Morphometric changes detected in Hepatits C (HCV) and HCV/HIV co-infected adults

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Introduction: Hepatitis C virus (HCV) infection is a rapidly increasing global health problem. Both HCV and human immunodeficiency virus (HIV) have same routes of transmission and establish chronic infections; therefore, co-infection is common [1]. Overall, 20% of HIV-infected individuals worldwide are chronically infected with HCV [2]. Although studies have been done on neuropsychological sequelae of co-infection with HIV and HCV [3], little is known about how the co-infection effect the cortex, including which cortical regions are affected. In this study we investigated the cortical thickness/volume and cerebral white matter (WM) volume across a group of HCV/HIV co-infected and HCV mono-infected adult patients employing an automated method for regional parcellation that uses curvature landmarks and gray matter (GM)/WM surface boundary information. We did a cortical surface-based analysis of the whole cortical mantle obtained from volumetric magnetic resonance imaging (MRI) data. The main objective of the study is to compare cortical thickness and volumetric changes in the cortex of HIV/HCV co-infected versus HCV mono-infected patients.

Materials and Methods: We assessed ten male patients with HCV (age 57.5y ± 5.2). They were compared to eight male HCV/HIV patients (age 51y ± 5.4). All subjects gave informed consent according to an institutionally approved research protocol. A Siemens 3T Trio-Tim MRI scanner (Siemens Medical Solution, Erlangen, Germany) was used and a 3D structural MRI was acquired on each subject using a T1-weighted a magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence (TR = 2200 msec; TE = 2.18 msec; inversion time = 900 msec; FA = 9°; matrix size = 256 x 256; FOV = 240 mm x 240 mm; slice thickness = 1 mm; number of slices = 176) for evaluation of structural brain abnormalities.

We used FreeSurfer Image Analysis Suite [4, 5] for cortical reconstruction and volumetric segmentation. Briefly, processing consisted of motion correction and averaging of multiple volumetric T1 weighted images, removal of non-brain tissue [6], automated Talairach transformation, automatic segmentation of the subcortical white matter and deep gray matter structures [7], tessellation of the gray/white matter boundary, inflation of the folded surface tessellation, automatic correction of topological defects and the extraction of cortical surfaces. Estimates of cortical thickness were made by measuring the shortest distance from the gray/white boundary to the gray/CSF boundary at each vertex on the tessellated surface and averaging between these two values. Subsequent to cortical reconstruction, the cortex is subdivided into 34 units based on gyral and sulcal structures [8]. These parcellations were subsequently used to assign a label to the underlying subcortical WM. Furthermore, Statistical thickness difference maps were constructed using a t statistic. We used a General Linear Model in which the main effects of group (thickness differences between HCV mono- and HCV/HIV co-infected) are shown.

Regions	HCV/HIV co-Infected		HCV mono-infected		F
	Mean	SD	Mean	SD	
Left Hemisphere					
Caudal middlefrontal	6302.9	1285.2	6565.2	1100.2	15.1
Inferior temporal	6320.1	1220.3	6398.8	1316.9	33.5
Isthmus cingulate	3566.4	630.7	3943.2	748.5	22.2
Lateral orbitofrontal	6304	915.6	6895.2	1115.5	14.0
Parsopercularis	3551.6	648.7	3598.9	695.7	26.6
precuneus	9512	2060.9	9458.8	1308.3	11.5
Superior frontal	18947.5	2079.2	18045.4	2098.0	13.3
Right hemisphere					
Inferior temporal	5754	1397.9	6063.8	974.5	12.4
Isthmuscingulate	3363.6	630.0	3245.4	609.6	16.8
lateralorbitofrontal	6642.8	1134.5	6483.7	871.3	12.9
Parsopercularis	3167.3	954.4	3322.5	767.8	19.1
Parstriangularis	3293	682.8	3300.1	610.5	15.5
Precuneus	10253.9	1392.4	10110.8	1639.2	16.3
Superior frontal	18439.1	2782.1	18178	2179.1	27.9
Supramarginal	8958.1	1858.8	8769.6	1241.4	11.3

Table1 1: Cerebral WM regions significant at Bonferroni's corrected threshold of p <0.0016. All volumes are in cubic millimeters.

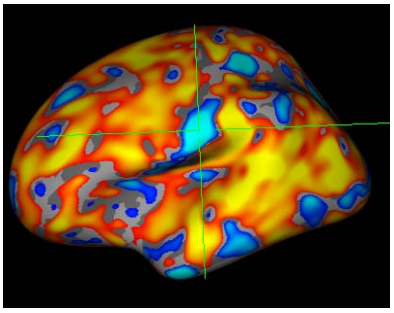

Figure 1: An inflated surface representation of cortical P value representing thickness (light and dark blue are areas of reduced thickness in HCV/HIV co-infected patients compared to HCV mono-infected).

Regions	HCV/HIV co-infected		HCV mono-infected		F
	Mean	SD	Mean	SD	
Left hemisphere					
Caudal middlefrontal	5777.1	1328.6	5983.1	1334.5	14.0
Inferiortemporal	10578.8	2279.3	10672.7	1791.1	11.4
Lateral orbitofrontal	6981.3	1276.1	7022.6	1066.7	12.9
Medial orbitofrontal	4922.6	838.1	5129.4	883.4	13.0
Precentral	13033	1910.7	12737.1	1895.2	22.8
Superiortemporal	11719.5	2574.7	10746.5	1017.9	17.0
Right hemisphere					
Fusiform	10774.6	2782.6	9507.9	1735.2	18.1
Inferiortemporal	9941.4	3059.1	10354.9	1610.2	13.43
Paracentral	3635.5	1082.0	4001.1	584.7	13.2
Precuneus	9898.8	1529.8	9822.6	1125.9	13.4
Superior temporal	11056.8	1844.3	10260.5	1085.6	17.1
Insula	6755.1	1339.4	7117.7	612.8	17.8

Table1 2: Cortical regions significant at Bonferroni's corrected threshold of p <0.0016. All cortical volumes are in cubic millimeters.

Results and Discussion: We used a contrast [1 -1 0 0 0 0] to regress out age and total intracranial volume (TIV) factors in GLM analysis of CT in both hemisphere with a false discovery rate (FDR) of p<0.05. There was a significant thinning of CT in HCV/HIV co-infected patients compared to HCV mono-infected (Figure 1). The areas with significant reduction in CT are inferior temporal, post central, lateral occipital, parahippocampal, pericalcarine, superior parietal, caudal anterior cingulate, superior frontal, superior frontal, parsopercularis, middle temporal, supramarginal, insula, lingual in both hemisphere. Increased CT was observed in superior parietal, supramarginal, and parstriangularis in both hemisphere in HCV/HIV co-infected patients.

We conducted MANCOVA on cortical parcellations and cerebral WM parcellations in each hemisphere using age, and cerebral volume as covariate. We observed WM volume reduction in left caudal middlefrontal**,** inferior temporal, isthmus cingulate, lateral orbitofrontal, parsopercularisin and right inferior temporal, parsopercularis, parstriangularis in HCV/HIV co-infected patients compared to mono (Table 1). WM volume increases in left precuneus, superior frontal and right isthmuscingulate, lateralorbitofrontal, precuneus, superior frontal, supramarginal. The cortical volume changes are shown in Table 2.

Conclusion: Our results showed widespread brain regions with thinning of CT in HCV/HIV co-infected adults relative to HCV mono-infected. Thickening of CT in some regions need explanation and further study. We also observed cerebral white matter volume and cortical volume changes between HCV/HIV co-infected and HCV mono-infected.

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