Changes in Intracellular pH (pH_i) in the Basal Ganglia of HIV-Infected Adults

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Introduction: HIV infection can lead to impaired neuropsychological function and to the development of HIV-associated dementia (HAD). Since neurons are not directly infected by HIV, its deleterious effects on the nervous system may be due to alterations in neuronal enviroment, changes in ion and solute transport. Intracellular alkalinization in HIV-infected astrocyte-cultures1 and in the cerebellum of asymptomatic HIV+subjects2 were observed previously. We extended our examination to the basal ganglia which play a pivotal role in the development of HAD carrying the heaviest viral load in the brain.

Subjects and Methods: ^{31}P-MRSI was performed on 25 HIV+subjects with various degree of HAD and 21 HIV- (healthy) controls to investigate the changes in pH_i associated with the progression of HAD.All 46 subjects underwent MRI and ^{31}P-MRSI on a 4.1T MR spectroscopy/imaging system and completed a standard neuropsychological battery to determine HAD stage. Anatomical FLASH images were obtained using a home built ^{1}H birdcage head coil with a mounted headrest. The imaging coil was replaced with a homebuilt ^{31}P transmit/receive head coil without moving the subject's head. Localized spectra were acquired from 11.5 cc voxels located in the basal ganglia using ^{31}P-MRSI (TR=74 ms, 18° block pulse, 22x22x22 phase encoding scheme with spherical gaussian weighting in k-space). Data processing was by time domain fitting using prior knowledge including J-coupling multiplets. The pH_i was calculated from chemical shift of inorganic phosphate from the phosphocreatine peak[3].

Results: No pH_i change was observed comparing all HIV-infected subjects to controls (mean=7.024±0.007 versus 7.021±0.008). In asymptomatic HIV+ subjects (HAD0, n=5) there was a tendency toward pH_i elevation compared to controls (mean=7.046±0.016 versus 7.021±0.008) while in patients with more severe dementia (HAD4, n=6) pH_i tended towards acidic resulting in significant pH_i difference between HAD0 and HAD4 patient groups (mean=7.046±0.016 versus 6.999±0.015 p=0.0458).

Conclusion: It is interesting that this study found larger pH diffences in asymptomatic patients than in patients with advance dimentia. The elevation of pH_i in asymptomatic patients may correspond to astrocyte activation, proliferation and the initial hypermetabolism in the basal ganglia during the development of HAD observed also with PET[4]. Intracellular acidification at later stage maybe associated with hypometabolism resulted from cellular damage and neuronal death. ^{31}P-MRSI may be used for non-invasive monitoring of the cellular changes associated with the progression of HAD.

References:

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