

Comparison the effect of two analysis methods of brain volume: Absolute brain volume and brain volume normalized with intracranial volume in methamphetamine abusers

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ABSTRACT

Introduction: Magnetic Resonance Imaging (MRI) documented abnormal brain structure in methamphetamine abusers with inconsistent results. It is likely that this discrepancy could be from different analysis methods for example absolute volume analysis method and intracranial volume(ICV) normalization.

Objectives: To compare the effect of analysis method between absolute volume analysis and normalized volume with ICV analysis among methamphetamine abusers (MA) and healthy controls (HC) groups.

Materials and methods: Ten MAs and 14 HCs with gender and age matched were recruited. MRI of brain were acquired on 1.5 Tesla MR Scanner (Achieva, Philips, Netherland). Axial T1-weighted images with 3D FFE pulse sequence were used for MRI acquisition with the following data acquisition parameters: TE/TR =4.6/20 ms, FOV = 24 cm, 256x128 imaging matrix and 120 slices. Measurement of brain volume were performed with Freesurfer (FS) version 5.3. Absolute volume and normalized volume with ICV between HCs and MAs groups were compared. Pearson correlation was used to find the correlation of the brain volume between the two methods.

Results: In absolute volume analysis method, we observed consistent significant larger brain volumes in HCs compared to MAs. A positive correlation in most parts of brains was observed between absolute volume analysis method and ICV in HCs and MAs group. In contrast, negative correlation in most parts of brains was observed between ICV normalized volume method and ICV between HC and MA. The different of correlation for each brain region between HCs and MAs could be associated with the effect of methamphetamine.

Conclusion: The difference of the two analysis methods give similar results but varied in different brain regions. The choice of analysis method should be carefully selected in brain imaging study.

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Introduction

Human brain is considered a vital organ of human body. Its primary functions include controlling and commanding muscle coordination of movement, seeing, hearing, speaking, thinking process, memory, emotion and all kinds of feeling. Brain structure abnormalities could be fetal. These abnormalities can occur from various causes such as head injury,^{1,2} some infection,^{3,4} and poison or addictive substance receiving.⁵ There are several methods for brain structure analysis such as the absolute and intracranial corrected volume.⁶ In previous studies, Magnetic resonance imaging (MRI) has been widely used,⁷⁻⁹ together with software programs to evaluate brain volume.^{10,11} The method is noninvasive, no side effect and can be done repeatedly. The analysis software that widely used for brain volume evaluation include Statistical Parametric Mapping (SPM) and Freesurfer (FS). Previous studies revealed that FS software package give more accurate results than SPM.^{12,13} A study of brain volume can indicate brain atrophy or changes in brain structure at the macroscopic level and increase understanding if changes occur in a certain area of the brain resulting in treatment or prevent any potential abnormality of the brain in the future.¹⁴

Studies of brain volume in methamphetamine users showed some conflict results. Some reports showed an increase in size of the caudate nucleus, putamen and globus pallidus,^{8,15,16} in drug abusers while other reports indicated a decrease in the brain volume.¹⁷ The inconsistency results may come from different analysis techniques or methods. Some researchers used absolute volume obtained from a software program for analysis,^{8,16,18-20} while the others used the brain volume normalized with intracranial volume.^{7,17} Consequently, this study aimed to find a correlation between the 2 analysis methods; with the absolute volume and the analysis with the brain volume normalized with intracranial volume. The results obtained from the 2 methods were compared between groups of methamphetamine abuser and healthy control.

Materials and methods

Study Participants

Twenty-four participants aged between 19 -35 years old were recruited. All are required to pass inclusion and exclusion criteria approved by Internal Review Board (IRB) of the Research Institute for Health Sciences (RIHES), Chiang Mai University. Participants were divided into 2 groups: 10 methamphetamine abuser group (MAs) and 14 healthy control group (HCs) (Table 1).

Inclusion criteria for MAs included: 1) passing the evaluation of Diagnostic and Statistical Manual of Mental Disorder IV (DSM-IV), 2) having history of using methamphetamine regularly at least 12 months and the latest usage was not over than 1 week before participating in the research and the methamphetamine was the main addictive substance, and 3) having negative Human Immunodeficiency Virus (HIV), Hepatitis B, and Hepatitis C Virus tests.

Inclusion criteria for the HCs were: 1) no history of drug abuse, 2) healthy and no regularly medicines for

treatment, 3) no history of addictive substance and methamphetamine confirming with negative urine test, and 4) negative HIV, Hepatitis B Virus, and Hepatitis C Virus tests.

Exclusion criteria were those who had history of mental illness regardless of addictive substance use, depression or schizophrenia, history of head injury, claustrophobia, having devices or implants in bodies such as cardiac peacemaker, aneurysm clips, and ear implant. All the subjects were recruited from Chiang Mai Thanyarak Hospital, Chiang Mai Province, and within the community areas.

Table 1 Demographics information of the subjects.

	Healthy Control (HCs) (n=14)	Methamphetamine Abuser (MAs) (n=10)
Mean age (SD)	22.701(3.361)	24.50(4.696)
Intracranial volume (ICV)		
- Max	1718.443 cm ²	1505.800 cm ²
- Min	1383.234 cm ²	1301.250 cm ²
- Mean	1507.501 cm ²	1415.246 cm ²
Gender (females)	14(0)	9(1)
Education (grade)	Secondary school	Secondary school
Race (%asian)	100%	100%

Image acquisition

Philips Achieva 1.5 tesla, Netherlands. A quadrature channel head coil was employed. Axial Images were acquired and covered from the vertex of the skull to the lowest part of the cerebellum. Pulse sequence used was 3D FFE with the scanning parameters similar to that of British Imaging Research Network (BIRN) as shown in Table 2.

Table 2 Magnetic resonance imaging acquisition parameters.

Parameters	
Pulse sequence	Three-Dimensional Fast Field Echo (3D FFE)
Plane	Axial
Repetition Time (TR)	20 ms.
Echo Time (TE)	4.6 ms.
Flip angle	30°
Voxel size	0.94 x 0.94 x 1 mm ³
Field of view (FOV)	240 x 240 mm ²

Image analysis with FreeSurfer

Axial T1-weighted images were analyzed using FreeSurfer software version 5.3 developed by Martinos Center for Biomedical Imaging (<http://surfer.nmr.mgh.harvard.edu/>). Analyzed data was used to measure brain volume in each region. Working flow of the software was shown in Figure 1 starting with T1W file in DICOM format which was converted to FreeSurfer file format following with motion correction along with affine transformation. The images were then normalized into the Talairach space along with image intensity inhomogeneity correction. Skull stripping was done automatically by FreeSurfer and manually removed

for the remaining. Finally, segmentation was done based on image intensity histogram and FreeSurfer atlas.²¹⁻²⁴ Volume

and area of each brain region was obtained for the next statistical analysis.

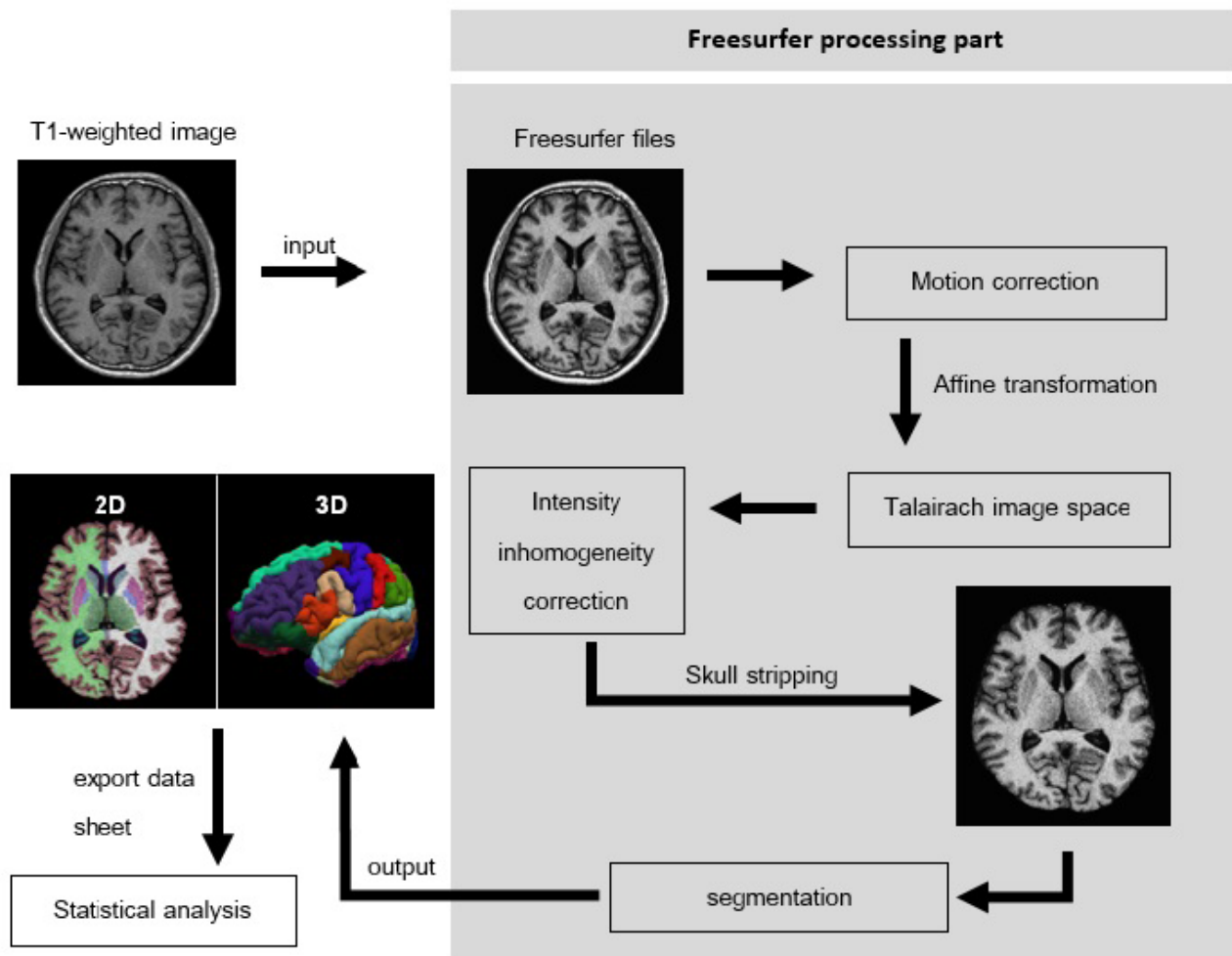


Figure 1. FreeSurfer workflow in diagram. First the raw data (T1-weighted image) were automated motion correction and transform to Talairach image space. Then, FreeSurfer will correct a non-uniform intensity and performed skull stripping followed by segmentation for separating brain to each region. Finally, the volume data was exported in a table format for statistical analysis.

Data analysis

In Absolute volume method, the volume in each brain region was obtained from the calculation of the FreeSurfer software. For the brain volume normalized with intracranial volume method, the absolute volume of each brain region was divided by an individual's intracranial volume.

Different parts of brain volumes were compared between groups using independent student t-test while the correlation between the 2 analysis methods and the intracranial volume were analyzed with Pearson correlation upon a confidence level of 95%, $p < 0.05$.

Results

Comparison of results from the 2 analysis methods

Using the absolute volume analysis, 8 areas of brain volume from the HCs were significantly higher than MA group ($p < 0.05$): at right (Rt) and left (Lt) frontal gray matters, Rt and Lt temporal gray matter, Rt parietal gray

matter, Rt occipital gray matter, Lt insular gray matter and Lt insular white matter. All the 8 areas are shown in Figure 2a, mean $\pm$ SD are shown in Table 3.

However, analyzing from ICV method showed 2 areas of different cortical volume between the two study group; Rt and Lt temporal gray matter (that exhibits larger volume for HC than MA) with a statistical significance ($p < 0.05$). ICV approach also showed significant higher Rt insular white matter volume in MA compared to HC with $p < 0.05$. All of these 3 areas are shown in Figure 2b and mean $\pm$ SD are shown in Table 4.

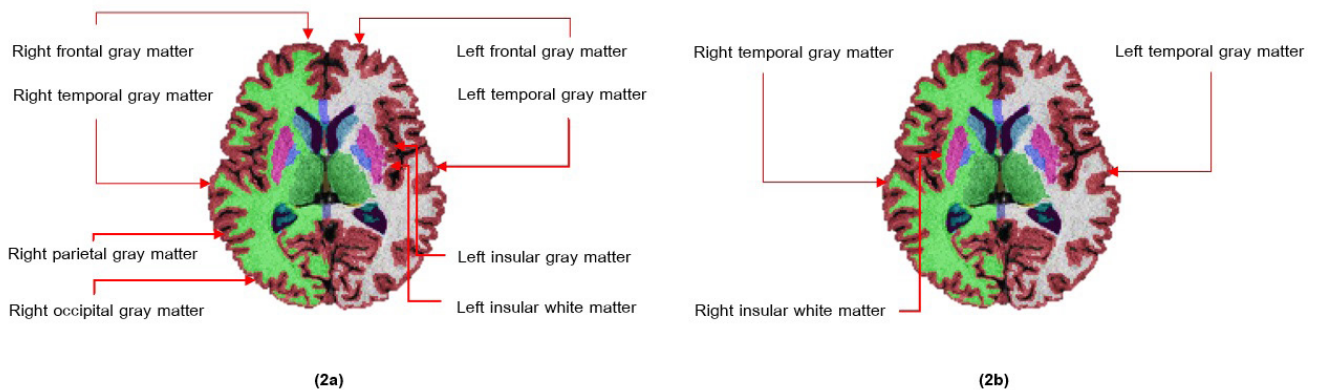


Figure 2. Significant different regions on brain between HCs and MAs with absolute brain volume analysis (2a) and brain volume normalized with intracranial volume analysis (2b)

Table 3 Absolute volume difference between groups of HCs and MAs on each brain region.

Regional brain volume (mm ³)	HCs (n=14)		MAs (n=10)		p-value
	Mean	SD	Mean	SD	
Left frontal gray matter	89587.000	7572.766	83398.800	5876.683	0.042*
Right frontal gray matter	87776.210	9071.645	80653.200	6703.253	0.047*
Left temporal gray matter	53688.290	4225.039	47538.400	2601.378	0.001*
Right temporal gray matter	51979.430	3913.410	45731.700	3797.214	0.001*
Right parietal gray matter	64302.210	6574.633	58209.400	2674.766	0.006*
Right occipital gray matter	24628.290	2567.025	22289.700	1715.632	0.020*
Left insular gray matter	7100.360	537.894	6556.300	459.313	0.017*
Left insular white matter	8831.471	694.384	8172.050	601.599	0.024*
Right insular white matter	8988.014	698.344	9057.710	607.925	0.802

* p-value <0.05 was statistically significant difference.

Table 4 Show normalized volume difference between groups of HCs and MAs on each brain region.

Regional brain volume (mm ³)	HCs (n=14)		MAs (n=10)		p-value
	Mean	SD	Mean	SD	
Left temporal gray matter	0.0356	0.0016	0.0336	0.0020	0.013*
Right temporal gray matter	0.0345	0.0016	0.0323	0.0024	0.013*
Right insular white matter	0.0060	0.0004	0.0064	0.0005	0.026*

* p<0.05 was statistically significant difference.

Correlation between two analysis methods between healthy controls (HC) and methamphetamine abusers (MA)

Figure 3 demonstrates Pearson correlation between the ICV and the two methods for volume determination in HC group. It could be observed that the analysis method from the absolute volume gave positive correlation with a statistical significance ($p<0.05$) in almost every area except the Lt and Rt basal ganglia, Lt parietal gray matter, Lt and Rt occipital gray matter, Lt and Rt occipital white matter and Lt insular white matter. The analysis method using the brain volume normalized with ICV gave negative correlation

with a statistical significance ($p<0.05$) in only Lt and Rt basal ganglia areas.

The correlation of the 2 analysis methods with the ICV in the MAs group was shown in Figure 4. The analysis method from absolute volume provided positive correlation with a statistical significance ($p<0.05$) in Lt frontal gray matter and Rt parietal gray matter areas and with the analysis of brain volume normalized with ICV, no correlation with a statistical significance in all areas was found.

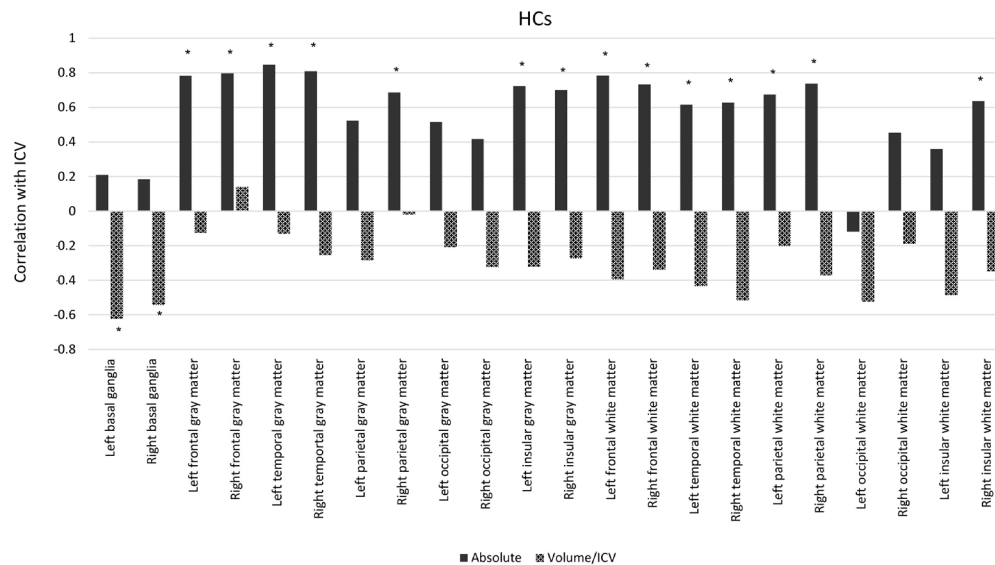


Figure 3. Correlation pattern for each regional of brain volume in HCs using different methods. * $p < 0.05$ was considered to indicate statistically significant correlation

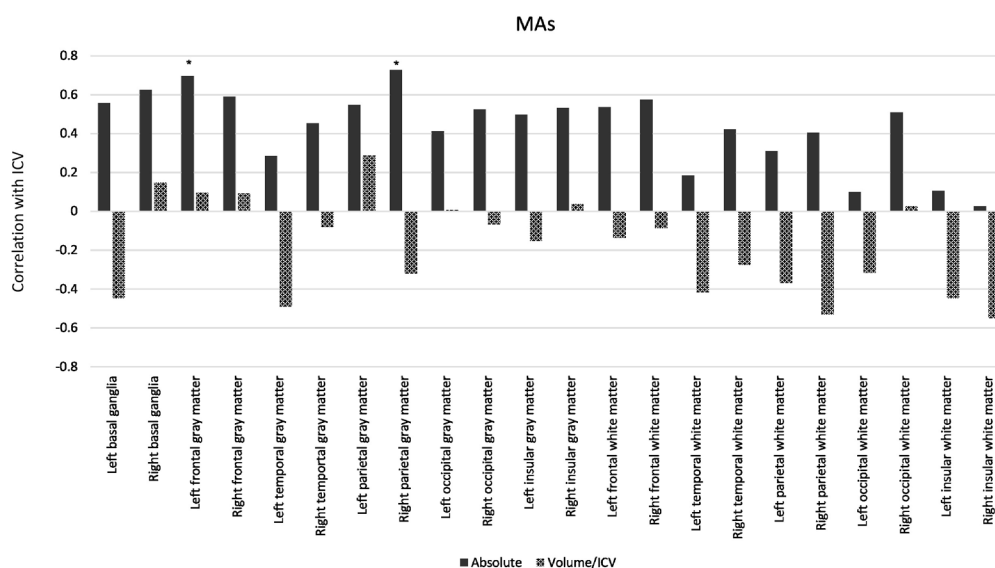


Figure 4. Correlation pattern for each regional of brain volume in MAs using different methods. * $p < 0.05$ was considered to indicate statistically significant correlation

Discussion

Our study showed that the gray matter volume of both sides of the temporal lobes were lower and the white matter volume of right insular was higher in MAs compared with HCs regardless of analysis methods (Table 3 and Table 4). Brain volume in MAs group that lower than that of HCs group is most likely appeared in gray matter which was consistent with previous studies.^{18, 19}

The significant larger of brain volume in Rt insular

white matter in MAs was explained by Thompson¹⁹ that it was probably from proliferation of glial (astrocyte) in MAs.

When compared with ICV, our study demonstrated positive correlation of absolute area volume in most areas in HCs. This implied larger ICV giving larger area volumes and agreed with the previous studies.²⁵⁻²⁷ Correlation found in the 2 analysis methods with the ICV in our study agrees with the report of Voevodskaya²⁸ that conducted a study with 406 volunteers. The different correlation result in some

areas in our study from the previous study may be due to lower numbers of subjects in our study.

It was found in MAs group that the absolute volume gave positive correlation to the ICV in only two areas, at Lt frontal gray matter and RT parietal gray matter (Figure 4). Normalized volume did not show significant correlation with the ICV. This pattern of correlation in MAs group was different from that of the HCs group. This may be caused by the effect of methamphetamine to most of the brain volume.^{15, 29}

Correlation between the two analysis methods and ICV performed in HCs and MAs groups is not the evidence to conclude for which method was superior to others. However, different patterns of the correlation found in both groups may be a trigger for brain change due to methamphetamine use in MAs. Limitation of this study is a small sample size and most of volunteers were male. Larger sample size is needed to confirm our observation. Moreover, results from other techniques such as magnetic resonance spectroscopy (MRS) and neuropsychological tests (NP test) should be applied to support for the results.

Conclusion

The study shows that using the analysis with absolute volume and the analysis with brain volume normalized with ICV provided similar results. However, the difference is numbers of significant different areas between study groups. To prove for the reliable analysis method, other techniques such as magnetic resonance spectroscopy (MRS) and neuropsychological (NP) test may be needed. In addition, ICV is an internal reference for normalization, and may not be appropriate for diseases with brain atrophy.

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