Electronic Supplementary Material (ESI) for Analyst.

Electronic Supporting Information

Comparison of the biological effects of Gadodiamide (Omniscan) and Gadoteridol (ProHance) by means of multi-organ and plasma metabolomics

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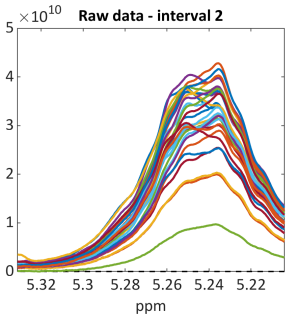
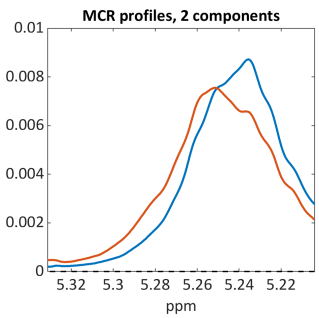
Table of Contents

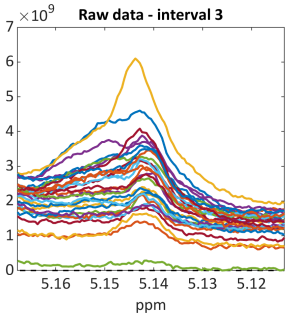
Key:
Resolved component 1 = blue profile
Resolved component 2 = red profile
Resolved component 3 = yellow profile

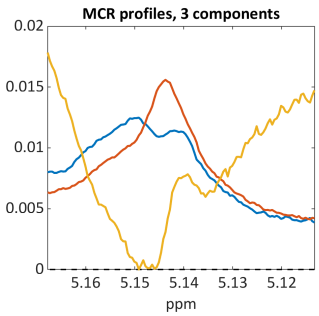




Interval assignment:
Methine (CH) of unsaturated lipids

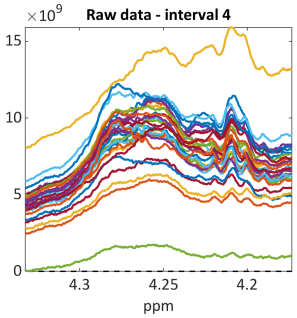
comp.1: lipid 1
comp.2: lipid 2

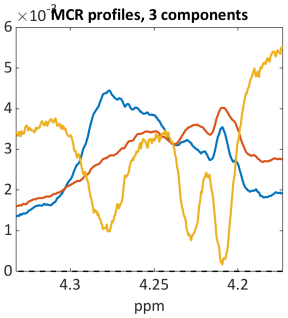




Interval assignment:
Methine (CHOCOR) of glyceryl lipids

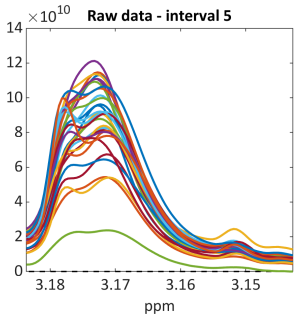
comp.1 + comp.2: glyceril lipid 1

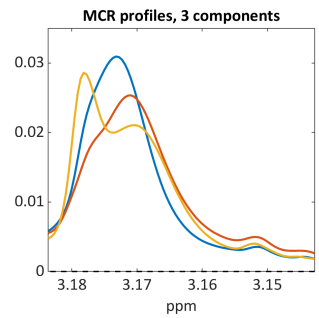




Interval assignment:
Methilene (CH_2OCOR) of glyceryl lipids
and methylene (CH_2OH) of choline

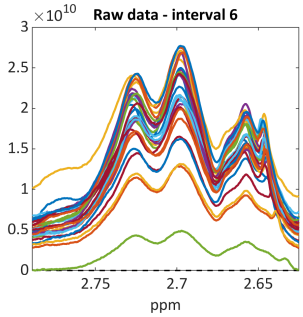
comp.1: glyceril lipid 2
comp.2: glycerophosphocholine

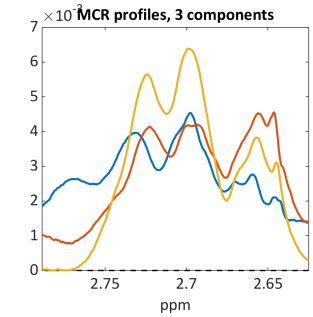




Interval assignment:
$N(CH_3)_3$ Choline

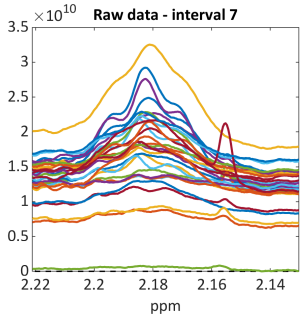
comp.1: phosphatidylcholine 1
comp.2: phosphatidylcholine 2
comp.3: phosphatidylcholine 3

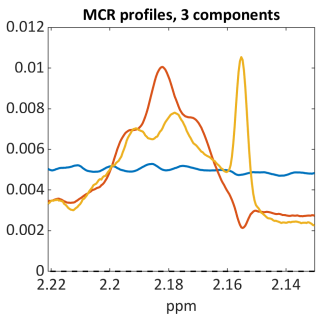




Interval assignment:
CH=CH-CH2-CH=CH of lipids

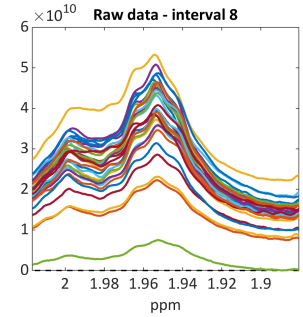
comp.1: Lipid 3
comp.2: Lipid 4
comp.3: Lipid 5

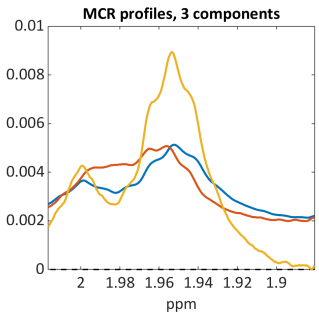




Interval assignment:
CH_2CO of lipids

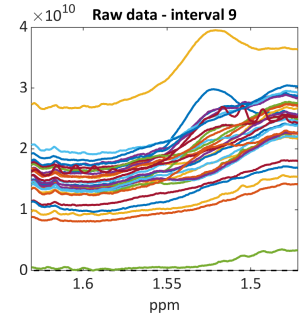
comp.2: lipid 6

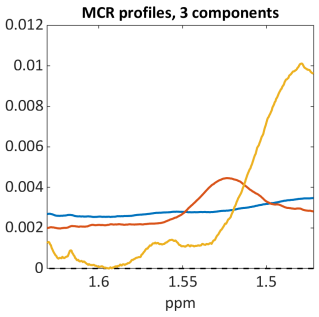




Interval assignment:
$CH_2C=C$ of lipids

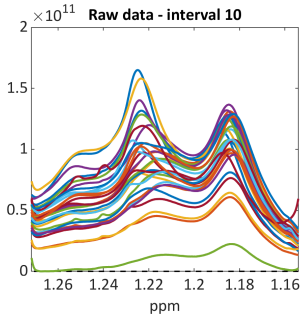
comp.1: lipid 7

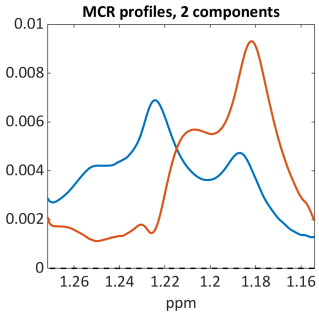




Interval assignment:
CH_2CH_2CO of lipids

comp.2: lipid 8





Interval assignment:
$(CH_2)_n$ of lipids

comp.1: VLDL_1
comp.2: LDL_1

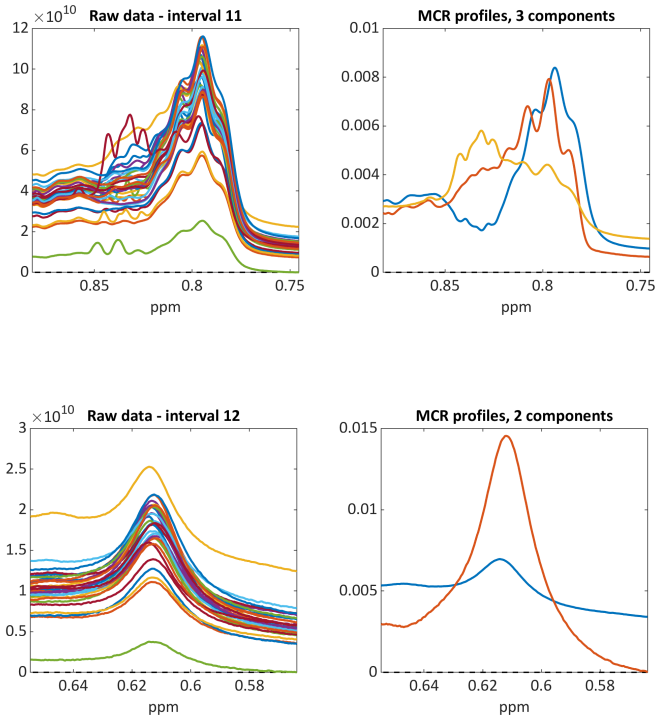


Figure S1. List of resolved intervals from NOESY ^{1}H-NMR spectra. The left panels represent the raw superimposed spectra for each selected interval while the right panel reports the spectral profiles obtained by the MCR model. PC1-3 stand for Principal Component 1-3 and they are referred to the actual MCR-resolved components which were identified as meaningful chemical signals in each individual model.

Key:
Resolved component 1 = blue profile
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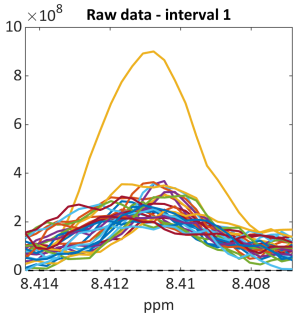
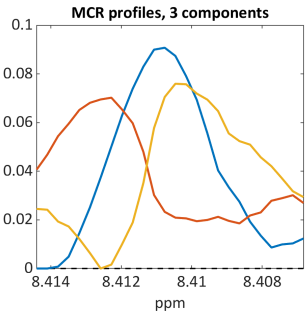
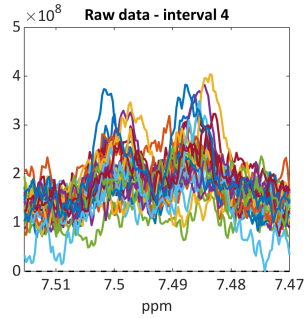
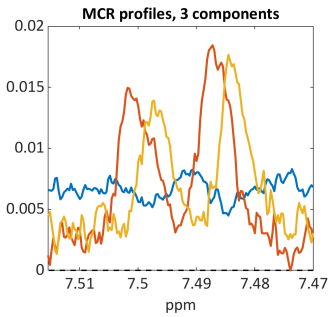




Interval assignment:
Formate

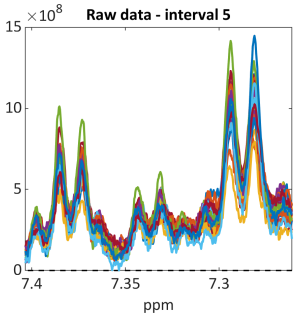
comp.1: Formate

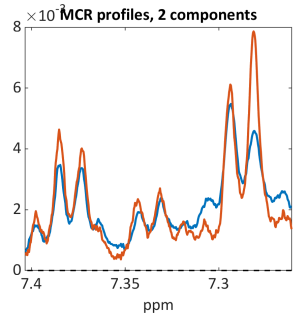




Interval assignment:
Tryptophan

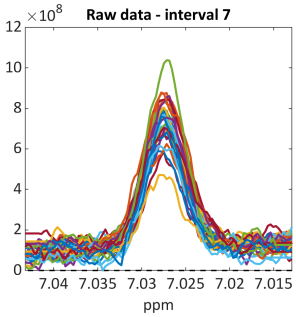
comp.2 + comp.3: Tryptophan

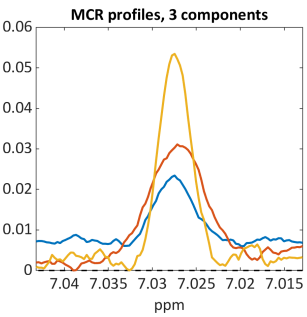




Interval assignment:
Phenylalanine

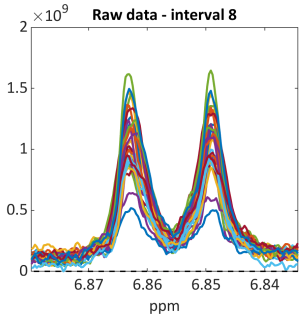
comp.1 + comp.2: Phenylalanine

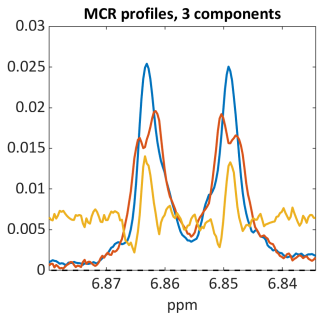




Interval assignment:
Histidine

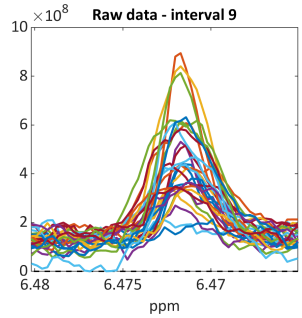
comp.2 + comp.3: Histidine

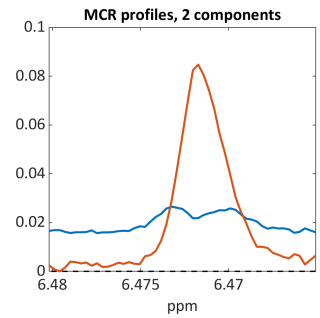




Interval assignment:
Tyrosine

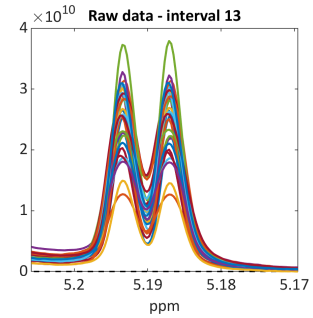
comp.2 + comp.3: Tyrosine

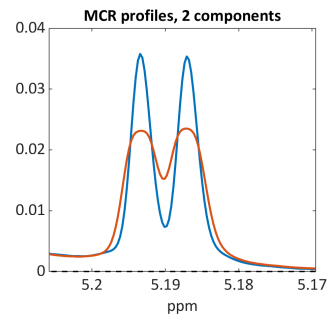




Interval assignment:
Fumarate

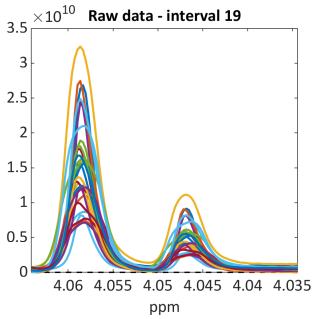
comp.2: Fumarate

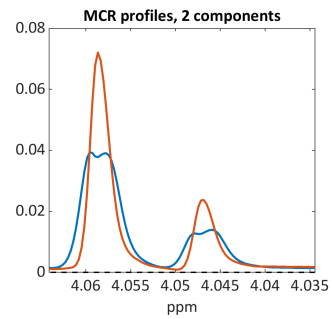




Interval assignment:
Glucose

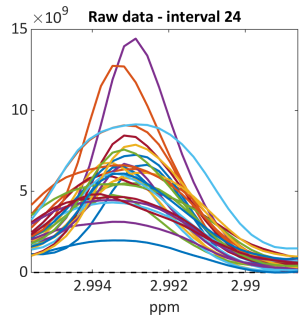
comp.1 + comp.2: Glucose

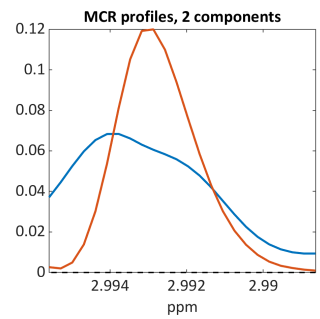




Interval assignment:
Lactate

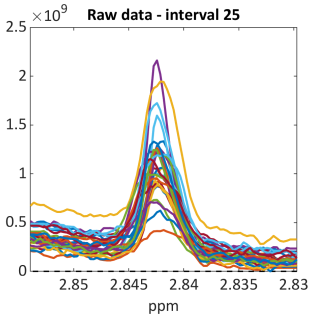
comp.1 + comp.2: Lactate

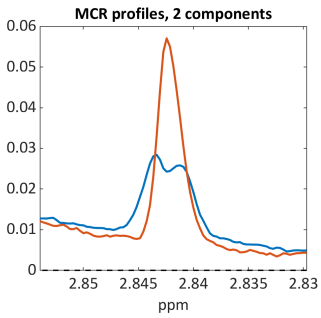




Interval assignment:
Creatine

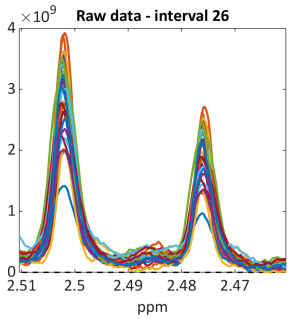
comp.2: Creatine

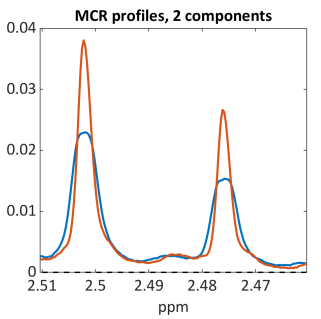




Interval assignment:
N,N–Dimethylglycine

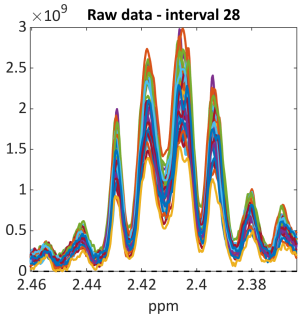
comp.1 + comp.2: N,N–Dimethylglycine

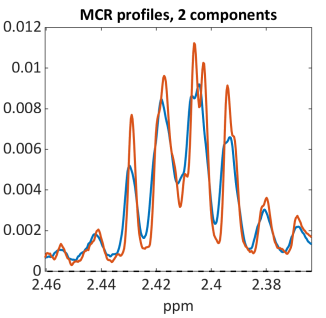




Interval assignment:
Citrate

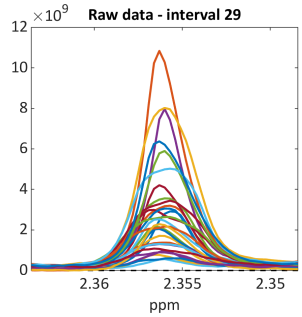
comp.1 + comp.2: Citrate

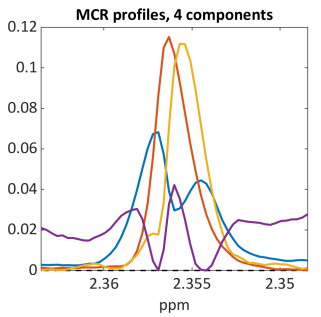




Interval assignment:
Glutamine

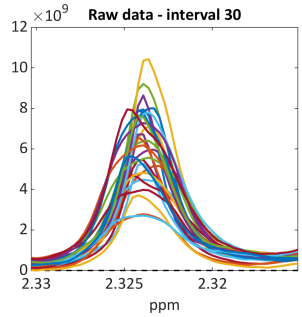
comp.1 + comp.2: Glutamine

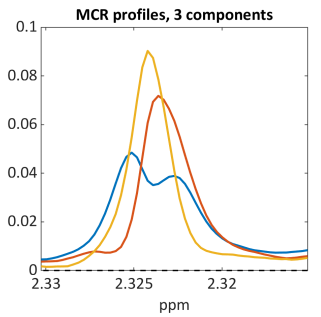




Interval assignment:
Succinate

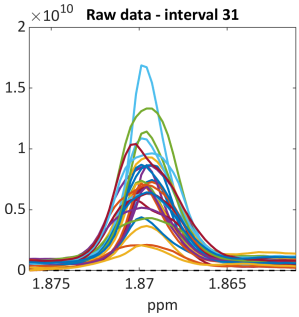
comp.2 + comp.3: Succinate

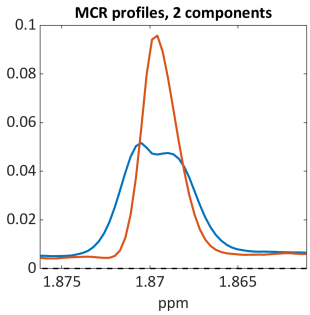




Interval assignment:
Pyruvate

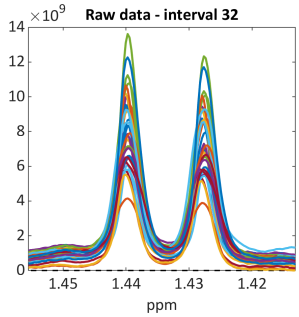
comp.2 and comp.3: Pyruvate

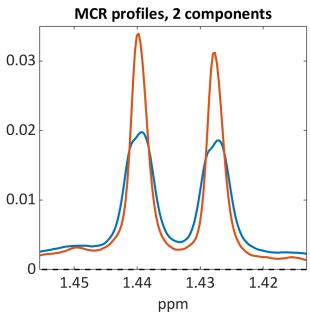




Interval assignment:
Acetate

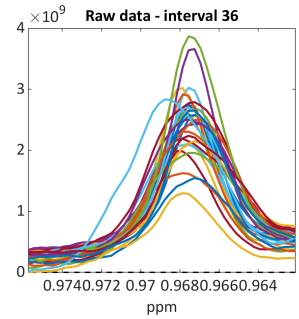
comp.2: Acetate

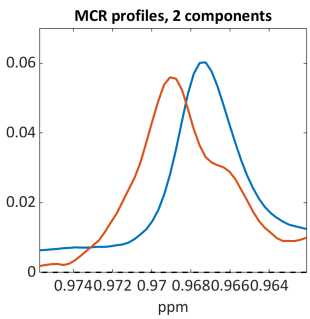




Interval assignment:
Alanine

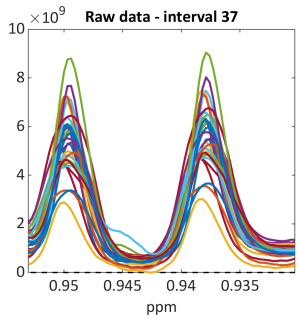
comp.1 + comp.2: Alanine

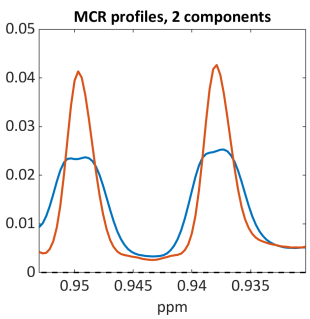




Interval assignment:
Isoleucine

comp.1: Isoleucine





Interval assignment:
Valine

comp.1 + comp.2: Valine

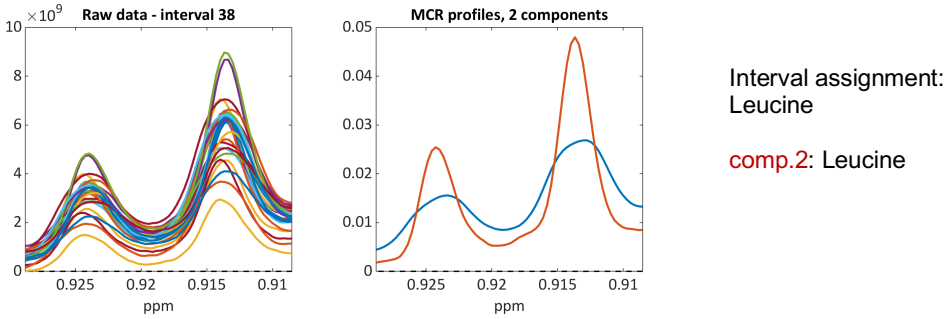


Figure S2. List of resolved intervals from CPMG ^{1}H-NMR spectra. The left panels represent the raw superimposed spectra for each selected interval while the right panel reports the spectral profiles obtained by the MCR model. Comp.1-3 stand for component 1-3 and they are referred to the actual MCR-resolved components which were identified as meaningful chemical signals in each individual model.

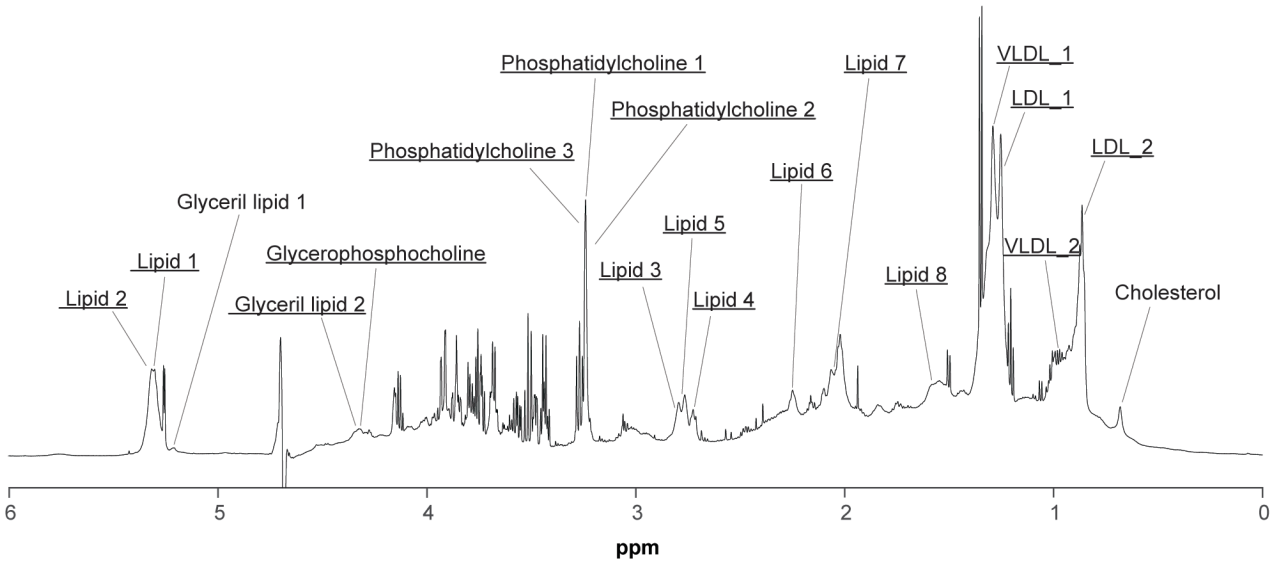
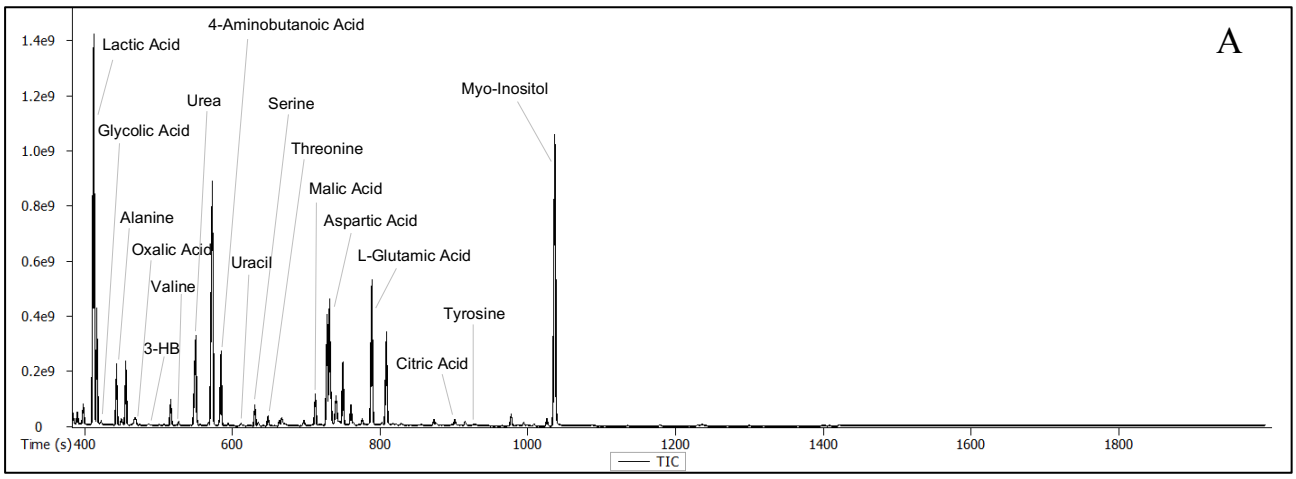
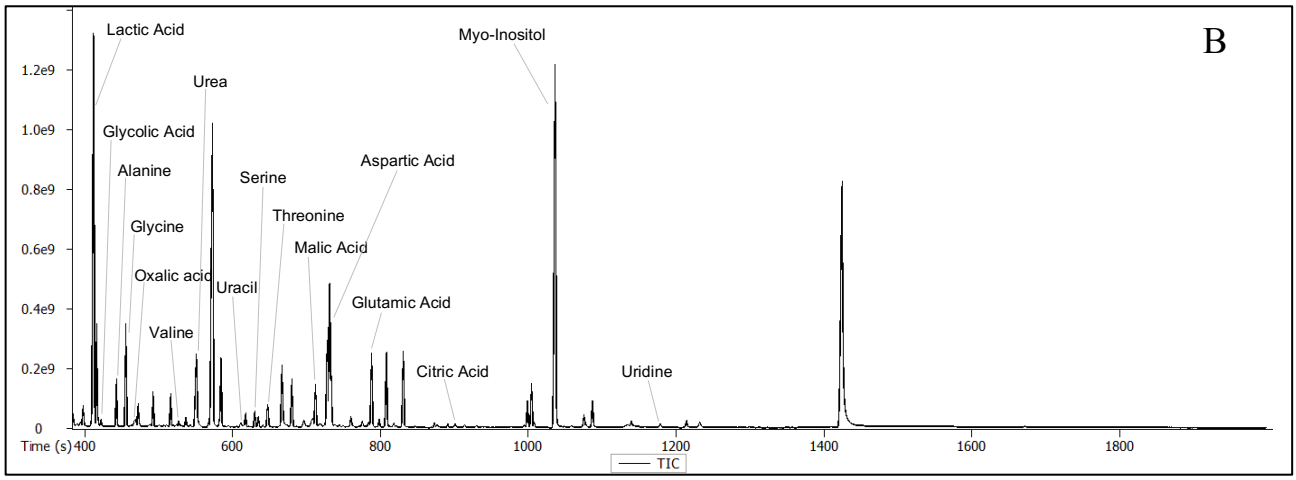
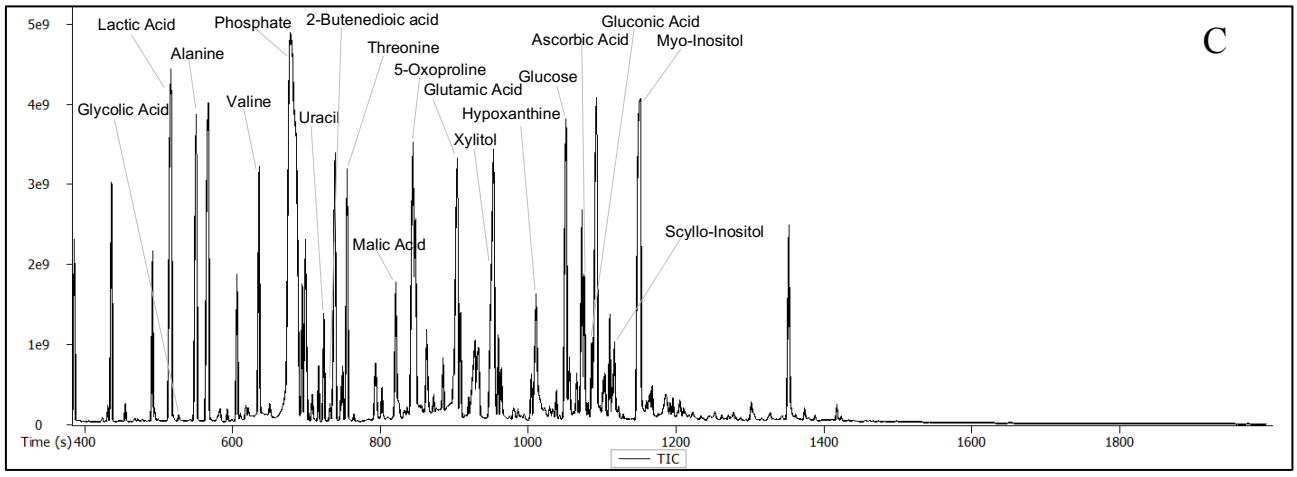


Figure S3. 1D NOESY spectrum of a representative control sample along with the signal assignment. Keys: Lipid 1 and Lipid 2: -CH=CH-; Glyceril lipid 1: =CH-OCOR; Glyceril lipid 2: $-CH_2OCOR$; Glycerophosphocholine: $-CH_2OH$; Phosphatidylcholine 1, Phosphatidylcholine 2 and Phosphatidylcholine 3: $-N(CH_3)_3$; Lipid 3, Lipid 4 and Lipid 5: $-CH=CH-CH_2-CH=CH-$; Lipid 6: $-CH_2CO-$; Lipid 7: $-CH_2C\equiv C-$; Lipid 8: $-CH_2CH_2CO-$; VLDL_1 and LDL_1: $(CH_2)_n$; VLDL_2 and LDL_2: CH_3.


A
Lactic Acid
4-Aminobutanoic Acid
Glycolic Acid
Urea
Serine
Myo-Inositol
Threonine
Malic Acid
Alanine
Aspartic Acid
Oxalic Acid
Uracil
L-Glutamic Acid
Valine
Tyrosine
3-HB
Citric Acid
1.4e9
1.2e9
1.0e9
0.8e9
0.6e9
0.4e9
0.2e9
0
Time (s)
400
600
800
1000
1200
1400
1600
1800
TIC


B
Lactic Acid
Myo-Inositol
Urea
Glycolic Acid
Aspartic Acid
Alanine
Serine
Threonine
Glycine
Malic Acid
Oxalic acid
Uracil
Glutamic Acid
Valine
Citric Acid
Uridine
1.2e9
1.0e9
0.8e9
0.6e9
0.4e9
0.2e9
0
Time (s)
400
600
800
1000
1200
1400
1600
1800
TIC


C
Lactic Acid
Phosphate
2-Butenedioic acid
Gluconic Acid
Ascorbic Acid
Myo-Inositol
Alanine
Threonine
5-Oxoproline
Glucose
Glutamic Acid
Glycolic Acid
Valine
Uracil
Hypoxanthine
Xylitol
Scyllo-Inositol
Malic Acid
5e9
4e9
3e9
2e9
1e9
0
Time (s)
400
600
800
1000
1200
1400
1600
1800
TIC

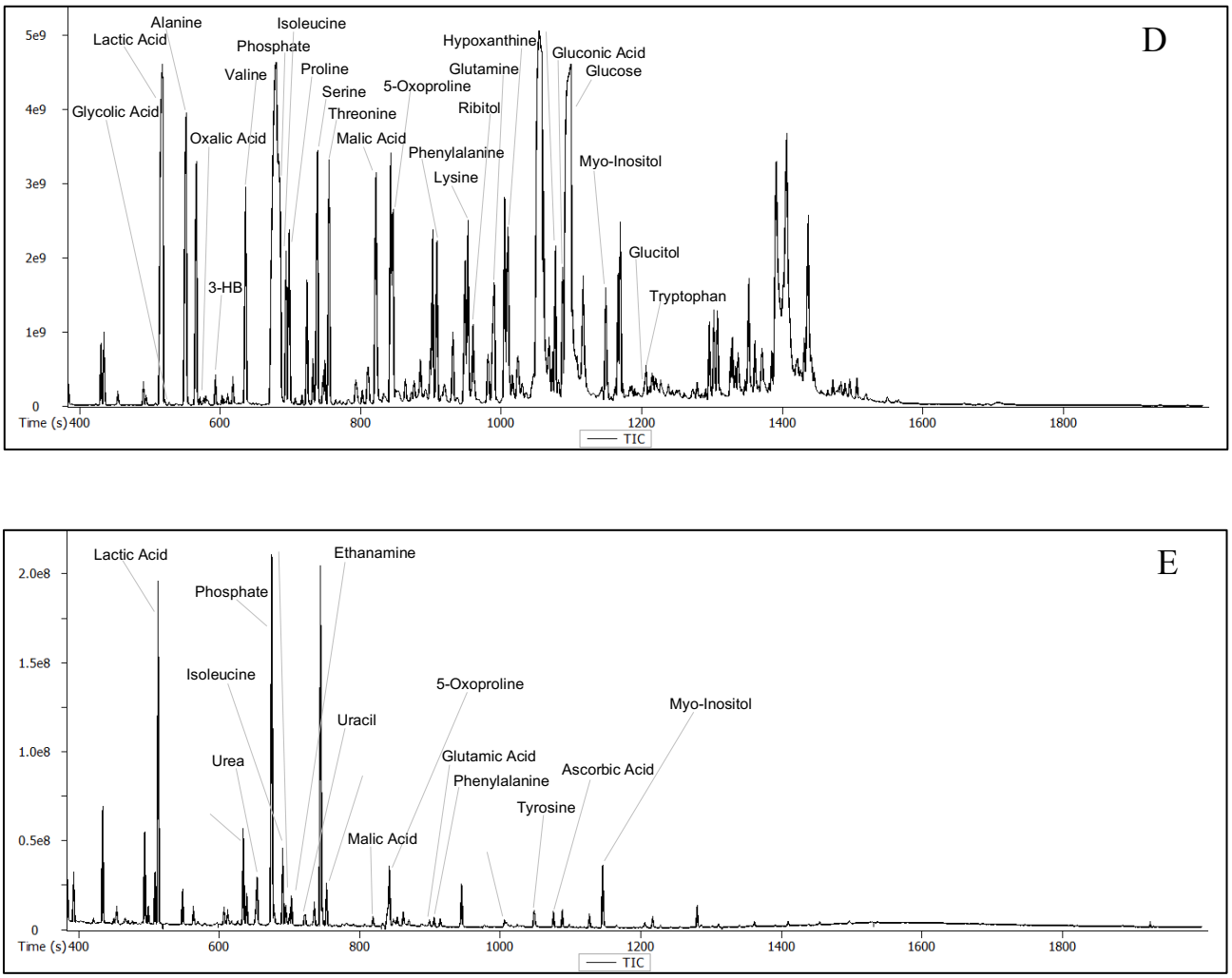


Figure S4. Representative GC-MS chromatograms along with the peak assignment. Chromatograms were obtained from the analysis of the aqueous extracts of (A) brain, (B) cerebellum, (C) kidney, (D) liver and (E) spleen.

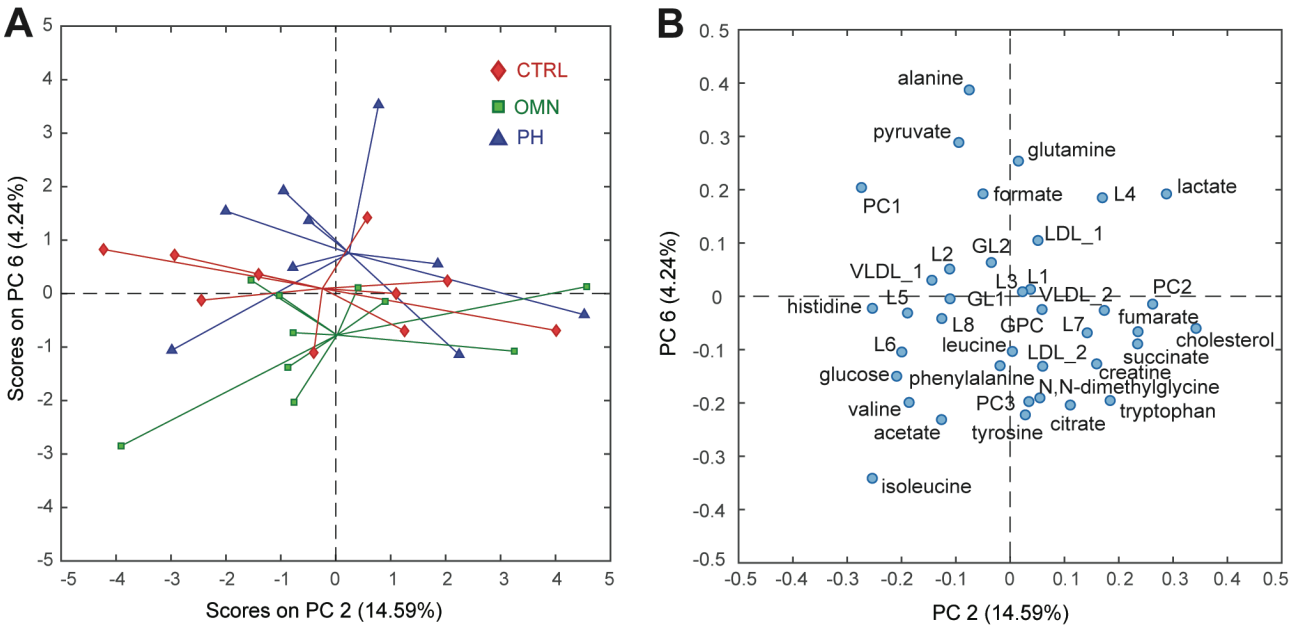


Figure S5. (A) PC 2/PC 6 scores and (B) loadings plots of the PCA model calculated using the MCR integrated peaks of the ^{1}H NMR NOESY and CPMG spectra of plasma. Keys: L1-8: lipid 1-8; GPC: glycerophosphocholine; GL1-2: Glyceril lipid 1-2; PC1-3: Phosphatidylcholine 1-3; VLDL_1 and VLDL_2: very low density lipoprotein; LDL_1 and LDL_2: low density lipoprotein.

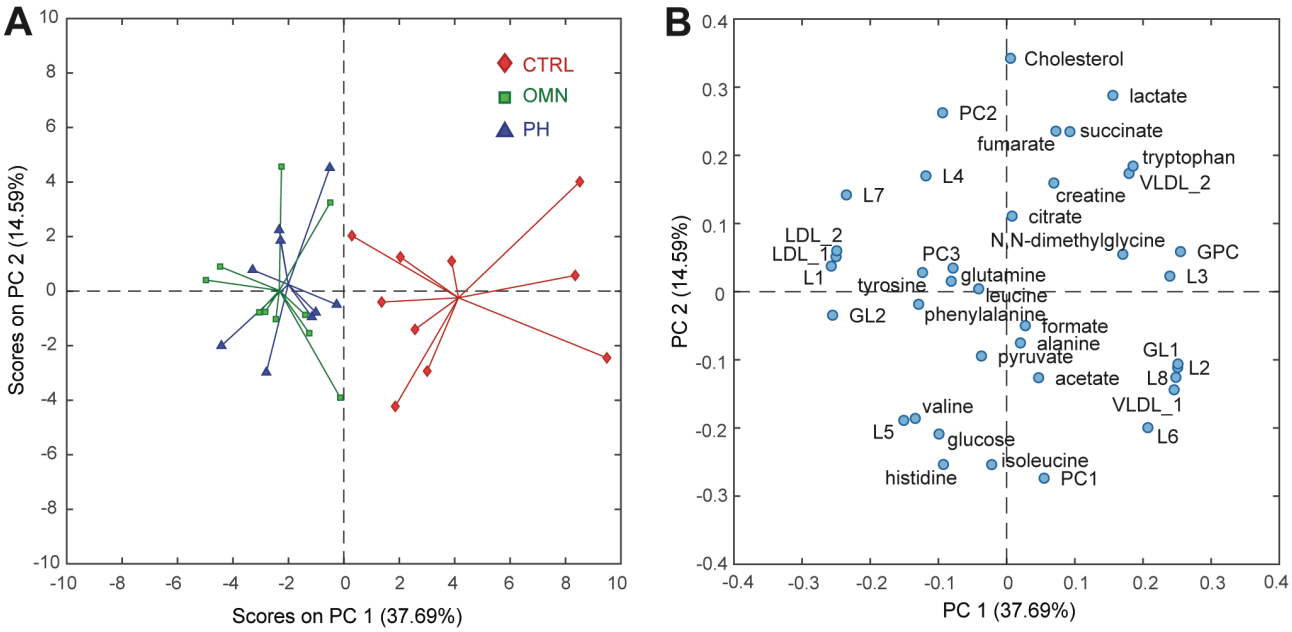


Figure S6. (A) PC1 vs. PC2 scores and (B) loadings plots of the PCA model calculated using the MCR integrated peaks of the 1D NOESY and CPMG spectra of plasma. Keys: L1-8: lipid 1-8; GPC: glycerophosphocholine; GL1-2: Glyceryl lipid 1-2; PC1-3: Phosphatidylcholine 1-3; VLDL_1 and VLDL_2: very low-density lipoprotein; LDL_1 and LDL_2: low-density lipoprotein.

Table S1. Average amounts of fresh tissues and buffer employed for sample homogenization.

Organ	Average weight of the fresh tissue (g)±SD	Buffer (μL)
Liver	1.20±0.11	1000
Kidney	0.41±0.03	400
Spleen	0.14±0.03	200
Brain	0.28±0.04	300
Cerebellum	0.12±0.01	200

Table S2. Amount of aqueous extract and TMSCN employed for GC-MS analysis.

Organ	Aqueous extract (μL)	TMSCN (μL)
Liver	60	60
Kidney	60	60
Spleen	80	80
Brain	60	60
Cerebellum	60	60

Table S3. List of all metabolites identified in organs extracts by GC-MS. Full name, short name, RT, RI, RI(NIST), ΔRI, ID level, CAS registry number and *p*-value from one-way ANOVA are indicated for each compound.

ID #	ID # general	Metabolite full name from NIST[a]	Metabolite short name[b]	RT (s)[c]	RI[d]	RI (NIST)[e]	ΔRI[f]	ID[g]	CAS[h]	One-way ANOVA[i]		
										Untreated-Gadodiamide	**Untreated-Gadoteridol**	**Gadodiamide-Gadoteridol**
		Brain										
1	**1**	Lactic Acid, 2TMS derivative	Lactic Acid, 2TMS	412	1057.4	1066	-8.6	2	17596-96-2	N.S.	N.S.	N.S.
2	**2**	Glycolic acid, 2TMS derivative	Glycolic acid, 2TMS	422.3	1072.4	1081	-8.6	2	33581-77-0	N.S.	N.S.	N.S.
3	**3**	L-Alanine, 2TMS derivative	Alanine, 2TMS	443	1102.7	1100	2.7	2	27844-07-1	N.S.	N.S.	N.S.
4	**4**	Oxalic acid, 2TMS derivative	Oxalic acid, 2TMS	467.3	1138.2	1136	2.2	2	18294-04-7	N.S.	N.S.	N.S.
5	**5**	Hydracrylic acid, 2TMS derivative	β-Lactic acid, bis-TMS	474.1	1148.1	1151	-2.9	2	55162-32-8	N.S.	N.S.	N.S.
6	**6**	3-Hydroxybutyric acid, 2TMS derivative	3-Hydroxybutyric acid, 2TMS	486.7	1166.5	1167	-0.5	2	55133-94-3	6.20E-03	N.S.	N.S.
7	**7**	L-Valine, 2TMS derivative	Valine, 2TMS	527.3	1225.9	1224	1.9	2	7364-44-5	N.S.	N.S.	N.S.
8	**8**	Urea, 2TMS derivative	Urea, 2TMS	544.3	1250.7	1249	1.7	2	18297-63-7	N.S.	N.S.	926E-04
9	**9**	Ethanolamine, 3TMS derivative	Ethanolamine, 3TMS	562.3	1277.0	1262	15.0	2	5630-81-9	N.S.	N.S.	N.S.
10	**10**	L-Leucine, 2TMS derivative	Leucine, 2TMS	567.5	1284.6	1276	8.6	2	7364-46-7	N.S.	N.S.	N.S.
11	**11**	4-Aminobutanoic acid, 2TMS derivative	4-Aminobutyric acid, bis-TMS	584.1	1308.9	1308	0.9	2	39538-11-9	N.S.	N.S.	N.S.
12	**12**	Glycine, 3TMS derivative	Glycine, 3TMS	584.2	1309.0	1314	-5.0	2	5630-82-0	N.S.	N.S.	N.S.
13	**13**	Butanedioic acid, 2TMS derivative	Succinic acid, 2TMS	593.9	1323.2	1321	2.2	2	40309-57-7	N.S.	1.67E-02	1.25E-02
14	**14**	Picolinic acid, TMS derivative	Picolinic acid, TMS	596.9	1327.6			2	17881-49-1	N.S.	N.S.	N.S.
15	**15**	Glyceric acid, 3TMS derivative	Glyceric acid, 3TMS	610.7	1347.8	1344	3.8	2	38191-87-6	N.S.	N.S.	N.S.
16	**16**	Uracil, 2TMS derivative	Uracil, 2TMS	612	1349.7	1343	6.7	2	10457-14-4	N.S.	N.S.	N.S.
17	**17**	Serine, 3TMS derivative	Serine, 3TMS	630.2	1376.3	1368	8.3	2	64625-17-8	N.S.	N.S.	N.S.
18	**18**	L-Threonine, 3TMS derivative	Threonine, 3TMS	648	1402.5	1367	35.5	2	7537-02-2	N.S.	N.S.	N.S.
19	**19**	Malic acid, 3TMS derivative	Malic acid, 3TMS	712	1507.8	1497	10.8	2	38166-11-9	N.S.	N.S.	N.S.
20	**20**	L-Aspartic acid, 3TMS derivative	Aspartic acid, 3TMS	730.7	1538.5	1522	16.5	2	55268-53-6	N.S.	N.S.	N.S.
21	**21**	DL-Phenylalanine, TMS derivative	Phenylalanine, TMS	738.4	1551.2	1559	-7.8	2	2899-42-5	N.S.	N.S.	N.S.
22	**22**	L-Glutamic acid, 3TMS derivative	Glutamic acid, 3TMS	787.9	1636.1	1651	-14.9	2	15985-07-6	N.S.	N.S.	N.S.
23	**23**	Citric acid, 4TMS derivative	Citric acid, 4TMS	901.2	1847.2	1845	2.2	2	14330-97-3	N.S.	N.S.	N.S.
24	**24**	Tyrosine, 2TMS derivative	Tyrosine, 2TMS	925.7	1896.5	1892	4.5	2	7536-83-6	N.S.	N.S.	N.S.
25	**25**	Scyllo-Inositol, 6TMS derivative	Scyllo-Inositol, 6TMS	1008	2067.8			2	14251-18-4	N.S.	N.S.	N.S.
26	**26**	Myo-Inositol, 6TMS derivative	Myo-Inositol, 6TMS	1035.6	2128.5	2129	-0.5	2	2582-79-8	N.S.	N.S.	N.S.
27	**27**	Uridine, 3TMS derivative	Uridine, 3TMS	1178.8	2469.6	2470	-0.4	2	10457-16-6	N.S.	N.S.	N.S.
		Cerebelllum										
1	**28**	Lactic Acid, 2TMS derivative	Lactic Acid, 2TMS	411.8	1057.1	1066	-8.9	2	17596-96-2	N.S.	N.S.	N.S.
2	**29**	Glycolic acid, 2TMS derivative	Glycolic acid, 2TMS	422.2	1072.3	1081	-8.7	2	33581-77-0	N.S.	1.64E-03	N.S.
3	**30**	L-Alanine, 2TMS derivative	Alanine, 2TMS	442.9	1102.5	1100	2.5	2	27844-07-1	N.S.	N.S.	N.S.
4	**31**	Glycine, di-TMS	Glycine, 2TMS	455.5	1120.9	1105	15.9	2	7364-42-3	N.S.	N.S.	N.S.
5	**32**	Oxalic acid, 2TMS derivative	Oxalic acid, 2TMS	467.2	1138.0	1136	2.0	2	18294-04-7	N.S.	N.S.	N.S.
6	**33**	2-Pyrrolidinone, TMS derivative	2-Pyrrolidinone, TMS	468.7	1140.2	1144	-3.8	2	14468-90-7	N.S.	N.S.	N.S.
7	**34**	3-Hydroxybutyric acid, 2TMS derivative	3-Hydroxybutyric acid, 2TMS	486.3	1165.9	1167	-1.1	2	55133-94-3	N.S.	3.02E-03	N.S.
8	**35**	L-Valine, 2TMS derivative	Valine, 2TMS	527.1	1225.6	1224	1.6	2	7364-44-5	N.S.	N.S.	N.S.
9	**36**	L-Leucine, 2TMS derivative	Leucine, 2TMS	567.4	1284.5	1276	8.5	2	7364-46-7	N.S.	N.S.	N.S.
10	**37**	Butanedioic acid, 2TMS derivative	Succinic acid, 2TMS	593.7	1322.9	1321	1.9	2	40309-57-7	1.68E-02	N.S.	N.S.
11	**38**	Picolinic acid, TMS derivative	Picolinic acid, TMS	596.7	1327.3			2	17881-49-1	N.S.	N.S.	N.S.
12	**39**	Uracil, 2TMS derivative	Uracil, 2TMS	611.9	1349.5	1343	6.5	2	10457-14-4	N.S.	N.S.	N.S.
13	**40**	Pipecolic acid, 2TMS derivative	Pipecolic acid, 2TMS	626.9	1371.4	1363	8.4	2	55255-44-2	N.S.	N.S.	N.S.
14	**41**	Serine, 3TMS derivative	Serine, 3TMS	630	1376.0	1368	8.0	2	64625-17-8	N.S.	N.S.	1.58E-02
15	**42**	L-Threonine, 3TMS derivative	Threonine, 3TMS	647.9	1402.4	1367	35.4	2	7537-02-2	N.S.	N.S.	N.S.
16	**43**	Pyroglutamic acid, TMS derivative	Pyroglutamic acid, TMS	708.1	1501.4	1511	-9.6	2		N.S.	N.S.	N.S.
17	**44**	Malic acid, 3TMS derivative	Malic acid, 3TMS	711.9	1507.6	1497	10.6	2	38166-11-9	N.S.	N.S.	N.S.
18	**45**	L-Aspartic acid, 3TMS derivative	Aspartic acid, 3TMS	730.6	1538.3	1522	16.3	2	55268-53-6	N.S.	2.46E-02	1.31E-02
19	**46**	4-Aminobutanoic acid, 3TMS derivative	4-Aminobutyric acid, bis-TMS	732.6	1541.6	1532	9.6	2	39508-23-1	N.S.	N.S.	N.S.
20	**47**	L-Glutamic acid, 3TMS derivative	Glutamic acid, 3TMS	787.8	1635.9	1651	-15.1	2	15985-07-6	N.S.	N.S.	4.35E-02
21	**48**	L-Phenylalanine, 2TMS derivative	Phenylalanine, 2TMS	788.6	1637.4			2	7364-51-4	N.S.	N.S.	1.07E-02
22	**49**	Citric acid, 4TMS derivative	Citric acid, 4TMS	900.9	1846.6	1845	1.6	2	14330-97-3	N.S.	N.S.	4.64E-02
23	**50**	Tyrosine, 2TMS derivative	Tyrosine, 2TMS	925.3	1895.7	1892	3.7	2	7536-83-6	N.S.	N.S.	N.S.
24	**51**	D-Mannitol, 6TMS derivative	Mannitol, 6TMS	965.1	1975.7	1964	11.7	2	14317-07-8	N.S.	N.S.	N.S.

25	**52**	Myo-Inositol, 6TMS derivative	Myo-Inositol, 6TMS	1035.3	2127.8	2129	-1.2	2	2582-79-8	N.S.	N.S.	N.S.
26	**53**	Urea, 2TMS derivative	Urea, 2TMS	544.9	1251.6	1249	2.6	2	18297-63-7	N.S.	N.S.	N.S.
27	**54**	Uridine, 3TMS derivative	Uridine, 3TMS	1178.8	2469.6	2470	-0.4	2	10457-16-6	N.S.	N.S.	N.S.
		Kidney										
1	**55**	Formamide, 2TMS derivative	Formamide, 2TMS	423.7	929.4			2	15500-60-4	N.S.	N.S.	N.S.
2	**56**	N,N-Dimethylglycine, TMS derivative	N,N-Dimethylglycine, TMS	454.8	968.1	1001	-32.9	2		N.S.	N.S.	N.S.
3	**57**	Glycolic acid, 2TMS derivative	Glycolic acid, 2TMS	526.9	1057.6	1081	-23.4	2	33581-77-0	N.S.	N.S.	N.S.
4	**58**	Propanoic acid, 2-oxo-3-(trimethylsilyl)-, trimethylsilyl ester	Pyruvic acid, TMS derivative	536	1068.9			2	55887-51-9	N.S.	N.S.	N.S.
5	**59**	Tris(trimethylsilyl)amine	Amine, 3TMS	565.2	1110.6			2	1586-73-8	N.S.	N.S.	N.S.
6	**60**	L-Valine, 2TMS derivative	Valine, 2TMS	635.3	1212.7	1224	-11.3	2	7364-44-5	N.S.	N.S.	N.S.
7	**61**	L-Leucine, 2TMS derivative	Leucine, 2TMS	676.4	1272.3	1276	-3.7	2	7364-46-7	N.S.	N.S.	N.S.
8	**62**	L-Proline, 2TMS derivative	Proline, 2TMS	696.8	1300.9	1305	-4.1	2	7364-47-8	N.S.	N.S.	N.S.
9	**63**	Glycine, 3TMS derivative	Glycine, 3TMS	701.6	1307.7	1314	-6.3	2	5630-82-0	N.S.	N.S.	N.S.
10	**64**	Glyceric acid, 3TMS derivative	Glyceric acid, 3TMS	715.7	1327.4	1344	-16.6	2	38191-87-6	5.50E-02	4.10E-03	N.S.
11	**65**	Uracil, 2TMS derivative	Uracil, 2TMS	722.7	1337.2	1343	-5.8	2	10457-14-4	N.S.	N.S.	N.S.
12	**66**	2-Butenedioic acid, (E)-, 2TMS derivative	Fumaric acid, 2TMS	731.3	1349.3	1353	-3.7	2	17962-03-7	N.S.	N.S.	N.S.
13	**67**	Erythritol, 4TMS derivative	Erythritol, 4TMS	831.2	1498.2			2	25258-02-0	N.S.	N.S.	N.S.
14	**68**	L-Aspartic acid, 3TMS derivative	Aspartic acid, 3TMS	841.9	1516.5	1522	-5.5	2	55268-53-6	8.56E-03	N.S.	N.S.
15	**69**	L-5-Oxoproline, 2TMS derivative	Pyroglutamic acid, 2TMS	845.4	1522.5	1522	0.5	2	30274-77-2	N.S.	N.S.	N.S.
16	**70**	L-Glutamic acid, 3TMS derivative	Glutamic acid, 3TMS	902.4	1620.2	1651	-30.8	2	15985-07-6	N.S.	N.S.	N.S.
17	**71**	Phenylalanine, 2TMS derivative	Phenylalanine, 2TMS	907.5	1629.0	1636	-7.0	2	2899-52-7	N.S.	N.S.	N.S.
18	**72**	Xylitol, 5TMS derivative	Xylitol, 5TMS	955.7	1715.7	1741	-25.3	2	14199-72-5	N.S.	N.S.	N.S.
19	**73**	D-Pinitol, pentakis(trimethylsilyl) ether	Pinitol, 5TMS	1016.4	1827.2	1815	12.2	2		N.S.	N.S.	N.S.
20	**74**	D-Gluconic acid, 6TMS derivative	Gluconic acid, 6TMS	1102.7	1998.5	2043	-44.5	2	34290-52-3	N.S.	N.S.	N.S.
21	**75**	Lactic Acid, 2TMS derivative	Lactic Acid, 2TMS	515.7	1043.7	1066	-22.3	2	17596-96-2	N.S.	N.S.	N.S.
22	**76**	Silanol, trimethyl-, phosphate (3:1)	Phosphoric acid, TMS	680.8	1278.5	1286	-7.5	2	10497-05-9	N.S.	N.S.	N.S.
23	**77**	L-Isoleucine, 2TMS derivative	Isoleucine, 2TMS	692.5	1294.9	1301	-6.1	2	7483-92-3	N.S.	N.S.	N.S.
24	**78**	L-Threonine, 3TMS derivative	Threonine, 3TMS	754.1	1381.3	1367	14.3	2	7537-02-2	N.S.	N.S.	N.S.
25	**79**	Malic acid, 3TMS derivative	Malic acid, 3TMS	820.2	1479.3	1497	-17.7	2	38166-11-9	N.S.	N.S.	N.S.
26	**80**	D-Glucose, 5TMS derivative	Glucose, 5TMS	1050	1892.6	1926	-33.4	2	6736-97-6	N.S.	N.S.	N.S.
27	**81**	Scyllo-Inositol, 6TMS derivative	Scyllo-Inositol, 6TMS	1115.9	2025.1			2	14251-18-4	N.S.	N.S.	N.S.
28	**82**	Myo-Inositol, 6TMS derivative	Myo-Inositol, 6TMS	1149.3	2095.4	2129	-33.6	2	2582-79-8	N.S.	N.S.	N.S.
29	**83**	2,3,4-Trihydroxybutyric acid tetrakis(trimethylsilyl) deriv., (, (R*,R*)-)	Threonic acid, 4TMS	853.1	1535.7			2	38191-88-7	N.S.	N.S.	N.S.
30	**84**	Ribitol, 5TMS derivative	Ribitol, 5TMS	948.2	1701.9	1747	-45.1	2	32381-53-6	N.S.	N.S.	N.S.
		Liver										
1	**85**	3-Methylbutanoic acid, TMS derivative	Isovaleric acid TMS	413.9	933.5	932	1.5	2	55557-13-6	4.22E-02	N.S.	N.S.
2	**86**	Ethanolamine, 2TMS derivative	Ethanolamine, 2TMS	491.4	1029.5	1021	8.5	2	17165-52-5	N.S.	N.S.	N.S.
3	**87**	Lactic Acid, 2TMS derivative	Lactic Acid, 2TMS	514.5	1058.2	1066	-7.8	2	17596-96-2	4.55E-02	N.S.	1.88E-02
4	**88**	Glycolic acid, 2TMS derivative	Glycolic acid, 2TMS	527.2	1073.9	1081	-7.1	2	33581-77-0	N.S.	N.S.	N.S.
5	**89**	L-Alanine, 2TMS derivative	Alanine, 2TMS	549.1	1101	1100	1	2	27844-07-1	N.S.	N.S.	N.S.
6	**90**	Glycine, di-TMS	Glycine, 2TMS	564.2	1119.7	1105	14.7	2	7364-42-3	N.S.	N.S.	N.S.
7	**91**	Oxalic acid, 2TMS derivative	Oxalic acid, 2TMS	571.1	1128.3	1136	-7.7	2	18294-04-7	N.S.	N.S.	N.S.
8	**92**	3-Hydroxybutyric acid, 2TMS derivative	3-Hydroxybutyric acid, 2TMS	593.1	1155.5	1167	-11.5	2	55133-94-3	N.S.	N.S.	2.01E-02
9	**93**	2-Aminobutanoic acid, 2TMS derivative	2-Aminobutyric acid, 2TMS	602.4	1167.1	1188	-20.9	2	55133-91-0	5.60E-03	N.S.	N.S.
10	**94**	Propanedioic acid, 2TMS derivative	Malonic acid, 2TMS	626.1	1196.4	1216	-19.6	2	18457-04-0	N.S.	N.S.	N.S.
11	**95**	L-Valine, 2TMS derivative	Valine, 2TMS	635.2	1208.8	1224	-15.2	2	7364-44-5	N.S.	N.S.	1.75E-02
12	**96**	Urea, 2TMS derivative	Urea, 2TMS	656.9	1239.6	1249	-9.4	2	18297-63-7	N.S.	N.S.	N.S.
13	**97**	Benzoic Acid, TMS derivative	Benzoic acid, TMS	661.6	1246.2	1249	-2.8	3	2078-12-8	N.S.	N.S.	N.S.
14	**98**	Silanol, trimethyl-, phosphate (3:1)	Phosphoric acid, 3TMS	675.7	1266.2	1286	-19.8	2	10497-05-9	N.S.	N.S.	N.S.
15	**99**	L-Isoleucine, 2TMS derivative	Isoleucine, 2TMS	691.3	1288.4	1301	-12.6	2	7483-92-3	N.S.	N.S.	N.S.
16	**100**	L-Proline, 2TMS derivative	Proline, 2TMS	695.8	1294.7	1305	-10.3	2	7364-47-8	N.S.	N.S.	N.S.
17	**101**	Butanedioic acid, 2TMS derivative	Succinic acid, 2TMS	706.2	1309.5	1321	-11.5	2	40309-57-7	N.S.	N.S.	N.S.
18	**102**	Glyceric acid, 3TMS derivative	Glyceric acid, 3TMS	715.5	1322.7	1344	-21.3	2	38191-87-6	N.S.	N.S.	N.S.
19	**103**	Uracil, 2TMS derivative	Uracil, 2TMS	722.5	1332.6	1343	-10.4	2	10457-14-4	9.68E-03	N.S.	N.S.
20	**104**	2-Butenedioic acid, (E)-, 2TMS derivative	Fumaric acid, 2TMS	731.3	1345.1	1353	-7.9	2	17962-03-7	N.S.	N.S.	N.S.
21	**105**	L-Serine, 3TMS derivative	Serine, 3TMS	736.7	1352.7	1388	-35.3	2	7364-48-9	N.S.	N.S.	N.S.
22	**106**	L-Threonine, 3TMS derivative	Threonine, 3TMS	753.7	1376.8	1367	9.8	2	7537-02-2	N.S.	N.S.	N.S.

23	**107**	L-Aspartic acid, 3TMS derivative	Aspartic acid, 3TMS	840.5	1512.4	1522	-9.6	2	55268-53-6	N.S.	N.S.	N.S.
24	**108**	L-5-Oxoproline, 2TMS derivative	Pyroglutamic acid, 2TMS	843.2	1516.7	1522	-5.3	2	30274-77-2	N.S.	N.S.	N.S.
25	**109**	L-Glutamic acid, 3TMS derivative	Glutamic acid, 3TMS	900.9	1609.8	1651	-41.2	2	15985-07-6	N.S.	N.S.	N.S.
26	**110**	Phenylalanine, 2TMS derivative	Phenylalanine, 2TMS	907	1620.7	1636	-15.3	2	2899-52-7	N.S.	N.S.	N.S.
27	**111**	L-Lysine, 3TMS derivative	Lysine, 3TMS	951.3	1699.4	1718	-18.6	2	24595-69-5	N.S.	N.S.	N.S.
28	**112**	Ribitol, 5TMS derivative	Ribitol, 5TMS	959.2	1713.5	1747	-33.5	2	32381-53-6	N.S.	2.98E-03	N.S.
29	**113**	L-Glutamine, 3TMS derivative	Glutamine, 3TMS	987.6	1764	1768	-4	2	70591-28-5	N.S.	N.S.	N.S.
30	**114**	9H-Purin-6-ol, 2TMS derivative	Hypoxanthine, bis-TMS	1007	1798.5	1811	-12.5	2	17962-89-9	5.1675E-02	N.S.	N.S.
31	**115**	D-Fructose, 5TMS derivative	Fructose, 5TMS	1010	1804.2	1842	-37.8	2	19126-98-8	N.S.	N.S.	N.S.
32	**116**	Adenine, 2TMS derivative	Adenine, 2TMS	1039.7	1862.5	1880	-17.5	2	17995-04-9	N.S.	N.S.	N.S.
33	**117**	Methyl galactoside (1S,2R,3S,4R,5R)-, 4TMS derivative	Methyl galactoside, 4TMS	1042.6	1868.2			2	2641-79-4	3.24E-03	N.S.	N.S.
34	**118**	D-Glucitol, 6TMS derivative	Sorbitol, 6TMS	1071.4	1924.7	1979	-54.3	2	14199-80-5	2.97E-05	4.35E-04	N.S.
35	**119**	L-Tyrosine, 3TMS derivative	Tyrosine, 3TMS	1074.5	1930.8	1959	-28.2	2	51220-73-6	N.S.	N.S.	N.S.
36	**120**	Ascorbic acid, 4TMS derivative	Ascorbic acid, 4TMS	1077	1935.7	1971	-35.3	2	55517-56-1	N.S.	N.S.	N.S.
37	**121**	D-Gluconic acid, 6TMS derivative	Gluconic acid, 6TMS	1085,8	1953	1997	-44	2	34290-52-3	N.S.	N.S.	N.S.
38	**122**	Myo-Inositol, 6TMS derivative	Myo-Inositol, 6TMS	1147.2	2080.5	2129	-48.5	2	2582-79-8	1.29E-02	N.S.	N.S.
39	**123**	L-Tryptophan, 3TMS derivative	Tryptophan, 3TMS	1205.2	2205.7	2225	-19.3	2	55429-28-2	N.S.	N.S.	N.S.
40	**124**	D-Glucose, 5TMS derivative	Glucose, 5TMS	1091.1	1963.4	1926	37.4	2	6736-97-6	N.S.	N.S.	N.S.
41	**125**	2-Hydroxybutyric acid, 2TMS derivative	2-Hydroxybutyric acid, 2TMS	567.7	1124.1	1136	-11.9	2	55133-93-2	N.S.	N.S.	N.S.
42	**126**	Malic acid, 3TMS derivative	Malic acid, 3TMS	820.1	1479.9	1497	-17.1	2	38166-11-9	N.S.	N.S.	N.S.
		Spleen										
1	**127**	Disilathiane, hexamethyl-	Sulfide, 2TMS	429.6	953.0	978	-25.0	2	3385-94-2	N.S.	N.S.	N.S.
2	**128**	L-Alanine, 2TMS derivative	Alanine, 2TMS	548.1	1099.8	1100	-0.2	2	27844-07-1	N.S.	N.S.	N.S.
3	**129**	L-Valine, 2TMS derivative	Valine, 2TMS	634.3	1207.5	1224	-16.5	2	7364-44-5	N.S.	3.32E-03	N.S.
4	**130**	Benzoic Acid, TMS derivative	Benzoic acid, TMS	661.2	1245.7	1249	-3.3	2	2078-12-8	N.S.	N.S.	N.S.
5	**131**	Silanol, trimethyl-, phosphate (3:1)	Phosphoric acid, TMS	674.4	1264.4	1286	-21.6	2	10497-05-9	N.S.	1.42E-02	N.S.
6	**132**	L-Leucine, 2TMS derivative	Leucine, 2TMS	675.1	1265.4	1276	-10.6	2	7364-46-7	N.S.	8.79E-03	N.S.
7	**133**	L-Isoleucine, 2TMS derivative	Isoleucine, 2TMS	690.4	1287.1	1301	-13.9	2	7483-92-3	N.S.	2.04E-03	N.S.
8	**134**	L-Proline, 2TMS derivative	Proline, 2TMS derivative	694.8	1293.3	1305	-11.7	2	7364-47-8	N.S.	N.S.	N.S.
9	**135**	Glycine, 3TMS derivative	Glycine, 3TMS	700.3	1301.1	1314	-12.9	2	5630-82-0	N.S.	N.S.	N.S.
10	**136**	Ethanamine, 2TMS derivative	Ethylamine, 2TMS	702.9	1304.8			2	2477-39-6	N.S.	N.S.	N.S.
11	**137**	2-Butenedioic acid, (E)-, 2TMS derivative	Fumaric acid, 2TMS	730.5	1343.9	1353	-9.1	2	17962-03-7	N.S.	5.25E-02	N.S.
12	**138**	Malic acid, 3TMS derivative	Malic acid, 3TMS	818.9	1478.0	1497	-19.0	2	38166-11-9	N.S.	5.03E-02	N.S.
13	**139**	L-Aspartic acid, 3TMS derivative	Aspartic acid, 3TMS	839.4	1510.7	1522	-11.3	2	55268-53-6	N.S.	N.S.	N.S.
14	**140**	L-Glutamic acid, 3TMS derivative	Glutamic acid, 3TMS	899.6	1607.5	1651	-43.5	2	15985-07-6	N.S.	N.S.	N.S.
15	**141**	Phenylalanine, 2TMS derivative	Phenylalanine, 2TMS	905.9	1618.7	1636	-17.3	2	2899-52-7	N.S.	N.S.	N.S.
16	**142**	Taurine, 3TMS derivative	Taurine, 3TMS	928.9	1659.6			2		N.S.	N.S.	N.S.
17	**143**	9H-Purin-6-ol, 2TMS derivative	Hypoxanthine, bis-TMS	1006.2	1797.0	1811	-14.0	2	17962-89-9	N.S.	N.S.	N.S.
18	**144**	Tyrosine, 2TMS derivative	Tyrosine, 2TMS	1048.7	1880.2	1892	-11.8	2	7536-83-6	N.S.	N.S.	N.S.
19	**145**	Ascorbic acid, 4TMS derivative	Ascorbic acid, 4TMS	1075.8	1933.4	1971	-37.6	2	55517-56-1	1.78E-02	N.S.	N.S.
20	**146**	Myo-Inositol, 6TMS derivative	Myo-Inositol, 6TMS	1145.9	2077.7	2129	-51.3	2	2582-79-8	N.S.	2.89E-02	N.S.
21	**147**	Lactic Acid, 2TMS derivative	Lactic Acid, 2TMS	513.3	1056.7	1066	-9.3	2	17596-96-2	N.S.	N.S.	N.S.
22	**148**	Tris(trimethylsilyl)amine	Amine, 3TMS	564.7	1120.4			2	1586-73-8	N.S.	N.S.	N.S.
23	**149**	Urea, 2TMS derivative	Urea, 2TMS	654.7	1236.5	1249	-12.5	2	18297-63-7	N.S.	N.S.	N.S.
24	**150**	Uracil, 2TMS derivative	Uracil, 2TMS	721.7	1331.4	1343	-11.6	2	10457-14-4	N.S.	N.S.	N.S.
25	**151**	L-Threonine, 3TMS derivative	Threonine, 3TMS	752.9	1375.7	1367	8.7	2	7537-02-2	N.S.	N.S.	N.S.
26	**152**	L-Methionine, TMS derivative	Methionine, TMS	775.5	1408.7	1416	-7.3	2		N.S.	N.S.	N.S.
27	**153**	L-5-Oxoproline, 2TMS derivative	Pyroglutamic acid, 2TMS	842.4	1515.5	1522	-6.5	2	30274-77-2	N.S.	N.S.	N.S.

[a]Full names of metabolites are directly extracted from the NIST11 metabolite database. [b]Metabolite short names are IUPAC or generic names of the identified metabolites. [c]Retention times of deconvoluted peaks were calculated as a mean of RTs of each peak across all samples. [d]Based on these RTs, retention indices (RI) of metabolites were estimated using all even alkane mixture sample (C10-C40). [e]Reported RIs of identified metabolites were extracted from NIST 11 *version 2.3*. [f]Difference between the reported RI and the calculated RI. [g]Identification level of the metabolites. Level 2 when the peaks are identified based on their EI-MS ≥ 80 (%) and RI match (±50). [h]CAS number of identified metabolites. For the metabolites with no CAS number the PubChem CID number has been reported followed by a (*). [i]One-way ANOVA test were performed to see if there are some variables significantly different among the groups: Untreated, Gadodiamide treated, and Gadoteridol treated. Significance of effects within the different pairs of groups is evaluated by *P*-values. "N.S." = Not Significant (P>0.05).

Table S4. List of non-polar and polar compounds detected in plasma by using both NOESY and CPMG ^{1}H-NMR experiments. Short name and *p*-value from one-way ANOVA are indicated for each compound. ANOVA was performed on the three analyzed class.

		One-way ANOVA[i]		
ID #	**Metabolite full name**	**Untreated - Gadodiamide**	**Untreated - Gadoteridol**	**Gadodiamide - Gadoteridol**
1	Lipid 1	1.04E-06	3.66E-06	N.S.
2	Lipid 2	1.07E-05	1.76E-04	N.S.
3	Glyceril lipid 1	8.21E-06	1.61E-05	N.S.
4	Glyceril lipid 2	1.41E-04	8.30E-05	N.S.
5	Glycerophosphocholine	5.72E-05	2.36E-04	N.S.
6	Phosphocholine 1	N.S.	N.S.	N.S.
7	Phosphocholine 2	N.S.	N.S.	N.S.
8	Phosphocholine 3	N.S.	N.S.	N.S.
9	Lipid 3	N.S.	N.S.	N.S.
10	Lipid 4	N.S.	N.S.	N.S.
11	Lipid 5	N.S.	N.S.	N.S.
12	Lipid 6	2.76E-04	3.92E-04	N.S.
13	Lipid 7	2.81E-04	N.S.	N.S.
14	Lipid 8	1.15E-05	2.08E-05	N.S.
15	VLDL_1	6.59E-06	2.08E-05	N.S.
16	LDL_1	1.15E-05	3.45E-06	N.S.
17	LDL_2	6.94E-06	1.69E-04	N.S.
18	VLDL_2	N.S.	N.S.	N.S.
19	Cholesterol	N.S.	N.S.	N.S.
20	Formate	N.S.	N.S.	N.S.
21	Tryptophan	N.S.	N.S.	N.S.
22	Phenylalanine	N.S.	N.S.	N.S.
23	Histidine	N.S.	N.S.	N.S.
24	Tyrosine	N.S.	N.S.	N.S.
25	Fumarate	N.S.	N.S.	N.S.
26	Glucose	N.S.	N.S.	N.S.
27	Lactate	N.S.	N.S.	N.S.
28	Creatine	N.S.	N.S.	N.S.
29	N,N-dimethylglycine	N.S.	4.27E-04	N.S.
30	Citrate	N.S.	N.S.	N.S.
31	Glutamine	N.S.	N.S.	N.S.
32	Succinate	N.S.	N.S.	N.S.
33	Pyruvate	N.S.	N.S.	N.S.
34	Acetate	N.S.	N.S.	N.S.
35	Alanine	N.S.	N.S.	N.S.
36	Isoleucine	N.S.	N.S.	N.S.
37	Valine	N.S.	N.S.	N.S.
38	Leucine	N.S.	N.S.	N.S.