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The relationship between brain morphometry and neuropsychological performance in alcohol dependence

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Abstract

The aim of this study was to explore local brain atrophy of patients with alcohol dependence using a voxel-based analysis of magnetic resonance images and to investigate the relationship of those atrophic regions with drinking history and neuropsychological performances. Statistical parametric mapping was applied for the global and regional comparison of segmented gray matter and white matter images from 20 patients with alcohol dependence and with those from 20 controls. The Rey auditory-verbal learning test, Rey-Osterrieth complex figure test, Stroop test, trail-making test, and Wisconsin card sorting test were conducted as neuropsychological evaluations. There was a significant decrease in both gray matter and white matter globally in alcohol dependence. Bilateral parahippocampal white matter areas were reduced in particular. Perseverative responses and perseverative errors in the Wisconsin card sorting test had significant correlation with the decrease of gray matter decrease including the left superior temporal gyri and right postcentral region. The psychological performance measures correlated with gray matter rather than white matter, whereas right temporal white matter correlated with drinking amount for last 4 weeks. This may imply that alcohol consumption in heavy amounts damages both gray matter and white matter, and gray matter atrophy mainly leads to cognitive impairment, whereas white matter is related to drinking history.

Keywords: Voxel-based morphometry; Alcoholism; Drinking history; Neuropsychological impairment

It is well known through animal experiments, postmortem, and neuroimaging studies that the chronic alcohol consumption is associated with brain deformation [6,14,24]. Wide spread gray matter (GM) and white matter (WM) losses in alcohol dependence were reported including in the frontal lobe, temporal lobe, and subcortical area [18,24]. In addition to structural brain atrophy, neuropsychological impairments have been one of main symptoms of alcohol dependent subjects [37]. According to previous reports, alcohol dependent subjects are particularly susceptible to executive function impairment that is related to the impairment of frontal lobe function [8,22]. Some studies have reported the association between frontal lobe function and brain volume in alcohol dependence [10,32,36]. However, one study showed no cognitive impairment in alcoholics [10] and the others focused on particular regions of the brain [32,36]. Furthermore, there was a report of no significant relationship between the volume of frontal regions and executive function deficits [29]. Although Chanraud et al. [5] recently showed that regional alteration in gray and WM volume was associated with impairment of executive function, the relationship between executive function impairment and brain atrophy in alcoholism has been less fully studied.

Voxel-based morphometry (VBM) has become an effective tool for the analysis of local brain impairment in the whole brain due to operator independent and automatic processing. Thus, VBM has been used to assess brain deformation in alcohol dependence [5,20]. Widespread cerebral atrophy in patients with alcohol addiction including precentral, middle frontal gyrus,

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insular cortex, hippocampus, thalamus and cerebellum was reported [20].

Here we reanalyze the brain abnormalities in individuals with alcohol dependence, using a voxel-based analysis of segmented magnetic resonance images, and investigate which specific cortical regions correlate with drinking history and neuropsychological executive function performance.

Twenty male patients with alcohol dependence, as diagnosed by Diagnostic and Statistical Manual of mental disorder-IV [2], were selected from among those seeking treatment at Severance Mental Health Hospital, Yonsei University College of Medicine. We included 20 age-matched control subjects who had no history of alcohol abuse in lifetime, drank fewer than 14 standard drinks per week, and no drinks for last 4 weeks. All subjects signed written informed consents.

Two psychiatrists (EL and SP) performed clinical interviews to exclude those with current or past psychiatric disorders, traumatic brain injury, neurological illness, and other substance use disorder except for caffeine or nicotine. This study was carried out under the guidelines for the use of human subjects established by the institutional review board. The demographics and information on subjects are summarized in Table 1.

Three-dimensional T1-weighted spoiled gradient echo magnetic resonance images were acquired on a 3.0T GE Signa scanner (General Electric Medical Systems, Milwaukee, WI, USA). Imaging parameters were as follows: 1.0-mm axial slices, echo time 5.5 ms; repetition time 14.4 ms; number of excitations 1; rotation angle 20°; field of view 21 cm × 21 cm; and a matrix of 256 × 256.

Magnetic resonance images were processed using ANALYZE (version 6.0, Rochester, MN, USA). Images were resampled to 1.0 mm^3 voxels, reoriented to the conventional position and spatially normalized so that the anterior–posterior axis of the brain was aligned parallel to the inter-commissural line. The data sets were then filtered using anisotropic diffusion methods to improve the signal-to-noise ratio [40].

Skull stripping was done by BET (Brain Extraction Algorithm) algorithm, which is known as a robust used independent automated brain extraction algorithm [34]. The extracted brain images were segmented into GM, WM, and cerebrospinal fluid (CSF), employing the FAST algorithm, which is robust and reliable, compared to most finite mixture model-based methods [41]. GM, WM and CSF voxels in each segmented data set were set to a uniform intensity value of unity and others were set to a value of zero.

Processing of GM and WM for the regional analysis was performed using statistical parametric mapping (SPM2) [9] (Institute of Neurology, University College of London, UK) implemented in MATLAB (The MathWorks, Natick, MA, USA). Binary GM and WM images were smoothed using an 8 mm full width at half-maximum (FWHM) Gaussian kernel to assign weighted sum of tissue (GM and WM) values to each voxel for voxel-based analysis of tissue differences. These images were normalized with the following two steps. First, to determine the transformation parameters, filtered T1-weighted images were normalized spatially to the MNI (Montreal Neurological Institute, McGill University, Canada) standard T1 template in the standard Talairach space [39], and affine transformation was performed to determine the 12 optimal parameters to register the brain on the template. Second, by applying the parameters produced in the first step, the smoothed GM and WM were transformed spatially. All processing was applied following that of the previous studies [16,40].

Total intracranial volume (ICV), global GM, and WM volume measured before processing for regional analyses were calculated, and the relative GM and WM volumes normalized with ICV were measured. Mean values were compared between the patients and the controls using Student's t-test, and $P < 0.05$ was considered significant.

Voxel-based regional analyses of the processed GM and WM images were performed using SPM2. The effects of global GM intensity were removed by proportional scaling in which the count of each voxel was normalized relative to the total count of the GM. Any significant changes of regional density that is defined as a probability of a subject's voxel containing gray or whiter matter in transformed space, in alcohol dependence were then estimated by comparing their pre-processed images with those of the controls using t-statistics at every voxel. For ease of interpretation, t values were transformed to Z scores in the standard Gaussian distribution. The clusters consisting of

Table 1
Demographic and drink history variables for the subjects

Variables	Alcoholics ($n = 20$)	Controls ($n = 20$)	t	P
Age (years)	43.5 ± 6	44.5 ± 7.4	−0.447	−0.658
IQ (estimated)	111.9 ± 15.7	114.7 ± 8.5	−0.651	0.521
Education (years)	14.3 ± 4.2	15.3 ± 2.6	−0.905	0.371
Lifetime alcohol consumption[a] (× 10^3drinks)	8.6 ± 7.0		–	
Drink amount for last 4 weeks[a]	360 ± 196	0		
Age at onset of illness	33.2 ± 7.8	–	–	
Days of sobriety before the neuropsychological testing	7.8 ± 6.5	–	–	
The number of smokers	18	20		
ADS[b]	21.2 ± 7.2			
CIWA-Ar[c]	6.2 ± 4.7			

All values are mean ± standard deviation.

[a] Unit of alcohol consumption: standard drink unit (12 g of alcohol).

[b] Alcohol dependence scale [17].

[c] Clinical Institute Withdrawal Assessment for Alcohol Scale [33].