Review of: "Modelling Skeletal Muscle Motor Unit Recruitment Contributions to Contractile Function: Part 3 - Substrate Oxidation of Phosphagen, Lipid, and Carbohydrate Metabolism"

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Potential competing interests: No potential competing interests to declare.

Abstract Feedback

The text is technically detailed, but certain sections could benefit from improved clarity and organization to enhance readability and flow.

Structure and Clarity:

- The paragraph could be divided into smaller sections for easier reading. Suggested sections:
  - Introduction to the model and methods.
  - Main results by energy system.
  - Interpretation and implications.
- Some sentences are long and challenging to interpret quickly, such as:

"The model utilized repeated contractions of varied frequency and fraction of motor unit recruitment, and four different genetic expressions of motor unit proportions."
Suggested improvement: Introduce key concepts separately.
"The model simulated repeated contractions varying in frequency and recruitment fraction, incorporating four genetic profiles of motor unit distribution."

Consistency in Terminology:

- Ensure technical terms are used consistently. For instance, "ATPto" seems to refer to "ATP turnover," but it could be confusing without an initial definition and should be used homogeneously (e.g., "ATPto" and "known ATP_{to} ").

Coherence Between Ideas:

- Some sentences have abrupt transitions. For example:

"This is to be expected for modelled research involving temporal summation of metabolism."

Improvement: Integrate it better with the previous context, connecting the explanation with the results.

- Some explanations are isolated and not well-connected to the results. Briefly explain *why* temporal summation is relevant for modeling and how it influences the presented results.

Simplification and Elimination of Redundancy:

- Sentences like:

"Using LabVIEW™ programming, the model then used the prior data of ATPto..."

Could be streamlined to:

"The model, implemented in LabVIEW™, used prior ATP turnover data..."

Stylistic Adjustments for Objectivity:

- Qualitative expressions like "far larger" or "logical" may appear subjective in a scientific context.
  Suggested replacements:
  - Replace *"far larger"* with *"significantly higher or greater."*
  - Replace *"logical"* with *"consistent with known physiological mechanisms."*

Results and Interpretation:

- The text presents results but lacks a smooth transition to interpretation. For example:

"Fatty acid oxidation was larger for lower motor unit recruitment conditions, and highest for type I-IIa and IIa motor units."

Improvement: Use clearer connectors to directly relate the results to the interpretation:

"This finding aligns with the recruitment patterns of oxidative fibres predominant in type I-IIa and IIa motor units."

Redundancy:

- Some information is repeated or unnecessarily prolonged. For example:

"Creatine phosphate is continually broken down and partially replenished during low-intensity exercise, with such partial replenishment sustained during more intense exercise thanks to the creatine kinase shuttle."

Improvement: Eliminate repetition and retain only:

"Creatine phosphate breakdown and partial replenishment occur during low- and high-intensity exercise via the creatine kinase shuttle."

Introduction

The introduction has a comprehensive background:

- Provides extensive detail on muscle biopsy methodologies, fibre type classification, and motor unit recruitment.
- The progression from biopsy limitations to motor unit-specific metabolic considerations is logical and sets up the research aim effectively.
- Table 1 and numerical data support the discussion effectively, offering concrete information about fibre type characteristics.

Areas for Improvement

Overly Detailed Descriptions

The explanation of biopsy procedures is too detailed for an introduction and could distract from the main focus.

Example:

"This procedure involves an incision to be made through the skin, subcutaneous fat and muscle fascia which allows a biopsy needle to be inserted through this incision and into the inner regions of the underlying muscle of interest."

Summarize briefly:

"Muscle biopsy involves extracting a small muscle sample through an incision for metabolic and enzymatic analysis."

Clarity in Sentence Construction

Some sentences are long and dense, making the information harder to follow.

Example:

"Since the early 1990s, more elaborate muscle fibre type classification methods have been pursued, with the most prominent being based on different genetic expressions of the structure of the myosin heavy chain."

Suggestion: Break down into simpler sentences:

"Since the 1990s, muscle fibre type classification has advanced significantly. One prominent method uses genetic differences in myosin heavy chain structures."

Consistency in Terminology

Ensure consistency in terms like *"slow twitch oxidative"* vs. *"Type I," "Type IIb,"* etc. Using multiple terms for the same concept can confuse readers.

Suggestion: Decide on a naming convention and adhere to it throughout (e.g., Type I, Type IIa, etc.).

Repetition

Some concepts are repeated unnecessarily, such as the description of motor unit recruitment principles.

Example:

"According to the 'all or none' principle, when muscle contraction occurs, each motor unit recruited contracts maximally."

This idea is repeated in the same paragraph.

Suggestion: Remove redundant statements and streamline explanations.

Table Presentation

While Table 1 is useful, it interrupts the narrative. Consider moving it to supplementary materials or referencing it more fluidly in the text.

Research Gap and Objectives

The gap and objectives are stated, but they could be more concise and impactful.

Example:

"Consequently, the purpose of this research was to use prior research and knowledge of cellular and whole-body markers of muscle metabolism to explore the more in-depth understanding of the important roles of motor unit recruitment in changing skeletal muscle metabolism during increasing contractile power."

Suggestion:

"This study aims to deepen our understanding of motor unit-specific substrate oxidation during varying contractile powers using existing VL contraction and ATP turnover models."

Overloading the Introduction

The introduction includes methodological details (e.g., ATP turnover models and prior data retrieval). These belong in the Methods section.

Suggestion: Mention briefly:

"This study employs prior models of VL contraction and ATP turnover to compute substrate oxidation, as detailed in the

Methods section."

You can improve:

- Briefly describe the importance of studying skeletal muscle metabolism and the limitations of traditional biopsy methods.
- Highlight advances in fibre type characterization and motor unit recruitment principles.
- Explain the limitations of existing methods in studying fibre-specific substrate oxidation.
- State the study's objective and the high-level approach.

Methods

Clarity and Flow:

1. **Complexity and sentence structure:** Some sentences are long and could be broken down to improve readability. For example:
    - *"Now that the cellular ATPto data was known for each motor unit recruited, across four different genetic expressions of motor unit proportions (80-20, 60-40, 40-60, 20-80 % ST-FT, respectively), five frequencies of muscle contraction (0.5, 1, 1.5, 2, 2.5 Hz), and nineteen different percentages of motor unit recruitment (5% increments from 5-95%), the task for this study was to obtain data for the fibre type specific capacities..."*
    - Could be rewritten as:
        - *"Having established the cellular ATP turnover (ATPto) data for each motor unit recruited, we examined four genetic expressions of motor unit proportions (80-20, 60-40, 40-60, 20-80 % ST-FT), five contraction frequencies (0.5, 1, 1.5, 2, 2.5 Hz), and nineteen levels of motor unit recruitment (in 5% increments, from 5% to 95%). The next task was to obtain data for fibre type-specific capacities..."*
2. **Introduce and define abbreviations early:** The abbreviation *"ATPto"* should be defined upon its first use, and its full term should be provided for clarity (e.g., ATP turnover).

Consistency and Terminology:

1. Consistent terms for energy pathways:

The terms "CK-AK," "CHO-GLY," "CHO-MR," and "FA-MR" should be clearly defined the first time they appear in the text. Consider writing out the full names for these abbreviations (e.g., "creatine kinase-adenylate kinase," "carbohydrate glycolysis," "carbohydrate mitochondrial respiration," and "fatty acid mitochondrial respiration") and using abbreviations consistently throughout.

1. ATP yield coefficients: Explain the rationale behind the ATP yield coefficients (1.1 for phosphagen, 129 for fatty acid oxidation, 3 for carbohydrate glycolysis, and 34 for carbohydrate mitochondrial respiration). This will make the methods more comprehensible to readers unfamiliar with these values.

Structure

- Procedure steps: The sequence of steps in the model could be made clearer:

1. Introduce the overall methodology briefly before delving into technical details.
2. More clarity on curve fitting and adjustments: The method of using Prism software for curve fitting could benefit from a clearer explanation.
3. Partitioning and summing data: The part about partitioning and summing motor unit data could be stated more clearly.

Technical Detail:

1. **Lactate production:** The assumption regarding lactate production is explained, but further clarification could be helpful.

Why this method over others? It would be useful to briefly mention why this method is being applied instead of other available techniques or methods for modeling ATP turnover or substrate oxidation. Maybe this approach was selected due to its ability to simulate the incremental recruitment of motor units and its previous successful application in modeling ATP turnover in skeletal muscle.

Methods

Overall Structure

The section is well-detailed and supported by figures and tables, but the dense information can overwhelm readers. To improve readability:

- Subdivide the section into clear subsections based on the systems or conditions studied (e.g., "CK-AK Energy System," "Fatty Acid Oxidation").

Summarize the main findings at the start of each subsection.

Example:

"CK-AK Energy System"

The CK-AK energy system demonstrated progressive increases in substrate oxidation with higher contraction frequencies and greater motor unit recruitment, particularly in muscles with higher fast-twitch (FT) fibre proportions (Figure 3).

Integration of Figures and Tables

- While figures and tables are referenced, the connection between the text and visuals could be stronger. You need to highlight the specific insights each figure or table provides.

Avoid repeating numbers in the text when they are already in the figures or tables. Instead, interpret or summarize the trends.

Example:

Before:

"The lower frequency and percent recruitment conditions had much higher contributions from fatty acid oxidation, as shown in Figure 7c, d."

After:

"Figures 7c and 7d illustrate increased reliance on fatty acid oxidation at lower contraction frequencies (1 Hz) and reduced motor unit recruitment (35%). This pattern aligns with the oxidative capacity of Type I fibres."

Main Findings and Interpretation

- Relate the results back to the study's objectives.
- What is the significance of increased carbohydrate dependency in FT fibres at higher frequencies?
- How do differences in genetic ST-FT proportions influence the overall findings?

Lactate and Practical Implications

- The section on lactate production describes it as the difference between CHO-GLY and CHO-MR but could emphasize its broader relevance.

Redundancies and Conciseness

- Some descriptions, such as those about "motor unit recruitment" and "energy system contributions," are repeated and could be streamlined.
- Simplify where possible to keep the focus on the results without repeating background or methodological details.

DISCUSSION

Comprehensive Analysis:

The discussion integrates a thorough interpretation of results, linking them to physiological principles like the All or None Principle and prior research.

Comparisons to Literature:

The comparison with other studies strengthens the validity of the findings and situates them within the broader research context.

Acknowledgment of Limitations:

The section explicitly addresses the study's assumptions and limitations, which is crucial for scientific rigor.

Practical Implications:

The inclusion of insights on training optimization and fiber-specific metabolism adds applied value to the research.

DISCUSSION:

Areas for Improvement and Suggestions

Organization and Flow

The section is lengthy and includes dense blocks of text.

Conciseness and Clarity

Some sentences are unnecessarily long and could be simplified.

Linking Results to Broader Implications

Some insights could be more explicitly tied to practical or theoretical implications.

For example:

"The significant role of the phosphagen system across all contraction frequencies suggests it is not limited to high-intensity exercise....

Interpretation of Energy Systems

The detailed discussion of energy systems could benefit from summarizing the key takeaways for each system in a bullet-point format.

Perspectives and Practical Implications

While the perspectives section is valuable, it could better emphasize actionable insights for training and performance. The findings suggest that contraction frequency and motor unit recruitment could be optimized to enhance energy efficiency during exercise. This is particularly relevant for designing training programs that target specific muscle fibre types or metabolic pathways.

Limitations

The limitations section is thorough but maybe could be condensed and focused on the most critical points.

CONCLUSIONS

The section effectively links the model to its practical and theoretical applications, such as sports and neuromuscular diseases, and it highlights the potential for further research to refine the model and its implications.

You can improve that:

Expand on Practical Implications

Provide more detail on how the findings could be applied in real-world contexts. For example, in sports science, the model could guide the design of training programs tailored to optimize energy utilization by targeting specific motor unit types. In neuromuscular diseases, the model may aid in understanding metabolic alterations and developing rehabilitation strategies. (Yes or NOT). And strengthen the emphasis on how the findings contribute to the understanding of muscle physiology and bioenergetics.

Next Steps

While the model offers valuable insights, it relies on theoretical assumptions that should be validated experimentally.

- Future research could focus on integrating real-time data from advanced imaging or biochemical techniques to refine predictions of fibre-specific substrate turnover.
- Validation of the model using experimental data on fibre-specific metabolism.
- Application of the model to other muscles with diverse fibre type compositions.
- Integration of genetic and molecular data to enhance understanding of fibre-type variability.