A Novel Automatic Quantitative Measurement of the Metabolites in Hippocampal Subfields by Combining 2D ^{1}H-MRSI and 3D Volumetric MRI in Patients With AD

Yu Sun[1,2,3], Dadi Zhao[1,2], Renyuan Liu[4], Zhao Qing[4], Ben Babourina-Brooks[5,6], Andrew C Peet[1,2], Bing Zhang[4]

[1]Institute of Cancer and Genomic Sciences, University of Birmingham [2]Institute of Child Health, Birmingham Children's Hospital [3]Laboratory of Biomedical Imaging and Artificial Intelligence, School of Biological Science and Medical Engineering, Southeast University, China [4]Department of Radiology, the Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China [5]Radiological Sciences, Division of Neuroscience, University of Nottingham [6]Sir Peter Mansfield Imaging Centre, University of Nottingham

Background and Objective Several subfields with different cellular and molecular characteristics construct the hippocampal formation, which were found differentially vulnerable to Alzheimer's Disease (AD). The metabolite changes of a specified subfield have not been investigated for their functions in AD, and only the most significant voxel was selected manually to represent metabolites within the hippocampus or hippocampal subfield. This study aims to investigate the hippocampal metabolite concentrations on the subfields level that are supposed as more sensitive biomarkers for Alzheimer's disease (AD) than the whole hippocampal level, while their alterations are still unclear.

Materials and Methods Group comparison was obtained from 17 patients of AD, 24 patients with mild cognitive impairment (MCI) and 21 matched normal controls (NC), using a novel automatic quantitative method of metabolite ratios for hippocampal subfields, via registration between the 2D proton magnetic resonance spectroscopy imaging (1H-MRSI) and the 3D T1W volumetric magnetic resonance imaging (MRI). Co-registration between the subfields segmented using FreeSurfer 6.0 and the 1H-MRSI voxels was used to estimate the metabolite ratios accumulatively with the volumetric proportion as weight, followed by analysis of variance and receiver operating characteristic to observe diagnostic performance.

Results Cornu ammonis (CA) 1 is the biggest among the 7 meaningful segmented subfields, occupying 69.158±13.768 voxels with the corresponding volumetric proportion as 11.0%±2.1% in the bilateral hippocampus. Comparing the MCI and NC group, N-acetylaspartate (NAA)/Creatine (Cr) of CA1 and CA2/3 in the bilateral hippocampus significantly decreased ($P<0.05$). Comparing the AD and MCI group, myo-inositol (Ins)/Cr of CA4, fimbria, granule cell layer of dentate gyrus (GC-DG), presubiculum and subiculum in the bilateral hippocampus significantly increased ($P<0.05$). Diagnostic power of segmented subfields performed more significant (average AUC=0.81, $P<0.001$) rather than that of the whole hippocampus (average AUC=0.72, $P=0.004$) for distinguishing both AD/MCI and MCI/NC.

Conclusion By proposing a novel measurement of the metabolites of the hippocampus and hippocampal subfields combining 3D TFE T1W MRI and 2D PRESS MRS, the study indicated that NAA/Cr and Ins/Cr may be sensitive predictors of AD progress in different stages respectively, and demonstrated that the metabolic alteration in AD progress have similar specificity in hippocampal subfield level compared with the whole level. This study suggests that metabolite ratios of some hippocampal subfields are able to better distinguish AD and MCI from normal controls through implementing co-registration between segmented MRI and CSI.

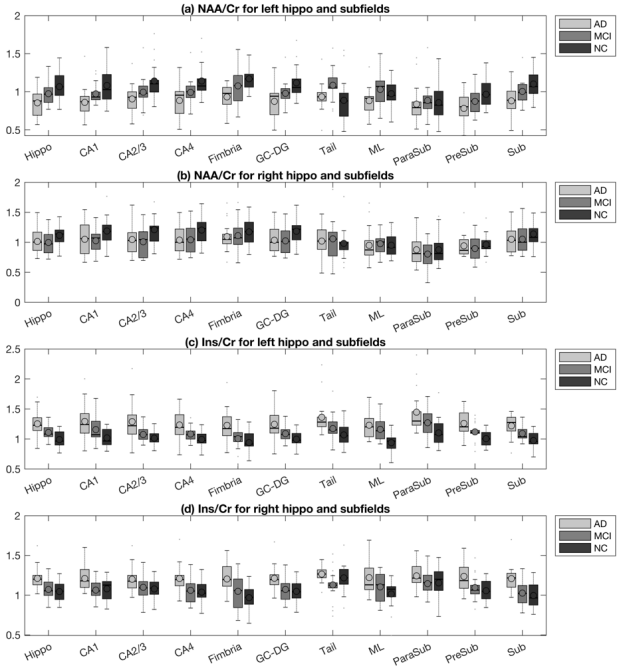

Figure The box statistic plot of metabolite ratio NAA/Cr and Ins/Cr for left and right hippocampus and subfields. The y-axis records the metabolite concentration ratio NAA/Cr and Ins/Cr of corresponding hippocampal subfields. Hippo. = hippocampus, GC-DG = granule cell layer of dentate gyrus, HATA = hippocampal–amygdaloid transition area, ML = molecular layer, ParaSub. = parasubiculum, PreSub. = presubiculum, Sub. = subiculum.