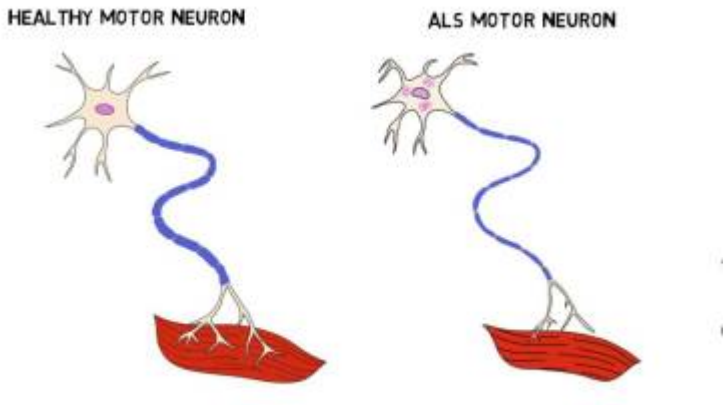
Amyotrophic lateral sclerosis treatment



Much of care is directed towards minimizing disability:

1. risk of aspiration may be reduced with

a) tracheostomy

b) gastrostomy tube to allow continued feeding

c) vocal cord injection with Teflon

2. noninvasive ventilation: e.g. BiPAP spasticity that occurs when upper motor neuron deficits predominate may be treated (usually with short-lived response) with:

a) baclofen: also may relieve the commonly occurring cramps b) diazepam

3. riluzole (Rilutek®): inhibits presynaptic release of glutamate. Doses of 50-200 mg/d increases tracheostomy-free survival at 9 &12 months,but the improvement is more modest or may be non-existent by ≈ 18 months [1) 2)].

Data recorded from the cortical surface of the motor and prefrontal cortex with an implanted brain-computer interface device was evaluated for 36 months after implantation of the system in an individual with late-stage ALS. In addition, electrode impedance and BCI control accuracy were assessed. Key measures included frequency of use of the system for communication, user and system performance, and electrical signal characteristics.

User performance was high consistently over the three years. Power in the high frequency band, used for the control signal, declined slowly in the motor cortex, but control over the signal remained unaffected by time. Impedance increased until month 5, and then remained constant. Frequency of home use increased steadily, indicating adoption of the system by the user.

The implanted brain-computer interface proves to be robust in an individual with late-stage ALS, given stable performance and control signal for over 36 months.

These findings are relevant for the future of implantable brain-computer interfaces along with other

brain-sensing technologies, such as responsive neurostimulation [3].

The main objective of a phase I trial was to assess the feasibility and safety of microtransplanting human neural stem cell (hNSC) lines into the spinal cord of patients with amyotrophic lateral sclerosis (ALS). Eighteen patients with a definite diagnosis of ALS received microinjections of hNSCs into the gray matter tracts of the lumbar or cervical spinal cord. Patients were monitored before and after transplantation by clinical, psychological, neuroradiological, and neurophysiological assessment. For up to 60 months after surgery, none of the patients manifested severe adverse effects or increased disease progression because of the treatment. Eleven patients died, and two underwent tracheotomy as a result of the natural history of the disease.

They detected a transitory decrease in progression of ALS Functional Rating Scale Revised, starting within the first month after surgery and up to 4 months after transplantation. The results show that transplantation of hNSC is a safe procedure that causes no major deleterious effects over the short or long term. This study is the first example of medical transplantation of a highly standardized cell drug product, which can be reproducibly and stably expanded ex vivo, comprising hNSC that are not immortalized, and are derived from the forebrain of the same two donors throughout this entire study as well as across future trials. This experimental design provides benefits in terms of enhancing both intra- and interstudy reproducibility and homogeneity. Given the potential therapeutic effects of the hNSCs, this observations support undertaking future phase II clinical studies in which increased cell dosages are studied in larger cohorts of patients [4].

References

1)
Bensimon G,Lacomblez L,Meininger V,et al.A Controlled Trial of Riluzole in Amyotrophic Lateral Sclerosis. N Engl J Med. 1994; 24:585–591
2)
Lacomblez L, Bensimon G, Guillet P, et al. Riluzole: A Double-Blind Randomized Placebo-Controlled Dose-Range Study in Amyotrophic Lateral Sclerosis (ALS). Electroenceph Clin Neurophysiol. 1995; 97
3)
Pels EGM, Aarnoutse EJ, Leinders S, Freudenburg ZV, Branco MP, van der Vijgh BH, Snijders TJ, Denison T, Vansteensel MJ, Ramsey NF. Stability of a chronic implanted brain-computer interface in late-stage amyotrophic lateral sclerosis. Clin Neurophysiol. 2019 Jul 27;130(10):1798-1803. doi: 10.1016/j.clinph.2019.07.020. [Epub ahead of print] PubMed PMID: 31401488.
4)
Mazzini L, Gelati M, Profico DC, Sorarù G, Ferrari D, Copetti M, Muzi G, Ricciolini C, Carletti S, Giorgi C, Spera C, Frondizi D, Masiero S, Stecco A, Cisari C, Bersano E, Marchi F, Sarnelli MF, Querin G, Cantello R, Petruzzelli F, Maglione A, Zalfa C, Binda E, Visioli A, Trombetta D, Torres B, Bernardini L, Gaiani A, Massara M, Paolucci S, Boulis NM, Vescovi AL; ALS-NSCs Trial Study Group. Results from Phase I Clinical Trial with Intraspinal Injection of Neural Stem Cells in Amyotrophic Lateral Sclerosis: A Long-Term Outcome. Stem Cells Transl Med. 2019 May 18. doi: 10.1002/sctm.18-0154. [Epub ahead of print] PubMed PMID: 31104357.