iScience

CellPress

Correction

ALS-Linked SOD1 Mutants Enhance Neurite Outgrowth and Branching in Adult Motor Neurons

Zachary Osking, Jacob I. Ayers, Ryan Hildebrandt, Kristen Skruber, Hilda Brown, Daniel Ryu, Amanda R. Eukovich, Todd E. Golde, David R. Borchelt, Tracy-Ann Read,* and Eric A. Vitriol*

*Correspondence:
taread@ufl.edu (T.-A.R.),
evitriol@ufl.edu (E.A.V.)

https://doi.org/10.1016/j.isci.2019.08.004

(iScience *11*, 294–304; January 25, 2019)

In the originally published version of this article, the authors concluded that the observed effects of SOD1 mutation were elicited in adult cells only. This statement was meant to summarize the results of this article. In light of other studies that have examined the morphology of motor neurons at early post-natal stages, the text referring to the effects of mutant SOD1 expression in adult cells has been modified. An expanded discussion and references have also been added to the manuscript.

Specifically, these sentences:

"Enhanced regeneration of mutant SOD1 motor neurons only occurs in adult cells and is independent of ALS onset."

"Increased outgrowth only occurs in adult neurons and is independent of ALS symptoms."

"Figure 2. Enhanced outgrowth and branching of adult motor neurons from mutant SOD1 mice is specific to adult cells and independent of ALS onset."

now read

"Enhanced regeneration of adult mutant SOD1 motor neurons is independent of ALS onset."

"Increased outgrowth in adult motor neurons is independent of ALS symptoms."

"Figure 2. Enhanced outgrowth and branching of adult motor neurons from mutant SOD1 mice is independent of ALS onset."

The sentence "In fact, the enhanced outgrowth and branching phenotypes only becomes apparent after the mouse is two months old (Figure 2D)." has been deleted. Finally, the authors have expanded the discussion and added the references reported below.

"In this study, we do not see a difference in the outgrowth and branching of cultured G93A-DL embryonic or P30 motor neurons (Figures 2A–2D). The enhanced outgrowth phenotype was observed in motor neurons cultured from mice at P60 or older (Figures 2C and 2D). Contrary to our findings in adult cells, most previous studies have shown that mutant SOD1 expression has an inhibitory effect on neurite outgrowth in embryonic and stem-cell-derived motor neurons (Azzouz et al., 2000; Bhinge et al., 2017; Karumbayaram et al., 2009; Lemmens et al., 2007). An exception to this would be an *in vivo* tracing analysis of early post-natal (P3–9) lumbar motor neurons in the G85R mouse, where an increase in the length and branching of dendritic processes was observed (Amendola et al., 2007; Filipchuk and Durand, 2012). However, these results did not translate to the G93A mouse model, where dendritic arborization of lumbar motor neurons was reduced at E17.5 (Martin et al., 2013) and unaltered in mice at P8–15 (Fogarty et al., 2017). Our analysis of G85R-het motor neurons showing increased neurite outgrowth and branching was only performed on

mice that were 5 months old (Figures 2E and 2F) and we did not examine earlier timepoints as we had with G93A-DL motor neurons (Figures 2C and 2D). *In vivo* tracing is often done on very small (~5) groups of cells (Amendola et al., 2007), and results can vary depending on the region of the spinal cord where the analysis is being performed (Fogarty et al., 2017). To enhance the rigor of our findings from our *in vitro* neurite outgrowth/branching analysis, we analyze approximately 40–120 cells/condition and culture neurons from the entire spinal cord. Another significant difference between this work and *in vivo* tracing studies is that they measure development and maintenance of the neuron's existing branch structure, whereas we are measuring the regrowth of these processes after they are severed. Previous studies examining the ability of adult motor neurons to regenerate after injury in G93A models have shown both increased (Sharp et al., 2018) and decreased (Schram et al., 2019) regeneration. Consequently, additional experiments are needed before we can determine how our results showing that G93A expression enhances *in vitro* regeneration (Figures 1, 2, and 3) translate to the more complex, three-dimensional environment *in vivo*."

The publisher apologises for this inconvenience.

REFERENCES

Amendola, J., Gueritaud, J.P., Lamotte d'Incamps, B., Bories, C., Liabeuf, S., Allene, C., Pambo-Pambo, A., and Durand, J. (2007). Postnatal electrical and morphological abnormalities in lumbar motoneurons from transgenic mouse models of amyotrophic lateral sclerosis. Arch. Ital. Biol. *145*, 311–323.

Azzouz, M., Poindron, P., Guettier, S., Leclerc, N., Andres, C., Warter, J.M., and Borg, J. (2000). Prevention of mutant SOD1 motoneuron degeneration by copper chelators in vitro. J. Neurobiol. *42*, 49–55.

Bhinge, A., Namboori, S.C., Zhang, X., VanDongen, A.M.J., and Stanton, L.W. (2017). Genetic Correction of SOD1 Mutant iPSCs Reveals ERK and JNK Activated AP1 as a Driver of Neurodegeneration in Amyotrophic Lateral Sclerosis. Stem Cell Reports *8*, 856–869.

Filipchuk, A.A., and Durand, J. (2012). Postnatal dendritic development in lumbar motoneurons in mutant superoxide dismutase 1 mouse model of amyotrophic lateral sclerosis. Neuroscience *209*, 144–154.

Fogarty, M.J., Mu, E.W.H., Lavidis, N.A., Noakes, P.G., and Bellingham, M.C. (2017). Motor Areas Show Altered Dendritic Structure in an Amyotrophic Lateral Sclerosis Mouse Model. Front. Neurosci. *11*, 609.

Karumbayaram, S., Kelly, T.K., Paucar, A.A., Roe, A.J., Umbach, J.A., Charles, A., Goldman, S.A., Kornblum, H.I., and Wiedau-Pazos, M. (2009). Human embryonic stem cell-derived motor neurons expressing SOD1 mutants exhibit typical signs of motor neuron degeneration linked to ALS. Dis Model Mech *2*, 189–195.

Lemmens, R., Van Hoecke, A., Hersmus, N., Geelen, V., D'Hollander, I., Thijs, V., Van Den Bosch, L., Carmeliet, P., and Robberecht, W. (2007). Overexpression of mutant superoxide dismutase 1 causes a motor axonopathy in the zebrafish. Hum. Mol. Genet. *16*, 2359–2365.

Martin, E., Cazenave, W., Cattaert, D., and Branchereau, P. (2013). Embryonic alteration of motoneuronal morphology induces hyperexcitability in the mouse model of amyotrophic lateral sclerosis. Neurobiol. Dis. *54*, 116–126.

Schram, S., Chuang, D., Schmidt, G., Piponov, H., Helder, C., Kerns, J., Gonzalez, M., Song, F., and Loeb, J.A. (2019). Mutant SOD1 prevents normal functional recovery through enhanced glial activation and loss of motor neuron innervation after peripheral nerve injury. Neurobiol. Dis. *124*, 469–478.

Sharp, P.S., Tyreman, N., Jones, K.E., and Gordon, T. (2018). Crush injury to motor nerves in the G93A transgenic mouse model of amyotrophic lateral sclerosis promotes muscle reinnervation and survival of functionally intact nerve-muscle contacts. Neurobiol. Dis. *113*, 33–44.