The pattern of metabolic heterogeneity in the hippocampus by 3T multi-voxel proton spectroscopy in Alzheimer's disease.

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Table 1 Metabolites ratios in AD and CN groups.

	NAA/Cr	NAA/Cr	MI/Cr	MI/Cr	MI/NAA	MI/NAA
Groups	AD	CN	AD	CN	AD	CN
RHP	1.99±0.36**	2.61±0.44	0.91±0.40*	0.63±0.24	0.46±0.19**	0.25±0.09
RHP-A	2.09±0.54	2.12±0.34	0.79±0.27	0.65±0.21	0.39±0.12	0.31±0.10
RHP-M	1.92±0.28**	2.65±0.47	0.88±0.33**	0.61±0.23	0.46±0.13**	0.24±0.10
RHP-P	1.92±0.37**	2.71±0.50	0.80±0.23**	0.54±0.16	0.44±0.20**	0.21±0.18
LHP	1.98±0.37**	2.50±0.37	0.82±0.21**	0.61±0.15	0.41±0.12**	0.25±0.07
LHP-A	2.06±0.52	2.02±0.54	0.80±0.21*	0.66±0.17	0.42±0.16	0.35±0.14
LHP-M	1.89±0.32**	2.46±0.32	0.89±0.29**	0.59±0.17	0.48±0.14**	0.24±0.08
LHP-P	2.10±0.61*	2.50±0.49	0.79±0.22**	0.59±0.18	0.42±0.19**	0.24±0.09

Note: AD represents probable AD. CN represents cognition normal control. RHP represents whole right hippocampal. RHP-A represents right hippocampal head. RHP-M represents right hippocampal body. RHP-P represents right hippocampal tail. LHP represents whole left hippocampal. LHP-A represents left hippocampal head. LHP-M represents left hippocampal body. LHP-P represents left hippocampal tail. * P<0.01 significant difference from AD to CN. ** P<0.001.

Table 2 The statistical results of hippocampal head, body and tail metabolites concentration distribution in CN group.

	Sta	RHP	RHP-A RHP-M	RHP-A RHP-P	RHP-M RHP-P	LHP	LHP-A LHP-M	LHP-A LHP-P	LHP-M LHP-P
NAA/Cr	F	15.882				10.280			
	p	<0.001	<0.001	<0.001	0.575	<0.001	<0.001	<0.001	0.713
MI/Cr	F	2.404				1.725			
	p	0.096	0.436	0.033	0.171	0.184	0.120	0.104	0.941
MI/NAA	F	9.583				11.478			
	p	<0.001	0.004	<0.001	0.197	<0.001	<0.001	<0.001	0.916

Note: Sta means Statistic method. CN represents cognition normal control. RHP represents whole right hippocampal. RHP-A represents right hippocampal head. RHP-M represents right hippocampal body. RHP-P represents right hippocampal tail. LHP represents whole left hippocampal. LHP-A represents left hippocampal head. LHP-M represents left hippocampal body. LHP-P represents left hippocampal tail.

Table 3 The statistical results of hippocampal head, body and tail metabolites concentration distribution in AD group.

	Statistic	RHP	RHP-A RHP-M	RHP-A RHP-P	RHP-M RHP-P	LHP	LHP-A LHP-M	LHP-A LHP-P	LHP-M LHP-P
NAA/Cr	F	1.749				1.566			
	p	0.180	0.325	0.413	1.000	0.215	0.187	0.729	0.097
MI/Cr	F	1.060				1.566			
	p	0.351	0.178	0.824	0.260	0.215	0.133	0.977	0.126
MI/NAA	F	1.653				1.294			
	p	0.197	0.088	0.179	0.710	0.279	0.160	0.959	0.175

Note: AD represents probable AD. RHP represents whole right hippocampal. RHP-A represents right hippocampal head. RHP-M represents right hippocampal body. RHP-P represents right hippocampal tail. LHP represents whole left hippocampal. LHP-A represents left hippocampal head. LHP-M represents left hippocampal body. LHP-P represents left hippocampal tail.

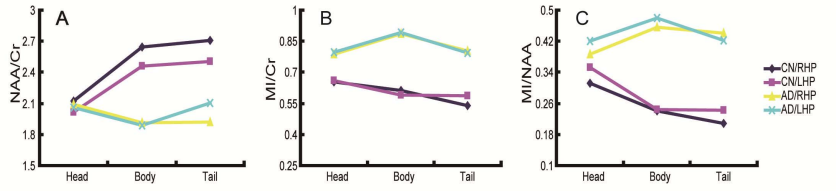

Fig.1 A-C Bilateral hippocampal head, body and tail metabolites concentration distribution of NAA/Cr, MI/Cr and MI/NAA in CN and AD groups.

TARGET AUDIENCE: Hippocampus is crucial for memory consolidation, spatial cognition, perception of temporal ordering of events. The abnormalities of the hippocampus play a major role in many prevalent neurologic disorders, such as Alzheimer disease.Proton MR spectroscopy(^{1}HMRS) can serve as estimates of neuronal cell viability, cell energetics, membraneturnover, gliosis, glycolysis, and inflammatoryprocesses in vivo. ^{1}HMRS with multi-voxel has revealed hippocampal metabolic differences between patients andcontrol subjects. This work will benefit for radiologists and scientists for evaluating metabolites changes in hippocampi.

Purpose: We explore the metabolic changes in the head, body and tail of hippocampal in Alzheimer's disease (AD) compared with normal control. We also investigate the distribution rules of metabolites concentration among different parts of the hippocampus for more accurate clinical diagnosis of AD.

Methods: Thirty patients with AD and 30 cognitively normal person (CN) were scanned by a 3.0 T magnetic resonance (MR) by Multivoxel proton spectroscopy (Achieva, Philips Medical Systems, Netherlands). The 8channels-HEAD coil was employed. The data was processed by commercially available postprocessing workstation (Extended Workspace (EWS), Philips Medical Systems, Netherlands). The hippocampus was divided equally into three parts (head, body and tail). N-acetylaspartate (NAA)/creatine (Cr), myoinositol (MI)/Cr and MI/NAA ratio were calculated separately from each part. We compared with each metabolites concentration data of AD and CN groups and analyzed the anteroposterior metabolic profile in hippocampus.

Result: The mean value of NAA/Cr is decreased and that of MI/Cr, MI/NAA are elevated in the bilateral hippocampi and hippocampal body and tail in AD group ($p < 0.01$). MI/NAA in the head of left hippocampus is also increased statistically ($p < 0.01$). Fig.1 shows NAA/Cr in the bilateral hippocampi from head to tail have the gradually rising trend ($p < 0.01$) and MI/NAA gradually declines in CN group ($p < 0.01$). MI/Cr in CN group and each metabolite concentration in AD group have no anteroposterior metabolic heterogeneity in bilateral hippocampil. (Fig.1). All detail data are recorded in Table 1-3.

Discussion: There were two advantages in ^{1}HMRS (MVS), also called chemical shift imaging[1], compared with single-voxel ^{1}HMRS (SVS). First, MVS collected many small SVS meanwhile, which could effectively avoid partial volume effect according to the specific post-process site. Second, MVS was able to analysis different parts metabolism distribution of the diffuse lesions and inhomogeneity lesions at the same time, it was more conducive to compare the different parts in region of interest than SVS. NAA is a marker who promotes neurons metabolic abilit, its decrease can be considered to the number or functional of neurons decline. In this study, NAA/Cr of bilateral hippocampi decline agrees with previous research [2]. MI only exists in glial cells, which makes it be the marker of them [2]. The MI/Cr increasing was report in former studies, while some results indicated it did not change in the hippocampus in AD. Ostojic J etc.[3] divided hippocampus into head, body and tail and indicated that NAA/Cr in hippocampal head was minimum, which had significant difference with that in hippocampal body and tail. Meanwhile, NAA/Cr in hippocampal body and tail were found no statistical differences. In our study, NAA/Cr gradually rises and MI/Cr, MI/NAA gradually decreases from hippocampal head to tail. NAA/Cr and MI/NAA have statistical difference between hippocampal head and body/tail. Each metabolite concentration in bilateral hippocampal head, body and tail has no statistical differences, which demonstrates neuron degeneration of the hippocampus is diffuse changes in AD. At present, absolute quantitative of MVS has become the trend of the research, our group has imported Lc model to further analyze absolute quantitative concentration of each metabolite, which will be reported in the next paper in detail.

Conclusion: The anteroposterior metabolic heterogeneity is dismissed in AD, which might be helpful on the early clinical diagnosis of AD.

Key words: Alzheimer's disease； Hippocampus ; Multivoxel proton spectroscopy; Magnetic resonance

Reference: 1. Doelken MT, Mennecke A, Stadlbauer A, et al. Multi-voxel magnetic resonance spectroscopy of cerebral metabolites in healthy adults at 3 Tesla. Academic radiology 2009;16:1493-1501. 2. Yang Z, Huo SS, Cheng XF, et al. Quantitative multivoxel proton MR spectroscopy study of brain metabolites in patients with amnestic mild cognitive impairment: a pilot study. Neuroradiology 2012;54:451-458. 3. Ostojic J, Kozic D, Konstantinovic J, et al. Three-dimensional multivoxel spectroscopy of the healthy hippocampus-are the metabolic differences related to the location? Clinical radiology 2010;65:302-307.