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IGF-I and insulin induce different intracellular calcium signals in skeletal muscle cells - Evidence review

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1. ABSTRACT

The analyzed study compared the immediate effects of insulin and IGF-I on intracellular calcium in myotubes, i.e., cultured skeletal muscle cells. The authors observed that insulin induced a very rapid and transient increase in calcium, with characteristics different from those produced by IGF-I. The insulin signal was abolished in the absence of extracellular calcium and was sensitive to inhibitors of channels involved in calcium mobilization.In “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, this publication contributes to the narrative that insulin can early mobilize calcium signals in skeletal muscle through a mechanism distinct from that of IGF-I. Independent studies in mouse muscle fibers, isolated muscles, and myotubes confirm that insulin can increase local calcium entry and activate additional intracellular release circuits. However, there are non-overlapping results in other experimental models. The confirmation is therefore primarily mechanistic and does not directly demonstrate clinical effects in humans.

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Through articles, reviews, in-depth analyses and expert contributions, the Journal champions evidence-based medicine and science, fostering a correct interpretation of scientific data and countering misinformation. Every piece of content is developed with the aim of translating the complexity of research into understandable, useful and applicable information, while keeping intact the principles of accuracy, transparency and scientific independence.

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2. ANALYZED STUDY

The research question was whether two hormones that act on skeletal muscle, insulin and insulin-like growth factor 1 (IGF-I), induce the same calcium signal within cells. Intracellular calcium is a small portion of the calcium present in the cell that also acts as a signal, meaning it contributes to activating or modulating cellular functions.The hypothesis evaluated was that insulin produces an early calcium signal with its own specific characteristics, not simply overlapping with those of IGF-I. This is the reason for its relevance to the section "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi: the publication documents that, in the muscle cells examined, the insulin signal and the IGF-I signal differ in mechanism and dependence on specific cellular structures.The study can demonstrate that insulin rapidly modifies the calcium signal in the cell models used and that this response depends on certain experimental conditions. However, it cannot demonstrate that the same phenomenon occurs with identical intensity in intact human muscle, nor that the signal alone is sufficient to activate cPLA2a, an enzyme that releases fatty acids from membrane phospholipids.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The publication available as an abstract describes experiments on cultured primary myotubes, which are cells obtained from muscle and maintained in the laboratory until they form structures similar to immature muscle fibers. The authors measured changes in intracellular calcium using fluo-3, a fluorescent probe whose emission increases when it binds to calcium.The main comparison concerned the response to IGF-I and insulin. To explore the mechanisms, conditions lacking extracellular calcium and substances that interfere with specific signaling pathways or calcium channels, including nifedipine and ryanodine, were used. Normal muscle cell lines, cells lacking the alpha1 subunit of the dihydropyridine receptor, and cells lacking ryanodine receptors were also used. These latter proteins participate in the regulation of calcium movement in muscle cells.The number of cell preparations, the number of independent experiments, the concentrations of insulin and IGF-I, the sample selection criteria, the statistical procedures, the P-values, and the confidence intervals are not reported in the available material. There is no follow-up, as these are acute experiments in cultured cells.

4. RESULTS

In simple terms, both hormones rapidly increased calcium in muscle cells, but they did so through different pathways. IGF-I caused a rapid and transient increase in calcium, associated with an increase in IP3, or inositol-1,4,5-trisphosphate. IP3 is a molecule that can promote the release of calcium from internal cell stores. Inhibitors of the IP3 pathway blocked the signal induced by IGF-I.Insulin, on the other hand, induced a transient and very rapid increase in calcium, described as occurring in less than a second from the start of the response. The signal induced by insulin was abolished in a calcium-free medium and reduced by nifedipine or ryanodine. This direction of the result is important: removing external calcium eliminated the observed response, suggesting that the entry of calcium from the outside is necessary in the experimental model.In NLT muscle cells, considered normal by the authors, the calcium responses provoked by the two hormones were similar to those of primary myotubes. Cells lacking the alpha1 subunit of the dihydropyridine receptor responded to IGF-I but not to insulin; restoring the alpha1 subunit allowed the response to both hormones once again. Similarly, cells lacking ryanodine receptors maintained the response to IGF-I but did not show the insulin-induced increase in calcium. Inhibition of G proteins, which are proteins that transmit signals between receptors and intracellular targets, also blocked the insulin response without significantly altering the response to IGF-I.Since the available abstract does not report complete quantitative values, sample sizes, data dispersion, or statistical analyses, it is not possible to estimate the effect size or the precision of the differences between experimental conditions.

5. INTERPRETATION

The primary significance is that, in the examined cells, insulin did not merely activate well-known metabolic pathways, but also produced an extremely early calcium pulse. This pulse appears to require both the calcium present outside the cell and components that regulate the release of calcium from intracellular

stores.From a technical standpoint, the study distinguishes an insulin response dependent on the dihydropyridine receptor, ryanodine receptors, and G proteins, from the IGF-I response, which is more closely linked to the IP3 pathway. This does not mean that the two pathways are completely isolated in the body, nor that every muscle fiber responds in the same way.In the section of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, the segment actually supported by the publication is: insulin early calcium mobilization in skeletal muscle a mechanism different from that induced by IGF-I. The study did not measure the activation of cPLA2a, the release of arachidonic acid, or inflammation; these steps remain outside its experimental design.

6. INDEPENDENT SUPPORTING EVIDENCE

Initial independent confirmation comes from intact skeletal muscle fibers isolated from mice. Bruton and colleagues observed that insulin did not increase the average calcium level of the entire fiber, but it did increase calcium near the cell membrane by approximately 70%. This local increase was lost in a low-calcium medium and following the inhibition of L-type calcium channels. The result directly confirms the step suggesting that insulin can promote the entry of extracellular calcium into the muscle, while specifying that the signal can be localized and therefore not necessarily visible as a global increase in cellular calcium [1].In a second study on single fibers and isolated mouse muscles, Lanner and colleagues found that insulin increased calcium influx. Maneuvers that reduced this influx also reduced the entry of 2-deoxyglucose, an experimental measure of glucose transport; conversely, conditions that increased calcium influx were associated with greater insulin-stimulated glucose uptake. This work supports the functional role of calcium in the late stages of insulin signaling, although it remains an animal and pharmacological experiment [2].A third study in myotubes added a mechanistic level. Contreras-Ferrat and colleagues observed that insulin promoted two calcium release pathways: one associated with reactive oxygen species and the ryanodine receptor, the other dependent on IP3. Inhibition of these pathways reduced the translocation of GLUT4, the transporter that allows glucose to enter the muscle cell. This confirms that the calcium signal can integrate with the metabolic action of insulin, but it does not prove that a single mechanism dominates under all physiological conditions [3].Taken together, these studies do not identically replicate the original model, but they converge on a specific point of the narrative: in skeletal muscle, insulin can mobilize calcium in rapid, spatially localized, and cell-context-dependent ways.

7. CONFLICTING EVIDENCE

Not all research has observed the same effect. In a study on isolated mouse diaphragms, Naitoh and colleagues did not observe changes in the efflux or influx of radioactive calcium following insulin alone. In the same model, an artificial increase in calcium influx via an ionophore was associated with a reduction in insulin-stimulated glucose uptake [4].This evidence does not negate the signal observed in the original study, but it does define the scope of its interpretation. Measuring total calcium flux in an isolated muscle may fail to detect a signal that is very brief or confined near the membrane. Furthermore, the artificial and sustained increase in calcium produced by an ionophore is not equivalent to an early physiological pulse induced by insulin. The results therefore suggest that the location, duration, and intensity of the signal matter: a local and transient increase may have different effects than a more widespread or prolonged calcium overload.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the study that is the subject of the Evidence Review from the independent publications used to confirm or define the narrative passage of the book.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Experimental cellular	Primary myotubes and muscle cell lines	Insulin induced a rapid and transient increase in calcium; the response was abolished without extracellular calcium and in cells lacking specific signaling components.	direct confirmation	moderate
[1]	Animal, isolated muscle fibers	Single mouse skeletal muscle fibers	Insulin increased membrane-proximal calcium by approximately 70%, without increasing global fiber calcium.	direct confirmation	moderate
[2]	Animal, isolated fibers and muscles	Skeletal fibers and muscles from normal and ob/ob mice	Insulin increased calcium influx; reducing it decreased insulin-induced glucose transport.	indirect confirmation	moderate
[3]	Experimental cellular	Cultured skeletal muscle cells	Insulin activated calcium release pathways associated with ROS, ryanodine receptors, and IP3, contributing to GLUT4 translocation.	biologically consistent evidence	moderate
[4]	Animal, isolated muscle	Mouse diaphragms	Insulin alone did not change total radioactive calcium fluxes; an artificial increase in calcium reduced insulin-induced glucose uptake.	discordant evidence	low

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The study analyzed directly supports the claim that insulin can trigger a rapid and transient calcium signal in skeletal muscle cells and that this signal is distinct from the one induced by IGF-I. Independent evidence primarily confirms the existence of a local calcium influx and complementary intracellular pathways in the muscle of animal or cellular models. The narrative is therefore supported at a mechanistic level. However, it has not been demonstrated by this research that the same pathway occurs identically in humans or that it leads directly to the activation of cPLA2a and the subsequent pro-inflammatory cascade.

Aggiornato al 24/11/2026. Questo contenuto riflette una sintesi divulgativa delle evidenze scientifiche al momento della pubblicazione e non sostituisce il parere medico.

10. TRANSPARENCY AND SCIENTIFIC RESPONSIBILITY

Artificial Intelligence was used solely as a tool for editorial and documentary support. All content, interpretations, bibliographic citations and conclusions have been verified, reviewed and approved by the author, who assumes full scientific responsibility for them.

The manuscript was also subjected to independent peer review prior to publication.

To ensure the greatest transparency, the complete history of the article, including the dates of submission, revision, acceptance and publication, as well as information on the peer review process, is available on the dedicated Article History page.

11. RIFERIMENTI BIBLIOGRAFICI

[1] **Insulin increases near-membrane but not global Ca 2+ in isolated skeletal muscle**
Bruton et al., 1999
Proceedings of the National Academy of Sciences
DOI: https://doi.org/10.1073/pnas.96.6.3281

[2] **The Role of Ca2+ Influx for Insulin-Mediated Glucose Uptake in Skeletal Muscle**
Lanner et al., 2006
Diabetes
DOI: https://doi.org/10.2337/db05-1613

[3] **Insulin elicits a ROS-activated and an IP3-dependent Ca2+ release; both impinge on GLUT4 translocation**
Contreras-Ferrat et al., 2014
Journal of Cell Science
DOI: https://doi.org/10.1242/jcs.138982

[4] **Intracellular Ca2+ and Mg2+ Regulation for Insulin-Stimulated Glucose Uptake into Mouse Diaphragm Muscles**
Naitoh et al., 1991
Japanese Journal of Pharmacology
DOI: https://doi.org/10.1254/jjp.56.241