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Impaired Ca²⁺ signaling indicates disturbed mitochondrial function in fibroblasts from patients with sporadic and familial ALS

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Reviewer 2: Subhas Chandra Biswas

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Manuscript reviewed 2022-06-03: *Only major points included.*

Reviewer 2

Dysregulation of calcium ion homeostasis and abnormal protein aggregation have been proposed as central pathophysiological features to ALS. However it is not known whether familial and sporadic ALS share a common or disparate mechanism of pathogenesis. Therefore, the study reported in this article is interesting and very relevant to the field. The work is very brief with some important aspects. Nonetheless there are few minor comments that need to be addressed before a final decision is taken on this manuscript.

The authors showed that the cytosolic Ca²⁺ concentrations was 28 % higher in sALS and 20 % lower in fALS compared to the control fibroblasts (Figure 1A). It seems that this result is representation of Figure 1A,B,C,D; not just Figure A. Please clarify. It is also suggested that an explanation on this findings may be addressed in the Discussion.

Authors

We appreciate the feedback of Dr Biswas and agree with his comment on assignment of the data in Figure 1. We made the corresponding adjustments.

With regards to the addressing the explanations in Discussion, we would like to let the text in Results remain as it is, as we believe this helps the readers to better understand the graphs and the purpose and order of adding different modulators. Yet, the Discussion was designed in a way that the experimental setup used in the work is reflected almost in every paragraph of this section.