LOWER ABSOLUTE CBF IN HEAVY DRINKERS AND COMPENSATORY BLOOD FLOW CHANGES IN TREATED HIV+ HEAVY DRINKERS

D. J. Meyerhoff[1], F. Ezekiel[2], N. Schuff[1], J. Kmiecik[3], C. Studholme[1], M. W. Weiner[1]

[1]Radiology, University of California San Francisco, DVA Medical Center, San Francisco, CA, United States, [2]DVA Medical Center, San Francisco, CA, United States, [3]Radiology, University of California San Francisco, San Francisco, CA, United States

Introduction

Studies in mildly impaired human immunodeficiency virus infected (HIV+) patients using bolus contrast MRI found lower cerebral blood flow (CBF) in frontal and parietal brain and higher CBF in parietal white matter (Chang et al. Neurology 54:389, 2002). However, to the best of our knowledge, since the introduction of antiretroviral therapy (ART) there have been no spin-labeled perfusion MRI studies of CBF in treated HIV+ patients. Furthermore, lower CBF throughout the brain has been generally detected in chronic alcoholics by SPECT, especially in frontal lobe. In the context of studying separate and interactive brain effects of HIV infection and comorbid chronic heavy drinking, we used arterial spin-labeled perfusion MRI to measure absolute CBF in gray and white matter of frontal and parietal lobes.

Methods

All studies were performed on a Siemens Vision 1.5 T. Our pulsed arterial spin-labeled perfusion MRI method used a multislice QUIPSSII-modified EPISTAR sequence (Wong et al. Magn Reson Med, 39(5): 702-8, 1998) with 6 contiguous 9mm thick slices and 2.0mm2 in-plane resolution, TI = 1500ms. Absolute CBF was measured in 39 HIV- individuals ((10 light drinkers (LD), 29 heavy drinkers (HD)) and 22 HIV+ patients (15 LD and 7 HD), 20 of whom received antiretroviral therapy (ART). The LD individuals drank < 20 alcoholic drinks/mo over lifetime, HD drank > 100 alcoholic dri/mo within 3 years prior to study and were matched on drinking severity. The HIV+ groups had a similar degree of immunosuppression (LD: CD4 383 ± 213, log viral load 3.23 ± 1.43; HD: CD4 244 ± 109, log viral load 3.11 ± 1.78). Perfusion images were co-registered with an MPRAGE data set (TR/TE/TI = 10/4/300 ms), which was segmented into gray matter (GM), white matter (WM), and cerebro-spinal fluid (CSF) of major lobes using probabilistic segmentation and atlas-based non-linear transformation (Studholme et al. Neuroimage 13(4):561-76, 2001). All perfusion voxels with 100% WM were analyzed to derive WM perfusion, all GM perfusion voxels were at least 90% GM with no WM. Mean absolute perfusion was expressed in units of ml/100mg/min as described by Wong et al. (1), except that T2 was calculated for each subject from double-spin-echo images. All participants also underwent neuropsychological testing. Statistical analyses used a 2x2 ANOVA with HIV status (positive or negative) or viral status (suppressed or >400) and drinking status (light or heavy) as main factors and t-tests where appropriate.

Results

Chronic heavy drinking was associated with significant reductions of CBF in frontal and parietal GM (both $p=0.01$, -9%), and with trends to lower CBF in frontal and parietal WM ($p<0.17$, -6%). HIV infection tended to be associated with hypoperfusion in frontal cortex ($p=0.15$, -7%) and hyperperfusion in parietal WM ($p=0.13$, +10%). There were negative HIV-by-heavy drinking interactions in frontal and parietal WM ($p<0.05$).

Among 25 LD, HIV+ patients had significantly lower CBF than HIV- controls in frontal GM ($p = 0.03$, -16%) and parietal GM ($p<0.08$, -11%). Among 36 HD, HIV infection was associated with higher parietal WM perfusion ($p<0.01$, +24%) and a trend to higher frontal WM perfusion ($p<0.09$, +14%), leading to a lower GM-to-WM perfusion ratio in frontal and parietal brain ($p<0.02$). Nine virally suppressed HIV+ individuals on ART had similar CBF than 10 viremic HIV+ patients on ART.

HD had ataxia and global cognitive impairment, in particular in the domains of working memory and processing speed. Within HIV- HD, our largest group, a higher ratio of GM-to-WM perfusion in frontal lobe was associated with a worse ataxia score (Spearman $r=0.77$, $p<0.0001$), reflecting imbalance and postural sway. Lower ataxia scores were also correlated with lower absolute CBF in frontal and parietal cortex and in frontal WM of 9 HIV+ LD (all $r>0.77$, $p<0.02$).

Discussion

Arterial spin-labeled perfusion studies yield absolute lobar CBF without the need for contrast or radiotracer injections. The results are largely consistent with results of bolus-contrast perfusion MRI in mildly impaired HIV+ patients and with SPECT perfusion studies in treated alcoholics. They show regionally lower CBF in HIV+ light drinkers on stable antiretroviral medication relative to HIV- light drinkers, suggesting the possibility that the HIV-infected brain sustains perfusion deficits despite "successful" virus-suppressing therapy in half the treated HIV+ sample. Furthermore, findings in heavily drinking HIV infected individuals of hyperperfusion in some brain regions and hypoperfusion in others supports the notion of a compensation in distribution of CBF, as observed in alcohol-abusing cocaine dependent individuals (Gottschalk, Kosten, Drug Alcohol Depend 68(1): 95, 2002). Correlations between regional perfusion and ataxia scores suggest clinical/functional relevance of perfusion changes in HIV infection and chronic heavy drinkers.