Interferon-alpha Induced Metabolic Alterations in Basal Ganglia
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Introduction
Chronic administration of interferon (IFN)-alpha (a pro-inflammatory cytokine) for the treatment of hepatitis C virus (HCV) infection is associated with depression and fatigue in 40-50% of the patients. These behavioral outcomes have been correlated with alterations in glucose metabolism in basal ganglia (BG). Based on these results, we hypothesized that the IFN-alpha induces metabolic changes in basal ganglia, underlying the aforementioned changes in behavior. In this study, our main purpose is to investigate the changes of metabolites in BG in HCV infection patients before and after interferon-alpha treatments.

Methods
Seventeen patients with HCV infection participated in this study. These patients were divided into two groups: (1) an IFN-alpha treated group (IFN group, n=8) who underwent two MRI sessions, one before and another after a 4-week treatment; (2) a control group (who were on the waiting list for IFN-alpha treatment, n=9) who underwent the same two MRI sessions with a 4-week interval. In each MRI session, T1-weighted images were obtained on a 3.0 Tesla Siemens Magnetom TRIO scanner (Siemens Medical Solutions, Malvern, PA) with an MPRAGE sequence (TR = 2300 ms, TE = 3.02 ms, TI = 1100 ms, Flip Angle = 8°, voxel size = 1 × 1 × 1 mm³). Spectroscopic data were acquired by 2D PRESS-based MRSI sequence (TR = 1590 ms, TE = 30 ms, sampling size = 1024, matrix=16 × 16, voxel size= 11.3 × 11.3×15 mm³). All MRSI data were analyzed with LCModel, using an 18-metabolites basis file and the water signal as the internal reference. Within each group, the changes of metabolites were tested by paired t-test.

Results
The spectroscopic data result showed that mI/Cre decreased (mean=0.6433 SD=0.121 at 0 week; mean=0.6092 SD=0.117 at 4 week P<0.05 *) and Glx/Cre increased (mean=1.19 SD=0.24 at 0 week; mean=1.2811 SD=0.208 at 4 week P<0.05 *) after 4 weeks interferon treatment in BG (red box) of IFN group. For control group, mI/Cre has no significant change between 0 weeks (mean=0.6766 SD=0.293) and 4 weeks (mean=0.66 SD=0.27); however the ratio of combination of glutamate and glutamine (glx) to Cre significantly decreased from 1.3975±0.332 at 0 week to 1.28±0.31 at 4 week which has an opposite trend compared with that in INF group.

Discussion and Conclusion
It has been reported that chronic administration of interferon-alpha (a pro-inflammatory cytokine) can precipitate astrocytic dysfunction resulting in a decrease in glutamate deactivation by astrocytes. mI has been reported to be an astroglial marker. The increase in glutamate and decrease in mI can be explained on the basis of astrocytic dysfunction induced by chronic IFN-alpha administration. Furthermore, reduction in the number of astroglia (or astrocytes) has been reported in depressive disorders from previous postmortem studies. Our findings indicate interferon-alpha may reduce the astrocytes in BG and induce a depression in HCV infection patients. The decrease in the glx/Cr values among controls probably represents decreasing levels of stress and increased comfort associated with the study procedures including scanning.

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References