International Journal of Sport Studies for Health

Journal Homepage

The Effect of Exercise Activity on Pannexin and NLRP3 in Neuromuscular Function with the Approach of The Role of New Peptides: A Narrative Review

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1. Round 1

1.1 Reviewer 1

Reviewer:

In the first paragraph of the Introduction, the term “neuro-muscular function” is used repeatedly. Consider standardizing terminology (e.g., neuromuscular vs. neuro-muscular) for consistency throughout the paper.

The sentence "Exercise has been found to strengthen muscles, increase nerve conduction velocity..." could benefit from more precise citation of primary studies, as reference (6) is too general. Specify which findings support each listed effect.

The figure caption for Figure 1 lacks any detailed description. Please expand on what the figure illustrates about exercise-induced pannexin-1 modulation.

In the paragraph beginning “The relationship between exercise and NLRP3 activation is multifaceted…”, the dual role of exercise is described but lacks synthesis. Add a summarizing sentence reconciling these opposing effects (activation vs. inhibition).

The phrase “NLRP3-mediated inflammation has the ability to trigger extreme adaptations” is ambiguous. Please clarify what is meant by “extreme adaptations” and whether these are desirable or pathological.

The sentence “NLRP3 is an undisputed key player in the area of exercise-induced adaptation” (paragraph 1 of Exercise and NLRP3) is too definitive. Consider softening the claim or providing broader supporting evidence.

The sentence “Exercise-activated irisin release would be involved in muscle contraction and fatigue…” should clearly differentiate between evidence from animal models vs. human studies and cite accordingly.

In “the potential interaction between irisin, pannexin-1 channels, and NLRP3 is a new area of study…” (Irisin section), consider stating if any current empirical data exist or whether this is purely theoretical.

Author revised the manuscript and uploaded the updated document.

1.2 Reviewer 2

Reviewer:

The sentence “These hemichannels in gap junction serve a pathway...” (paragraph 3 of Introduction) is syntactically awkward. Consider rephrasing to: “These hemichannels, functioning within gap junctions, serve as pathways for small ions and signaling molecules…”

In the Methods section, you mention including literature from 2013 to 2025, yet later state a focus on "studies published within the last decade.” This inconsistency should be resolved or clarified.

The phrase “reference lists of highlighted articles were meticulously searched…” is vague. Clarify what constitutes a “highlighted” article and whether a PRISMA or other structured approach was used in selection.

In the paragraph starting with “Pannexin channels, and particularly pannexin-1…”, several hypotheses are presented as fact. Rephrase to maintain a critical tone, especially for mechanisms “under investigation” (e.g., ATP release roles and channel phosphorylation).

The phrase “IL-6 is also involved in ‘browning’ white fat...” is repeated in two places in the Interleukin-6 section. Streamline the content to avoid redundancy while emphasizing the physiological relevance.

The sentence “Muscle pannexin-1 channels are responsible for ATP release to control IL-6 production” requires elaboration. Explain the causal pathway or intermediary steps, or clarify if this is still hypothetical.

The sentence “Exercise-stimulated pannexin-1 activation and ATP release can influence muscle contraction…” contains a redundancy. Consider rephrasing: “Pannexin-1 activation during exercise releases ATP, which modulates muscle contraction…”

Author revised the manuscript and uploaded the updated document.

2. Revised

Editor’s decision after revisions: Accepted.

Editor in Chief’s decision: Accepted.