Biomechanical Properties and Mechanotransduction of Skeletal Muscles as The Basis for The Use of Myofascial Osteopathic Techniques

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Abstracts: Skeletal muscles are an important link in human biomechanics. Every movement depends on muscle strength and is important for maintaining health and quality of life. Mechanical loads on the human body directly depend on the state of muscle tissue, so it is necessary to understand the cellular composition and regulation of the tissue responsible for the processes of mechanotransduction . This, in turn, makes it possible to develop methods of effective manual intervention in complex rehabilitation for patients with dysfunctions of the musculoskeletal system. This review describes the molecular basis of mechanotransduction in muscle tissue.

Keywords: Hypertrophy, mTORC, Wnt Growth, Mechanical Load, Mechanotransduction, Skeletal Muscles.

1. INTRODUCTION

Any movement is carried out by our skeletal muscles. We are used to thinking that a muscle can contract and stretch, but a large number of chemical reactions take place in these tissues. This is an important component in human physiology, providing a greater range of motion in joints and improving microcirculation of all organs. For example, a number of chemical reactions occur in skeletal muscle, as well as the storage of amino acids and glucose. Produces various myokines that influence metabolism in other tissues [1-3] .

We must understand the factors that influence skeletal muscle metabolism to prevent loss of muscle mass, which can lead to functional instability and increase the risk of injury and ultimately reduce quality of life.

A huge number of factors influence muscles, both genetic and epigenetic: hormonal levels , nutrition, mechanical stimuli [4,5]. Mechanical loading is necessary for the growth of muscle tissue (i.e., muscle hypertrophy) [6-8].

The structural unit of skeletal muscles is muscle fiber and the application of a mechanical load on it will give a biochemical reaction, the so-called process is mechanotransduction

Muscle fiber consists of myofibrils, which include molecules actin and myosin, as well as auxiliary proteins - titin, troponin, tropomyosin and other proteins. All these components are found in sarcaplasm.

When skeletal muscles contract, sarcoplasm, like water in a balloon, presses on the outer shell muscle fiber and expands it, activating chemical signals inside fibers. Chemical signals activate a variety of enzymes found in the

sarcoplasm. These enzymes act on the myonuclei and cause increased protein synthesis. This ultimately leads to muscle hypertrophy.

The lack of muscle function even in the womb leads to impaired development of fetal bones and joints [13-17], and during postnatal skeletal growth (2-20 years), the more muscle mass increases, the more bone mass becomes [18]. If we compare muscle and bone tissue, we can say with confidence that they are similar [19, 20]. This is how muscles work to grow bones. And a decrease in muscle mass can lead to bone loss, which will lead to spinal cord damage [23], and the development of neuromuscular diseases (cerebral palsy, Duchenne muscular dystrophy [21, 22].

In the practice of a manual medicine doctor, dysfunctions of the musculoskeletal system are often encountered, caused by weakness of skeletal muscles, with the formation of local muscle compactions (triggers) in them. To eliminate them, myofascial release techniques are used. release, soft tissue, muscle-energy techniques, strain - counterstrain techniques. In addition to manual treatment, special exercises and a corrective diet are prescribed to consolidate the therapeutic effect. However, the doctor does not always fully understand the specifics of the physiological processes occurring in muscle tissue as a result of manual mechanical action. In this article, we focused on mechanotransduction, a physiological process in which mechanical load is converted into biochemical reactions.

1.1. Mechanotransduction And Regulation of Skeletal Muscle Mass

The development of muscle tissue depends on protein synthesis and degradation [24]. The greater the synthesis, the stronger the muscle hypertrophy, and conversely, reduced synthesis leads to muscle atrophy. Currently, there are a number of signaling mechanisms that influence protein synthesis under mechanical load [25-34]. For example, a protein kinase called mechanical target of rapamycin (mTOR), [6, 11]. Also, satellite cells (SC) play an important role in mechanotransduction [7, 35 – 38] .

1.2. Mechanical Signaling Messengers in Skeletal Muscle

mTOR

mTOR is a conserved serine / threonine kinase that is contained in two complexes: mTORC1 (whose signaling is partially inhibited by the drug rapamycin) and mTORC2 (resistant to rapamycin) [39]. mTORC1 is the main regulator of cell growth, ensures the rate of mRNA translation), and regulates the number of ribosomes [40].

Under the influence of mechanical forces, mTORC1 is activated in skeletal muscles [6]. As a result, protein synthesis increases and induces hypertrophy of muscle fibers (*in vivo)* [41, 42], which lead to muscle hypertrophy [43, 44].

Potential candidates for mechanically induced mTORC1 activation include increased intracellular Ca2, amino acids, insulin-like growth factor 1 (IGF -1), extracellular signal-regulated kinase 1 and 2 (ERK1/2), phosphatidic acid (PA), TSC2 (tuberin). Additional research is needed to clarify the role of the above factors.

1.3. Increased Intracellular Calcium Content

The sarcoplasmic reticulum (SR) stimulates the release of calcium, which causes skeletal muscle contraction [45]. There is also a downside - with passive muscle stretching, the amount of intracellular calcium increases by activating stretch-sensitive ion channels [46, 47]. Studies in non-muscle cells have shown that mTORC1 signaling can be regulated by changes in [$Ca2^+$], with an increase in [$Ca2^+$] activating mTORC1 signaling and a decrease in [$Ca2^+$] resulting in inhibition of mTORC1 signaling [48, 49]. Increasing [$Ca2^+$] has been shown to also increase the rate of protein synthesis *ex vivo* in resting skeletal muscle [50]. Thus, contraction or stretch induced increases in [$Ca2^+$] appear to be an ideal candidate for mechanical activation of mTORC1 and protein synthesis in muscle tissue.

Chronic mechanical overload activates $Ca2^{+}$ / calmodulin-dependent protein kinase α (CaMKKα), and together with the increase in $Ca2^{+}$ stimulates mTORC1 signaling and protein synthesis [52, 53]. On the other hand, there is no requirement for CaMKK α for muscle growth [53].

Thus, an increase in [$Ca2^{+}$] may stimulate mechanical activation of mTORC1, but this requires further study.

1.4. Amino Acids

Amino acids are important regulators of mTORC1 signaling, which plays a key role in the regulation of protein synthesis and skeletal muscle mass. Studies have shown that decreasing amino acid levels leads to decreased mTORC1 activation, while increasing amino acid availability increases mTORC1 activation [60].

Particularly important are branched chain amino acids such as leucine, which can activate mTORC1 signaling and increase protein synthesis. Therefore, increased amino acid intake may play a role in the mechanical activation of mTORC1 signaling [61, 62].

However, there is still no evidence to support this hypothesis. Some studies have shown that resistance exercise increases muscle leucine content and class III PI3K, Vps34 activity, which is associated with mTORC1 activation [63 - 67]. However, other studies have reported a decrease in leucine following acute resistance exercise [68].

Thus, although there is some indirect evidence suggesting a role for amino acids in the mechanical activation of mTORC1 signaling, more research is required to more fully understand this process.

1.5. Prostaglandins

There is evidence that prostaglandin (PG) signaling may also play a role in the mechanical regulation of protein synthesis and muscle hypertrophy. Studies have shown that PGs stimulate an increase in protein synthesis in skeletal muscle and cause hypertrophy of cultured myotubes [69 - 74].

In addition, mechanical stimulation of skeletal muscle also leads to increased production of PGs, including PGF2α [75, 76]. This supports a possible role for PG in mechanical activation of mTORC1 and muscle hypertrophy. It is also worth mentioning that after eccentric exercise there is an increase in protein synthesis, and large doses of Cox inhibitors , acetaminophen and ibuprofen can reduce it [77].

Not all PGs can stimulate protein synthesis. Some studies have shown that PGE2 stimulates protein degradation in skeletal muscle [70]. Therefore, additional research is required to more fully understand the role of various PGs in the mechanical regulation of protein synthesis and skeletal muscle mass.

Overall, although there is some evidence suggesting a role for amino acids and prostaglandins in the mechanical regulation of mTORC1 signaling and protein synthesis, more research is required to more fully understand these processes.

1.6. Wnt Signaling

In skeletal muscle embryogenesis as regeneration, Wnt molecules play a major role [78, 79]. It is also worth noting that exercise increases Dsh/GSK3β interaction and also decreases GSK3β activity and β- catenin phosphorylation in humans [80]. In addition, muscle fiber hypertrophy induced by resistance training is associated with increased expression of various elements of the Wnt signaling pathway (e.g., Wnt1, β- catenin , LEF1, cyclin D1) [81]. Muscle loading also influences muscle hypertrophy, and β-catenin is required for this [82]. It follows that Wnt/β- catenin signaling takes place in mechanotransduction and muscle tissue enlargement.

CONCLUSION

In conclusion, we note that the molecular mechanisms regulating mechanotransduction in skeletal muscle are complex and, in many ways, similar to the processes in bone tissue. In this case, several mechanisms likely work in synergy.

In skeletal muscle, mTORC1 has been established as a major messenger for stimulating protein synthesis, as well as intracellular calcium and amino acids. However, much remains to be studied to prove the acceleration of skeletal muscle growth due to mechanotransduction messengers.

The role of prostaglandins and Wnt signaling in the mechanical activation of mTORC1 in skeletal muscle needs to be understood.

This review explains the basic processes of mechanotransduction in skeletal muscle. It is necessary to understand the importance of studying this topic to explain the application of myofascial osteopathic techniques, physical exercises for the development and growth of muscle tissue and stimulate ideas for future research.

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