Age-related Increase in brain reserve in HIV subject during attention tasks

L. Chang[1], R. Yakupov[1], L. Girton[2], T. Nash[1], H. Nakama[3], T. Ernst[1]

[1]Department of Medicine, University of Hawaii, John A. Burns School of Medicine, Honolulu, Hawaii, United States, [2]Imaging Department, Queens Medical Center, Honolulu, Hawaii, United States, [3]Department of Psychiatry, University of Hawaii, John A. Burns School of Medicine, Honolulu, Hawaii, United States

INTRODUCTION: Prior fMRI studies have demonstrated increased usage of reserve brain regions during working memory and attention tasks in HIV patients with mild dementia,[1, 2] as well as in those who were neuroasymptomatic.[3] With effective antiretroviral treatments, these HIV-infected individuals are living longer and the prevalence of HIV dementia is increasing[4]. Whether aging exacerbates HIV-associated brain injury and leads to greater usage of the reserve network was evaluated in this study.

METHODS: Fifty-eight subjects [22 HIV neuroasymptomatic (HIV-NA: aged 41±2, 22-60 years), 17 with cognitive deficits (HIV-CD: aged: 52±2, 40-67 years) and 19 seronegative controls (SN, aged 42±3, 21-68 years)] with similar education completed detailed clinical assessments, including neuropsychological tests. All performed fMRI during a set of visual-attention tasks with increasing levels of difficulty, mental tracking of multiple targets (2, 3, or 4 balls) amongst 10 moving balls.[2,5] After a brief training session, subjects had fMRI in a 3 T Siemens Trio MRI scanner, using single-shot gradient-echo EPI (TE/TR=30/3000ms, 3 mm slices, 1 mm gap, typically 42 axial slices, 64^2 matrix, 20cm FOV, 126 time points). Task performance and subject motion were monitored in real-time during fMRI, to assure accuracy > 80% and motion < 1mm-translations and < 1°-rotations. Motion and distortion corrections were performed on the scanner. After spatial normalization to the Talairach frame and spatial smoothing, activation maps and positive or negative age correlations in each group, as well as contrasts between the aging effects in the three groups, were calculated with SPM2.

RESULTS: Clinical: HIV-NA and HIV-CD subjects had similar immune status: CD4 count (495±47 vs. 381±49/mm^3), nadir CD4 (218±32 vs. 157±30/mm^3), plasma viral load (Log 2.8±0.3 vs. 2.7±0.3 copies/mL). Compared to HIV-NA subjects, HIV-CD subjects had lower HIV dementia scale (15.4±0.2 vs. 13.2±0.4) and poorer Karnofsky score (97±1 vs. 90±2). HIV-CD subjects also had AIDS dementia stage 0.7±0.06, and poorer performance on several neuropsychological tests (domains affected include motor, fine motor, psychomotor, and memory function). **fMRI:** All subjects showed similar activation patterns during the attention tasks. However, despite similar fMRI task performance (all had >80% accuracy) and reaction times, age-dependent increases in BOLD signals were observed in the parietal cortices bilaterally in HIV-NA and in the frontal cortices in HIV-CD, but not in SN, on the more difficult tasks (tracking 3 or 4 balls) (Figure 1). HIV-NA showed greater age-related increase in activation than HIV-CD in the parietal brain regions that showed load effects.

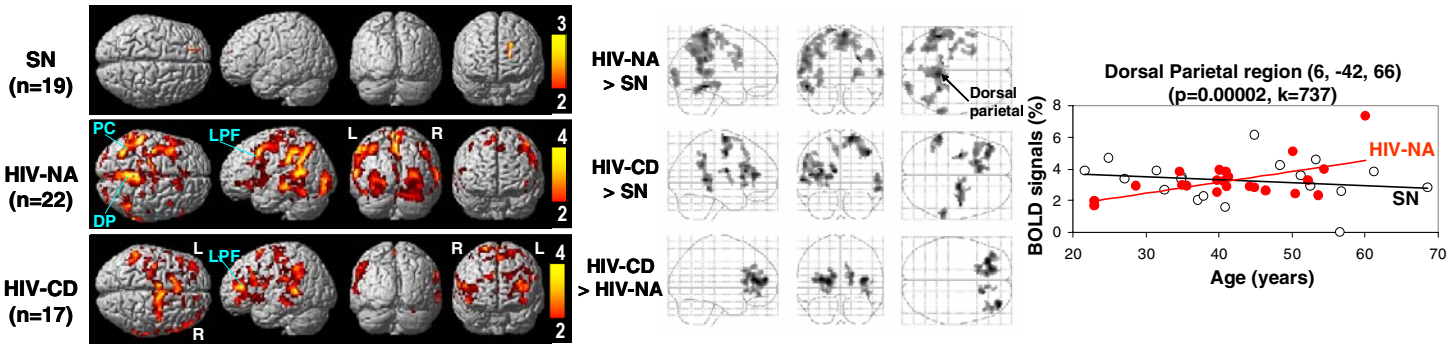

Figure 1: *Left*: Surface maps for the 4-ball tracking task show age-related increases in BOLD signals only in the HIV groups (T ≥2, p = 0.025, k>10 voxels); *Middle:* Glass brain views showing group differences in age-related changes in brain activation (T ≥ 2.5, p<0.008, k>50 voxels); *Right:* Correlation plots showing age-related increase in BOLD signals in SN-NA but not in SN controls.

DISCUSSION: Compared to SN, HIV-NA showed age-related increased usage of regions with load effects (reserve brain regions), as observed previously.[2] Older HIV patients with cognitive deficits could not activate all of the reserve brain regions, but additionally activated the frontal regions in order to maintain performance on the visual attention tasks. These findings suggest that with aging, HIV-associated brain injury leads to less efficient usage of the normal attention network, and greater usage of the reserve brain regions. Cognitive deficits ensued in HIV-CD subjects when the capacity of the reserve network was exhausted, as shown in the more difficult tasks on standard neuropsychological tests. Since the inter-subject variability on fMRI is large, longitudinal follow-up of these subjects will further validate these cross-sectional observations.

ACKNOWLEDGEMENTS: Studies were supported by NIMH (R01 MH61427) and NIDA (K24-DA16170; K02-DA16991). We also thank Dr. Christine Cloak, Dr. Kenneth Yue, Darlene Ramones, Kathryn Taketa and Trevor Wu for their assistance in data collection.

REFERENCES

1. Chang, L, et al, Neurology, 2001;57:1001-1007.
2. Chang, L, et al, Ann Neurol, 2004;56(2):259-272.
3. Ernst, T, et al, Neurology, 2002;59(9):1343-1349.
4. Sacktor N et al, J Neurovirol 2002;8 Suppl 2:115-121.
5. Culham, J.C., et al., Invest Ophthal Vis Sci 1997;38(4):S1174.