Associations of dietary n-3 polyunsaturated composition quantified by ^{1}H magnetic

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fatty acids with liver fat content and resonance spectroscopy

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Background

- Dietary intake long train poly-unsaturated fatty acids (n-3 PUFAs) was reported to improve non-alcoholic fatty liver disease while the mechanism is still unknown.
- In non-alcoholic fatty liver disease (NAFLD) patients,

1) elevation in hepatic triglycerides;

2) increase in the degree of saturation in fatty acid composition of the deposited fat;

were reported.

Objectives

- We aimed to investigate the relationship between the Diet History Questionnaire (DHQ) measured n-3 PUFAs intake and

1) ^{1}H magnetic resonance spectroscopy (^{1}H-MRS) quantified liver fat content
2) Estimated liver fat Saturation Index

Participants

55 local government retirees in Aichi Pref. Japan

Exclusion:

- current smoker (n=9)
- heavy drinker (2 *go [46g/day]* or more) (n=4)
- missing necessary variables for the analysis (n=1)

40 (men 34, women 6)

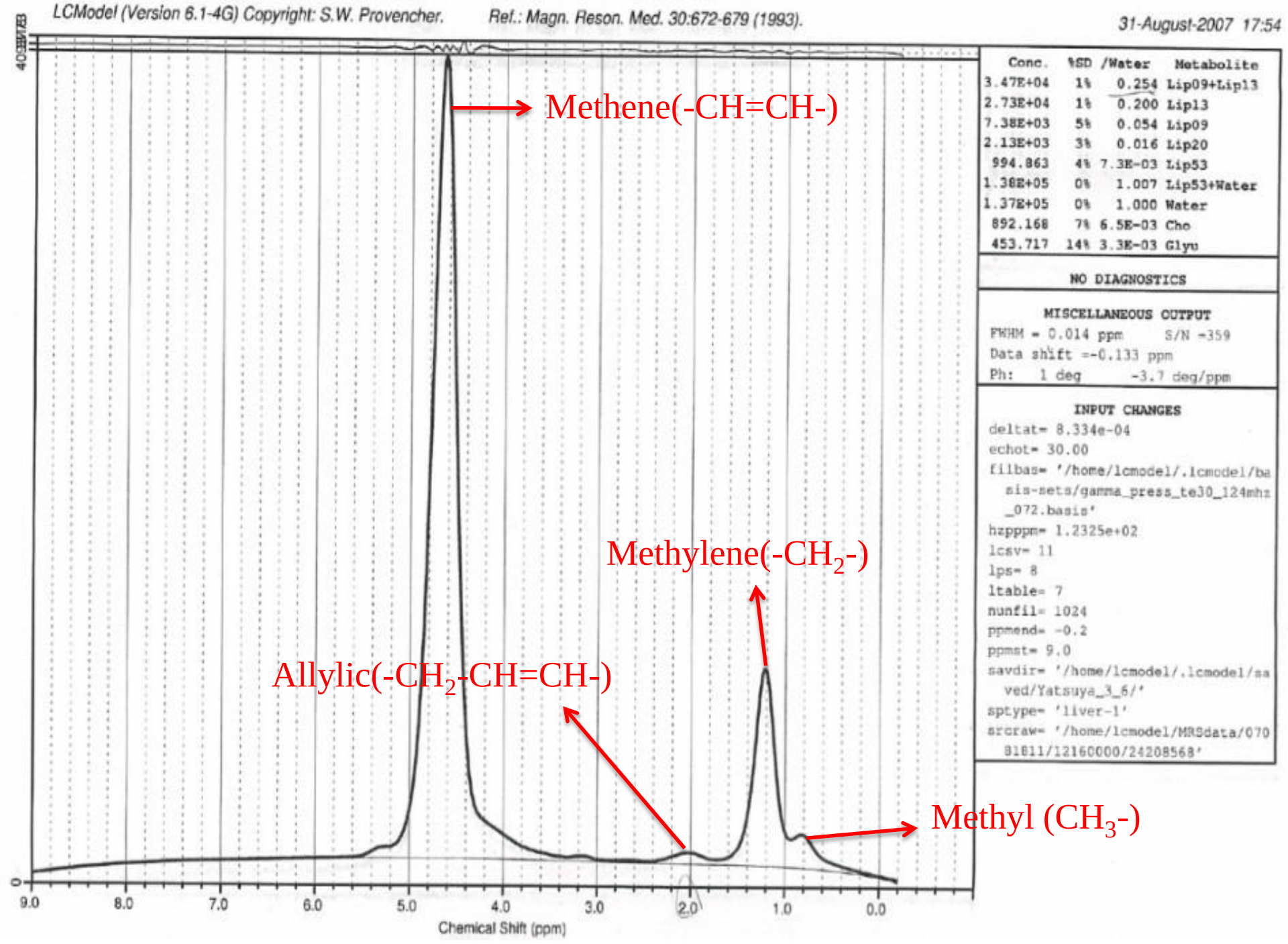
Methods: MRS

- MRS is a reliable and non-invasive method to quantify liver fat content.
- ^{1}H magnetic resonance spectroscopy (^{1}H-MRS)

✓ 3T Siemens Magnetic Resonance Scanner (TE=30ms)

✓ Volume of interest: right liver lobe (4×4×4 cm)

✓ Spectrogram was analyzed by LCModel software


LCModel (Version 6.1-4G) Copyright: S.W. Provencher.
Ref.: Magn. Reson. Med. 30:672-679 (1993).
31-August-2007 17:54
Methene(-CH=CH-)
Methylene(-CH2-)
Allylic(-CH2-CH=CH-)
Methyl (CH3-)
Chemical Shift (ppm)
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
0
Conc. %SD /Water Metabolite
3.47E+04 1% 0.254 Lip09+Lip13
2.73E+04 1% 0.200 Lip13
7.38E+03 5% 0.054 Lip09
2.13E+03 3% 0.016 Lip20
994.863 4% 7.3E-03 Lip53
1.38E+05 0% 1.007 Lip53+Water
1.37E+05 0% 1.000 Water
892.168 7% 6.5E-03 Cho
453.717 14% 3.3E-03 Glyu
NO DIAGNOSTICS
MISCELLANEOUS OUTPUT
FWHM = 0.014 ppm S/N =359
Data shift =-0.133 ppm
Ph: 1 deg -3.7 deg/ppm
INPUT CHANGES
deltat= 8.334e-04
echot= 30.00
filbas= '/home/lcmodel/.lcmodel/basis-sets/gamma_press_te30_124mhz_072.basis'
hzpppm= 1.2325e+02
lcsv= 11
lps= 8
ltable= 7
nunfil= 1024
ppmend= -0.2
ppmst= 9.0
savdir= '/home/lcmodel/.lcmodel/saved/Yatsuya_3_6/'
sptype= 'liver-1'
srcraw= '/home/lcmodel/MRSdata/07031811/12160000/24208568'

Saturation Index

- The degree of lipid saturation can be calculated based on chemical shifts (peaks) corresponding to different fatty acid functional structures.
  - ✓ $SI = 1 - UI$
  - ✓ UI is unsaturation index
  - ✓ $UI = (I_{allylic}+I_{diallylic})/(I_{allylic}+I_{diallylic}+I_{methylene}+I_{methyl})$ [1]
  - ✓ I_x are the signal amplitudes of the fatty acid functional groups peak in ^{1}H-MRS spectra

[1] Johnson, N.A., et al., *Noninvasive assessment of hepatic lipid composition: Advancing understanding and management of fatty liver disorders.* Hepatology, 2008. **47**(5): p. 1513-23.

Methods

- Self-administered Diet History Questionnaire

  Diet was assessed by a self-administered diet history questionnaire (DHQ) that required recalling dietary habits over a 1-month period which included 148 kind of food items.

- The reproducibility and validity of the DHQ

  Pearson correlation coefficients in 92 Japanese men and 92 Japanese women aged 31-76 years were 0.42 and 0.45 for n-3 PUFA, 0.30 and 0.32 for ALA, 0.27 and 0.37 for EPA, and 0.26 and 0.27 for DHA, respectively. [2]

[2] Sasaki S(2004). Development and evaluation of dietary assessment methods using biomarkers and diet history questionnaires for individuals. (head investigator: Tanaka H) Research for Evaluation Methods of Nutrition and Dietary Lifestyle Programs held on Healthy Japan 21. Summary Report of the Ministry of Health, Labour and Warfare. Ministry of Health, Labour and Warfare: Japan, pp10-44(in Japanese)

Table 1. Subject characteristics

	Range	Mean(SD)
Age (y)	37-69	63.1 (5.5)
Body mass index (kg/m^2)	18.4-32.0	23.9 (5.6)
Body fat (%)	13.5-39.7	23.1 (2.4)
Waist circumference (cm)	72.1-101.3	86.4 (6.7)
n-3 PUFA intake (g/d)	0.94-5.25	2.7 (1.1)
Liver fat content（%）	0.7-25.4	0.72 (0.006)
Saturation index	0.35-1.0	0.9 (0.1)

n-3 PUFA : n-3 polyunsaturated fatty acid

Partial correlation coefficients of liver fat content with dietary fat intakes controlling for sex, age, BMI, and alcohol intake

Table 4

		p
Fat	0.135	0.43
SFA	0.183	0.28
MUFA	0.077	0.65
PUFA	0.183	0.28
n6-PUFA	0.021	0.9
n3-PUFA	0.09	0.6
EPA(C20:5)	0.076	0.66
DHA(C22:6)	0.072	0.67
ALA(C18:3)	0.065	0.7
AA(C20:4)	0.105	0.54
LA(C18:2)	0.016	0.92
cholesterol	0.168	0.32

SFA: saturated fatty acid; MUFA: monounsaturated fatty acid; PUFA: polyunsaturated fatty acid; EPA: Eicosapentaenoic acid; DHA: Docosahexaenoic acid; ALA: α-Linolenic acid; AA: Arachidonic acid; LA: Linoleic acid

Partial correlation coefficients of SI with dietary fat intakes controlling for sex, age, BMI, and alcohol intake

Table 3

		p
Fat	0.23	0.18
SFA	0.16	0.35
MUFA	0.2	0.25
PUFA	0.16	0.35
n6-PUFA	0.24	0.16
n3-PUFA	0.37	0.03
EPA(C20:5)	0.35	0.04
DHA(C22:6)	0.31	0.06
ALA(C18:3)	0.29	0.08
AA(C20:4)	0.13	0.46
LA(C18:2)	0.24	0.16
Cholesterol	0.16	0.35

SFA: saturated fatty acid; MUFA: monounsaturated fatty acid; PUFA: polyunsaturated fatty acid; EPA: Eicosapentaenoic acid; DHA: Docosahexaenoic acid; ALA: α-Linolenic acid; AA: Arachidonic acid; LA: Linoleic acid

Partial correlation coefficients of SI with dietary fat intakes controlling for sex, age, BMI, and alcohol intake in subjects with lower or higher than median liver fat content

Table 4

	lower liver fat content subjects(n=24)		higher liver fat content subjects(n=16)	
		p		p
Fat	.37	.102	-.02	.950
SFA	.27	.238	.05	.883
MUFA	.33	.150	.03	.923
PUFA	.27	.238	.05	.883
n6-PUFA	.39	.080	-.05	.869
n3-PUFA	.44	.049	.03	.935
EPA(C20:5)	.45	.042	.00	.995
DHA(C22:6)	.39	.077	.01	.970
ALA(C18:3)	.40	.071	.05	.882
AA(C20:4)	.21	.366	-.12	.586
LA(C18:2)	.39	.079	-.05	.875
Cholesterol	.24	.296	-.16	.599

SFA: saturated fatty acid; MUFA: monounsaturated fatty acid; PUFA: polyunsaturated fatty acid; EPA: Eicosapentaenoic acid; DHA: Docosahexaenoic acid; ALA: α-Linolenic acid; AA: Arachidonic acid; LA: Linoleic acid

Summary

- Dietary n-3 PUFA intake did not have association with liver fat content

- Dietary n-3 PUFA intake was positively related to the degree of lipid saturation of the deposit fat particularly in subjects without high liver fat content.

Discussion

- The reasons we did not find association of liver fat content with dietary n-3PUFA and total fat intakes are not clear; however the number of subjects might not have been sufficient (n=40).
- Another reason may be the lower contribution of dietary fat to liver fat content. Various sources of intrahepatic deposition of TG were reported (60% from serum nonesterified fatty acids, 15% from diet and 25% from de novo lipogenesis.) [3]

[3] Donnelly KL, Smith CI, Schwarzenberg SJ, Jessurun J, Boldt MD, Parks EJ (2005). *Sources of fatty acids stored in liver and secreted via lipoproteins in patients with nonalcoholic fatty liver disease.* J Clin Invest 115, 1343-1351

Discussion

- Present findings may conflict with some of the previous studies which suggested that dietary n-3 PUFAs supplementation improves NAFLD. However there was a rodent study that implied that hepatic SFA levels were high when diets were enriched in PUFA. [4]

[4] Sealls W, Gonzalez M, Brosnan MJ, Black PN, DiRusso CC. Dietary polyunsaturated fatty acids (C18: 2 omega6 and C18: 3 omega3) do not suppress hepatic lipogenesis. *Biochim Biophys Acta*. 2008;**1781**:406–14.