

Study of Imaging Patterns in Magnetic Resonance Imaging and Magnetic Resonance Spectroscopy of Brain in Alcohol Dependence

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A B S T R A C T

Introduction: Alcohol is one of the most commonly abused substances in the world. Excessive alcohol consumption can result in chronic brain changes as well as acute life threatening neurologic disorders. It results in morphological, metabolic and functional brain damage which can be detected on MRI, and even early on MRS. Some changes are reversible with abstinence. The recognition of potentially reversible pathological changes in the brain could enhance preventive medical approaches, and treatment efforts.

Material and methods: This study was conducted on 30 alcohol dependent cases with a consumption history of more than 5 years. All the individuals were subjected to MRI and MRS using 1.5 TESLA PHILIPS ACHIEVA 16 channel machine equipped with proton spectroscopy package, NV coil and software for spectral acquisition and processing.

Results: MRI findings include Brain global volume loss and regional volume losses (80%-frontal region, 60%-cerebellum and 48%-temporal white matter). On MRS Ratios obtained shown decreased levels of NAA/Cr, Cho/Cr in frontal lobe (70% and 36.7% respectively) and cerebellar white matter (76.7% and 40% respectively).

Conclusion: Thus MRI and MRS are useful in studying early diagnosis of chronic alcoholism effects on brain and MRS detects these degenerative changes, earliest at metabolic level before the structural changes are obvious

Keywords: Magnetic Resonance Imaging, Spectroscopy, Alcohol Consumption, Brain Atrophy, N Acetyl Aspartate, Choline, Creatine

INTRODUCTION

Alcohol is one of the most commonly abused substances in the world. Drinking alcohol is widely socially accepted and associated with relaxation and pleasure. However, many experience physical, social and psychological harmful effects of alcohol.¹

Excessive alcohol consumption can result in chronic brain changes as well as acute life threatening neurologic disorders. It results in morphological, metabolic and functional brain damage which can be detected on MRI and, even early on MRS.

Some changes are reversible with abstinence. The recognition of potentially reversible pathological changes in the brain could enhance preventive medical approaches, and treatment efforts.²

Study objectives were to assess the structural changes of brain on Magnetic Resonance Imaging in 'Alcohol Dependence' with a history of 5 yrs of consumption and to study the alterations in endogenous metabolites such as NAA, Choline,

Creatine in specific brain regions on Magnetic Resonance Spectroscopy in the same group.

MATERIAL AND METHODS

It was a cross sectional study done at Dr.Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinnavutapalli.

This study was conducted on 30 alcohol dependent cases with a consumption history of more than 5 years, referred from medicine and psychiatry departments at our institute. All the patients included in the study were carefully explained about the purpose of the study and consent was taken. Data was collected by taking detailed history and using described proforma, meeting the objectives of the study. All the individuals were subjected to MRI and MRS using 1.5 TESLA PHILIPS ACHIEVA 16 channel machine equipped with proton spectroscopy package, NV coil and software for spectral acquisition and processing. 1 H MRS data obtained from 4.2 to 1.8 ppm in the spectral dimension and were analyzed using LC

Model.

Inclusion criteria

All patients with “Alcohol Dependence” with a history of 5yrs or more of consumption.

Exclusion criteria

Patients with known pathology including encephalopathies. Patients with Alzheimer’s disease or age related dementia. Patients who are abstinent for more than 5 weeks (as abstinence for 5 weeks can lead to brain recovery in the form of volume gain and changes in MRS pattern). Patients who are also dependent on other substances other than tobacco.

Scanning technique

T2-weighted localizer images (TR/TE=2000/144, slice thickness 128 mm) were acquired in the axial, coronal, and sagittal planes. T1- weighted multiplanar reconstructions were taken. Localized MR spectroscopy included single-voxel measurements in the frontal lobe(20x20x20 mm) and in the left cerebellar hemisphere(20x20x20 mm).

To achieve a reproducible position, the frontal voxel was placed with its inferior edge at the calloso marginal sulcus and its posterior edge at the central sulcus. The cerebellar voxel was placed with its medial edge in the left cerebellar hemisphere adjacent to fourth ventricle, and its superior edge adjacent to the tentorium.

For every voxel position, a PRESS sequence (2000/144), with 128 signals was applied with water suppression. The patient is positioned inside the gantry in supine position. NV- 16 channel was selected. Scanning was done at TE 31mS and TE 144 mS in selected frontal and cerebellar voxels.

STATISTICAL ANALYSIS

Present study is a Cross sectional study with descriptive statistical analysis. Spectroscopic continuous results are presented on Mean +/- standard deviation.

RESULTS

The total study group consisted of 30 individuals of alcohol dependence, with a 5 year or more consumption history. Age ranged between 26 to 45 years.

The parameters taken in brain MRI and MRS study are Regional brain volume loss - assessed by cortical and white matter atrophic changes and prominent ventricles and adjacent sulci (Table 1).

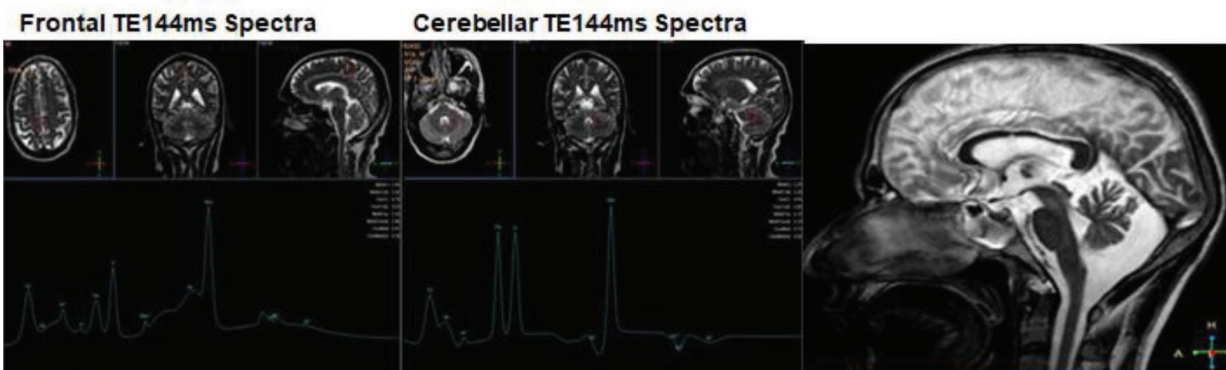
Metabolite concentrations depicted in TABLE-2 were computed for total NAA, total choline, and total creatine compounds from selected frontal and cerebellar (TABLE-3) voxels. Metabolite ratios for choline and NAA were obtained, creatine as the reference. Ratios taken are NAA/Cr, Cho/Cr, NAA/Cho, Cho/NAA. NAA/Cho, Cho/NAA are obtained to prospect the metabolite variations precisely.

Brain global volume loss and regional volume losses at frontal, parietal, temporal, occipital gray and white matter regions noted (case:1, and case:2). Gray matter volume loss was pronounced by prominent sulcal spaces and white matter volume loss by increased ventricular volume in lateral, third ventricles. Brainstem region and cerebellar volume loss was appreciated by prominent cisternal and sulcal spaces and by prominent folia in cerebellar region which are depicted in Table 1.

Sl no	Region	Percentage Involved
1	Frontal white matter	80%
2	Temporal white matter	48%
3	Parietal white matter	40%
4	Cerebellum	60%
5	Anterior superior vermis	34%
6	Corpus callosum	33%
7	Brainstem	31%
8	Mammillary bodies	20%
9	Anterior hippocampus	20%
10	Basal ganglia	7%

Table-1: Brain parenchymal changes observed are

Case: 1



Frontal TE144ms Spectra	
NAA/Cr	1.84
Cho/Cr	0.75
NAA/Cho	2.45
Cho/NAA	0.41

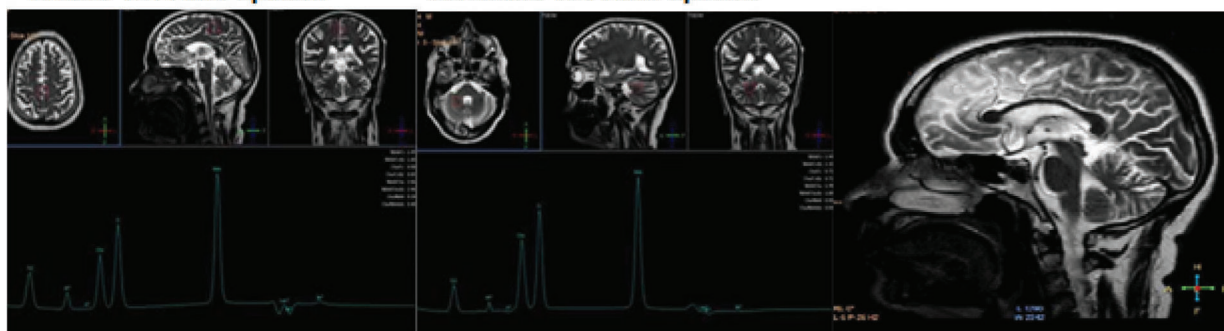
Cerebellar TE144ms Spectra	
NAA/Cr	1.35
Cho/Cr	0.82
NAA/Cho	1.65
Cho/NAA	0.61

MRI Findings (Atrophic changes)
Frontal
Temporal
Corpus callosum
Cerebellum
Anterior superior vermis

Case:2

Frontal TE144ms Spectra

Cerebellar TE144ms Spectra



Frontal TE 144ms Spectra	
NAA/Cr	1.49
Cho/Cr	0.58
NAA/Cho	2.56
Cho/NAA	0.39

Cerebellar TE 144ms Spectra	
NAA/Cr	1.44
Cho/Cr	0.72
NAA/Cho	1.99
Cho/NAA	0.5

MRI Findings (Atrophic Changes)
Frontal
Parietal
Temporal
Corpus callosum
Cerebellum

Metabolite ratios	Normal	Abnormal
NAA/Cr	1.6 to 2	<1.6
Cho/Cr	<1.6 to 1.5	<0.6 to >1.5
NAA/Cho	>1.2	<1.2
Cho/NAA	0.34 to 0.76	>0.76

Table-2: Normal and abnormal ratios of neurometabolites

Metabolite – Ratios	Abnormal Percentage involved in frontal white matter	Abnormal Percentage involved in cerebellar white matter
NAA/Cr	Decreased in 70%	Decreased in 76.7%
Cho/Cr	Decreased in 36.7%	Decreased in 40%
NAA/Cho	Decreased in 3.3%	Decreased in 30%
Cho/NAA	Decreased in 6.7%	Decreased in 16.7%

Table-3: MRS findings in frontal white matter and cerebellar white matter

Region specific atrophic changes were compared with brains of age matched normal individuals.

Table-2: Changes in the metabolite ratios for NAA/Cr, Cho/Cr, NAA/Cho, and Cho/NAA were compared with standard baseline ratios given by Huntington medical research and control data.³

Table-3: Spectroscopy data in frontal voxel and cerebellar voxel shown, significant decrease in NAA/Cr and Cho/Cr ratios compared with the standard ratios taken, and changes noted in NAA/Cho and Cho/NAA are statistically insignificant in frontal white matter and are statistically significant in cerebellar white matter.

DISCUSSION

Alcoholism is a universal health problem. Its toxic effects on various organs, its dependence producing properties, significant morbidity and mortality associated, and its effects on social and economic sectors worldwide, is a cause of concern.

Neuronal loss due to chronic alcohol use has been the subject of debate. Several authors have shown brain volume loss in different regions of brain which are detected by MRI, and brain shrinkage is the preferred term to brain atrophy, which assumes more specific neuropathological lesion.⁴ The effects of alcohol are not consistent, some parts of the brain and some cell types are affected preferentially. And these changes are detected at the earliest at metabolic level by alterations in neuro metabolite concentrations.

Magnetic Resonance imaging (MRI): Techniques have greatly influenced the field of brain imaging because they allow non invasive measurement of both the anatomy (using structural MRI) and the functioning (using functional MRI)

Magnetic Resonance Spectroscopy (MRS): detects metabolic changes in affected regions of brain, even earlier than by anatomical MR imaging. MRS is an adjunct to MRI, as can be done with the same equipment used for MRI. MR spectroscopy provides a measure of brain chemistry. The most common nuclei used are 1 H(proton), 23 Na(sodium), 31P(phosphorus). Protons (1H) are the most used nuclei for clinical applications in human brain mainly because of its high sensitivity and abundance. As MRS needs to detect weak signals from metabolites, requires a higher strength field (1.5 T or more).The proton MRS is altered in almost all neurological disorders. In clinical practice, 1 H-MRS is used for analysis of stroke, brain Tumors, inflammatory diseases, dementia and metabolic diseases. Higher signal strength units have the advantage of higher signal-to-noise ratio, better resolution (better separation of the metabolites) and shorter acquisition times.^{5,6,7}

Basic physical principle of MRS⁸: In a proton spectrum at 1.5 T, the metabolites are spread out between 63,000,000 and 64,000,000 Hertz. The resonant frequencies will be expressed in parts per million (ppm), the ppm scale can be read from right to left. The predominant metabolites, displayed from right to left are NAA, creatine, choline, and myo-inositol. The line formed by the metabolites on the white matter

spectrum is called HUNTER'S angle. If angle and the peak corresponds to 45° , then the curve is said to be normal.

Chronic heavy alcohol consumption is associated with global brain atrophy and smaller regional brain volumes, functional and metabolic deficits. A reduction in brain volume has been demonstrated in neuroimaging and pathological studies. The structural basis for brain atrophy in patients with chronic alcoholism and its reversibility in sobriety are poorly understood. sprouting of dendrites and axons (Carlen PL Wetz)⁹, glial hyperplasia (or) and rehydration of brain tissue have been suggested as possible mechanism. Neuro metabolite abnormalities in chronic heavy drinking may vary as a function of duration of abuse.

In alcohol dependent patients MRI imaging of brain and MRS were done at the same time. For MRS the voxels selected were frontal and cerebellar, as these are the more vulnerable and more commonly studied regions. The results of the present study are consistent with the observations made by authors of previous studies

Brain Parenchymal Changes on MR Imaging: The present study on MR imaging reported frontal white matter volume loss along with global parenchymal volume loss. Frontal white matter volume loss is the predominant observation in this study reaching upto 80% and corresponds with the observations made by Kubota et al¹⁰, Pfefferbaum et al¹¹ and moselhy et al 2001¹² in their studies

And the second most observation of brain volume loss was made out in the cerebellum in 60% of cases and signal intensity changes with shrinkage noted in 34% of cases in anterior superior vermis, these findings are associated with behavioral and coordination disturbances. And these results are in consistent with the observations made by Oscar-Berman and Marincovic.¹³

Parietal cortex and white matter changes were noted in 40% of chronic alcoholics accompanied with other regional volume losses. And 48% of alcoholics exhibited volume loss in the temporal parenchyma, without a positive history of seizures. And the results correlate with the studies done by Fein G et al¹⁴ and Pfefferbaum A¹¹, Sullivan EV et al.¹⁵

Corpus callosal atrophy, mammillary body atrophy and anterior hippocampal atrophies were noted in a significant number of cases. Corpus callosal volume loss was accompanied by global brain volume loss in majority of cases. And the mammillary body atrophy was noted in chronic alcoholics without a history of thiamine deficiency, and these findings are in consistent with the conclusions made by Pfefferbaum A et al¹¹, Sullivan et al¹⁵, Agartz et al.¹⁶

Atrophic changes with signal intensity changes noted in basal ganglia of two chronic alcoholics, but without a statistical significance.

MRS Findings observed: MR spectroscopy data for the selected voxels in the frontal and cerebellar white matter was obtained. MR spectroscopy revealed significantly decreased levels of NAA/Cr and Cho/Cr in both frontal lobe and cerebellum in comparison with the standard baseline ratios given by Huntington medical research and control data.

NAA levels decrease pattern in the present study: In the frontal lobe Present study reported decrease NAA /Cr

ratios in frontal lobe in 70% of alcoholics. These results are in support of studies conducted by Mayerhoff, Durazzo and Ende in 2011¹⁷ and reduced levels of NAA is supporting their observations that, the single most widely reported MRS effect is reduced NAA.

Studies conducted by Fein et al¹⁴ and O'Neil et al²⁶, within two weeks of abstinence found lower NAA levels, lower NAA/Cr, NAA/Cho in the frontal lobe Cortex. Study done by Bartsch et al²³, Durazzo et al²¹, Ende et al²⁴ and Gazdzinski et al²² emphasizes on frontal white matter NAA changes.

In the cerebellum decreased NAA/Cr ratios noted in 76.7% of alcoholics in the present study. These are in keeping with observations made by Park et al²⁵ and Bartsch et al²³ in their studies.

Choline levels decrease pattern in the present study: In the frontal lobe Decreased Cho/Cr ratios in frontal lobe noted in 36.7% of alcoholics in the present study. Studies conducted by Ende et al in 2006²⁴, in frontal white matter have shown lower choline and Cho/Cr ratios suggesting alterations in myelin or cell membrane, or decreased cellular synthesis.

In the cerebellum Decreased Cho/Cr ratios were noted in cerebellum in 40% of alcoholics in the present study. Study done by Bartsch et al in 2007²³ have shown lower choline levels and lower Cho/Cr or Cho/NAA in the cerebellum, supporting this observation.

Findings regarding choline levels are ambiguous and dependent on localization. Shifts between different choline compounds may contribute to the heterogeneous results with choline.

Bendszus et al²⁰ conducted study on both the frontal and cerebellar white matter regions and observed lower NAA, NAA/Cr and decreased choline, Cho/Cr levels in both the regions.

Reversible changes noted in early abstinence: Brain damage caused by chronic alcohol consumption is reversible to some extent. Morphometric, spectroscopic and neuropsychological indicators studies support this.

Joseph o'Neill; Dieter J Meyerhoff in 2006²⁶ documented Region specific structural recovery from chronic alcohol-induced brain injury, but also region- specific long-term damage in abstinent alcoholics. Recovering alcoholics had greater volumes of frontal white matter and gray matter volumes in the orbital frontal pole and post central gyrus but, smaller white matter volumes in basal frontal and temporal lobes, the cerebellum and the brainstem and gray matter volumes in the anterior cingulate gyrus. Proton MRS measures, as applied in this cross sectional study, were largely ineffective in revealing metabolic effects in brain.

Andreas J. Bartsch et al study²³, Structural Image Evaluation using Normalization of Atrophy (SIENA) detected global brain volume gain of nearly 2% on an average and was spatially significant around the superior vermis, perimesencephalic, infra and supra tentorial periventricular region and to a lesser extent, on frontomesial and orbital edges. Reversibility of brain shrinkage in patients with alcoholism is noted in the early stages of abstinence. Significant augmentation of cerebellar choline and frontomesial NAA levels upon short term sobriety. And NAA gains were below cerebellar

choline increase. A significant increase in NAA/Cr occurs with significant period of abstinence, indicating either an augmentation of neuronal tissue or reversibility of neuronal dysfunction. Moderate increase of Cho /Cr in abstinent cases, indicates a limited potential for membrane regeneration. sequential MRS study on alcoholic abstinence reported increased levels of Cho / NAA. Increasing choline and stable NAA levels are an expression of gliosis (or) a partially reversible cholinergic deafferentiation.

Present study reported 16.7% increase in Cho/NAA in the cerebellum probably due to increased Choline and stable NAA levels in early abstinence and also noted decreased NAA/Cho levels in the cerebellum significantly, representing gains of NAA which were below the cerebellar choline increases as proposed by Bartsch et al.²³

Brain parenchymal changes noted in present study are compared with the previous studies done by Kubota et al in 2001¹⁰, Pfefferbaum et al 2000¹¹ and Oscar – Berman and Marinovic in 2007¹³ on chronic alcoholism and, found to be in correlation with their observations. In significant number of cases metabolite changes are noted, without significant parenchymal changes.

MRS results been compared with 1H MRS study done by Meyerhoff, Durazzo and Ende in 2011¹⁷, Durazzo et al in 2004²¹, Ende et al in 2006²⁴ and the study done by Martin Bendszus et al in 2001²⁰, and supports their observations

The present study hence supports that, chronic alcoholism causes regional brain volume loss and metabolic deficits especially NAA and choline in frontal lobe and in the cerebellum. NAA losses are more in both frontal and cerebellar regions and decreased choline levels in significant proportion in frontal lobe along with cerebellum noted.

Limitations

Various consumption patterns, Different intervals from abstinence and the time point studied may alter the spectroscopic results. Multiple level MRS sampling is needed to study its entire effects. A common limitation of many studies on the chronic effects of alcohol is the retrospective nature of estimated alcohol consumption and the consumption history is based on the patients recollect. And as the variables studied are many, large sample size is to be considered for statistical purposes.

CONCLUSION

With high prevalence of alcohol abuse and the limited and inefficient current treatment options, the need for better understanding of the effects of alcohol is required. MRI findings include Brain global volume loss and regional volume losses. On MRS ratios obtained from the present study have shown decreased levels of NAA/Cr, Cho/Cr in frontal lobe and cerebellar white matter. The Predominant Correlation is with frontal and Cerebellar NAA Levels with the Previous studies

Thus MRI and MRS are useful in studying early diagnosis of chronic alcoholism effects on brain and MRS detects these degenerative changes, earliest at metabolic level before the structural changes are obvious. Combined morphologic and spectroscopic data adds to the emerging evidence of brain

injury in chronic alcoholism.

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