Relationship between Alcohol Use Disorders Identification Test Fractional Anisotropy Value of Diffusion Tensor Image in Brain White Matter Region

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ABSTRACT

Magnetic resonance diffusion tensor imaging (DTI) has revealed the disruption of brain white matter microstructure in normal aging and alcoholism undetectable with conventional structural MR imaging. we plan to analyze the FA measurements of the ROI of dangerous drinkers selected from Alcohol Use Disorders Identification Test (AUDIT) and Tract-Based Spatial Statics (TBSS) tool was used to extract FA values in the ROI from the image acquired through the pre-processing process. TBSS has a higher sensitivity of the FA value and MD value in the white matter than the brain gray matter, and has the advantage of quantitatively deriving the unlimited degree of brain nerve fibers, and more specialized in the brain white matter. We plan to analyze the fractional anisotropy (FA) measurement value for damage by selecting the center of the anatomical structure of the white matter region of the brain with high anisotropy among the brain neural networks that are particularly vulnerable to alcohol as the region of interest (ROI). In this study, we expected that alcohol causes damage to the brain white matter microstructure from FA value in various areas including both Choroid plexus. Especially, In the case of the moderate drunker, the mean value of FA in Lt, Rt. Choroid plexus was 0.2831 and 0.2872, whereas, in the case of the severe drunker, the mean value of FA was 0.1972 and 0.1936. We found that the higher the score on the AUDIT scale, the lower the FA value in ROI region of the brain white matter. Using the AUDIT scale, the guideline for the FA value of DTI can be presented, and it is possible to select a significant number of potentially severe drinkers. In other words, AUDIT was proved as useful tool in screening and discrimination of severe drunker through DTI.

Keyword: Alcohol Use Disorders Identification Test (AUDIT), Tract-Based Spatial Statics (TBSS), FA (Fractional Anisotrpy)

I. INTRODUCTION

Over the past half century. Magnetic Resonance Imaging technology (MRI) has been developed to the extent of studying the molecular displacement of biological tissues, and it has become possible to display the diffusion of water molecules. Especially, the magnetic resonance imaging technology using diffusion is called Diffusion Tensor Imaging (DTI) or Diffusion Tensor Magnetic Resonance Imaging. It is the only technique known to date to express neural pathways of white matter in a non-invasive way. It has revealed the disruption of brain white matter and gray matter microstructure in normal aging and alcoholism undetectable with conventional structural MR imaging[1].

The cerebral white matter has a clear directionality in its structure, and the inside is filled with water molecules, so, we can know the nerve pathways indicated by the white matter by using the diffusion

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direction of the water molecules. A technique that implements neural pathways in the brain through diffusion is called Tractography and is widely used as a method for exploring functional areas of the brain. In particular, by diagnosing nerve structures that do not appear in MRI with diffusion tensor imaging, it is possible to a diagnose of motor nerve pathway damage and know the degree of recovery from motor paralysis.

Chronic alcohol intake affects the structure and function of the brain, and structural changes in the brain have been suggested through many studies such as ventricular dilatation, cerebellar volume reduction, subcortical volume reduction, and cerebral cortex overall atrophy. For example, brain MRI has revealed that several brain structures in people with a history of chronic alcohol dependence are smaller in volume than the same brain structures in nonalcoholic control subjects[2]. Although side effects to alcohol continue to be reported, there are few studies related to discrimination against alcohol use disorders, which are studies of predictors of alcohol use disorders.

Alcohol abuse is not defined separately in the WHO's International Classification of Disease, Tenth Revision, ICD-10, due to its ambiguity in definition, and in the recent revision DSM-V, alcohol use disorders (AUD) were classified into three levels of mild, moderate, and severe according to severity instead of alcohol abuse and dependence[3]. The Alcohol Use Disorders Identification Test (AUDIT) was developed by a multinational investigation team at the request of the WHO, consists of key questions and auxiliary physical examinations, and follows the diagnostic criteria of ICD-10. With 3 questions about the amount of drinking, 3 questions about the type of drinking, and 4 questions about the presence or absence of psycho social problems, the quantitative aspect of drinking is important, and rather than the presence or absence of symptoms of alcohol, the question of the behavioral aspect of drinking is asked.

The AUDIT is developed by the World Health Organization in 1983 to identify risky drinkers early by evaluating the amount, frequency, and harm levels of alcohol in various ways. After the reliability test, the Cronbach alpha coefficient was 0.92, and the test re-reliability was 0.96. The first three items out of 10 questionnaires consist of questions to understand the quantitative aspects of drinking, such as alcohol consumption and drinking habits. The rest of the items consist of alcohol dependence and hazardous drinking levels such as mental and social problems or harm. AUDIT is used as the most appropriate standard test to screen for risky drinkers as well as alcohol use disorders.

In general, AUDIT is the most used questionnaire used to discriminate between patients with alcohol dependence. AUDIT is being used as the most appropriate standard test for screening high-risk drinkers as well as AUD. AUDIT is a ten-item questionnaire approved by the World Health Organization to screen patients for hazardous and harmful alcohol consumption. It was developed from a WHO multi-country collaborative study the items being selected for the AUDIT being the best performing of approximately 150 items including in the original survey. It is widely used as a summary measure of alcohol use and related problems. It has application in primary health care, medical clinics, and hospital units and performs well in these settings .Using different cut-off points, it can also screen for Alcohol Use Disorder (DSM-5) and alcohol dependence. Guidelines for the use of the AUDIT have been published by WHO and are available in several languages. It has become a widely used instrument and has been translated into approximately fifty languages[4].

In this study, the score was scaled using the AUDIT, brain DTI were obtained, and then classified into I group, II group and III group : AUDIT score scale of men was classified as I group: 0 to 9 points

or less for men , and as II group: 10 to 19 points for men and as III group: 20 points or higher for men.

Fractional anisotropy (FA) is the most widely used quantitative index that can be obtained through diffusion tensor imaging. We plan to analyze FA measurement value for damage by selecting the center of the anatomical structure of the white matter region of the brain with high anisotropy among the brain neural networks that are particularly vulnerable to alcohol as the region of interest (ROI). In addition, we plan to visualize a three-dimensional neural network using tractography, which is a technique that reconstructs neural bundles using information from diffusion tensors[5].

The purpose of this study is statistically analyzed by FA value of DTI after dividing them into I group, II group and III group according to AUDIT scale. This study is expected to confirm the usefulness of AUDIT. And we want to screen and appropriately intervene and manage a number of potential AUD by AUDIT.

II. MATERIAL AND METHODS

1. Research subjects and Calculation of the number of samples

A 30 between 50-year-old who visited departments of mental health in our hospital was selected as research subjects from January 1 to December 31, 2021. In this study, the study subjects were limited to men aged 30 to 50 years. We explained the purpose of this study and the examination method, and agreed to the examination. The number of study subjects was calculated using Statistical power analysis using G*power 3.1 analysis, and the expected number of samples was a median effect size of 0.15, power 95%, significance level 0.05 for multiple regression analysis, and correlation with alcohol consumption. A total of 170 patients were selected in consideration of the number of responses and insufficient responses.

2. Research method

2.1. Experiment equipment

The examination equipment for data acquisition in this study was a 3.0 Tesla magnetic resonance imaging system (SIEMENSE Medical system, Germany, MAGNETOM Skyra), and a 64 channel head coil was used as a receiving coil for data acquisition. (Axial plane).

2.2. MRI Image parameters

(1) Brain Diffusion Tensor Imaging Parameter

In this study, brain stem which is a neural network of white matter regions, anterior and central, posterior of corpus callosum, both cerebellum, and both choroid plexus were defined as a region of interest (ROI)

Table 1. Brain DTI parameter

PS	TR	TE	FA	NEX	FOV
EPI	4600	74	90	2	250
-	Voxel size	b-value	slice thickness	direction	scan time
-	2.0×2.0×2.0	1000	2.0	30	5:27

*PS (pulse sequence), *EPI (echo planner image), *TR (time repetition time), ms *TE (echo time), ms *FA(flip angle) *NEX (number of exciting) *FOV (field of view), mm

(2) Brain diffusion tensor image preprocessing method

DTI data were analyzed using tract-based spatial statistics (TBSS). The acquired images were analyzed using FSL (FMRIB Software Library version 6.0) software package. In order to analyze the images of all subjects under the same conditions, the acquired images were pre-processed. First, FSL and FDL tools were used to correct eddy current generated by gradient coils applied in various directions when DTI image is acquired and head movement when image is acquired. When the skull was removed, the brain mask image was output and then used to calculate FA values. The TBSS tool was used to extract FA values

in the ROI from the image acquired through the pre-processing process. After proceeding with the process of rearranging and inputting data according to the TBSS analysis type, a normalization process was performed to move all images to the same space. At this time, the normalization space was normalized using the MNI atlas used as a standard space for brain image analysis. In the normalization process, each image was linearly transformed and then nonlinearly transformed to normalize it to the standard MNI space[6].

(3) Brain diffusion tensor image analysis method

In order to extract FA values of the normalized image for each region of interest (ROI), MNI atlas and Harvard-Oxford cortical and subcortical structural atlases provided by FSL were used for the sub-brain region, as shown in Fig 1.

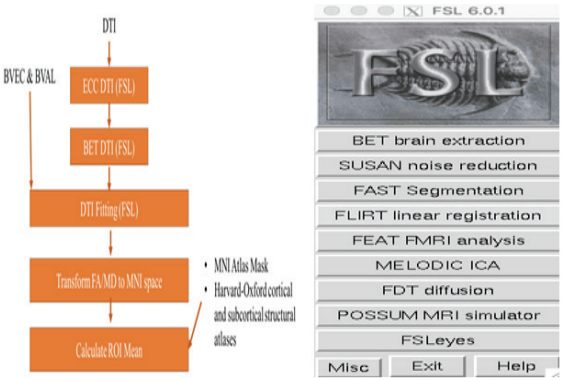

Fig. 1. Analysis pipeline of brain diffusion tensor images using FSL (FMRIB Software Library version 6.0) software package.

3. Statical analysis method

The statistics program uses SPSS 26.0 Version, and the alcohol use disability questionnaire scale score is classified into descriptive statistics and frequency analysis, and classified into I, II and III group according to AUDIT scale After acquiring brain diffusion tensor images, FA values were analyzed using corresponding statistical techniques. Descriptive Statistical Analysis, One-way ANOVA analysis, Pearson correlation analysis and multiple regression analysis was performed based the results of the analysis. All data were considered to be statistically significant if the p-value was less than 0.05.

III. RESULT

1. Distribution by demographic and sociological characteristics of study subjects

The distribution of research subjects by demographic and sociological characteristics is shown in Table. 2. For 170 men (100%), the average age was 41.89 years, 45 (26.5%) were 30-39 years old and younger, 125 (73.5%) were 40-50 years old or younger. The drinking period was 16 people (9.4%) under 10 years, 70 people (41.2%) under 20 years, 84 people (49.4%) under 30 years, and the body mass index was 38 people (22.4%) in the normal group , and the overweight group. There were 45 (26.5%), 72 (42.4%) in the obese group, and 15 (8.8%) in the ultra-high obesity group. The average AUDIT score of the study subjects was 15.54, with 44 moderate drinkers (I group) (25.9%), dangerous drinkers (II group) 63 (37.1%), and alcohol use disorder drinkers 63 (III group) (37.1%).

Table. 2 Distribution by demographic and sociological characteristics of study subjects

Characteristic	Division	Frequency (N)	Ratio (%)
Sex	Male	170	100
Age	30 ≤ 39	45	26.5
	40 ≤ 50	125	73.5
Drinking period (year)	≤ 10	16	9.4
	≤ 20	70	41.2
	≤ 30	84	49.4
BMI	Normal (18.5-22.9)	38	22.4
	Overweight (23-24.9)	45	26.5
	Obesity (25-29.9)	72	42.4
	High obesity (<30)	15	8.8
AUDIT (scale)	I group	44	25.9
	II group	63	37.1
	III group	63	37.1

Table 3. One-way-ANOVA of FA values of white matter in the brain according to AUDIT scale

Brain region	Moderate drunker (a)		Dangerous drinker (b)		alcohol use disorder drinkers (c)		F-value/ p-value	Post-hoc
	Mean	SD	Mean	SD	Mean	SD		
Brain Stem	0.4145	0.0123	0.3995	0.0150	0.3861	0.0151	50.076/0.000	a>b.c(scheffe)
CC Anterior	0.5953	0.0195	0.5728	0.0247	0.5539	0.0246	40.450/0.000	a>b.c(scheffe)
CC Central	0.5460	0.0363	0.5269	0.0322	0.5073	0.0333	17.284/0.000	a>b.c(scheffe)
CC Posterior	0.7519	0.0184	0.7383	0.0259	0.7296	0.0346	8.284/0.000	a>b.c(scheffe)
Lt. Cerebellum	0.3578	0.0108	0.3456	0.0136	0.3339	0.0.38	43.622/0.000	a>b.c(scheffe)
Rt. Cerebellum	0.3711	0.0095	0.3576	0.0154	0.3447	0.0134	51.327/0.000	a>b.c(scheffe)
Lt. Choroid plexus	0.2831	0.0155	0.2200	0.0197	0.1972	0.0225	298.120/0.000	a>b.c(scheffe)
Rt. Choroid plexus	0.2872	0.0150	0.2298	0.0833	0.1936	0.0241	39.744/0.000	a>b.c(scheffe)

2. One-way ANOVA of FA values in the brain white matter area according to the AUDIT scale

Table 3 shows the results of One-way-ANOVA of FA values of white matter in the brain according to AUDIT scale. In this study, brain stem which is a neural network of white matter regions, anterior and central, posterior of corpus callosum, both cerebellum, and both choroid plexus were defined as a region of interest. The ROI in this study was selected as region which is vulnerable to the alcohol in white matter based on advice of a the specialist psychiatrist and of our hospital.

One-way-ANOVA of FA value of white matter region according to AUDIT scale showed statistically significant difference in measured ROI region of I, II and III group. When the I and III group are compared, there was statistically difference (*$p<0.05$) at brain stem, anterior and central, posterior of corpus callosum and both cerebellum, as shown in Table 3. The highest FA mean value 0.7519 was measured in posterior of corpus callosum in the I group. The mean difference of FA value was between 0.0239 and 0.0414 in brain stem, anterior and central, posterior of corpus callosum, and both cerebellum when I and III group are compared. But, in both choroid plexus, the mean difference of FA value was the largest in the III group more than in the I group. In the case of I group, the mean value of FA in Lt, Rt. Choroid was 0.2831 and 0.2872, whereas, in the case of III group, the mean value of FA in Lt, Rt. Choroid was 0.1972 and 0.1936. Our result show the higher the score on the AUDIT scale, the lower the FA value of the white matter region of the brain. A neural network related to alcohol by FA values indirectly can check. degree of damage to nerve fibers.

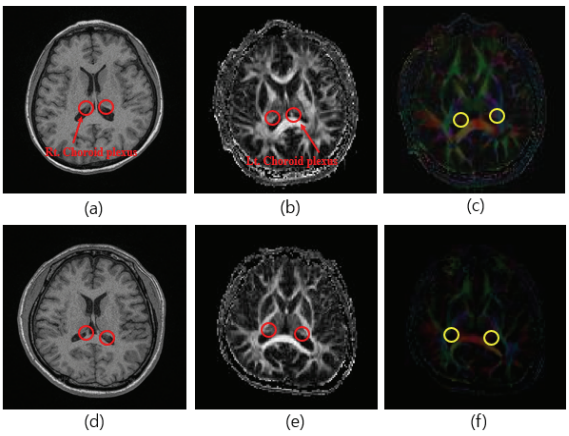

Fig. 2. The region of both Choroid plexus for FA measurement (a) Axial T1 3D mprage image, (b) Axial DTI (c) DTI color mapping image: I group (d) Axial T1 3D mprage image (e) Axial DTI (f) DTI color mapping image: III group.

Figure 2 shows the region of both Choroid plexus in I and III group for FA measurement. Despite the significant difference in the FA value of I and III group in Tbale 3, the color mapping image did not show any abnormalities of the neural network circuit in III group, as shown in Fig 2 (f).

3. Image analysis of T1 and Tractorgrapy

DTI tractography can be used to assess white matter characteristics over the entire extent of white matter tracts and aggregated fiber bundles. DTI tractography entails propagation of fibers along the path of greatest diffusivity. The tractography is RGB color mapped according to the direction, and it is indicated with blue for up/down movement, red for left/right movement, and green for forward/backward movement, as shown in Fig 3 (b), (c).

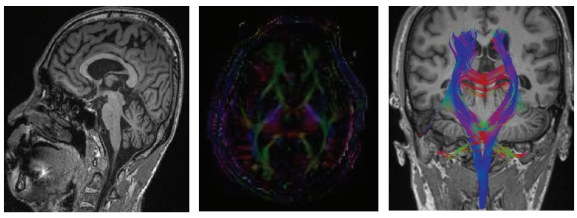

Fig. 3. DTI tractography entails propagation of fibers along the path of greatest diffusivity from each voxel, creating a 3D map of all white matter connections (a) Sagittal T1 mprage weighted image related to tractography mapping: whole-brain diffusion-weighted MRI data were acquired using dual spin-echo diffusion-weighted sequences (b) Axial color FA map (c) AP tractography image.

Figure 3 shows that the tract architecture of whole region in III group reveals connections between white matter nerve tract fiber. In the result of evaluation using whole brain tractography, The tractography image of whole region did not show any abnormalities of the neural network circuit in III group.

IV. DISCUSSION

Alcohol causes changes in nerve synaptic plasticity and nerve cell function when consumed for a long time, and eventually induces chemical and structural changes in nerve cells. It is thought that alcohol damages nerve fibers in region of the white matter, affects the structure, and affects functional abnormalities related to it. In addition, changes in the brain caused by alcohol play an important role in creating a vicious cycle that accelerates and related complications due to continuous alcohol intake. In other words, it accelerated brain aging looking at changes in the brain of alcoholic addictions[7].

Generally, DTI can provide information about ultrastructure brain white matter by quantifying water diffusion. In addition, DTI can confirm the disruption of brain white matter microstructure in normal aging and alcoholism undetectable with conventional structural MR imaging. Our study was to assess FA values by alcohol based on AUDIT. FA can well be described due to the active brownian motion of water in white matter. In this research, we studied brain white matter instead of gray matter.

MNI atlas and Harvard-Oxford cortical and subcortical structural atlases provided by FSL were used for ROI selection. The change of FA values by alcohol statistically analyzed to present the relevance of three group. Our statistical results show that FA value can distinguish between I and III group based on detailed information concerning brain brownian motion of water by alcohol.

In previous studies, it mainly dealt with corpus callosum which is vulnerable to alcohol. In other words, the geun and splenium of corpus callosum and centrum semiovale had already been established that alcoholic men had a significant disruption of brain white matter microstructure, observed as low regional anisotropy, beyond that occurring in normal aging[8]. However, in our study, the significant difference of

FA was shown in the both Choroid plexus by alcohol. The correlation between AUDIT scale and brain white matter area showed a strong negative correlation in all areas measured by ROI, and there was a statistically significant difference. Lt. Choroid plexus showed the strongest negative correlation at r=-0.862 ($p<0.01$).

Individuals with alcohol use disorders show white matter abnormality relative to normal samples. The III group demonstrated reduced FA values in all measured ROI region compared with I group. In brain white matter of III group, our result show that the decrease in FA value may arising from cell swelling of alcohol toxicity effect and reduce the spacing between the myelin fiber bundles.

The metrics of DTI can be useful in establishing the nature of the observed microstructural aberrations[9]. However, the relationship between microscopic tissue damage and the macroscopic diffusivity parameters measured by DTI is complex and not fully understood. We indirectly checked that alcohol caused damage to the brain white matter microstructure through comparison of FA value with I group in various areas including both Choroid plexus. From this research result, we predicted more microstructural damage in both Choroid plexus compared with other region of brain white matter. DTI tractography reveals connections of white matter nerve tract fiber. We confirmed the fiber tract architecture using whole brain tractography. However, in the result of evaluating tractography, there did not show any abnormalities of the neural network circuit in III group.

The first limitation of this study is that AUDIT scale differed between men and women, so the study subjects were only limited to men. Second, the FA value of DTI was only measured with the score of the AUDIT, without discriminating between smokers and non-smokers, which have a lot of association with drinking. So, it is necessary to study how the presence of smoking influences the FA value in I, II and III group. Third, TBSS is a program with higher sensitivity of FA, MD values in white matter than brain gray matter. Although TBSS has the advantage of being able to quantitatively derive the anisotropy of brain nerve fibers, but it has the disadvantage that values of the gray matter region aer measured low. In other words, it is a more specialized program for white matter.

In the future, study on comparison of III group and real alcohol use disorders is needed. It is needed to measure the FA value of brain diffusion tensor images by dividing the control group who received medical confirmation about alcohol use disorder, not the AUDIT scale. We expect that AUDIT will be useful as a test method for judging alcoholism symptoms, or guidelines for FA values alcoholism. Our research is expected to screen out AUD. For a comprehensive strategy for reducing alcohol damage, various ministries within the public, private and government need to participate and cooperate[9].

V. CONCLUSION

DTI can detect changes in brain white matter after acute alcohol consumption that are not detectable by conventional MR imaging. In this study, we indirectly conformed the microstructural change by FA value in the white matter region of ROI. Using the AUDIT, the guideline for the FA value of DTI can be presented, and it is possible to select a significant number of potentially AUD. In other words, AUDIT was proved as useful tool in screening and discrimination of alcohol abuse.

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알코올 선별 검사법(Alcohol Use Disorders Identification Test)과 뇌 백질 영역의 확산텐서 비등방도 계측 값의 관련성

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요 약

AUDIT(Alcohol Use Disorders Identification Test)에서 정상 음주자, 위험 음주자 및 알코올 사용 장애자로 분류하여 뇌 백질 영역의 ROI(Region Of Interest)에 대한 FA 측정값을 분석하였다. TBSS(Tract-Based Spatial Statics) 도구를 사용하여 ROI의 FA 값을 추출하였다. TBSS라는 도구는 뇌 회백질보다는 백질에 대한 FA 값과 MD 값의 민감도가 더 높고 뇌 신경섬유의 비등방도를 정량적으로 도출해 낼 수 있는 장점이 있고 백질에 더 특화된 프로그램이라 할 수 있다. 특히 양쪽 맥락총 평균 차이가 높았고 정상 음주자에서는 FA의 평균값이 0.2831과 0.2872로 나타났으며, 알코올 사용 장애자의 경우 0.1972와 0.1936로 나타났다. 즉, AUDIT 척도에서 점수가 높을수록 뇌 백질의 계측한 모든 ROI 영역에서 FA 값이 더 낮게 측정되는 것을 알 수 있었으며 뇌 백질에 신경 섬유로의 손상에 대한 미세구조 변화를 확인할 수 있었다. AUDIT 척도를 사용하여 DTI의 FA 값에 대한 지침을 제시할 수 있으며 혈액학적 인자의 가이드인 처럼 FA 값을 산정한다면 알코올 사용 장애자의 선별 및 진단에 유용한 검사법이라 사료 된다.

중심단어: AUDIT(Alcohol Use Disorders Identification Test), TBSS(Tract-Based Spatial Statics) FA(Fractional Anisotrpy)

연구자 정보 이력

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