Time course of changes in lipoprotein lipase activity in rat skeletal muscles during denervation-reinnervation

E. ZERNICKA,1 E. SMOL,2 J. LANGFORT,1 AND M. GÓRECKA1

1Department of Applied Physiology, Medical Research Center, 02-106 Warsaw; and
2Department of Physiology, Academy of Physical Education, 40-065 Katowice, Poland

Received 2 August 2001; accepted in final form 27 September 2001

Zernicka, E., E. Smol, J. Langfort, and M. Górecka.

Time course of changes in lipoprotein lipase activity in rat skeletal muscles during denervation-reinnervation. J Appl Physiol 92: 535–540, 2002; 10.1152/japplphysiol.00820.2001.—The effects of denervation-reinnervation after sciatic nerve crush on the activity of extracellular and intracellular lipoprotein lipase (LPL) were examined in the soleus and red portion of gastrocnemius muscles. The activity of both LPL fractions was decreased in the two muscles within 24 h after the nerve crush and remained reduced for up to 2 wk. During the reinnervation period, LPL activity was still reduced in the soleus and started to increase only on the 40th day. In the red gastrocnemius, LPL activity increased progressively with reinnervation, exceeding control values on the 30th day post-crush. The LPL activity in the soleus from the contralateral to denervated hindlimb was also affected, being increased on the postoperation day and then gradually decreased during the following days. In conclusion, the time course of changes in muscle LPL activity after nerve crush confirmed the predominant role of nerve conduction in controlling muscle potential to take up free fatty acids derived from the plasma triacylglycerols. However, other factors, such as muscle fiber composition and the fiber transformation, should also be considered in this aspect of the denervation-reinnervation process. Moreover, it was found that denervation of muscles from one hindlimb may influence LPL activity in muscles from the contralateral leg.

skeletal muscle; denervation; reinnervation

PERIPHERAL NERVE CRUSH leads to functional denervation of muscles with a variety of degenerative changes in muscle morphology and biochemistry that subsist until the regeneration of injured nerve takes place. The changes include an immediate loss of muscle activity followed by atrophy and degeneration of muscle fibers, a decrease in mitochondrial oxidative enzyme activities, and a fall in high-energy phosphate contents (6, 8, 21, 38). Reinnervation and regeneration of skeletal muscles result in restoration, to some degree, of the original muscle fiber structure and contractile activity accompanied by a reversal of some previous biochemical alterations (8, 12, 24, 25). The rate of recovery of metabolic alterations induced by denervation is different for enzymes of various metabolic pathways, and so it depends on the muscle fiber type (33, 38).

Lipoprotein lipase (LPL) is a major enzyme responsible for hydrolysis of triacylglycerols (TG) derived from circulating TG-rich lipoproteins, making fatty acids available for cellular uptake. LPL in skeletal muscles, as in other tissues, is under a complex control by dietary and hormonal factors that modulate the enzyme activity at the cellular and molecular levels. In addition, LPL exhibits muscle fiber type-specific regulation that is closely related not only to the oxidative capacity of the muscle but also to its capability of replenishing the intramuscular TG stores (3, 20). LPL activity is greater in muscles composed mainly of high-oxidative slow-twitch “red” fibers (soleus), lower in the oxidative-glycolytic fast-twitch red fibers (e.g., red portion of gastrocnemius), and the lowest in “white” fast-twitch glycolytic fibers (e.g., white portion of gastrocnemius). These differences in LPL activity are probably due to not only the substrate preferences but also local alterations in the contractile activity of muscles (11, 27, 31, 32).

Our laboratory has previously found (34) a marked decrease in the activity of LPL (both the heparin-releasable (HLPL) and residual fractions (RLPL)) in the soleus and red portion of gastrocnemius muscles of the rat 12 h after inactivity caused by irreversible denervation induced by the sciatic nerve cut. The short-term electrostimulation, applied to the denervated muscles, increased activity of two LPL fractions, partly restoring it to control values. These findings support the regulatory role of muscle contractile activity in LPL activity and also suggest that the intact innervation is necessary for maintenance of normal enzyme activity in skeletal muscles. The purpose of this study was to follow up the time course of changes in the activity of two LPL fractions (i.e., active, endothelial HLPL and intracellular RLPL) as well as TG content in the rat skeletal muscles of different fiber composition after reversible denervation induced by sciatic nerve crush and during the subsequent period of self-reinnervation.

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

http://www.jap.org 8750-7587/02 $5.00 Copyright © 2002 the American Physiological Society 535
MATERIALS AND METHODS

Animal protocols. The study was carried out on male adult Wistar rats weighing 180–200 g. The animals were housed in groups of eight in a temperature-controlled room with 12:12-h light-dark cycle. They were fed a standard rodent Chow and had water available ad libitum. Food was withheld 12–15 h before the animals were killed.

Five groups of rats (8 per group) were examined at different time after unilateral denervation. The denervation was performed by the sciatic nerve crush while the animals were under light ether anesthesia. The nerve from the right hindlimb was exposed and crushed by pinching firmly three times with the ends of fine watchmaker’s tweezers. For consistency of the procedure, all sciatic nerve crushing was done by the same well-experienced person. This led to the complete, although reversible, denervation, resulting in morphological and histochemical changes similar to those occurring after the nerve cut. These alterations were maintained up to the 15th after the nerve crush, when the processes of reinnervation and regeneration started (15, 16).

Muscles from the contralateral intact hindlimb served as controls (C_i). Additionally, muscles from 16 intact rats were analyzed and used as separate, second controls (C_c).

During the postsurgical period, the rats were kept free in their home cages (8 per cage). They were able to move with one immobile, extended hindlimb. Within 2–4 h after denervation procedure, rats resumed normal feeding and behavior pattern without any overt signs of stress or pain.

On the 1st, 14th, 24th, 30th, and 40th days after the nerve crush, the rats were killed by decapitation. The soleus, and had water available ad libitum. Food was withheld 12–15 h before the animals were killed.

The experimental procedure was approved by the Ethical Committee of the Medical Research Center, Polish Academy of Sciences in Warsaw, Poland.

Biochemical assays. LPL activity in skeletal muscle samples was determined by measuring the release of [14C]oleic acid emulsion of glycerol-tri[14C]oleate in a Tris-buffer medium containing albumin and pooled human serum as an activator according to Taskinen et al. (35). For determination of HLPL activity, muscle samples (weighing ~5–10 mg) were incubated with gentle shaking at 28°C in 200 μl of Krebs-Ringer-0.1 M Tris-HCl buffer at pH 8.4, containing 1% bovine serum albumin and 5 IU of heparin. After 40 min the tissue was removed from the medium, 500 μl of the triolein substrate mixture were added, and the incubation was continued for a further 120 min.

To determine the activity of RLPL, the samples of muscle tissue removed from the medium after 40 min of incubation were homogenized in 500 μl of Krebs-Ringer-Tris-HCl buffer. Samples of the homogenate (200 μl) were incubated with 500 μl of substrate mixture for 120 min.

At the end of incubation, duplicate samples of the eluate and homogenate were taken from the incubation mixture and extracted with 3.25 ml of methanol-chloroform-heptane (1:41:1.25:1.00, vol/vol/vol). Then, 1.05 ml of 0.05 M potassium carbonate buffer were added (pH 10.05). After mixing, 1.0 ml of the upper phase was used for scintillation counting (LKB Wallac 1211). Each assay included two blank tubes.

LPL activity was expressed as micromoles of free fatty acids (FFAs) per gram of protein per hour.

Participated muscles were determined according to the enzymatic method of Eggstein and Kuhlmann (7) after an overnight extraction of muscle samples in chloroform-methanol mixture (2:1). TG content was expressed as micromoles per gram.

Total protein content was measured by the method of Lowry et al. (19).

Statistical analysis. The data are presented as means ± SE. Two-way multivariate analysis of variance followed by Tukey’s test was used to verify significance of differences between the experimental (denervated) and intact muscles from the contralateral hindlimbs as well as between the experimental and intact muscles taken from the second control group.

RESULTS

Muscle mass. Atrophy and muscle fiber degeneration appeared early after the muscle denervation. The average weight of the soleus muscle on the postcrush day was ~53 mg wet wt in both the denervated and contralateral intact hindlimbs (Table 1). After 14 days following nerve crush, the weight of soleus decreased by 62.9% in the denervated hindlimb compared with the contralateral one. In the subsequent days, when reinnervation process had started, the muscle mass from the denervated hindlimbs began to increase, but it was still below the values found in the contralateral hindlimbs by 25.30, 24.60, and 8.00% on the 24th, 30th, and 40th days, respectively.

LPL activity. In muscles taken from the hindlimbs C_i rats, the activity of LPL found in the high-oxidative soleus (35.82 ± 1.03 and 44.88 ± 1.06 μmol FFA·g protein−1·h−1 for HLPL and RLPL, respectively) was higher than in the oxidative-glycolytic red gastrocnemius (12.14 ± 0.65 and 22.68 ± 0.74 μmol FFA·g protein−1·h−1 for HLPL and RLPL, respectively).

Only 1 day after the sciatic nerve crush, activity of both LPL fractions was markedly reduced in denervated soleus (Fig. 1) and the red portion of gastrocnemius (Fig. 2) muscles compared with the respective muscles isolated from the C_c hindlimbs as well as with muscles obtained from C_i animals. The activity of LPL, especially HLPL, in the soleus muscle from the C_c hindlimb was higher than in the C_i rats. No such a

<table>
<thead>
<tr>
<th>Days After Nerve Crush</th>
<th>Muscle Mass, mg wet wt</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C_c</td>
</tr>
<tr>
<td>1</td>
<td>53.25 ± 1.69</td>
</tr>
<tr>
<td>14</td>
<td>59.13 ± 2.74</td>
</tr>
<tr>
<td>24</td>
<td>68.00 ± 3.15</td>
</tr>
<tr>
<td>30</td>
<td>90.63 ± 2.88</td>
</tr>
<tr>
<td>40</td>
<td>106.94 ± 2.26</td>
</tr>
</tbody>
</table>

Values are means ± SE. D–R, denervated-reinnervated; C_c, intact contralateral. *Significant differences between D–R and C_i muscles, P < 0.001.
difference was found in the red portion of gastrocnemius muscle.

During the entire degeneration-reinnervation process, the activity of LPL in the soleus from denervated-reinnervated (D-R) and intact, contralateral (C_i) rat hindlimbs was reduced (Fig. 1). However, on the 40th day, an increase in the activity of this enzyme occurred, especially in the RLPL fraction. These changes were accompanied by gradual reduction in the activity of both LPL fractions (more pronounced in RLPL) in the soleus from C_c hindlimbs. On the 24th, 30th, and 40th days, there were no significant differences between the RLPL activity in the denervated and C_c muscles. On the 40th day after denervation, the RLPL activity in both denervated and C_c muscles returned to the values found in C_i animals (Fig. 1).

The pattern of changes in LPL activity in the red portion of gastrocnemius differed from that in the soleus muscle. In the gastrocnemius from the denervated hindlimbs, activities of both LPL fractions were greatly decreased until the 14th day after the nerve crush. Coinciding with the beginning of reinnervation, activity of HLPL started to increase, and it reached the C_i value at the 24th day and then exceeded it at the 30th and 40th days after the nerve crush (Fig. 2). Activity of RLPL also slowly increased from the 24th day after denervation, and at the 40th day it was significantly higher than in C_i muscles (Fig. 2).

### TG content

In the soleus from the experimental hindlimbs, the TG content remained unchanged up to 14 days after the nerve crush, and it was similar to that of the contralateral muscles (Table 2). With the beginning of reinnervation process, the TG content in this muscle increased, being the highest 40 days after denervation. In the red portion of gastrocnemius, enhanced TG content was found in denervated-reinnervated muscles during the entire period after the nerve crush.

### Table 2. Triacylglycerol content in the soleus and red portion of gastrocnemius muscles from denervated-reinnervated and intact contralateral rat hindlimbs during 40 days after the sciatic nerve crush

<table>
<thead>
<tr>
<th>Days After Nerve Crush</th>
<th>Soleus</th>
<th>Red portion of gastrocnemius</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C_c</td>
<td>D-R</td>
</tr>
<tr>
<td>1</td>
<td>10.42 ± 0.45</td>
<td>11.49 ± 0.41</td>
</tr>
<tr>
<td>14</td>
<td>10.27 ± 0.25</td>
<td>10.81 ± 0.27</td>
</tr>
<tr>
<td>24</td>
<td>9.92 ± 0.38</td>
<td>11.25 ± 0.49</td>
</tr>
<tr>
<td>30</td>
<td>10.10 ± 0.57</td>
<td>12.07 ± 0.25†</td>
</tr>
<tr>
<td>40</td>
<td>9.79 ± 0.26</td>
<td>12.42 ± 0.50*</td>
</tr>
</tbody>
</table>

Values are means ± SE. TG, triacylglycerol. Significant differences between D-R and C_c muscles: *P < 0.001, †P < 0.05.
crush except for the 24th day, when the TG content was similar in the denervated and contralateral muscles.

**DISCUSSION**

To our knowledge, this is the first report in which the pattern of changes in the skeletal muscle potential to hydrolyze the plasma TGs has been described during the process of denervation-reinnervation.

Earlier studies have demonstrated that sciatic nerve crush results in the total lack of nerve conduction to the gastrocnemius and soleus muscles of rats for up to 2 wk after the injury. This is followed by axonal regeneration, with good functional recovery taking place between 2 and 3 wk after nerve crush and leading to an ~80% recovery in nerve conduction after 6 wk (9, 10, 18).

General rules concerning denervation atrophy and reinnervation recovery allow to treat changes in the soleus mass as an index of the muscle atrophy and recovery. Two weeks after the sciatic nerve crush, the weight of soleus in the denervated hindlimb was the lowest, indicating atrophy resulting from lack of nerve conduction. After that time, the soleus mass started to increase, which is in line with the beginning of nerve regeneration (16, 18). The decline of muscle mass is accompanied by reduction of fiber diameter and fiber-type transformation. These changes lead to more glycolytic metabolism in red muscles. In the recovering muscle during reinnervation, the fiber types are transformed back into more oxidative, the activity of oxidative enzymes increases and the muscle shifts back to more oxidative metabolism (6, 8, 38).

The present study showed an immediate and marked reduction in the activity of both HLPL and RLPL fractions in the soleus and red portion of gastrocnemius muscles for up to 2 wk after the sciatic nerve crush, when muscles remained totally denervated. The low LPL activity in the soleus was maintained for the following 2 wk despite the gradual recovery of the muscle during reinnervation. After 40 days from the nerve crush, the activity of LPL was markedly higher than that found in the earlier days; however, the control value was attained only by the RLPL fraction of the enzyme. Interestingly, in the red portion of gastrocnemius, the pattern of changes in the activity of LPL during nerve regeneration was different. Twenty-four days after the nerve crush, activity of both LPL fractions was already increased over the values found after denervation, and, at the end of the experiment, it even exceeded the control values.

Our laboratory has previously described (34) a marked reduction in LPL activity (both fractions) in gastrocnemius and soleus muscles 12 h after the sciatic nerve cut. We have suggested that this finding is associated with local postdenervation alterations and an immediate loss of the muscle contractile activity caused by muscle inactivity with diminished demand for FFA as an energy source. We have also taken into consideration a diminished rate of LPL synthesis or enhanced intracellular degradation. In the present study, 1 day after the sciatic crush, the HLPL and RLPL activities were also decreased in denervated soleus and red portion of gastrocnemius muscles. In the soleus, the magnitude of changes was similar to that found 12 h after nerve cut, and, in the red portion of gastrocnemius, the decrease in the activity of HLPL fraction was more pronounced.

According to Jakubiec-Puka et al. (16), it is possible to compare the results obtained after the sciatic nerve crush with those after nerve cut, because the rates of atrophy of the rat leg muscles for ~15 days after both types of nerve injuries are the same. It seems, therefore, probable that the mechanisms leading to reduction in LPL activity 24 h after the nerve crush found in the present study are similar to those after the nerve cut.

Unexpectedly, 24 h after the unilateral sciatic nerve crush, the reduced LPL activity in muscles from the injured leg was accompanied by slightly increased LPL activity in the muscles from the intact, contralateral hindlimbs, especially the HLPL fraction in the soleus. It seems likely that, during the period of postcrush recovery, rats do not use the injured leg, which leads to an overload of the contralateral leg and rise in LPL activity.

The reduced LPL activity found after the sciatic nerve crush persisted during the time of denervation and was accompanied by muscle weight loss and reduction in fiber diameter. It started to reverse during reinnervation of muscles, at different time in different fiber types. In the soleus muscle of control rats, 90% of fibers showed characteristics of the SO type, whereas, 27 days after the nerve crush, the proportion of SO fibers decreased to 27%. This was accompanied by the number of fibers simultaneously showing characteristics of both types SO and FOG increasing from 1 to 39% (16). At the same time, the transformation into SO and FOG fiber type during denervation took place in other red muscles (22, 23). This slow-to-fast and fast-to-slow transformation of muscle fibers may be responsible for the unexpectedly long-lasting low LPL activity in the soleus muscle, which is in contrast to increasing activity of this enzyme in the red portion of gastrocnemius from the 14th day after the nerve crush.

In agreement with our laboratory’s previous results (34), the present data showed that, in both the soleus and red portion of gastrocnemius muscles, the activity of the HLPL fraction is more affected by denervation than activity of the RLPL. This suggests that reduced LPL activity after the nerve crush may result from not only decreased synthesis of the enzyme but also restrained translocation of LPL particles to the plasma membrane and their reduced secretion from myocytes to capillaries. The process of intracellular translocation of LPL particles within the myocytes is poorly recognized, but structural damage like disruption of sarcoplasmic reticulum, related to denervation, may inhibit this transport, causing an accelerated intracellular inactivation and/or degradation of the enzyme.

Peripheral nerve injury affects not only muscle fiber structure, contractile ability, and energy metabolism
but also local circulation. It has been shown that denervation causes an immediate increase in blood flow to muscles (5, 14). Eisenberg and Hood (8) demonstrated that a 10-fold increase in blood flow in the tibialis anterior muscles of rats 7 days after nerve crush returned to the normal, control value 21 days after the injury. Disuse of muscles leads also to regression of microvascular structure, degeneration of the capillary wall, alteration in the endothelial barrier permeability, and progressive decrease of capillary density (37). All these changes result in lowered binding of LPL to the luminal endothelial surface and increased release of the enzyme from these cells, which may lead to the reduced HLPL activity found in our study. Changes in local circulation after denervation are more pronounced in oxidative than oxidative-glycolytic muscles (4), which additionally explains why LPL activity in the soleus muscle is more affected than that in the red gastrocnemius.

The sciatic nerve crush, with continuity of the nerve preserved, allows for complete axonal return and restoration of the nerve-muscle interaction. This leads to muscle regeneration; however, full recovery from denervation atrophy takes 4 mo in most muscles. During this time biochemical and physiological changes become reversed. When reinnervation takes place, local circulation dynamics of previously denervated skeletal muscle return to normal even faster than the energy state, which may facilitate the recovery of energy metabolism (12). In regenerating muscle, transformation of fiber types into a more oxidative pattern also takes place and is consistent with the dependence of oxidative metabolism on innervation. All these changes in gastrocnemius and soleus during reinnervation are reflected in gradually increasing LPL activity, although the time course of recovery depends on the muscle fiber composition. We have noted that activities of both LPL fractions in the red portion of gastrocnemius on the 40th day after nerve crush markedly exceeded the control values, which may be associated with a subsisting shift of FOG toward SO fibers. Moreover, it was demonstrated previously that some enzymes display an “overshoot” activity, possibly reflecting increased energy demand by growing muscle (6). The increased LPL activity during progressive reinnervation, which accompanies increasing contractile activity of muscles, supports also the results of our laboratory’s previous study, in which it was shown that enhanced contractile activity of denervated muscle by electrostimulation partly restored activities of both LPL fractions (34).

The gradual decrease in the activities of both LPL fractions in the soleus muscle from the contralateral leg was rather unexpected. The reduction of LPL activity was less pronounced than in the denervated-reinnervated muscles, and it occurred with some delay after the sciatic nerve crush. After denervation, the cross-extension reflexes disappear and contractile activity of extensor muscles like the soleus is decreased. Reichmann et al. (28) reported that unilateral cross-reinnervation of the soleus muscle is capable of altering the properties of this muscle in the unoperated contralateral leg after relatively long periods. These authors (28) described a slow-to-fast transformation of muscle fibers in the untouched soleus from the contralateral hindlimb, similar to that occurring in the injured muscle. Oki et al. (26) found that ~5% of the capillaries in the contralateral to immobilized soleus muscle had extremely thin endothelial cells that were perforated by fenestrations. All these changes in the contralateral to denervated soleus may contribute to the lowered LPL activity. LPL activity in the nonoperated soleus returned to control values after 40 days from the nerve crush. In view of these findings, the contralateral hindlimb does not seem to be a suitable control in the denervation-reinnervation studies.

It was found previously that the increased FFA concentration in denervated muscles is accompanied by decreased rate of fatty acid oxidation (17, 29), which may result in increased TG content. We have found an immediate increase in TG content in the red portion of gastrocnemius after the nerve crush and a marked increase in TG content in the soleus during reinnervation. It seems likely that decreased insulin sensitivity of skeletal muscle after denervation plays a role in elevation of TG content. This hypothesis is supported by findings that muscle insulin resistance induced by a high-fat diet, fructose infusion or genetic modifications results in an increase in TG and diacylglycerol contents (29). The above-mentioned authors suggested that this effect is due to an increase in the malonyl-CoA concentration, an inhibitor of long-chain fatty acyl-CoA transport into mitochondria, which leads to their retention in the cytosol and further incorporation into TG and diacylglycerol pool. According to Saha et al. (30) also in denervated muscles the concentration of malonyl-CoA is significantly enhanced. An elevation of neutral lipids in denervated muscles was also reported by others (2, 13, 36).

To summarize, muscle denervation after the sciatic nerve crush results in immediate reduction in LPL activity in the soleus and red portion of gastrocnemius muscles, lasting for up to 2 wk until the regeneration processes in the injured nerve start. This finding confirmed our earlier suggestions that lack of nerve conduction, leading to muscle disuse, plays a predominant role in controlling muscle potential to take up and utilize FFAs derived from plasma TG. The distinct pattern of changes in LPL activity during reinnervation in the muscles examined indicates that other factors, such as muscle fiber composition, slow-to fast and fast-to-slow muscle fiber transformation, and changes in local blood flow, should be considered for explaining the mechanism of muscle LPL dynamics in denervation-reinnervation processes. The reduced LPL activity in the soleus muscle from the contralateral to denervated hindlimb indicates that this leg may be unsuitable as a control in denervation-reinnervation studies on lipid metabolism.

We are grateful to Prof. H. Kaciuba-Uscilko for valuable comments in all stages of the study.
REFERENCES


2. Chen KS, Heydrick SJ, Brown ML, Friel JC, and Ruder-
man NB. Insulin increases a biochemically distinct pool of diac-

3. Corthn RN, Muoio DM, and Dohm GL. Skeletal muscle lipid metabolism: a frontier for new insights into fuel homeosta-

4. Delp MD and Armstrong RB. Blood flow in normal and dener-


6. Dubois DC and Max SR. Effect of denervation and reinnerva-
ton on oxidation of 6-C glucose by rat skeletal muscle homoge-


8. Eisenberg HA and Hood D. Changes in nerve conduction and 
control of vascular tone in muscles of different 


14. Jakubiec-Puka A and Drabikowski W. Influence of denerva-
tion and reinnervation on autolytic activity and on protein com-


Pi/PCr ratio during denervation-reinnervation of the gastroco-


20. Max SR, Young JL, and Mayer RF. Neural regulation of 
glucose 6-phosphate dehydrogenase in rat muscle: effect of de-

21. Midrio M, Danielli-Betto D, Betto R, Noventa D, and An-
tico P. Cordotomy-denervation interaction on contractile and 
myofibrillar properties of fast and slow muscles in the rat. Exp 

22. Midrio M, Danielli-Betto D, Megighian A, Velussi C, Ca-
tani C, and Carraro U. Slow-to-fast transformation of denerv-
ated soleus muscle of the rat, in the presence of an antifibril-

23. Nemeth PA, Cope TC, Kushner S, and Nemeth PM. Spatial 
arrangement and metabolic capacity of fiber types in self-rein-

24. Nemeth PM and Turk WR. Biochemistry of rat single muscle 
fibers in newly assembled motor units following nerve crush. 

25. Oki S, Desaki J, Tagucki Y, Matsuda Y, Shibata T, and Okumura H. Capillary changes with fenestrations in the 
contralateral soleus muscle of the rat following unilateral limb immob-

26. Oscai LB, Tsika RW, and Essing DA. Exercise training has a 
heparin-like effect on lipoprotein lipase activity in muscle. Can 

27. Reichmann H, Striha T, and Pette D. Ipsi- and contralat-
eral fibre transformation by cross-reinnervation. A principle of 

28. Ruderman N, Saha A, Vavvas D, and Witters L. Malonyl-
CoA, fuel sensing, and insulin resistance. Am J Physiol Endo-

29. Saha A, Kurowski T, and Ruderman N. A malonyl-CoA 
fuel-sensing mechanism in muscle: effects of insulin, glucose, 
and denervation. Am J Physiol Endocrinol Metab 269: E283– 

30. Seip RL, Mair K, Cole TG, and Semenkovich CF. Induction 
of human skeletal muscle lipoprotein lipase gene expression by 
short-term exercise is transient. Am J Physiol Endocrinol Metab 


32. Sesodia S, Choksi RM, and Nemeth PM. Nerve-dependent 

33. Smol E, Zernicka E, Czarnowski D, and Langfort J. Li-

34. Taskinen MR, Nikkila EA, Huttonen J, and Hilden HA. 
Micromethod for assay of lipoprotein lipase activity in needle 

35. Turinsky J, Bayly BP, and O’Sullivan DM. 1,2-Diacylglyc-

36. Tynl K and Mathieu-Costello O. Structural and functional 
changes in the microvasculature of disuse skeletal muscles. 

37. White KK and Vaughan DW. Age effects on cytochrome oxi-