Impact of Glutamate in Amyotrophic Lateral Sclerosis (ALS)

Dianabell Maldonado, Rajesh Jaiprashad and Patricia Snyder, Ph.D.
Florida Atlantic University. Department of Chemistry and Biochemistry

Introduction

Amyotrophic Lateral Sclerosis (ALS) is a disease that weakens muscles by affecting motor neurons. In the body, neurons serve to receive and transmit signals from the brain. Some of the 20 essential amino acids are used to stimulate the receiver cell membrane to transmit nerve impulses. In contrast with the other nerve stimulating amino acids, glutamate is the only one that cannot be broken down by enzymes (Garrett 2010). Instead, it gets recycled by glial cells. These cells uptake glutamate and convert it into glutamine, creating a glutamine-glutamate cycle. Glutamate also controls brain development which determines the formation or destruction of nerve contacts. Therefore, investigating the properties of glutamate through molecular modeling may help with understanding how it binds to the acceptor neuron cells and its interactions with glial cell receptors.

Method

Gaussian is a molecular modeling software that allows the calculation of complex theoretical problems. Glutamate was drafted into Gauss View and optimized using Gaussian (Figure 2), The optimized structure was then run through Gaussian again for energy calculations. All calculations were carried out in the ground state using Semi-empirical settings.

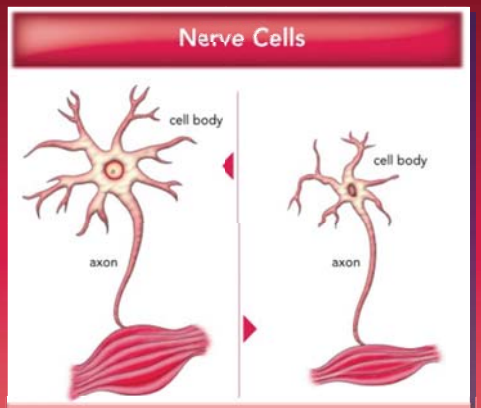


Figure 1: Healthy Nerve Cell and Muscle vs ALS Affected Nerve Cell and Muscle

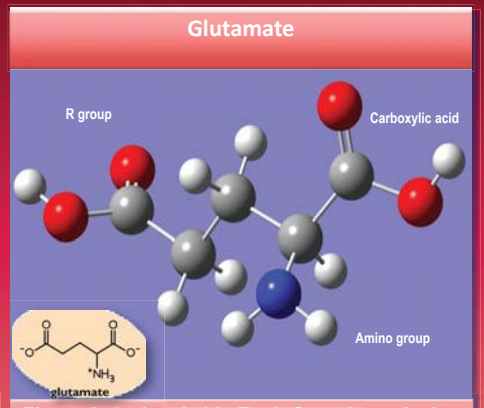


Figure 2: Amino Acids Each Contain an Amino Group and a Carboxyl Group but Differ in Their R Group

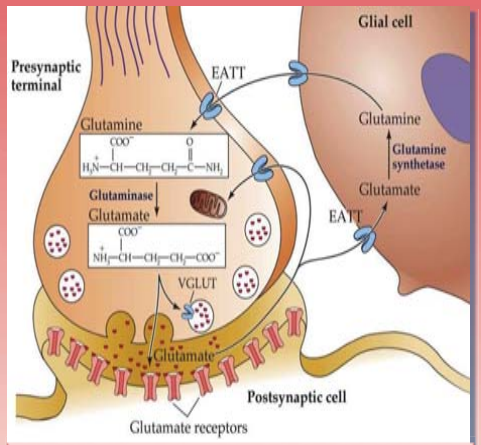


Figure 3: Glutamine Glutamate Cycle

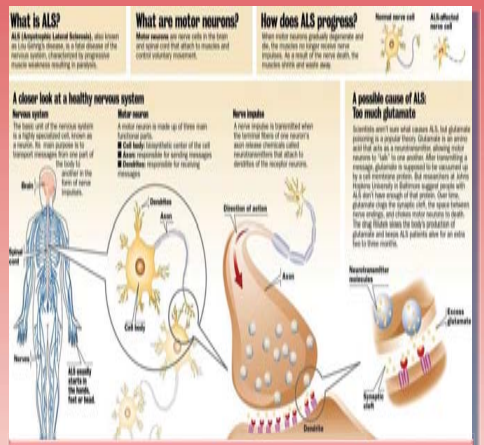
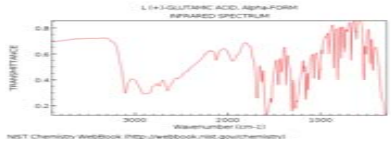


Figure 4: More About ALS

Results



The Infrared spectroscopy (IR) reading shows peaks consistent with amino and carboxyl functional groups. The strong, broad peak of the carboxylic acid can be observed in Gaussian as a hydroxyl functional group stretch. The fang like peak at 3150 cm^{-1} is characteristic of an amino group and is a primary amide. It can be observed as stretching as well. Both are intensified by hydrogen bonding.

Discussion

In the mammalian nervous system, the highest concentration of glutamate is found inside the nerve cell terminals (~100milimoles). After glutamate is released from these terminals, its unique properties shown above, are rapidly recognized by the receptors of the receiving cells. This binding opens the cell receptor, allowing Ca^{+} to enter the cell, producing an electric potential. If glutamate binds irreversibly to this receptor, accumulation of glutamate in the extracellular fluid would occur. This would result in over excitation of the nerve cell, excitotoxicity, and symptoms of ALS.

References

See Handout