nature portfolio

Peer Review File

Modulation of beta oscillatory dynamics in motor and frontal areas during physical fatigue

Corresponding Author: Mr Pierre-Marie Matta

This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
This manuscript deals with a seeming anomaly of beta-frequency EEG signals during physical fatigue. The authors present a suite of analyses that explore this phenomenon. I think the work is comprehensive, and raises some interesting questions. I only have a small number of comments for the authors.

I would alsoi like to apologise to the authors for my late review.

Major comments

1. My only substantial comment is that the authors' analyses seem to be focused only on the frequency range of interest. While this makes sense, in that the existing literature points to there being effects in beta, and indeed the authors have replicated and extended these findings, there is no 'control' frequency that could be used to explore alternative explanations. For example, the authors find a reduction in beta during movement, and a rise during rest (shown in Figure 2). I suppose my question is whether the increse in beta in rest is ONLY in beta, or if there is a general rise in EEG power in all bands during that phase. I think I believe that authors' explanation, but without a 'control' frequency it would not be possible to show this for ceratin. I don't think I expect the authors to add a whole new analysis, but peraps the authors could add some thoughts on this?

Minor comments

1. There are a couple of places (e.g. lines 75-79) where the text changes tense to the future tense. I think this should be in the past tense for consistency.

2. The topographies presented in Figure 1B seem very different between the two example participants for High and Low beta. Could the authors explain why this might be the case? Is this an artefact (or hallmark?) of the individual nature of the beta frequency?

3. I liked the computational model a lot, and it is very satisfying to see the output matching the 'real' data so well. Could the authors say a little more about the spiking units? Perhaps adding something equivalent to a Hodgkin-Huxley style action potential, or maybe a single-unit style raster plot to Figure 6 would help the naive reader (me) to connect these units to equivalent biological data.

4. In the Discussion (lines 483-499) the authors speculate about bidirectional coupling. I think another possible explanation here could be that a more fatigued body requires additional strategic control. For example when I carry a heavy load over a long distance, at some point I find myself shifting that load around. I wonder if this coupling could reflect the need to adapt motor strategies as muscular elements 'drop out' with fatigue?

Reviewer #2

(Remarks to the Author)
The authors present a study in which they seek to reconcile a contradiction in the understanding of sensorimotor beta band oscillations in motor cortex. They state that beta band oscillations are thought to reflect neural computations that promote the maintenance of the current state of the motor system, or the 'status quo'. They state that results from prior work in physical fatigue contradict the 'status quo' idea since they show that motor cortical beta oscillations actually increase during muscle contraction with increased fatigue. This is a contradiction since it is thought that motor cortex will need to recruit more motor units to produce movement when it is fatigued.

In their experiments, the authors show a reduction in motor cortex beta oscillations during muscle contraction with increased fatigue, an increase in rest-related beta oscillations with increased fatigue, and an increase in frontal beta oscillations with increased fatigue. The authors also present connectivity analysis showing an increase in frontal-motor cortex connectivity with fatigue. Finally, the authors present a spiking model demonstrating that increasing inhibition to motor cortex will reduce beta power during a simulated contraction event.

While the study is interesting, several concerns reduce my confidence in the results and interpretation.

Major concerns:

1. The "Status Quo" Framework is very simplified: The interpretation of beta oscillations as a mechanism for maintaining the "status quo" is oversimplified. There are a number studies that highlight exceptions to this view. For example 1,2 show that beta is related to cue processing and utilization, certainly an active process. Other studies show that beta is present during precision grip isometric contraction 3–5, a task that should required recruitment of motor cortex to support a sustained output. Other perspectives propose that beta is a rhythm that facilitates active peripheral sampling6 due to its prominence not only in motor cortex but also somatosensory cortex, spinal cord, and muscle activity recordings3. Finally other studies show that beta power is highest when there's most uncertainty (or least of a "status quo") in the task7. I believe that these alternatives to the "status quo" framework have been ignored in the discussion of the results in this manuscript due to a laser-focus on defending the status quo framework, and I would like to see more discussion around the possibility that the status quo is too simple of a framework and there are other ways to understand what beta is conveying about the underlying neural computations8.

2. Beta Band definition: Already in Figure 1B, there is a lack of clarity on the issue of whether beta power is high or low during the contractions. Both participants show sustained beta oscillations at ~18Hz and ~20 Hz respectively. Based on the beta oscillations literature, these dynamics are firmly within beta band limits. Why are the authors choosing to select individualized beta bands based on the assumption that beta will desynchronize during the contraction given the existing literature that beta can indeed persist during isometric contraction? Do all participants have this split between high and low beta? The authors need to discuss why they believe that the high beta / individualized beta results are more representative of true beta dynamics (i.e. are the results discussed with reference to the status quo framework) than the low beta results. This also needs to be discussed when comparing this result to other literature – do other physical fatigue studies use the full beta band for analysis (e.g. 13-30 hz) ? perhaps this could be one reason this study differs from previous ones?

3. Isometric contraction dynamics: As mentioned above, it is puzzling that beta oscillations are reported to desynchronize during isometric contraction since previous work has found that motor cortex during isometric contractions can exhibit high beta. This manuscript assumes that the desynch occurs, and uses this fact to define the beta band frequency bounds. It must be discussed prior to doing this why this is an appropriate criteria.

4. Small Effect Sizes: The main result that contracts previous literature is shown in Fig. 2B, -- the reduction in beta power during contraction over the course of fatiguing. The effect size of this reduction is small (~4%). It is not discussed whether this is a large effect, how it compares to the effect sizes of the studies it seeks to refute. Finally, it does not show the individual participant traces that would give confidence that this is a robust, reproducible result – not a result driven by a few outlier participants.

o Suggestion: Perhaps beta power is not a very sensitive metric during beta desynchronization events since there is only so much that beta can reduce – once it is gone it can't really reduce much further (as demonstrated by the model in Fig. 6 – differences between bin 3, 4, 5 are quite small). Possibly a more sensitive metric would be something like beta burst rate9.

5. Confusion in the Model's Mechanism: The model presented in Fig. 6 suggests that inhibition reduces beta oscillations, but this is counterintuitive given that excitation, rather than inhibition, is typically implicated in beta desynchronization during movement. This mechanism also contradicts the authors' own interpretation of the beta desynchronization – that motor cortex is engaged and must change to increase its output activity. How can motor cortex do that if it is receiving an inhibitory signal?

6. Unclear Granger Causality Analysis: The frontal beta increase alongside motor cortex beta decrease contradicts the notion of frontal areas driving the motor cortex (Fig. 4). The analysis in Fig. 4 does not clarify which frequency bands are driving the increase in frontal motor information. It is difficult to interpret this connectivity analysis without knowing whether these results are derived from beta frequencies or others.

Minor Points and Methodological Questions

1. Design Justification (Lines 73-75): “Importantly, this design allowed us to study the evolution of fatigue neural correlates with a relatively high temporal resolution while minimizing fatigue-related muscle artifacts and confounds such as muscular compensation “ Can you explain this more? I don’t understand how this design helps minimize fatigue-related muscle artifacts / compensation.

2. Error Bars and Individual Variability: Error bars are missing in Fig. 2C, making it difficult to interpret

3. EMG Activity and Fatigue (Fig. 2B): The observed increase in EMG root-mean-square values with fatigue contradicts my expectations – I would have expected reduced EMG output with increased fatigue. Can the authors elaborate on why this result is expected ?

4. Outliers in Correlation Analysis (Fig. 5C): The presence of outliers seems to heavily influences the results. It would be prudent to verify whether the correlations persist without these points (e.g. remove point (-5, 58) for the green set of points and point (2, -5) for the blue set of points. Do the correlations still hold ?).

5. Field Potential Simulation (Fig. 6B): The process for deriving field potentials from the computational model needs clarification. How was Fig. 6B made?

References:
1. Leventhal, D. K. et al. Basal ganglia beta oscillations accompany cue utilization. Neuron 73, 523–536 (2012).
2. Saleh, M., Reimer, J., Penn, R., Ojakangas, C. L. & Hatsopoulos, N. G. Fast and Slow Oscillations in Human Primary Motor Cortex Predict Oncoming Behaviorally Relevant Cues. Neuron 65, 461–471 (2010).
3. Oya, T., Takei, T. & Seki, K. Distinct sensorimotor feedback loops for dynamic and static control of primate precision grip. Commun Biol 3, 1–13 (2020).
4. Baker, S. N., Olivier, E. & Lemon, R. N. Coherent oscillations in monkey motor cortex and hand muscle EMG show task-dependent modulation. J. Physiol. (Lond.) 501 (Pt 1), 225–241 (1997).
5. Conway, B. A. et al. Synchronization between motor cortex and spinal motoneuronal pool during the performance of a maintained motor task in man. J Physiol 489, 917–924 (1995).
6. Baker, S. N. Oscillatory interactions between sensorimotor cortex and the periphery. Curr. Opin. Neurobiol. 17, 649–655 (2007).
7. Tzagarakis, C., Ince, N. F., Leuthold, A. C. & Pellizzer, G. Beta-Band Activity during Motor Planning Reflects Response Uncertainty. J. Neurosci. 30, 11270–11277 (2010).
8. Schmidt, R. et al. Beta Oscillations in Working Memory, Executive Control of Movement and Thought, and Sensorimotor Function. J. Neurosci. 39, 8231–8238 (2019).
9. Little, S., Bonaiuto, J., Barnes, G. & Bestmann, S. Human motor cortical beta bursts relate to movement planning and response errors. PLOS Biology 17, e3000479 (2019).

Reviewer #3

(Remarks to the Author)

The article "Modulation of beta oscillatory dynamics in motor and frontal areas during physical fatigue" investigates the role of beta-band oscillations (~13-30 Hz) in motor and frontal brain regions during physical fatigue. The authors propose a reconciliation of the functional role of beta oscillations during physical fatigue with the "status quo" theory, which posits that beta oscillations help maintain the motor system's current state. Using EEG data from participants performing submaximal isometric knee contractions, the study identifies two key findings namely increased beta-band power at rest, aligning with the status quo theory and decreased beta-band power during contractions, indicating heightened MC activation needed to counteract fatigue. Furthermore, Beta-band activity in the prefrontal cortex increases during contractions, particularly in mid-task stages, indicating a role in top-down cognitive control. Here are my points for improvement:

• The task focuses on isolated quadriceps activity, which may limit generalizability to whole-body or real-world tasks.
• While the authors provide a novel reconciliation, their explanation of conflicting results (e.g., increased beta during fatigue in previous studies) requires further experimental validation.
• Although sufficient for statistical analyses, a more diverse or larger cohort could strengthen the study's applicability.
• I am doubtful about Directed connectivity with Granger analyses on scalp EEG. Why not source analyses and then directed connectivity? Instead imaginary phase coherence for directionality
• Not sure about the modeling with real data at hand
• Which interpolation was used for the channels?
• Not sure why the CZ electrode was selected any specific reason more the motor cortex C3 and C4
• Frontal electrodes are not defined properly

In summary:
The study makes significant contributions to understanding the dual role of beta oscillations during physical fatigue and integrates these findings into the status quo framework. It sets a foundation for future research into motor and cognitive fatigue mechanisms, with potential applications in neurological rehabilitation and performance optimization. However, further studies are needed to expand its ecological validity and confirm the proposed mechanisms across different fatigue paradigms.

Version 1:

Reviewer comments:

Reviewer #2

(Remarks to the Author)
I am thankful for the authors' response to my comments, especially the extra supplemental figures and the discussion of beta during isometric contraction with pinching. I re-read the new manuscript as well as the rebuttal and have no further comments at this point.

Reviewer #3

(Remarks to the Author)
The authors have adequately answered all my questions in the revised version of the manuscript. I do not have further comments on this revised manuscript.

Dear Dr. Enzo Tagliazucchi,

We thank you for sending the Reviewer's comments and allowing us to revise our manuscript, which contributed to its improvement. We have carefully answered all the comments the Reviewers made and thoroughly revised the paper. Specifically, we added four supplementary figures to control for the specificity of our findings and provide more transparency in our results. We also modified several sections of the paper to justify our methodological choices, broaden the perspective around the status-quo theory, and better contextualize our results in the literature.

All changes have been made visible in the manuscript in red.

Please find below a point-by-point response to the Reviewers' comments.

Reviewers' comments:

Reviewer #1 (Remarks to the Author):

This manuscript deals with a seeming anomaly of beta-frequency EEG signals during physical fatigue. The authors present a suite of analyses that explore this phenomenon. I think the work is comprehensive, and raises some interesting questions. I only have a small number of comments for the authors.

I would alsoi like to apologise to the authors for my late review.

We thank the Reviewer for their thoughtful feedback and suggestions, which have helped improve the manuscript. We have added a control analysis to restrict our results to the beta band and have addressed all their minor comments. We hope the changes we have made will satisfy their concerns. We appreciate the time and effort they put into the review process.

Major comments

1. My only substantial comment is that the authors' analyses seem to be focused only on the frequency range of interest. While this makes sense, in that the existing literature points to there being effects in beta, and indeed the authors have replicated and extended these findings, there is no 'control' frequency that could be used to explore alternative explanations. For example, the authors find a reduction in beta during movement, and a rise during rest (shown in Figure

2). I suppose my question is whether the increse in beta in rest is ONLY in beta, or if there is a general rise in EEG power in all bands during that phase. I think I believe that authors' explanation, but without a 'control' frequency it would not be possible to show this for ceratin. I don't think I expect the authors to add a whole new analysis, but peraps the authors could add some thoughts on this?

We thank the reviewer for this thoughtful comment. We agree that our results are not shown to be specific to the beta-band, as we did not have a control frequency. We added an additional analysis (Supplementary Figure S1) to remediate this lack, using theta and alpha bands as control frequency bands. The results reveal some distinct power modulations (decreasing power during contractions in the theta band and increasing power at rest in the alpha band) that confirm the specificity of our effect in the beta-band (i.e., decreasing power during contractions and increasing power at rest). Furthermore, our effect was specific to the individualized and high-beta bands, as we did not find a decreasing power during contraction in the low-beta band, further corroborating its specificity and discarding a broad-band trend. We included this control analysis in the Supplementary Information of the manuscript and mentioned it in the Results section, as detailed below.

Figure S1: To control for the specificity of our main result to the β-band (decreasing beta power in Cz during contractions and increasing beta power at rest), we performed the same analyses on the theta (θ, 4-8 Hz) and alpha-band (α, 8-12Hz) in Cz. We first ran an RM-ANOVA with BIN (1 to 10) and SESSION (S10, S12) as fixed factors on θ Cz and α Cz in contractions. We found a BIN effect in θ Cz only ($F_{(9,207)} = 3.16$, $p = .001$, $\eta^2 = 0.12$, $BF = 10.54$), highlighting a decreasing θ power (Fig S1A). There was no other significant effect ($p > .33$, $BF < .55$, for the other factors for θ Cz; and $p > .26$, $BF < .39$ for all factors for α Cz). We then ran the same analysis on θ Cz and α Cz recorded at rest (i.e., between contractions). We found a significant BIN effect regarding α Cz only ($F_{(9,207)} = 3.56$, $p < .001$, $\eta^2 = 0.13$, $BF = 15.68$), revealing an increasing α power ($p > .73$, $BF < .34$, for the other factors for α Cz; and $p > .47$, $BF < .52$ for all factors for θ Cz) (Fig S1B). All in all, these analyses corroborate the specificity of our effect to the beta band.

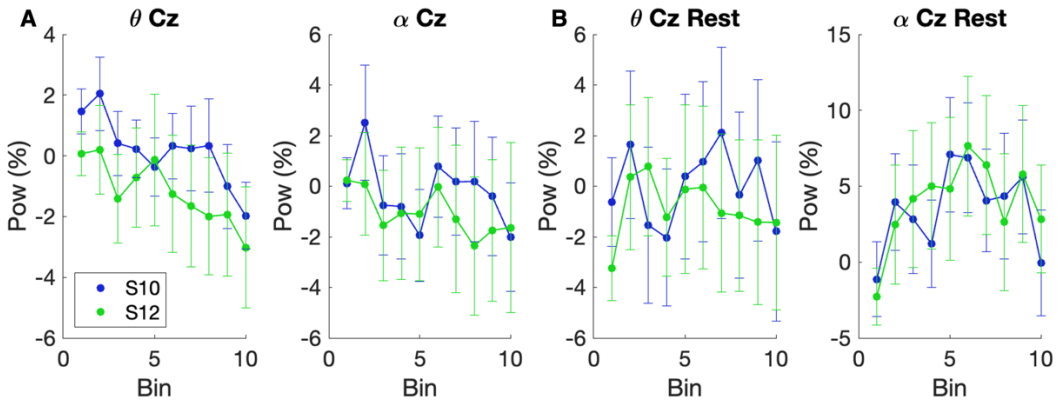

Figure S1 – Control Frequency-bands

EEG modulations during the main task. A. The two panels represent relative power changes (respective to the first contractions, see Methods for details) quantified in the theta (θ) and alpha band (α) in Cz in contraction. B. As in A, but during rest, that is between contractions. The dots represent the averaged distribution for all panels, and the error bars are the standard error mean (SEM).

Lines 182-184: In addition, we used two control frequency bands for both the contractions and rest phases and found only isolated modulations regarding the BIN factor (Fig S1), highlighting the specificity of our results to the beta-band.

Minor comments

1. There are a couple of places (e.g. lines 75-79) where the text changes tense to the future tense. I think this should be in the past tense for consistency.

We thank the Reviewer for their attention to this point. We have changed it to the past tense.

Lines 78-81: In addition, the relatively low submaximal load chosen (≤ 20% of maximal force) and the endurance of the muscle engaged (quadriceps) enabled us to observe the early stages of fatigue, where we were able to dissociate beta-band dynamics during the contraction and rest. These two temporal moments allowed us to observe different dynamics.

2. The topographies presented in Figure 1B seem very different between the two example participants for High and Low beta. Could the authors explain why this might be the case? Is this an artefact (or hallmark?) of the individual nature of the beta frequency?

Indeed, two types of differences can be pointed out in these topographies: between frequency bands (Low and High Beta bands) and between participants. As shown in Figure 1B, there is only a clear desynchronization in Cz in the High beta band for both participants but not in the

Low beta band. As reported in the literature, the desynchronization of the High-Beta band reflects the contraction of lower limbs (as in our study), whereas Low-Beta has been associated with upper limbs (Neuper & Pfurtscheller, 2001b; Pfurtscheller et al., 2000). The second difference between participants is more substantial in the Low Beta bands and may reflect cognitive processes or artifacts unrelated to our task. Importantly, both types of differences (between subjects and between frequency bands) highlight the importance of accounting for individualized frequency bands.

3. I liked the computational model a lot, and it is very satisfying to see the output matching the 'real' data so well. Could the authors say a little more about the spiking units? Perhaps adding something equivalent to a Hodgkin-Huxley style action potential, or maybe a single-unit style raster plot to Figure 6 would help the naive reader (me) to connect these units to equivalent biological data.

We thank the Reviewer for his support and enthusiasm about the computational model. The spiking units have been modeled as described in the original work of Izhikevich (Izhikevich, 2003), which is commonly used to model the membrane potential of biologically plausible spiking neurons. In the Methods section, we have detailed the equations in the 'Modelling' paragraph (Lines 750-775). According to the Reviewer's suggestions, we have included in the new figure (Figure 6) some panels with the raster plot and the averaged action potential to characterize the model's dynamics better. For visualization purposes only, we have included the plots below with the action potentials of a few excitatory and inhibitory neurons over time.

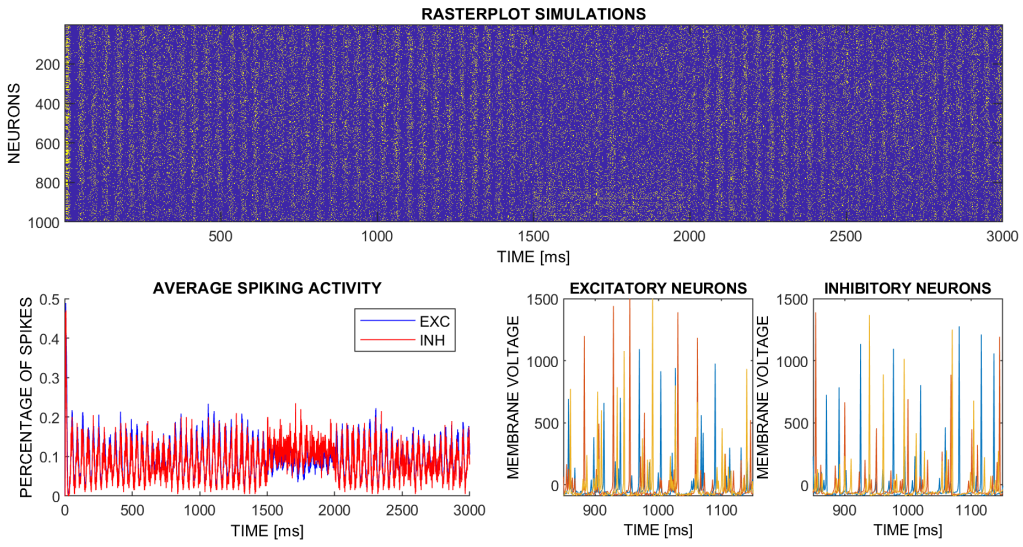

Figure R1: Upper panel: raster plot of one simulation. The x and y axes represent time (in ms) and neurons (the first 800 are excitatory and the last 200 are inhibitory), respectively. The lower

plot on the left shows the average spike activity, revealing a clear beta-band oscillation, which is disrupted at the onset of the movement (which marks the beginning of excitatory input to excitatory and inhibitory neurons for 500 ms). The last two bottom panels on the right show the voltage potential for three random neurons, excitatory and inhibitory (respectively, on the left and right panels).

4. In the Discussion (lines 483-499) the authors speculate about bidirectional coupling. I think another possible explanation here could be that a more fatigued body requires additional strategic control. For example when I carry a heavy load over a long distance, at some point I find myself shifting that load around. I wonder if this coupling could reflect the need to adapt motor strategies as muscular elements 'drop out' with fatigue?

We thank the Reviewer for this insight. The increasing coupling might indeed reflect the need to adapt motor strategies as the body becomes more fatigued. Accordingly, we added this hypothesis to the discussion.

Lines 538-540: Another possible explanation for such an increase in bidirectional coupling might be the need for motor strategies adaptation as fatigue rises (Taylor et al., 2016).

Reviewer #2 (Remarks to the Author):

The authors present a study in which they seek to reconcile a contradiction in the understanding of sensorimotor beta band oscillations in motor cortex. They state that beta band oscillations are thought to reflect neural computations that promote the maintenance of the current state of the motor system, or the 'status quo'. They state that results from prior work in physical fatigue contradict the 'status quo' idea since they show that motor cortical beta oscillations actually increase during muscle contraction with increased fatigue. This is a contradiction since it is thought that motor cortex will need to recruit more motor units to produce movement when it is fatigued.

In their experiments, the authors show a reduction in motor cortex beta oscillations during muscle contraction with increased fatigue, an increase in rest-related beta oscillations with increased fatigue, and an increase in frontal beta oscillations with increased fatigue. The authors also present connectivity analysis showing an increase in frontal-motor cortex connectivity with fatigue. Finally, the authors present a spiking model demonstrating that increasing inhibition to motor cortex will reduce beta power during a simulated contraction event.

While the study is interesting, several concerns reduce my confidence in the results and interpretation.

We thank the Reviewer for their appreciation of our paper and for constructive comments that improve the manuscript. We have taken all the Reviewer comments into consideration. The revised version of the manuscript brings more perspective around the status quo theory, better justifies our methodological choices, and confronts our results more directly with previous studies from the literature. We hope that these changes will satisfy the Reviewer's concerns.

Major concerns:

1. The "Status Quo" Framework is very simplified: The interpretation of beta oscillations as a mechanism for maintaining the "status quo" is oversimplified. There are a number studies that highlight exceptions to this view. For example 1,2 show that beta is related to cue processing and utilization, certainly an active process. Other studies show that beta is present during precision grip isometric contraction 3–5, a task that should required recruitment of motor cortex to support a sustained output. Other perspectives propose that beta is a rhythm that facilitates

active peripheral sampling6 due to its prominence not only in motor cortex but also somatosensory cortex, spinal cord, and muscle activity recordings3. Finally other studies show that beta power is highest when there's most uncertainty (or least of a "status quo") in the task7. I believe that these alternatives to the "status quo" framework have been ignored in the discussion of the results in this manuscript due to a laser-focus on defending the status quo framework, and I would like to see more discussion around the possibility that the status quo is too simple of a framework and there are other ways to understand what beta is conveying about the underlying neural computations8.

We thank the Reviewer for their insightful comment. We acknowledge the limitations of the status-quo theory and that several pieces of evidence relate beta-band activity to other relevant cognitive processes. In the revised manuscript, we have provided a broader perspective on the role of beta-band in cognition and included the suggested references.

Line 464-471: The interpretation of our results aligns with the status-quo theory. However, it is important to acknowledge that several studies highlighted processes related to beta-band oscillations that fall outside the scope of this theory (Schmidt et al., 2019). For example, beta oscillations have been linked to cue processing (Leventhal et al., 2012; Saleh et al., 2010), confidence (Tan et al., 2016), uncertainty (Tzagarakis et al., 2010), salience processing and sensorimotor adaption (Torrecillos et al., 2015), and sensorimotor integration (Baker, 2007). All in all, while the status-quo theory provides a valuable framework to interpret our findings, it may present too limited a perspective to fully explain the functional role of beta oscillations in physical fatigue.

2. Beta Band definition: Already in Figure 1B, there is a lack of clarity on the issue of whether beta power is high or low during the contractions. Both participants show sustained beta oscillations at ~18Hz and ~20 Hz respectively. Based on the beta oscillations literature, these dynamics are firmly within beta band limits. Why are the authors choosing to select individualized beta bands based on the assumption that beta will desynchronize during the contraction given the existing literature that beta can indeed persist during isometric contraction? Do all participants have this split between high and low beta? The authors need to discuss why they believe that the high beta / individualized beta results are more representative of true beta dynamics (i.e. are the results discussed with reference to the status quo framework) than the low beta results. This also needs to be discussed when comparing this result to other

literature – do other physical fatigue studies use the full beta band for analysis (e.g. 13-30 hz) ? perhaps this could be one reason this study differs from previous ones?

The Reviewer is correct in pointing out the importance of choosing a more or less broad range of frequencies in the beta-band. The beta-band is indeed quite broad (~20 Hz range), and several studies have demonstrated that narrower bands are related to specific cognitive or motor functions (Chandrasekaran et al., 2019; Neuper & Pfurtscheller, 2001b; Nougaret et al., 2024; Pfurtscheller et al., 2000; West et al., 2018; Zhang et al., 2008). For these reasons, we considered focusing on a narrower, individualized range within the beta-band more relevant (Kilavik et al., 2013). Here, we focused specifically on the individualized/high beta as it has been specifically related to lower limb contractions (Neuper & Pfurtscheller, 2001b; Pfurtscheller et al., 2000). This specificity is consistent across participants, as shown in Fig 1C, where almost all participants have an individualized peak desynchronization beyond 20Hz. Furthermore, as shown in Figure 3, the low and high beta-bands exhibit quite different dynamics during the contractions at the group level, confirming the importance of considering them separately. Importantly, we are aware that the individualized/high beta band is not representative of the whole beta-band dynamics, but it reflects the dynamics associated with the lower limb contraction. We have referred to these considerations in the Results section of the original manuscript (Lines 233-276).

The Reviewer is also correct in pointing out that previous studies on fatigue considered the whole beta range, which could explain the discrepancy between our findings. Accordingly, on top of presenting both the Low and High Beta bands, in line with the recommendation to focus on narrower beta bands (Kilavik et al., 2013; Nougaret et al., 2024), we also included an analysis of the whole beta band in the Supplementary Information and mentioned it in the Discussion.

Figure S4: To properly compare our main results with previous studies, we have performed our main analyses on the whole beta-band (13-31 Hz). We first ran an RM-ANOVA with BIN (1 to 10) and SESSION (S10, S12) as fixed factors on β Cz in contractions. We found a BIN effect ($F_{(9,207)} = 3.09$, $p < .002$, $\eta^2 = 0.12$, BF = 15.23), highlighting a decreasing power over the task, and a BIN-SESSION interaction effect ($F_{(9,207)} = 2.05$, $p = .035$, $\eta^2 = 0.082$, BF = .68). There was no session effect ($p = .25$, BF = .58). We then ran the same RM-ANOVA on β Cz quantified at rest. We found a BIN effect only ($F_{(9,207)} = 4.55$, $p < .001$, $\eta^2 = 0.17$, BF = 376.48; $p > .16$, BF < .85 for the other factors), revealing an increasing power over the task. Finally, we performed the same analysis considering the frontal electrodes. We found a significant SESSION effect ($F_{(9,207)} = 4.40$, $p = .047$, $\eta^2 = 0.16$, BF = 1.71), showing a higher

power in the S12 compared to the S10 session. We also found a significant BIN effect ($F_{(9,207)} = 3.81$, $p < .001$, $\eta^2 = 0.14$, BF = 55.79), revealing an increasing power over the task. There was no BIN-SESSION interaction effect (p = .79, BF = 0.38). All in all, these analyses yield to similar results to those found on Iβ.

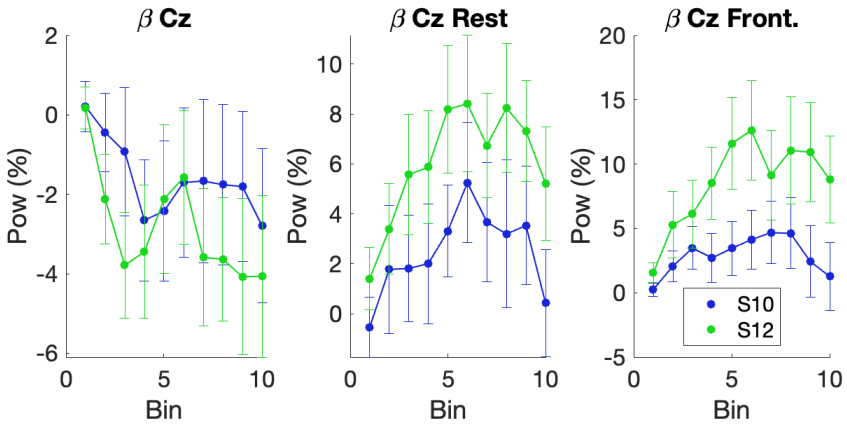

Figure S4 – Beta-band power modulations in the whole beta band (13-31 Hz)

EEG modulations over the main task. Panels 1 and 2 represent relative power changes (respective to the first contractions, see Methods for details) quantified in the beta-band (β) in Cz in contraction (Panel 1) and at rest (Panel 2). Panel 3 exhibits the power-relative changes in frontal electrodes quantified during contractions. The dots represent the averaged distribution for all panels, and the error bars are the standard error mean (SEM).

Lines 472-476: Furthermore, our results specifically concern a narrow and individualized range with the high beta band, whereas previous studies mainly included the whole beta range (~13-31 Hz). As this would not allow a direct comparison, we included a supplementary analysis (Fig S4) on the whole beta-band, which nonetheless corroborates the difference between our findings and the previous literature.

3. Isometric contraction dynamics: As mentioned above, it is puzzling that beta oscillations are reported to desynchronize during isometric contraction since previous work has found that motor cortex during isometric contractions can exhibit high beta. This manuscript assumes that the desynch occurs, and uses this fact to define the beta band frequency bounds. It must be discussed prior to doing this why this is an appropriate criteria.

The desynchronization that occurs when performing a contraction is a fact widely observed and consistently found in the literature (Alegre et al., 2006; Cassim et al., 2000; Crone et al., 1998; Dal Maso et al., 2012; Doyle et al., 2005; Kilavik et al., 2013; Neuper & Pfurtscheller, 2001a; Pfurtscheller & Lopes da Silva, 1999; Stancák et al., 1997; Tzagarakis et al., 2010). However, it is important to dissociate the contraction phase and the holding phase. As correctly pointed

out by the Reviewer, the desynchronization can be followed by a synchronization during a sustained contraction (in the holding phase), as shown in previous studies about static postural maintenance (Kilavik et al., 2013). For example, in a recent study (Oya et al., 2020), desynchronization occurs during the grip phase and synchronization during the holding phase (fig. 1e in Oya et al., 2020). In addition, we noticed that all studies showing a sustained beta synchronization during a contraction applied a low-intensity load (e.g., either postural or a precision grip task), and for contractions that lasted less than ~3 s. Altogether, we agree with the Reviewer that these differences from previous studies could be misleading, and we include these considerations in the Discussion section.

Lines 427-435: Interestingly, this pattern was also observed within a contraction along with the rising fatigue (reflected by the increasing EMG). This result appears at odds with previous studies investigating non-fatiguing sustained contraction, which reported sustained beta oscillations during the holding phase (Baker et al., 1997; Conway et al., 1995; Oya et al., 2020). However, since these studies were not designed to examine fatigue, the contraction duration was kept short (< 3 s), and the contraction intensity low (e.g., often postural or precision grip task). Therefore, the sustained desynchronization might be specific to higher-intensity contractions, while the decreasing power appears to be a distinct feature of physical fatigue.

4. Small Effect Sizes: The main result that contracts previous literature is shown in Fig. 2B, -- the reduction in beta power during contraction over the course of fatiguing. The effect size of this reduction is small (~4%). It is not discussed whether this is a large effect, how it compares to the effect sizes of the studies it seeks to refute. Finally, it does not show the individual participant traces that would give confidence that this is a robust, reproducible result – not a result driven by a few outlier participants.

From a statistical perspective, the effect size (η^2) is medium ($\eta^2 = 0.10$) (Cohen, 1988), while previous studies often reported a large effect size (Hosang et al., 2022). We mentioned it in the revised version of the manuscript, as detailed below. Even though our effect size appears smaller than in the previous literature (Hosang et al., 2022), it is hard to directly compare as our study has a novel design with a 10 BINS resolution, which significantly increases the degrees of freedom of our statistical models. It is also important to consider that effect size represents the variation between the conditions and the variability between the participants, indicating that not all participants are prone to the same variation due to fatigue. To detect if this small effect

size could be due to participants with very high or very low variations, we ran the same RM-ANOVA using BIN and SESSION as fixed factors on Iβ Cz after having removed two outlier participants (defined as participants with a power variation > than 10 Standard Deviation), which could be considered as a way to increase the statistical Signal to Noise Ratio. Without changing the results' pattern, we now get a more substantial effect size ($\eta^2 = 0.20$), comparable with those found in the literature (Hosang et al., 2022). We added these analyses in the Supplementary Information (Figure S3). As suggested, we also added individual traces and some fittings to help better visualize the individual traces.

Lines 420-422: Our effect demonstrates a medium effect size, which becomes large upon removing outliers (Fig S3), comparable to the opposite effects reported in the previous literature (Hosang et al., 2022).

Figure S3: To assess the robustness of the decrease in beta power during contractions, we ran again our main analysis for Iβ Cz after removing two outliers, defined as participants with a power variation larger than 10 Standard Deviation. We removed the two participants reaching ~ -40% and ~ +35% of power variation (Fig S3A). The RM-ANOVA displayed a significant BIN effect ($F_{(9,189)} = 5.34$, $p < .001$, $\eta^2 = 0.20$, $BF = 6917.11$), highlighting a decreasing power over the task. In contrast, no SESSION or BIN-SESSION interaction effects were found ($p > .25$, $BF < .39$, for both factors) (Fig S3A). These results corroborate our findings and reveal a more substantial statistical effect size due to the reduced inter-participant variability. We also analyzed the linear trend for these participants (excluding the two outliers) and observed a negative slope in both sessions (S10: $t_{(21)} = 2.72$, $p = .013$, $d = 0.58$, $BF = 4.04$; S12: $t_{(21)} = 2.75$, $p = .012$, $d = 0.59$, $BF = 4.24$) (Fig S3B). Finally, we also performed a 2nd-degree polynomial fit. We found a quadratic coefficient (a) almost significantly positive (S10: $t_{(21)} = 1.50$, $p = .074$, $d = 0.32$, $BF = 1.10$; S12: $t_{(21)} = 1.52$, $p = .072$, $d = 0.32$, $BF = 1.11$, unilateral one-sample t-test, H1: DV > 0) and a slope (b) negative (S10: $t_{(21)} = 2.12$, $p = .023$, $d = 0.45$, $BF = 2.77$; S12: $t_{(21)} = 1.97$, $p = .031$, $d = 0.42$, $BF = 2.17$, unilateral one-sample t-test, H1: DV < 0) (Fig S3C).

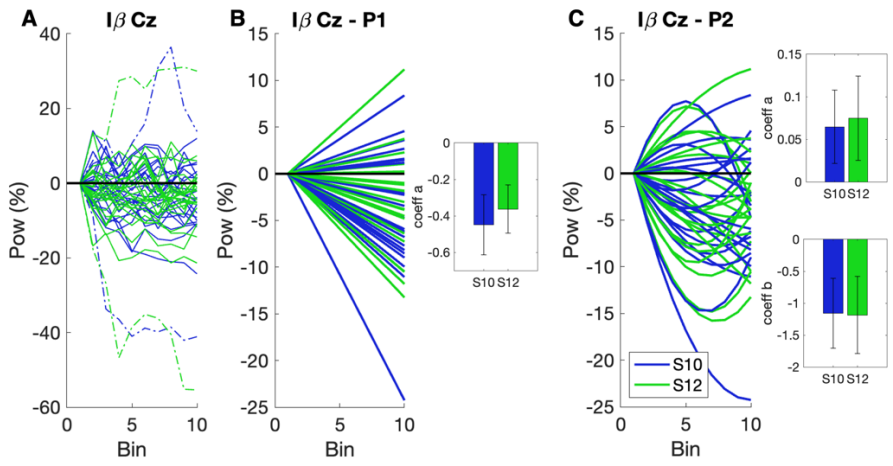

Figure S3 – Individual Iβ modulations over the main task

A. Relative power changes (respective to the first contractions, see Methods for details) quantified in the individualized beta band (Iβ) in Cz in contraction. Dotted lines represent outliers. B Linear fit of the individual traces; 'coeff a' is the linear slope of the fit. C. 2nd degree polynomial fit of the individual traces; 'coeff a' is the quadratic coefficient of the fit and 'coeff b' is the slope. All traces have their first bin zero-centered for visual purposes only.

Lines 459-461: Most of our participants follow this three-stage pattern (Fig S3), which might explain the heterogeneity of our findings, as less-endurant participants may reach the latest stage quicker than others.

o Suggestion: Perhaps beta power is not a very sensitive metric during beta desynchronization events since there is only so much that beta can reduce – once it is gone it can't really reduce much further (as demonstrated by the model in Fig. 6 – differences between bin 3, 4, 5 are quite small). Possibly a more sensitive metric would be something like beta burst rate9.

We thank the Reviewer for the interesting suggestion, and we agree extending our results to the beta burst metrics could be very interesting. However, we think it goes beyond the scope of the current work, and it could be, per se, the topic of another study (possibly with measures that are more sensitive at the trial level, such as MEG recordings). We have, however, mentioned this interesting possibility -and included the related reference- in the section about possible future perspectives.

Lines 554-558: Further studies will generalize our findings to a more ecological context (e.g., whole-body exercise), accounting for other relevant physiological parameters (fitness level, muscle typology, cardiovascular capacity, etc.), exploring how demographic factors (e.g.,

sex, age) may influence the results, and incorporating other physiological metrics, such as beta burst rate (Little et al., 2019; Lundqvist et al., 2024).

5. Confusion in the Model's Mechanism: The model presented in Fig. 6 suggests that inhibition reduces beta oscillations, but this is counterintuitive given that excitation, rather than inhibition, is typically implicated in beta desynchronization during movement. This mechanism also contradicts the authors' own interpretation of the beta desynchronization – that motor cortex is engaged and must change to increase its output activity. How can motor cortex do that if it is receiving an inhibitory signal?

We thank the Reviewer for the useful comment. We agree that the model's presentation and interpretation were rather confusing and not entirely in line with the theoretical ideas of the paper. Accordingly, we have modified it as detailed below, yet having the same results, qualitatively and quantitatively. Specifically, we have introduced an excitatory, rather than inhibitory, top-down modulation, which affects both excitatory and inhibitory neurons, which is in line with experimental studies (Okoro et al., 2022). This effect still produces the same beta desynchronization and aligns with previous studies and our interpretation. Additionally, we have modelled the fatigue effect over sessions with an increase in the number of recruited neurons, which causes a larger beta-desynchronization. We are aware of the model's simplicity, which does not aim at precisely modelling the motor cortex activity and does not allow us to support any novel biological insights. Yet, we deemed it interesting that we could propose a simple mechanism to support our experimental results.

Following the abovementioned modifications, we modified the modelling paragraphs in the Results and Method sections.

Lines 368-402: Somewhat contrary to previous studies that suggested an increase of beta power during contractions due to fatigue, our experimental data revealed that beta-band oscillations in the MC decrease over submaximal contractions due to physical fatigue (Fig 2B), supposedly driven by some top-down modulatory effect (Fig 4B). To understand such an effect, we implemented a simple but biologically plausible model composed of 1000 Izhikevic neurons (Izhikevich, 2003). This model, in line with previous studies (Kumar et al., 2011; Palmigiano et al., 2017), aims to support our hypothesis and experimental results by explaining our findings mechanistically. Specifically, the network comprised excitatory and inhibitory neurons (Fig 6A), whose baseline activity spontaneously generated bursts of beta-band oscillations. To simulate motor contraction's effect, excitatory and inhibitory neurons received a top-down

excitatory modulation at 1500 ms (Fig 6B) from frontal regions (as suggested by our experimental results – Fig 4B). Despite its simplicity, the network successfully replicates the beta-band desynchronization (Fig 6A, 6B). Next, to reproduce the fatigue effect, we increased the number of neurons whose activity was influenced by the top-down modulation over five repetitions, and we ran the simulations 10 times. To statistically test such fatigue effect, we performed an RM-ANOVA on the beta-band power changes with BIN (1 to 5) as a fixed factor. We found a strong BIN effect ($F_{(4,36)} = 33.71$, $p = < .001$, $\eta^2 = 0.79$, $BF = 8.59\times10^{+8}$), revealing an increase in the beta-band desynchronization over the bins due to a rise in the excitatory input (Fig 6A, 6C). These results, in line with our experimental data (Fig 2B), provide a simple yet plausible implementation of such beta-band desynchronization during the contraction, yielding a mechanistic explanation of our experimental observations.

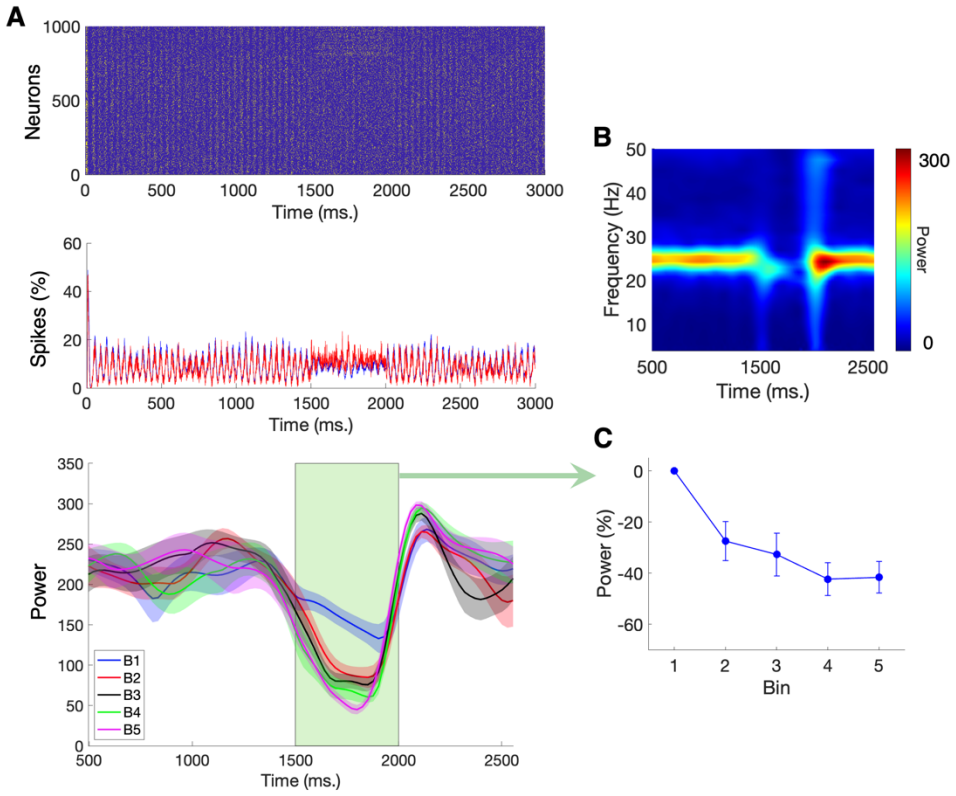

Figure 6 – Spiking network model of beta-band desynchronization during physical fatigue

A. Spiking network and beta-band modulations. The upper part of the panel illustrates the 1000 interconnected Izhikevich neurons, 80% excitatory and 20% inhibitory, with its averaged spiking activity represented in the middle part of the panel. The lower part of the panel displays the beta-band power generated by the spiking network and modulated over time. The contraction period (from 1500 to 2000 ms) corresponds to an excitatory modulation sent for 500 ms to a subset of excitatory and inhibitory neurons. As we can see on the lower part of the panel, a desynchronization occurs during the excitatory input (green area). The five Bins (B) represent an incremental number of recruited neurons (from Bin 1 to Bin 5) to simulate the fatigue effect. B. Typical time-frequency map.

The network generates beta power centered around 25 Hz, followed by a desynchronization and a slight rebound at the end of the movement. C. Beta-band power modulations. This panel represents the relative power changes quantified during the 'movement' period over Bins. The dots represent the averaged distribution of the 10 simulations, and the error bars the SEM.

Lines 765-775: After one second at rest, we modelled the onset of a motor contraction by providing 20% of both excitatory and inhibitory neurons with a top-down excitatory modulation from frontal regions (a weaker modulation was provided to the excitatory neurons, which are 80% of the whole population). We modelled the effect of fatigue by producing five contractions with a linear increase in the number of recruited neurons, both excitatory and inhibitory, and we ran the simulations 10 times. We assessed the effect on the network dynamic by computing the beta-band power over time, that is, before, during, and after the motor contraction. The spectral power was computed via wavelet decomposition on the membrane potential obtained by averaging the activity of all neurons. We eventually compared the beta-band desynchronization as a function of the top-down modulation strength.

6. Unclear Granger Causality Analysis: The frontal beta increase alongside motor cortex beta decrease contradicts the notion of frontal areas driving the motor cortex (Fig. 4). The analysis in Fig. 4 does not clarify which frequency bands are driving the increase in frontal □ motor information. It is difficult to interpret this connectivity analysis without knowing whether these results are derived from beta frequencies or others.

We thank the Reviewer for the valuable comments on the connectivity analysis. Regarding the first part, we don't think that the increase in frontal beta and the decrease in motor cortex are contradictory with a possible modulatory influence of the former on the latter. It is likely that, in this specific case, frontal areas have an overall inhibitory effect on the motor cortex, thus having an opposite trend (frontal increase driving a decrease in motor areas). Concerning the second point, we agree that our analysis does not allow us to clarify which frequency band is driving the increasing bidirectional flow between motor and frontal areas. We have added a supplementary analysis focusing on the individualized beta-band (Figure S2) and mentioned it in the Results. We did not replicate the findings found in the temporal domain, suggesting a non-specificity of this increasing communication to the beta-band.

Figure S2: To further identify the frequency band underlying our bidirectional Cz – Front. increasing communication (Fig 4B), we performed Granger Connectivity (GC) analyses in the

spectral domain. We looked at the Iβ frequency, as we found that Iβ oscillations were involved both in motor and frontal regions during physical fatigue. However, we did not replicate the effects we found in the temporal domain within the Iβ band ($p > .093$, $BF < 0.51$, for both directions), indicating a non-specificity of the Iβ band to the increasing communication.

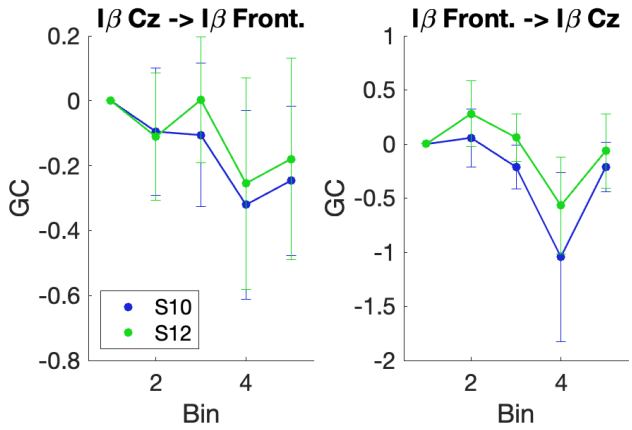

Figure S2 – Granger Causality in the frequency domain

Granger causality (GC) quantified in the Individualized Beta-band (Iβ). The dots represent the averaged distribution, and the error bars the SEM. The first bin is 0 centered for both sessions. One bin is the integration of 20 contractions.

Lines 311-312: Note that this effect was not specific to the beta frequency band (Fig S2).

Minor Points and Methodological Questions

1. Design Justification (Lines 73-75): "Importantly, this design allowed us to study the evolution of fatigue neural correlates with a relatively high temporal resolution while minimizing fatigue-related muscle artifacts and confounds such as muscular compensation "Can you explain this more? I don't understand how this design helps minimize fatigue-related muscle artifacts / compensation.

We apologize for the lack of clarity. As the design uses an isometric task in a standardized strapped position and a relatively low submaximal intensity in the lower limb, it allows to (i) minimize movements as well as the involvement of other muscles (in comparison to a cycling task, for example), (ii) have a more prolonged effort duration (in comparison with higher intensity), (iii) have a considerable distance between the muscle involved and EEG sensors (in

comparison with upper limbs task). Altogether, these considerations contribute to minimizing muscle compensation and artifacts. We added these points in the Introduction.

Lines 73-78: Importantly, this design incorporates an isometric task in a strapped position and a low submaximal intensity in the lower limb, which allows to (i) minimize movement artifacts, (ii) minimize the involvement of other muscles, (iii) extend effort duration, and (iv) increase the distance between active muscles and EEG sensors. These features reduce muscle compensation and EEG artifacts and provide a relatively high temporal resolution.

2. Error Bars and Individual Variability: Error bars are missing in Fig. 2C, making it difficult to interpret

We did not include error bars in this panel as its objective is to highlight the general trend in the two conditions. However, statistical analyses were performed on the slope parameters, represented in the adjacent panel, in which error bars show the inter-participant variability.

3. EMG Activity and Fatigue (Fig. 2B): The observed increase in EMG root-mean-square values with fatigue contradicts my expectations – I would have expected reduced EMG output with increased fatigue. Can the authors elaborate on why this result is expected ?

The interpretation of the EMG results may indeed not be straightforward. The EMG behavior during an isometric fatiguing task depends on the task intensity. During a submaximal exercise, it has been established that EMG activity increases throughout the contraction (Bigland-Ritchie et al., 1986). This characteristic evolution is thought to reflect an increase in the central motor command (Johnson et al., 2004; Taylor et al., 2016) to compensate for a failure of the contractile mechanisms (Hunter & Enoka, 2003) and to allow the recruitment of additional motor units, as well as a (transient) increase in their discharge frequency (Carpentier et al., 2001; Garland et al., 1994). On the other hand, when performing a maximal isometric contraction, there is a progressive decline of the central motor command, intrinsic adaptations of the motor neurons properties, and a de-recruitment of motor units, leading to a reduced EMG output. We added these details and references in the Results section.

Lines 149-156: We found a robust BIN effect ($F_{(9,207)} = 41.49$, $p < .001$, $\eta^2 = 0.64$, $BF = 3.30\times10^{+38}$), indicating increasing fatigue over contractions. This typical increase in the EMG activity during fatiguing submaximal contractions (Bigland-Ritchie et al., 1986) is thought to reflect an increase in the central motor command (Johnson et al., 2004; Taylor et al.,

2016) to compensate for a failure of the contractile mechanisms (Hunter & Enoka, 2003) and to allow the recruitment of additional motor units, as well as a (transient) increase in their discharge frequency (Carpentier et al., 2001; Garland et al., 1994). We also found a substantial BIN-SESSION interaction ($F_{(9,207)} = 3.43$, $p < .001$, $\eta^2 = 0.13$, $BF = 28.43$), highlighting a growing fatigue difference between the two sessions (with S12 > S10) (Fig 2B).

4. Outliers in Correlation Analysis (Fig. 5C): The presence of outliers seems to heavily influences the results. It would be prudent to verify whether the correlations persist without these points (e.g. remove point (-5, 58) for the green set of points and point (2, -5) for the blue set of points. Do the correlations still hold ?).

As suggested, we verified the correlations while removing the outliers identified as participants with a Cook's distance > 4/n (Bollen & Jackman, 1985). The correlation was consistent in the S10 session ($r = ¬–0.61$, $p = .002$, $BF = 28.30$) but not in the S12 session ($r = -0.027$, $p = .45$, $BF = 0.30$). We added it in the Results section, which is detailed below.

Lines 345-350: Note that we further examined the same correlation after removing outliers identified as participants with a Cook's distance greater than four divided by the number of participants (Bollen & Jackman, 1985). The effect remained consistent in the S10 session ($r = ¬–0.61$, $p = .002$, $BF = 28.30$) but not in the S12 one ($r = -0.027$, $p = .45$, $BF = 0.30$), potentially indicating a more complex relationship when reaching higher stages of fatigue.

5. Field Potential Simulation (Fig. 6B): The process for deriving field potentials from the computational model needs clarification. How was Fig. 6B made?

We apologize for the omission. We computed the field potential in Figure 6B, applying a wavelet decomposition on the average membrane potential (i.e., obtained averaging across the membrane potential of all neurons). This has now been specified in the method section.

Lines 772-774: The spectral power was computed via wavelet decomposition on the membrane potential, which was obtained by averaging the activity of all neurons.

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Reviewer #3 (Remarks to the Author):

The article "Modulation of beta oscillatory dynamics in motor and frontal areas during physical fatigue" investigates the role of beta-band oscillations (~13-30 Hz) in motor and frontal brain regions during physical fatigue. The authors propose a reconciliation of the functional role of beta oscillations during physical fatigue with the "status quo" theory, which posits that beta oscillations help maintain the motor system's current state. Using EEG data from participants performing submaximal isometric knee contractions, the study identifies two key findings namely increased beta-band power at rest, aligning with the status quo theory and decreased beta-band power during contractions, indicating heightened MC activation needed to counteract fatigue. Furthermore, Beta-band activity in the prefrontal cortex increases during contractions, particularly in mid-task stages, indicating a role in top-down cognitive control. Here are my points for improvement:

We thank the Reviewer for the time they put into the review process and for their suggestions that contribute to improving the manuscript.

• The task focuses on isolated quadriceps activity, which may limit generalizability to whole-body or real-world tasks.

We agree with the Reviewer that our task is not easily generalizable to an ecological situation. However, choosing an ecological task (e.g., cycling or running) would have made the EEG recordings extremely noisy and prevented us from controlling for several confounding factors, such as muscular compensation, change of muscle's position/speed/length, or muscular artifacts. However, we acknowledge that our study's generalizability remains to be tested, and we mentioned these considerations in the conclusion of the original manuscript (Lines 554-558).

• While the authors provide a novel reconciliation, their explanation of conflicting results (e.g., increased beta during fatigue in previous studies) requires further experimental validation.

We fully agree with the Reviewer's comment. We anticipate that our results will constitute a starting point for future experimental and theoretical studies to confirm further (or disprove) such theoretical explanations. We added this consideration to the Discussion.

Lines 461-463: Further studies will be necessary to shed light on the temporal dynamic of beta-band power during a fatigue task to exhaustion and to experimentally validate our theoretical explanation for conflicting results.

• Although sufficient for statistical analyses, a more diverse or larger cohort could strengthen the study's applicability.

We thank the Reviewer for this comment. The number of participants in our study is comparable, if not slightly higher, than most of the previous studies investigating fatigue using EEG (on average n = 22 in the previous literature (Hosang et al., 2022), and n ~ 12 regarding the studies using isometric contractions (Suviseshamuthu et al., 2021; Yang et al., 2009)). We have included a homogeneous pool of participants to decrease the variability in the data and increase the statistical power. However, we fully agree with exploring how different criteria, such as age, sex, and fitness level, may influence the results, and we anticipate that future studies will explore these questions. We have included this suggestion in the conclusion. We also added the minimum and maximum age in the Methods section for more transparency.

Lines 554-558: Further studies will generalize our findings to a more ecological context (e.g., whole-body exercise), accounting for other relevant physiological parameters (fitness level, muscle typology, cardiovascular capacity, etc.), exploring how demographic factors (e.g., sex, age) may influence the results, and incorporating other physiological metrics, such as beta burst rate (Little et al., 2019; Lundqvist et al., 2024).

Lines 562-563: Twenty-eight participants took part in this study (16 women, age: 24 ± 4 [min: 19; max: 33], weight: 70 ± 18, mean ± SD).

• I am doubtful about Directed connectivity with Granger analyses on scalp EEG. Why not source analyses and then directed connectivity? Instead imaginary phase coherence for directionality

We thank the Reviewer for their interesting suggestion. We agree that source analyses could provide more informative insights about the connectivity and the brain regions involved in this effect. However, source analysis may fall beyond the original scope of this work, besides requiring a much larger number of trials and better imaging techniques, such as MEG recordings.

• Not sure about the modeling with real data at hand

We understand the Reviewer's concerns about the link between the real data and our modeling efforts. As our findings challenge part of the previous literature on physical fatigue, we supposed that the modelling part could provide some support to strengthen our point. We clarified this justification at the beginning of the modelling section in the original manuscript (Lines 368-375).

• Which interpolation was used for the channels?

We apologize for the lack of clarity. A spherical interpolation was used (Perrin et al., 1989). We have added it in the Method section.

Lines 649-650: The previously removed channels were then spherically interpolated (Perrin et al., 1989).

• Not sure why the CZ electrode was selected any specific reason more the motor cortex C3 and C4

The Cz electrode was selected as it has been pointed out as best capturing the motor cortex activity associated with quadriceps contraction (Dal Maso et al., 2012; Forrester et al., 2006). Moreover, these previous findings were supported by the topographical representations of the current study (e.g., Fig 1B). C3 and C4 are usually associated with contraction in the upper limb (right or left, respectively) (Li et al., 2019; López-Larraz et al., 2014; Pfurtscheller & Lopes da Silva, 1999; Suwannarat et al., 2018). Finally, the somatotopic representation provided by a more locally precise neuro-imagery method aligned with these findings (Gordon et al., 2023; Meier et al., 2008). We added some references to justify our choice in the Methods section.

Lines 706-708: Cz was retained as reflecting the MC activity associated with the quadriceps contraction (Dal Maso et al., 2012; Forrester et al., 2006; Gordon et al., 2023; Meier et al., 2008), a location confirmed by visualizing topographically the beta desynchronization.

• Frontal electrodes are not defined properly

According to previous studies, we chose the F3, F4, F7, and F8 electrodes to represent the ventrolateral and dorsolateral prefrontal cortex activity, respectively (Medvedev et al., 2011; Okamoto et al., 2004; Robertson & Marino, 2015), while remaining aware of the spatial

limitations of EEG recordings. We have justified our choice in the Method section of the original manuscript (Lines 703-706).

In summary:

The study makes significant contributions to understanding the dual role of beta oscillations during physical fatigue and integrates these findings into the status quo framework. It sets a foundation for future research into motor and cognitive fatigue mechanisms, with potential applications in neurological rehabilitation and performance optimization. However, further studies are needed to expand its ecological validity and confirm the proposed mechanisms across different fatigue paradigms.

We thank the Reviewer for their appreciation of our paper. We hope our answers and modifications have addressed all their concerns and that our study will constitute a starting point for future studies aiming at expanding its ecological validity, exploring the different factors that may play a role in modulating this effect, and developing our theoretical interpretation.

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