Selective Vulnerability of Motor Neurons and Treatment for Amyotrophic Lateral Sclerosis

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BACKGROUND:

- ALS is a neurodegenerative disease that leads to the gradual deterioration of motor neurons (MNs).

- Oculomotor neurons (OMNs) and Onuf nuclei MNs (ONMNs) are resistant to deterioration.

- Vulnerability depends on physical characteristics along with function.

- Riluzole is the most effective treatment for ALS but there studies on Mesenchymal stem cells (MSCs).

QUESTION:

What are the characteristics that determine vulnerability and what is the most effective treatment?

	Spinal α-MN	Oculomotor neuron
Target muscle fiber	Single fiber type[1]	Multiple fiber types[1]
Soma size	Larger[2,3]	Smaller[2,3]
Dendrite branching	Larger[2]	Smaller[2]
Motor unit size (innervation ratio)	Larger[4,5,6,7]	Smaller[4,5,6,7]
Resting potential	Smaller[8,9,10]	Higher[8,9,10]
Discharge frequency	100 Hz[8,9,10]	100–600 Hz[8,9,10]
Affected in ALS	Yes[11,12,13,14]	No[11,12,13,14]
Affected in aging	Yes[15,16]	No[15,16]

Figure 1 shows the comparison between spinal MNs and OMNs through target muscle fiber, soma size, dendrite branching, motor unit size, resting potential, discharge frequence, affect in ALS, and affect in aging to pinpoint characteristics significant to vulnerability (Ragagnin, A., Shadfar, S., Vidal, M., Jamali, M. S., & Atkin, J. D., 2019).

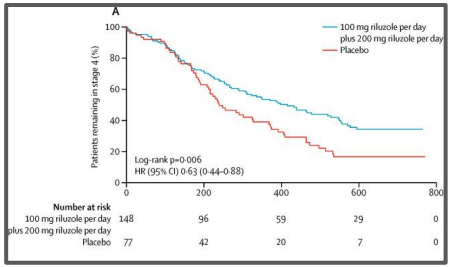

Figure 2 graphs the percentage of patients remaining remaining in stage 4 of ALS over time (days) between 100 mg riluzole per day plus 200 mg riluzole per day and placebo. Results reveal that riluzole is effective in prolonging survival (Fang, T., Al Khleifat, A., Meurgey, J. H., Jones, A., Leigh, P. N., Bensimon, G., & Al-Chalabi, A., 2018).

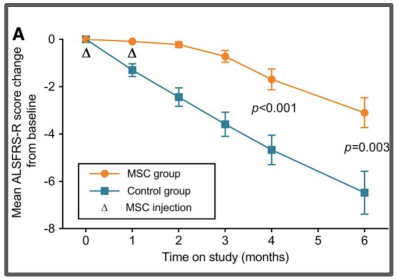

Figure 3 graphs the mean ALSFRS-R score change from baseline over time in months between the MSC group and the control group after the MSC injection (Oh, K. W., Noh, M. Y., Kwon, M. S., Kim, H. Y., Oh, S. I., Park, J., Kim, H. J., Ki, C. S., & Kim, S. H., 2018).

FUTURE DIRECTIONS:

Research should focus on the quality of life of ALS patients in regard to riluzole and focus on the effects of riluzole on months specifically. There should be a phase 3 clinical trial for MSCs to study long-term efficacy.

CONCLUSION:

Selective vulnerability, found in OMNs and ONMNs, in ALS can be attributed to ALS-related proteins and excitability. MNs that are resistant to deterioration are smaller, requires less energy to function, are slow-twitching, and differs in their ability to reinnervate. Treatments such as riluzole prolongs survival by blocking ACh receptors along with glutamate through its anti-excitotoxic properties. Patients that were injected with MSCs had greater function stability as they had better outcomes in terms of ALSFRS-R. However, riluzole is more effective as MSCs are not beneficial in advances stages and have unknown long-term effects due to lack of trials.

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