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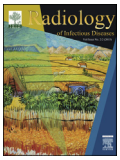
Radiology of Infectious Diseases 2 (2015) 61–64



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Research article

Cerebral metabolism in HIV infected patients with non-cognitive disorder using single voxel magnetic resonance spectroscopy

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Received 21 April 2015; revised 1 June 2015; accepted 1 June 2015
Available online 2 July 2015

Abstract

Objective: To investigate the variance of metablites, including N-Acetyl aspartate (NAA), Choline (Cho) and Creatine (Cr), in brain regions of HIV infected patients with non-cognitive disorder and healthy volunteers by a 3.0 T magnetic resonance spectroscopy.
Methods: Single voxel magnetic resonance spectroscopy was applied to measure the basal ganglia region, frontal lobe and parietal lobe in 69 HIV infected patients and 33 healthy volunteers. According to CD4 T cell count, the patients were divided into 2 groups, group A (≥200 cells/μL, 40 patients) and group B (<200 cells/μL, 29 patients). The normal control group, group C, consisted of 33 healthy volunteers.
Results: The patients in groups A and B had lower ratio of NAA/Cr but higher ratio of Cho/Cr in the basal ganglia region than group C ($P < 0.001$; $P = 0.021$). Compared to groups B and C, the patients in group A had higher ratios of NAA/Cr and Cho/Cr ($P = 0.013$; $P < 0.001$) in the frontal lobe. In the parietal lobe, the patients in group A had higher ratio of Cho/Cr than groups B and C ($P = 0.037$).
Conclusion: HIV infection induces inflammation in basal ganglia region, frontal lobe and parietal lobe before non-cognitive disorder occurs after HIV infection. However, the basal ganga region sees more neurons loss.

Keywords: HIV infection; MR spectroscopy; Cognitive disorder; N-Acetyl aspartate; Choline

1. Introduction

Due to the widespread use of highly active antiretroviral therapy (HAART) for HIV infected patients in China, the incidence of HIV/AIDS associated neurocognitive disorder (HAND) has been showing a gradual increase nowadays [1]. By studies intended to find the evidence for early diagnosis of HAND, intracephalic metabolic changes have been demonstrated to occur before HAND [2].

2. Materials and methods

A total of 69 HIV infected patients was enrolled in our present study, including 23 females and 46 males with a median age of 39 years (range: 23–63 years). The diagnosis of HIV infection was defined 2 weeks to 19 years ago. The patients with a mild condition, specifically a CD4 T cell count of above 200 cells/μL (≥200 cells/μL), were assigned into group A. The patients with a CD4 T cell count of <200 cells/μL, namely patients with severe condition, were assigned into group B. Healthy volunteers were recruited to constitute the normal control group, the group C, including 11 females and 22 males with a median age of 35 years (range: 22–59 years).

By using Siemens 3.0 T TIM TRIO magnetic resonance scanner with 32 channel head coil, single voxel magnetic resonance spectroscopy (MRS) imaging was performed in cerebral axis T2WI and 3-dimensional model voxel. The basal ganglia, the frontal lobe and parietal lobe were scanned. The scanning parameters of T2WI (TSE, fast spin echo) was TR/TE 4570/100 ms, 5 mm of layer thickness and 1.5 mm interval, while the scan parameters of 3-dimensional model voxel T1WI (TurboFLASH, fast and small angle

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Peer review under responsibility of Beijing You'an Hospital affiliated to Capital Medical University.

http://dx.doi.org/10.1016/j.jrid.2015.06.004

excitation sequence) was TR/TE 1900/2.52 ms, FOV 250 mm × 250 mm and voxel 1.0 mm × 1.0 mm × 1.0 mm. The scan parameters of MRS was Svs-se (Press sequence), TR/TE 2000/135 ms, number of excitation of 64 and bandwidth 1200 Hz with 20 mm * 20 mm * 20 mm volume of voxel. MRS was processed into wave spectrogram by the use of syngo B17 spectroscopy. The quality of MRS figure was accessed by an experienced radiologist who was also responsible for observing MRI plain scan and MRS figure. The values of NAA, Cho and Cr were recorded.

The recruitment criteria of HIV infected patients included: HIV positive and at least 10 points scoring for the, international HIV dementia scale (IHDS) [3]. According to MR T1WI and T2WI, the patients with obvious lesions of cerebral infection and/or obvious space occupying effect were excluded. The recruitment criteria for healthy volunteers included: no history of cerebrocardiovascular events, no brain parenchymal lesions on weighted T1 and/or T2 image when large noise was excluded, instability of base line or peak overlapping by MRS.

Statistical analysis was performed by using SPSS 16. T test was used for hypothesis test when the data was in line with normal distribution.

3. Results

The group A consisted of 40 patients, including 20 males and 20 females, with a median age of 37.5 years (range: 25–63 years). A total of 13 patients reported a history of unsafe homosexual/heterosexual behavior, and 2 other patients reported a history of receiving blood transfusion. The remaining 25 patients reported no known infection route. Their durations of HIV infection ranged from 3 months to 19 years with a median of 60 months. The CD4 T cell counts in the group A ranged from 202 cells/μL to 1200 cells/μL and 14 patients from the group A had a CD4 T cell count of ≥500 cells/μL (Fig. 1). And 10 patients from the group A reported a history of intracranial infection. The group B consisted of 29 patients with a median age of 40 years (range: 23–60 years). The 18 patients reported a history of unsafe homosexual or heterosexual behavior and another 1 patient reported a history of receiving blood transfusion. The other 10 patients showed no known route of HIV infection. Their durations of HIV infection ranged from 2 weeks to 19 years with a median of 2 months. The CD4 T cell count of the patients in the group B ranged from 3 to 194 cells/μL. Notably, 24 patients in this group had a history of intracranial infection. MRS showed no lactate peak in all the cases (Table 1).

4. Discussion

In the era of HAART, most HIV infected patients experience symptoms of the central nervous system [4]. When HIV infected patients are receiving HAART, 50% shows lower cognitive ability than the healthy controls of the same age [4]. HIV infection may impair the central nervous system to produce cognitive and behavioral impairment, and even dementia. MRS is optimal in diagnosing HIV-related dementia [5,6]. In recent years, MRS has gained widespread application in antiretroviral therapy [7], as well as the detecting of cerebral metabolism during its early period (within 1 year) and chronic period [8]. Our present study intended to evaluate the

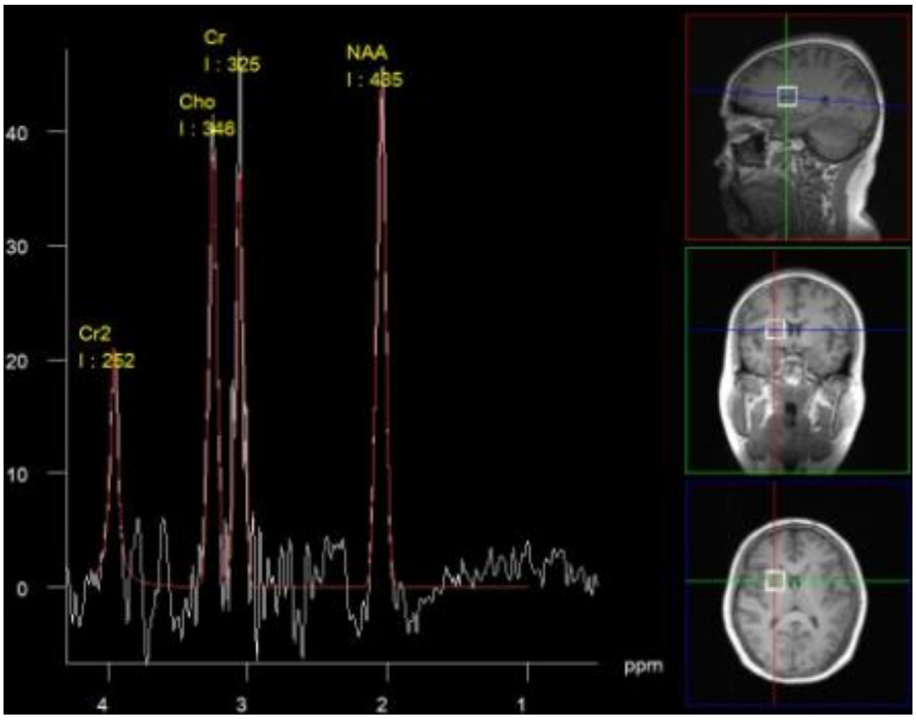

Fig. 1. A female patient aged 47 years with HIV infection for 8 years. She was treated by antiretroviral therapy for 7 years. The CD4 T cell count was 500 cells/μL. MRS of basal ganglia showed lower NAA and higher Cho.

Table 1
Analysis of intracranial infection in all the cases.

CD4+ T cell (cells/μL)	Basal ganglia				Frontal lobe				Parietal lobe			
	Cases	NAA/Cr	Cho/Cr	NAA/Cr	Cases	NAA/Cr	Cho/Cr	NAA/Cr	Cases	NAA/Cr	Cho/Cr	NAA/Cr
≥200 (A group)	29	1.36 ± 0.28	0.96 ± 0.19	1.45 ± 0.33	36	1.84 ± 0.20	1.19 ± 0.14	1.56 ± 0.19	37	2.05 ± 0.25	1.11 ± 0.16	1.88 ± 0.39
<200 (B group)	13	1.15 ± 0.28	0.98 ± 0.13	1.18 ± 0.25	22	1.66 ± 0.33	1.01 ± 0.18	1.69 ± 0.38	26	1.92 ± 0.22	1.03 ± 0.20	1.91 ± 0.36
Normal group (C group)	21	1.55 ± 0.22	0.84 ± 0.17	1.88 ± 0.29	33	1.73 ± 0.14	1.06 ± 0.13	1.66 ± 0.22	33	1.94 ± 0.18	1.02 ± 0.10	1.92 ± 0.24
P value (ANOVA)		<0.001	0.023	<0.001		0.013	<0.001	0.135		0.051	0.037	0.783
P value (A–B)		0.021	0.678	0.010		0.005	<0.001	0.077		0.030	0.042	0.595
P value (A–C)		0.016	0.017	<0.001		0.049	<0.001	0.110		0.051	0.021	0.522
P value (B–C)		<0.001	0.020	<0.001		0.277	0.298	0.730		0.726	0.902	0.948

application value of measurable brain metabolic abnormalities detected by MRS in diagnosing or assessing HIV infected patients with no cognitive impairment. A longer TE time (135 ms) was selected for the subjects of the study, accounting for a more stable basic line and a better reproducibility of the waveform of the main markers.

MRS is capable of demonstrating early cerebral trauma [8]. Even though MRS remains to be the only noninvasive examination for cerebral metabolism, the scanning can be greatly affected by the uniformity of magnetic field, the conditions of patient, and the scanning parameters. The neuropsychological examination is an additional way to MRS in the diagnosis of HIV/AIDS related dementia. In the studies about the use of MRS in detecting cerebral cognitive impairment, the data about basal ganglia and hippocampus tended to be consistent, suggesting that HIV infection could induce lower NAA/Cr. However, the studies showed variant MRS data about the frontal lobe, occipital lobe and cingulate cortex. Morgan [9] found that frontal lobe has higher inositol and lower glutamate complex but absence of NAA. However, Lentz [10] and Suwanwela [11] found that frontal lobe shows lower NAA in the early period of HIV infection.

The group of patients with mild condition was shown with higher Cho/Cr in basal ganglia, frontal lobe and parietal lobe than the normal control group. However, the group of patients with severe condition was shown with higher Cho/Cr only in basal ganglia. Because of the longer duration of HIV infection in the group of patients with mild condition, inflammation induced by HIV infection may contribute to the increase of Cho/Cr ratio. In combination to the ratio of NAA/Cr (no obvious decrease in frontal lobe), the frontal lobe of HIV infected patients with no symptomatic cognitive impairment showed inflammation induced by HIV virus, but no loss of neuron was demonstrated.

Based on grouping of patients by the CD4 T cell count, our study demonstrated that the basal ganglia of HIV infected patients, including those with high CD4 T cell count and low CD4 T cell count, has lower NAA/Cr than the normal control. And the decrease of NAA/Cr ratio is more obvious in the group of patients with lower CD4 T cell count (1.15/1.55). The finding indicated neuronal trauma in basal ganglia of HIV infected patients with no cognitive impairment, whose occurrence is not related to CD4 T cell count. Our finding is consistent to the results of most related studies. The frontal lobe of HIV infected patients with low CD4 T cell count was shown to have lower NAA/Cr than HIV infected patients with high CD4 T cell count, but no significant decrease by comparison to the normal control. The reason for such changes may be related to exclusion of HIV infected patients with cognitive impairment in our study. Therefore, we speculated that the frontal lobe of HIV infected patients with no cognitive impairment may experience mild neuronal trauma. The parietal lobe of the patients with low CD4 T cell count was shown with lower NAA/Cr than the patients with high CD4 T cell count ($P = 0.030$). The finding may be related to the measurement error, due to P (ANOVA) of about 0.051. As we know, in addition to a large amount of neuron, there are also a large amount of microglias in the basal ganglia. And in the brain of HIV infected patients, microglia is seriously affected by HIV virus. Because the microglia nourishes the neuron, the trauma of microglia may induce neuronal trauma. Although HIV virus could destroy the nerve cell of frontal lobe and parietal lobe, basal ganglia is mainly affected by HIV virus in the early period of its infection. Based on the previous reports [12,13], we came to a conclusion that regarding the central nervous system, HIV virus may spread from basal ganglia to frontal lobe, parietal lobe and occipital lobe.

Our findings may be insufficient to explain such an infection route because MRS with longer TE (135 ms) is incapable of detecting inositol and glutamate complex. However, the longer TE (135 ms) facilitates in observing NAA and Cho with favorable stability and repeatability. The metabolic conditions of NAA and Cho in the detected regions were precisely demonstrated in our study. In conclusion, inflammation induced by HIV infection in basal ganglia, frontal lobe and parietal lobe may occur before the period of no cognitive impairment, but the loss of neuron does occur in the region of cerebral basal ganglia.

Supported by

Beijing natural science foundation (No.7132108); The capital health research and development of special (No.2011-2018-01); Beijing Municipal Administration of Hospitals Clinical Medicine Development of Special Funding Support (No. ZYLX201511).

References

[1] Fengli Song, Yulin Zhang, Qiao Luxin, Wei Ding, Shuying Xu, Tong Zhang, et al. An initial screening for HIV-1 associated neurocognitive disorders in HIV-1 infected patients in China. J Cap Med Univ 2012;33(5):610−5.

[2] Walsh K, Megyesi J, Hammond R, Wiley CA, Hammond R. HIV-1/AIDS neuropathology in a Canadian teaching centre. Can J Neurol Sci 2003;31(2):235−41.

[3] Sacktor NC, Wong M, Nakasujja N, Skolasky RL, Selnes OA, Musisi S, et al. The international HIV dementia Scale: a new rapid screening test for HIV dementia. AIDS 2005;19(13):1367−74.

[4] Valcour V, Sithinamsuwan P, Letendre S, Ances B. Pathogenesis of HIV in the central nervous system. Curr HIV/AIDS Reports 2011;8(1):54−61.

[5] Paul RH, Yiannoutsos CT, Miller EN, Chang L, Marra CM, Schifitto G, et al. Proton MRS and neuropsychological correlates in AIDS dementia complex: evidence of subcortical specificity. J Neuropsychiatry Clin Neurosci 2007;19(3):283−92.

[6] Peluso MJ, Meyerhoff DJ, Price RW, Peterson J, Lee E, Young AC, et al. Cerebrospinal fluid and neuroimaging biomarker abnormalities suggest early neurological injury in a subset of individuals during primary HIV infection. J Infect Dis 2013;207(11):1703−12.

[7] Winston A, Duncombe C, Li PC, Gill JM, Kerr SJ, Puls RL, et al. Two patterns of cerebral metabolite abnormalities are detected on proton magnetic resonance spectroscopy in HIV-infected subjects commencing antiretroviral therapy. Neuroradiology 2012;54(12):1331−9.

[8] Masters MC, Ances BM. Role of neuroimaging in HIV-associated neurocognitive disorders. Semin Neurol 2014;34(1):89−102.

[9] Morgan RH, Barker PB, Skolasky RL, Selnes OA, Moxley RT, Pomper MG, et al. Brain metabolism and cognitive impairment in HIV infection a 3T magnetic resonance spectroscopy study. Magn Reson Imaging 2010;28(9):1251−7.

[10] Lentz MR, Kim WK, Lee V, Bazner S, Halpern EF, Venna N, et al. Changes in MRS neuronal markers and T Cell phentypes observed during early HIV infection. Neurology 2009;72(17):1465−72.

[11] Suwanwela N, Phanuphak P, Phanthumchinda K, Suwanwela NC, Tantivatana J, Ruxrungtham K, et al. Magnetic resonance spectroscopy of the brain in neurologically asymptomatic HIV-infected patients. Magn Reson Imaging 2000;18(7):859−65.

[12] Lentz MR, Kim WK, Kim H, Soulas C, Lee V, Venna N, et al. Alterations in brain metabolism during the first year of HIV infection. J Neurovirol 2011;17(3):220−9.

[13] J1 Harezlak, Cohen R, Gongvatana A, Taylor M, Buchthal S, Schifitto G, et al. Predictors of CNS injury as measured by proton magnetic resonance spectroscopy in the setting of chronic HIVinfection and CART. J Neurovirol 2014;20(3):294−303.