non-impulse interactions between peripheral tissues and the nervous system. One of Gutmann's last reviews on neurotrophic relations was published in 1976.

An attractive hypothesis about the basis of the "trophic" influence was formulated in the monograph "The Denervated Muscle" (Gutmann 1962). The co-authors of this book were: A. Bass, R. Beránek, Z. Drahotka, E. Gutmann, P. Hník, O. Hudlická, V. Škorpil, L. Vyklický, J. Zelená and R. Žák. The main idea was that muscle activity leads to a preponderance of catabolic processes (concerning both energy and protein metabolism).

However, following muscle activity, an overshoot phenomenon occurs in normally innervated muscles, indicating that energy and protein resynthetic processes are accentuated. This "supercompensation" of glycogen, first observed by Yampolskaya (1950) in normal muscles is present until neuromuscular connection is lost due to degeneration of nerve terminals following nerve section (Gutmann *et al.* 1954), and a similar situation was reported in the overshoot reaction of proteins and RNA by Žák and Gutmann (1960). This naturally led to the idea that perhaps the

trophic influence of the nervous system on skeletal muscles ensures metabolic restitution after the preceding catabolic load due to muscle activity. This question is still open, since it has not been decided, beyond any doubt, to what extent axoplasmic flow and impulse or artificially induced activity are closely coupled together under normal conditions, or whether the main factor influencing muscle characteristics is exclusively muscle activity itself. Certainly, several aspects of muscle properties, e.g. speed of contraction or prevention of acetylcholine denervation hypersensitivity (Vrbová *et al.* 1978) and vascularization (Hudlická 1973) and others can be altered by a chronic muscle stimulation pattern (e.g. Lomo and Gundersen 1988). Yet the application of nerve extracts onto the surface of innervated muscles can induce acetylcholine sensitivity in extrajunctional regions (Vyskočil and Srový 1979, Vyskočil *et al.* 1981). The most effective polypeptidic extract was found to be in the region of 10 000 D.

C. Nerve Regeneration, Muscle Transplantation, Muscle Differentiation and Morphogenetic Influence of Innervation

1. Nerve Regeneration

The problems of peripheral nerve regeneration and muscle reinnervation were started by E. Gutmann in collaboration with J.Z. Young in Oxford during world War II. The main aim of these studies was to obtain basic data about factors affecting nerve regeneration after peripheral nerve injuries. These early studies mainly concerned the rate of regeneration of motor and sensory nerve fibres in an attempt to speed up restitution of function. The results were recapitulated in monograph form first in Czech (Gutmann 1955) and subsequently in a German edition (1958).

2. Muscle Reinnervation, Cross-union Experiments and Muscle Transplantations

a) Muscle reinnervation

The basic facts about the factors affecting muscle reinnervation following peripheral nerve injury were summarized in the two above-mentioned monographs (Gutmann 1955, 1958). These included a detailed description of regenerating nerves, of reinnervated end-plates, muscle histology and reinnervation after repeated nerve crushes. An important observation was made by Gutmann (1942) concerning the earlier onset of muscle mass restitution before the return of functional neuromuscular transmission. This may be taken as an example of the dissociation of non-impulse "trophic" effects and the reappearance of nerve impulse transmission. The beneficial effect of electrostimulation of denervated muscles in retarding muscle wasting was shown in several papers (e.g. Gutmann and Guttmann 1944). Besides his studies on muscle reinnervation, Gutmann was also involved in the fate of skeletal muscles after vascular injury (Bowden and Gutmann 1949) and reinnervation of denervated skin areas (Weddell *et al.* 1941). Factors affecting the rate of regeneration of peripheral nerve fibres were also studied after spinal cord transection by Beránek and Gutmann (1953) and in flexor and extensor muscles (Beránek *et al.* 1957). Increased motor activity was shown to have a deleterious

effect on peripheral nerve regeneration in young rats (Gutmann and Jakoubek 1963).

b) Nerve cross-union experiments

An important contribution were the studies of Jirmanová and co-workers concerning the cross-innervation of the chick posterior latissimus dorsi (PLD), a fast muscle, and the anterior latissimus dorsi (ALD), a slow muscle with multiple innervation. When nerve cross-union was performed in the adult domestic fowl, the type of motor end-plates and the character of neuromuscular transmission was altered, but the changed innervation did not induce any substantial changes either in muscle fibre ultrastructure or in muscle contraction speed (Zelená *et al.* 1967, Hnák *et al.* 1967). An attempt was therefore made to cross-innervate chicken muscles at an earlier developmental stage. The ALD was transposed in newly hatched chickens and innervated by a predominantly fast nerve. These ALD muscles were mostly innervated focally with end-plates of the fast type and their ultrastructure closely resembled that of the control fast PLD (Zelená and Jirmanová 1973). The changes in ultrastructure correlated well with the change in function towards the fast type (Jirmanová *et al.* 1971). ATPase activity of myosin and light chains of myosin from cross-innervated ALD were similar to those of the control PLD (Syrový and Zelená 1975). A changeover of fibre types and contractile properties also occurred when the fast PLD muscle was cross-innervated by the ALD nerve (Jirmanová and Zelená 1973, Hnák *et al.* 1977b).

c) Muscle transplantations

Considerable effort was made to ascertain the possibilities of muscle transplantations and muscle regeneration. Most of this work was done by E. Gutmann in collaboration with B.M. Carlson. It was shown, for example, that the functional and histochemical characteristics of heterotopically grafted muscles do not depend on the new site of their implantation after denervation but rather on the type of innervation which they receive (Gutmann and Carlson 1975). Early regenerates of minced triceps surae muscles exhibited contractile properties of very slow muscles and it was concluded that regenerating muscles undergo "developmental recapitulation" (Carlson and Gutmann 1972).

However, the success of these and many other experiments is greatly limited by the size of muscle grafts. Hence muscle transposition appeared to be the method of choice for solving some clinical problems. For example, a new surgical approach was introduced for treating congenital anal incontinence in children. This method was developed in the Department of Child Surgery in Prague 5, in collaboration with the Institute of Anatomy, Faculty of Medicine and Institute of Physiology, Czechoslovak Academy of Sciences in Prague. The surgical procedure is based on the transposition of the gracilis muscle (including its neurovascular hilus) to act as substitute for the missing anal sphincter (Grim *et al.* 1981, Vejsada *et al.* 1981).

Systematic studies have also been carried out concerning muscle morphogenesis and differentiation in chicken and quail muscles in dependence on specific motoneurone innervation. It was found that individual muscle types are originally determined by the connective tissue. Subsequently, however, both the

differentiation and distribution of muscle fibre types, as well as the development of the motor end-plate pattern are controlled hierarchically by neurogenic and myogenic factors (Grim *et al.* 1989).

3. Muscle Differentiation During Development and Changes in Old Age

It was shown in a comparative study of slow and fast muscles in three mammalian species (rat, rabbit and guinea-pig) that the prolongation of contraction time in the slow soleus muscle occurs postnatally in all three species. This was also demonstrated in ATPase activity of slow and fast muscles and their muscle fibre pattern. It was suggested that the postnatal maturation process is of neurogenic origin and that it is an expression of developmental adaptation of the slow muscle to its antigravity function and that the postnatal differentiation of myosin is much more marked in slow than in fast muscles (Syrový and Gutmann 1977).

A "two phase" developmental change in acid phosphatase (AP) activity was also shown in both the fast extensor digitorum longus and slow soleus of the rat. AP activity is high at birth, decreases during later postnatal development and increases again in senescent muscles (Gutmann *et al.* 1976). Analogous results were obtained in the developmental properties of fast-phasic and slow-tonic muscles of the chick (Melichna *et al.* 1974).

A review of changes taking place in the neuromuscular system during old age were summarized in monograph form (Gutmann and Hanzlíková 1972).

4. Morphogenetic Influence of Innervation on Muscle Receptor Differentiation

One of the most convincing findings in favour of a non-impulse morphogenetic influence of innervation upon the periphery was first demonstrated by Zelená in 1957 (for review see Zelená 1976). Since then it has repeatedly been confirmed that muscle receptors - muscle spindles and Golgi tendon organs do not develop without sensory innervation. The differentiation of muscle spindles is prevented by early denervation of skeletal muscles in rat and rabbit fetuses *in utero* (Zelená 1957). Furthermore, developing muscle spindles degenerate and disintegrate in leg muscles transiently denervated after sciatic nerve crush in neonatal rats; only occasional intrafusal fibres survive denervation and can be reinnervated after nerve regeneration (Zelená and Hník 1963a). Thus, most rat muscles reinnervated after an early postnatal nerve crush, contain only occasional muscle spindles atypical in structure and, sporadically, a tendon organ; however, the gastrocnemius muscle, if reinnervated within a few days after the nerve lesion, is an exception in that it contains a normal, or even an increased number of atypical spindles (Zelená and Hník 1963b). The morphogenetic influence upon muscle spindle differentiation is exerted by primary sensory neurones of dorsal root ganglion cells (Zelená and Soukup 1973). When the distal segments of the spinal cord were excised at birth including ventral and dorsal lumbosacral roots, but preserving the spinal ganglia and their peripheral axons, the de-efferented skeletal muscles became extremely atrophic but contained a full complement of muscle spindles the structure of which was practically normal (Zelená and Soukup 1973). These receptors also responded to muscle stretch with a static and dynamic component (Hník *et al.* 1977c). Furthermore, the same heavy chains were

synthesized in de-efferented spindles as in the controls. The degree and extent of their staining, however, varied (Soukup *et al.* 1990).

The occasional atypical spindles to be found in adult muscles after neonatal sciatic nerve crush were found to respond to muscle stretch (Paleček *et al.* 1989), although with lower frequencies of responses. Electromyography (EMG) of reinnervated flexor and extensor muscles in adult rats showed that extensor muscles (soleus and medial gastrocnemius) are little affected by neonatal nerve crush, but abnormal activity was observed in the tibialis anterior (a flexor muscle), which exhibited spontaneous EMG at rest and two-burst activation during locomotion (Vejsada *et al.* 1991). This was taken to indicate that flexor motoneurons are coactivated with the extensor motoneurone pool. These results serve as evidence that postnatal nerve crush not only has severe late effects in the periphery, but also in spinal cord connectivity.

5. Humoral Factors Affecting Muscle Status

A review of hormonal and humoral factors acting on skeletal muscles was published in *The Denervated Muscle* (Gutmann 1962). This subsequently led to a series of studies concerning the survival of the levator ani muscle in female rats by testosterone administration (e.g. Čihák *et al.* 1970). Considerable effort was also invested into catecholamine mechanisms involved in stimulating muscle metabolism. It was found that the thermogenic response to noradrenaline (NA) is controlled by the efflux of NA into the extravascular space and that it depends on the increased flow rate conditioned by the microcirculation (Mejsnar and Jiráček 1981, Pácha *et al.* 1986).

D. Muscle Atrophies

A concentrated effort was made to assess the common features and differences between various types of muscle atrophy after denervation, tenotomy, immobilization, deafferentation and reflex atrophy induced by nociceptive stimulation.

1. Denervation Atrophy

The basic findings of Gutmann's group were first published in a monograph "The Denervated Muscle" (Gutmann 1962) and in "The Effect of Use and Disuse on Neuromuscular Functions" (Gutmann and Hník 1963). The first of these volumes contained the results of complex research concerning energy (Bass and Vodička), protein (Žák) and ion metabolism (Drahota), developmental data and morphogenetic aspects of neural influences (Zelená) and possible circulatory involvement in denervation atrophy (Hudlická). Furthermore, electrophysiological studies were made mainly about denervation fibrillations and factors affecting their onset and arrest (Hník and Škorpil). An interesting finding was made by Gutmann in 1960, which led him to postulate the hypothesis that denervated skeletal muscles pass through a transient, brief phase of hypertrophy of at least a few hours' duration. This phenomenon had been shown only in exceptional cases, e.g. in the denervated hemidiaphragm (Sola and Martin 1953) and later in the chick anterior latissimus

dorsi (ALD) (Feng *et al.* 1963). Extensive biochemical studies were performed in both these muscles by Hájek *et al.* (1966, 1967) and morphologically in the denervated ALD by Jirmanová and Zelená (1970).

2. Atrophy Due to Tenotomy

The loss of muscle weight and metabolic, circulatory and functional changes after section of the tendon were systematically studied in an effort to differentiate between this type of atrophy and that after nerve section. The results were found to be grossly similar to that after denervation, with the exception of fibrillation activity, which was exclusively found after denervation (see Gutmann 1962). The metabolic changes in tenotomized muscles cannot be due to decreased muscle blood flow, since that was increased at later periods after tenotomy and it was postulated that these muscles utilize surplus oxygen and glucose for lipid production (Hudlická 1962), similarly as denervated muscles (Bass and Hudlická 1960).

An enhanced monosynaptic response of the motoneurone pool supplying the tenotomized cat gastrocnemius was first reported by Beránek and Hník (1959) and was brought into context with increased afferent activity from the tenotomized muscles and plasticity of spinal cord synaptic functions (Hník *et al.* 1963). Section of the dorsal roots significantly reduced the rate of muscle atrophy following section of the tendon (Hník 1964).

3. Disuse Atrophy

Experiments were performed confirming previous findings that immobilization in the stretched position leads to smaller atrophy (or even hypertrophy) than immobilization in the "short" position. An EMG study of muscles thus immobilized showed that the "stretched" soleus received an analogous number of EMG impulses as the control. However, in the "short" position, i.e. when the ankle is immobilized in plantar flexion, the soleus lost weight almost to the same extent as after denervation, its EMG activity was reduced to about 10 %. The relatively low EMG activity in the control tibialis anterior (TA), a flexor muscle, was unchanged whether the muscles were immobilized in the "short" or "long" position. This led to the conclusion that extensor muscles depend more on neurally induced activity, while flexors are more dependent on muscle stretch (Hník *et al.* 1985, 1988). These differences were further confirmed in electrophysiological studies of Zemková *et al.* (1990). The membrane potential, frequency of m.e.p.s and ³H-ouabain binding were decreased in the soleus immobilized in the "short" position, but were unchanged when the muscles were stretched. Only minor changes were observed in the extensor digitorum longus, a flexor-muscle, whether it was stretched or shortened. Another set of experiments dealing with a different aspect of disuse atrophy dealt with suspension hypokinesia (SH). It was found that the lack of gravity arrests the normal developmental transformation of type IIA into type I fibres in the soleus muscles, if the suspension is performed in 3 to 4-week-old rats (Asmussen *et al.* 1988). Three to six weeks after SH, the histochemical fibre pattern and myosin light chain patterns corresponded to those present in the soleus at the time of suspension. SH also caused marked wasting of the soleus, mainly due to the severe atrophy of type I fibres. The latter change was the only one occurring in the

soleus after SH performed in adult 6-month-old rats. SH is thus followed by atrophy of slow-twitch muscles such as the soleus, but not of fast-twitch muscles such as the extensor digitorum longus muscle. Furthermore, the contractile properties of the slow soleus were altered in young rats with SH (Asmussen *et al.* 1989).

4. Deafferentation

Section of dorsal roots supplying the rat hind limbs leads to progressive atrophy of deafferented extensor muscles, but not the flexors (Hník 1956). This is accompanied by EMG symptoms of hyperexcitability of extensor motoneurons (Hník *et al.* 1981). A new phenomenon, named "stretch-induced inhibition" of this spontaneous activity of deafferented extensor muscles may be associated with ventral root afferents (Hník *et al.* 1984).

5. Reflex Muscle Atrophy

Chronic nociceptive stimulation (e.g. injection of turpentine oil into the planta) causes loss of weight of muscles around the appropriate joint. Gutmann and Vodička (1953) studied this model of muscle atrophy in which, although motor innervation is intact, loss of muscle weight is even more rapid than after denervation. Subsequently, a more detailed analysis demonstrated that this reflex atrophy is not due to muscle inactivity or reduced blood circulation (Hník *et al.* 1977a).

E. Muscle Hypertrophy

Denny-Brown's model of compensatory muscle hypertrophy was extensively studied by a number of authors including Gutmann and Hájek (1971), Gutmann *et al.* (1971b) and Macková and Hník (1973). The general consensus of these studies was a certain reluctance to accept this experimental situation (tenotomy of synergistic muscles) as a model of working hypertrophy. Firstly, it is transient in character (Macková and Hník 1973), it responds to denervation by a dramatic loss of weight (Hník *et al.* 1974) and by a sudden enhancement of lysosomal enzyme activities (Bass *et al.* 1984). In view of these findings and lack of increased EMG activity in hypertrophying muscles (Hník *et al.* 1986) it was concluded that "compensatory" muscle hypertrophy is not true working hypertrophy and that it is rather the result of other factors, e.g. muscle stretch or muscle activity against increased resistance of intact antagonistic muscles. Furthermore, muscle stretch by itself was found to enhance the rate of incorporation of amino acids (Burešová *et al.* 1969).

F. Physiology and Pathophysiology of Muscle Afferents

The responses of still immature rat muscle spindles in the early postnatal period were studied starting from the day of birth (Vejsada *et al.* 1985) and compared with the function of these receptors in very young kittens (Vejsada *et al.* 1988).

The transient increase of K^+ in the muscle interstitial space during activity measured with ion-selective electrodes (Hník *et al.* 1976) has been considered in context with non-proprioceptive myelinated fibres (Hník *et al.* 1969) and their probable role in triggering cardiovascular and respiratory responses to muscle work (Hník *et al.* 1986).

From the pathophysiological point of view, it was found that spindles from muscles undergoing atrophy either after tenotomy or after ventral root section have an enhanced response to stretch (Hník and Lessler 1971, 1973). Atrophying muscles also become a source of abnormal spontaneous activity of non-proprioceptive afferents (Hník and Payne 1966).

G. Neuromuscular Pathophysiology

a) The myotoxic effects of a local anaesthetic, methylbupivacaine, lead to rapid degeneration of skeletal muscle fibres after subcutaneous injection. However, within 10-14 days, muscle regeneration is practically complete due to a specific myotoxic action of the drug, which leaves the blood supply, basal lamina (Jirmanová and Thesleff 1972) and nerve supply (Jirmanová and Thesleff 1972, Jirmanová 1975) intact. In methylbupivacaine treated muscles only the postsynaptic part of the neuromuscular junction degenerates whereas the nerve terminals remain intact. The postsynaptic part of the neuromuscular junction and muscle regeneration already occur as early as the fourth day after drug administration, when the newly formed junctions almost attain maturity (Jirmanová 1975).

b) The effects of botulinum toxin on neuromuscular transmission was studied in collaboration with the Department of Pharmacology in Lund (Fex *et al.* 1966). It was shown that the block of impulse transmission leads to denervation changes in the affected muscles. It did not, however, affect the morphological redifferentiation of the postsynaptic part of the neuromuscular junction following muscle degeneration-regeneration induced by methylbupivacaine (Jirmanová and Thesleff 1970).

c) The mechanisms responsible for muscle degeneration in muscular dystrophy are largely unknown. It is possible that lysosomal enzymes, which are elevated in dystrophic muscles, participate in intracellular proteolysis resulting in muscle fibre breakdown. Electronmicroscopic and biochemical results showing intracellular uptake of horseradish peroxidase (HRP), proliferation of vesicles from T-tubules, muscle fibre vacuolization and lysosomal activation were obtained in an *in vitro* myopathy induced by protamine (Jirmanová *et al.* 1977). It was postulated on the basis of these results that endocytosis and lysosomal activation might be causally related. Moreover, evidence for increased endocytosis by vesicles derived from T-tubules and concomitant lysosomal activation was found in skeletal muscles of the genetically dystrophic mouse of the Bar Harbor 129 strain (Libelius *et al.* 1978) and dystrophic chicken (Libelius *et al.* 1979). It was demonstrated that endocytosis from T-tubules is an early and essential pathological phenomenon in dystrophic muscle fibres, and may be related to lysosomal function and muscle fibre degeneration.

d) CS_2 intoxication was found to induce pathological ultrastructural changes in peripheral axons, classified as giant filamentous axonopathy. Even during the intoxication, regeneration of damaged axons takes place, starting from intact internodes (Jirmanová and Lukáš 1984). Nerve regeneration results in an altered

innervation pattern of Pacinian corpuscles (Jirmanová 1987) and probably of other end-organs.

e) Congenital myofibrillar hypoplasia, called splayleg, is a muscle disease which affects newborn piglets in large pig industries. The similarity of electronmicroscopic changes in this disease and those of corticosteroid myopathy (Zelená and Jirmanová 1979) led to the hypothesis that splayleg is brought about in foetuses by increased levels of corticosteroids in pregnant sows kept under stressful conditions (Zelená and Jirmanová 1979, Jirmanová 1983). The conclusion that splayleg is a congenital form of glucocorticoid myopathy was further strengthened by the finding that glucocorticoids induced a myopathy in young rabbits resembling the splayleg disease (Jirmanová *et al.* 1982). The induction of splayleg in newborn minipiglets by the administration of dexamethasone to pregnant minisows confirmed this hypothesis (Jirmanová and Lojda 1985).

H. Muscle Fatigue and Biomechanics

a) Fatigue of respiratory muscles was studied especially during hypoventilation following phrenic nerve section (Paleček and Nacházel 1988) (Department of Pathophysiology, Third Medical Faculty in Prague). It was found that muscle performance (estimated according to respiratory volume) was decreased, while integrated EMG activity was augmented. Besides peripheral factors, central regulatory mechanisms are also involved, as was shown after administration of aminophylline (Nacházel and Paleček 1990).

b) Biomechanics are mainly studied at the Faculty of Physical Education and Sports (L. Karas) and concern the latency of volitional activation between a light signal, the onset of EMG activity and actual beginning of muscle shortening. An important aspect of this work is also volitional relaxation, i.e. the time which elapses between end of the light signal and end of EMG activity, and electromechanical delay occurring during relaxation. The basic findings are making it possible to assess the results of training, fatigue and correlate the changes with serum Na^+ levels (Karas and Otáhal 1979, Karas *et al.* 1981).

Attempts are also being made at the Department of Physiology of the same Institution to find noninvasive indicators for the prediction of skeletal muscle morphology and thus for assessing young athletes for their suitability to enter certain sports disciplines. A test of vertical jumping ability was correlated with muscle biopsies of the quadriceps muscle and it was shown that the muscle fibre ratio (type II:I) correlates with the height of the vertical jump (Macková *et al.* 1985).

However, this performance test seems to be of value for use in trained subjects and only of limited significance for selecting young athletes for their sports specialization (Melichna *et al.* 1990).

c) A systematic study was made of isotonic contractions of the rabbit gastrocnemius muscle *in situ*. By employing a very low resistance mechanical myograph, isotonic contractions could be obtained. This made it possible to compute the speed of isotonic contractions and correlate them with various contractile parameters (Wünsch 1987).

Conclusions

This survey is, of course, not complete, and I apologize to all other colleagues in this field whom I have not been able to include. However, it has given me the opportunity of informing members of the IUPS Regional Meeting in Prague 1991 about the trends of neuromuscular physiology in our country.

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