Glutamate is reduced in the Frontal Lobe of HIV Patients

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Background: Glutamate excitotoxicity has been linked to neurocognitive impairment in several diseases including complications of advanced HIV/AIDS. We measured the unobstructed single-line glutamate (Glu) resonance at 2.35 ppm on a 3T MR clinical scanner and derived absolute glutamate concentration [Glu] mM for HIV seropositive patients and gender matched seronegative controls.

Methods: Nine HIV positive subjects (1 female, age 42 ± 4 years) and ten healthy subjects (2 females, age 43 ± 3 years) underwent proton MRS examination using the single voxel TE-averaged PRESS method (1). Two brain regions were chosen: the frontal white matter (FW), a region associated with cognitive function; and posterior cingulate gyrus gray matter (GM), a common reference region for MRS study. The voxel size was 2x2x2 cm^3. HIV subjects had normal cognitive function and Mini Mental State Examination scores in the normal range (means ± SD= 28.0±2.0). The LCModel was used to analyze and quantify the MRS data.

Results: Figure 1 shows T1-weighted image, a representative TE-averaged FW spectrum from a normal and an HIV patient. Comparative results of the MRS analysis of the FW and GM regions are shown in Figure 2. Glutamate was significantly lower in the FW in HIV patients (3.5±1.5mM) compared to normal subjects (9.9±3.3mM) (p=0.02). N-acetylaspartate (NAA) was lower in the FW in HIV patients (12.02±1.55mM) compared to normal subjects (16.31±2.7mM) (p= 0.026). There were no significant differences in Glu and NAA concentrations in the GM of normal and HIV patients.

Discussion:

1. To our knowledge, this is the first time direct measurement of Glu level in HIV patients has been investigated. Several studies performed at 1.5T and 3T have previously reported significantly reduction of FW Glx (combined glutamate and glutamine) in HIV patients compared with normal subjects.
2. We found i) GM [Glu] > FW [Glu], ii) HIV FW [Glu] < normal FW [Glu], and iii) HIV GM [Glu] ~ normal GM [Glu]. Glu signals measured using the MRS method represent the neuronal and glial pools (about 10mM). Our observation indicates the loss of Glu exceeds the entire contribution from the glial and is therefore most probably loss exclusively from the neuronal pool as indicated by the concomitant loss of NAA, a neuronal marker.
3. Reduction of neuronal Glu may be relevant to the development of cognitive impairment in HIV. Therefore, early MRS followed by appropriate treatment may prevent neurocognitive decline in these patients.

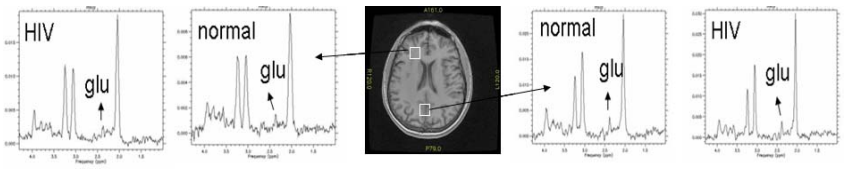

Figure 1: T1 weighted image and representative spectra from FW, and GM.

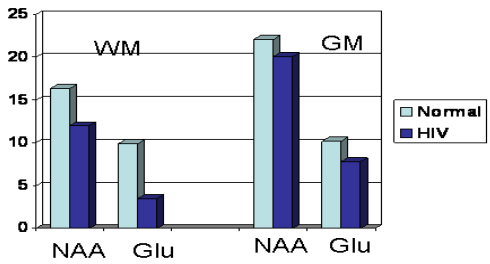

Figure 2: Comparison of NAA and Glu concentrations between normal and HIV patients in FW and GM.

Conclusion: Local changes in brain glutamate in HIV are profound and of neurologic significance.

References: 1). Hurd, R et al. MRM 2004; 51: 435-440.