Glutamate level in the frontal cortex decreases during young adulthood

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Introduction

Glutamate is the major excitatory neurotransmitter in the mammalian central nervous system and is involved in functions that alter with age, such as learning and memory, emotion, motivation, and motor behaviour. Rodent studies as well as human studies have found age-related decreases in glutamate levels in several brain areas. The purpose of this study was to measure glutamate concentrations in the frontal cortex of healthy subjects of different ages. Since measurement of glutamate with ^{1}H-MRS is challenging at lower field strengths, due to its spectral overlap with glutamine, a magnetic field strength of 7 Tesla was used in this study to accurately determine glutamate concentrations in the human brain.

Materials/Methods

Participants: 31 subjects from 18 to 31 years old (mean ± SD = 23.1 ± 3.2 years, 12 males, 19 females) participated in this study. Participants did not have a history of psychiatric or neurological disorders, did not have a history of alcohol or drug abuse, and did not have first degree family members with psychiatric or neurological disorders.

MR acquisition: ^{1}H-MRS experiments were performed on a 7 Tesla whole body MR scanner (Philips, Cleveland, USA), a birdcage transmit head coil (Nova Medical, Inc., Burlington, MA, USA) was used in combination with a 16-channel receive coil (Nova Medical, Inc., Burlington, MA, USA). We used a stimulated echo acquisition mode (STEAM) sequence (TR = 2000 ms, TE = 7 ms, TM = 11 ms acquisition time = 260 s, single voxel, voxel size = 2x2x2 cm, B_1 = 20 μT), and located the voxel of interest in the medial frontal cortex (fig.1). SWAMP water suppression was applied for the metabolite scan with the carrier frequency set to 3.0 ppm. A non water suppressed spectrum was obtained with the carrier frequency set to 4.7 ppm. First order shimming was based on the FASTERMAP algorithm [1,2]. After selecting the volume of interest, a localized B_1 field adjustment was applied [3].

Spectral fitting and quantification: Spectral fitting was performed with LCModel based software implemented in Matlab [4], which uses a priori knowledge from spectral components to fit metabolite resonances [5]. Metabolite concentrations were calculated as follows:

$$[met] = \frac{signal_{met}}{signal_{water}} x \frac{\#H_{water}}{\#H_{met}} x \frac{1 - e^{(-TR/T_1^{met})}}{1 - e^{(-TR/T_1^{water})}} x [water]$$

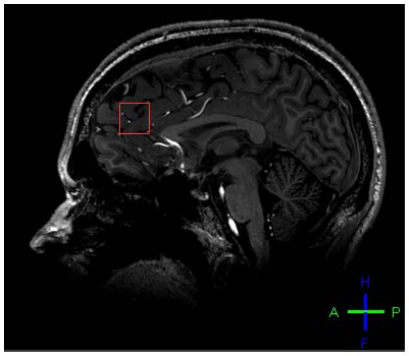

Fig.1: Voxel placement

Results/Discussion

Glutamate concentrations could be successfully determined with ^{1}H-MRS at 7 Tesla in the healthy adult brain. Moreover, we found a decrease in glutamate concentration in medial frontal cortex with increasing age in young adults up to 31 years (r=0.4,p=0.02) (fig.2). 7 Tesla ^{1}H-MR spectra are shown for the youngest (fig.3) and oldest participants (fig.4).

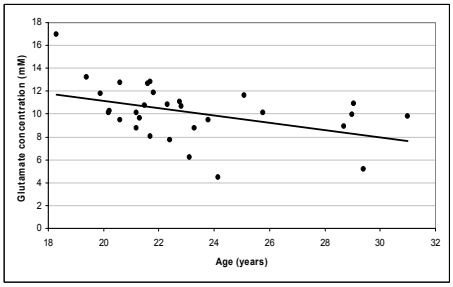

Fig.2: Glutamate concentrations during young adulthood

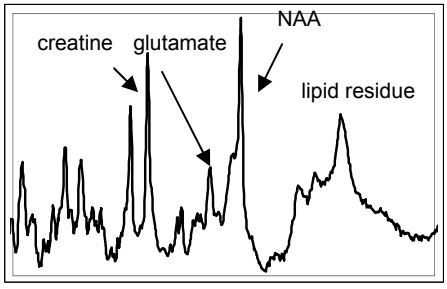

Fig.3: ^{1}H-MR spectrum from a younger participant

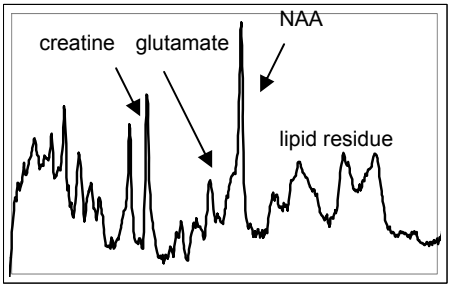

Fig.4: ^{1}H-MR spectrum from an older participant

Conclusion

At 7T the glutamate resonance at 2.3 ppm is well resolved and can be obtained with a high signal to noise ratio. Alterations in these concentrations were observed even in the relatively small age range of 18 to 31 years. The decrease in glutamate concentration is in line with the gray matter thinning in the medial frontal cortex [6] observed in this age range. However, the change in glutamate is larger than the change in gray matter, therefore we postulate that the observed effect is due to physiological changes rather than anatomical changes.

References

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