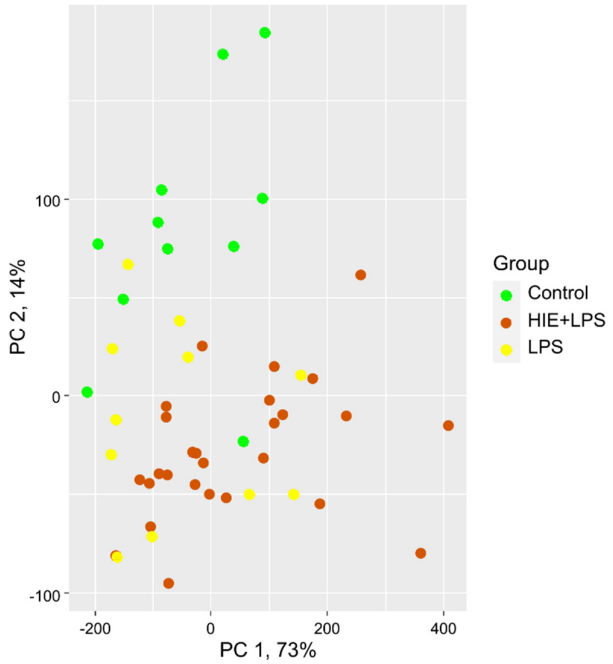

Figure S1. Principal component analysis (PCA) for the study of the effect inflammation influence on ischemia/hypoxia DBS metabolites, whose levels are statistically significantly different when comparing pairwise groups.

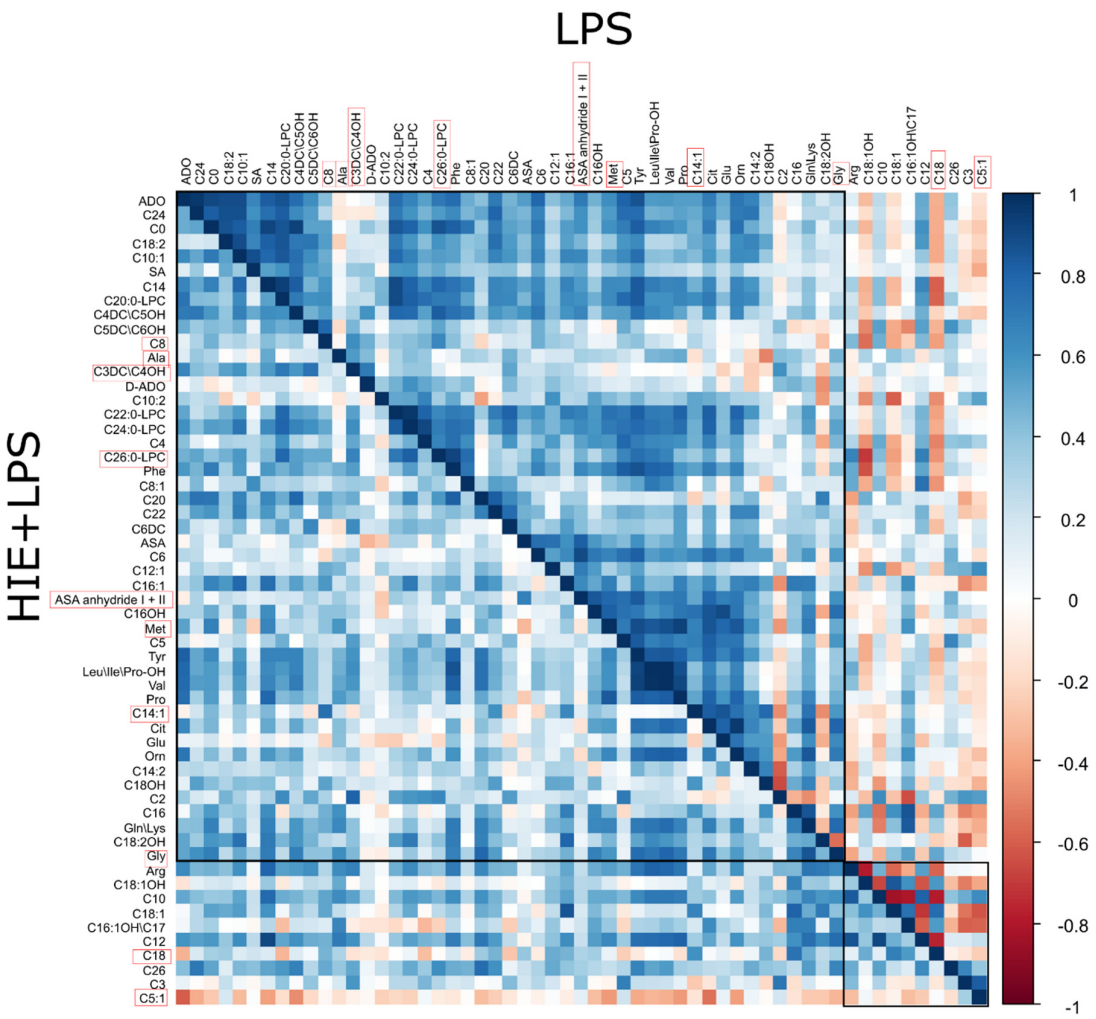

Figure S2. Comparison of correlations for the group with inflammation and the group with inflammation and hypoxia/ischemia. Compounds with a statistically significant difference in levels are highlighted in red, clusters of compounds are highlighted in black squares.

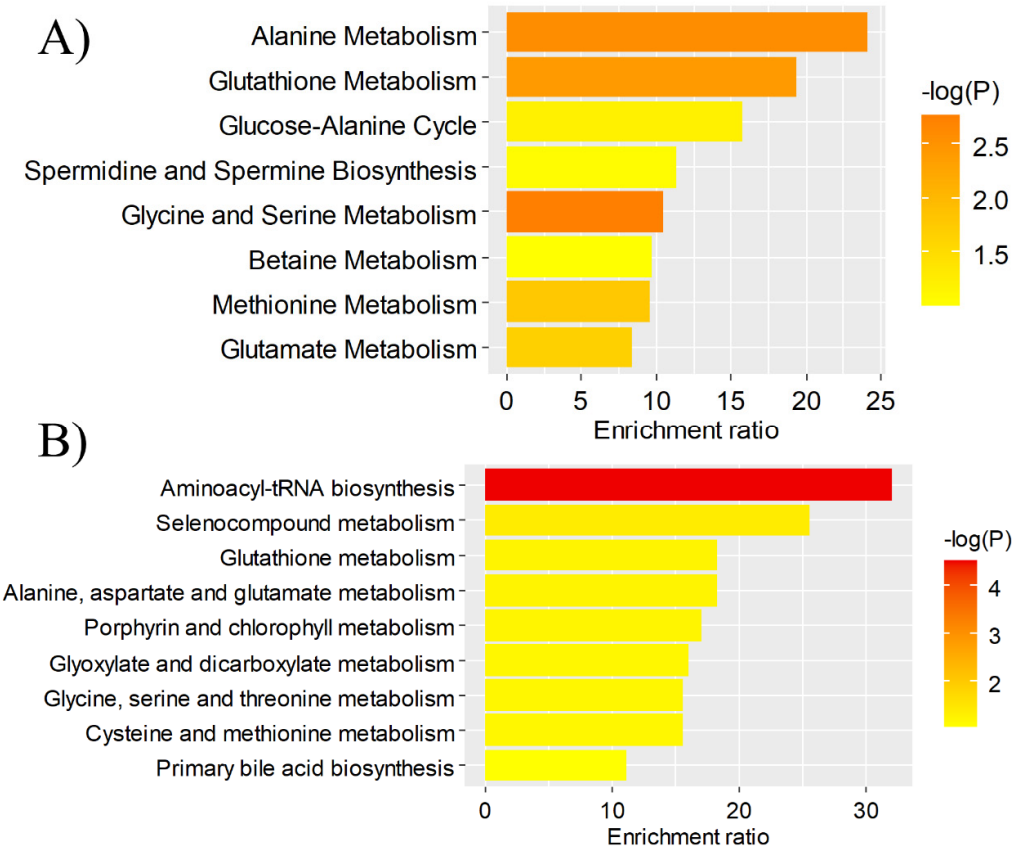

Figure S3. Enrichment levels of statistically significantly enriched pathways during ischemia/hypoxia against the inflammation according to **A**) the SMPDB library, **B**) the KEGG library.

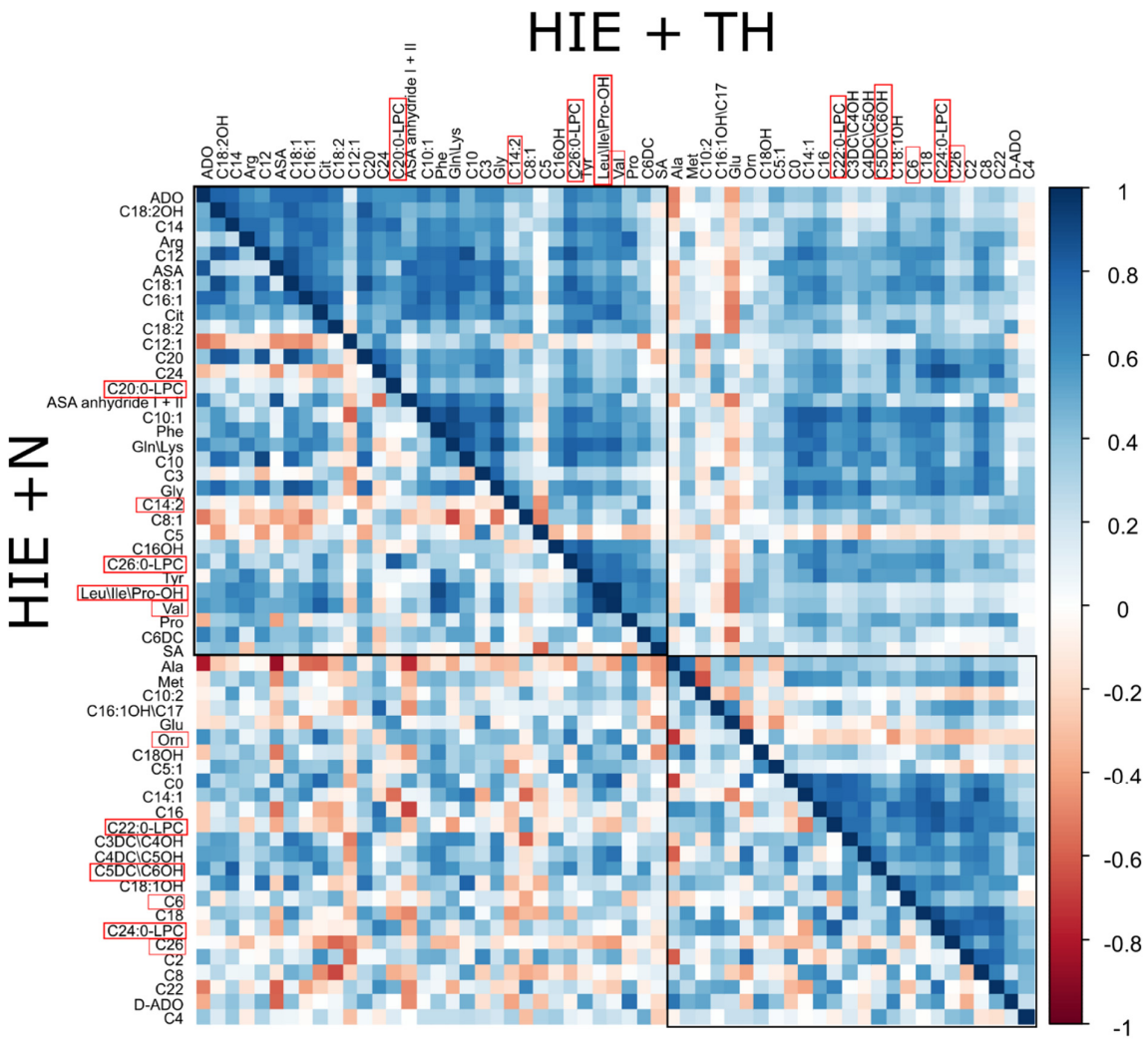

Figure S4. Comparison of correlations for the group with normothermia and the group with hypothermia after hypoxia/ischemia. Compounds with a statistically significant difference in levels are highlighted in red, clusters of compounds are highlighted in black squares.

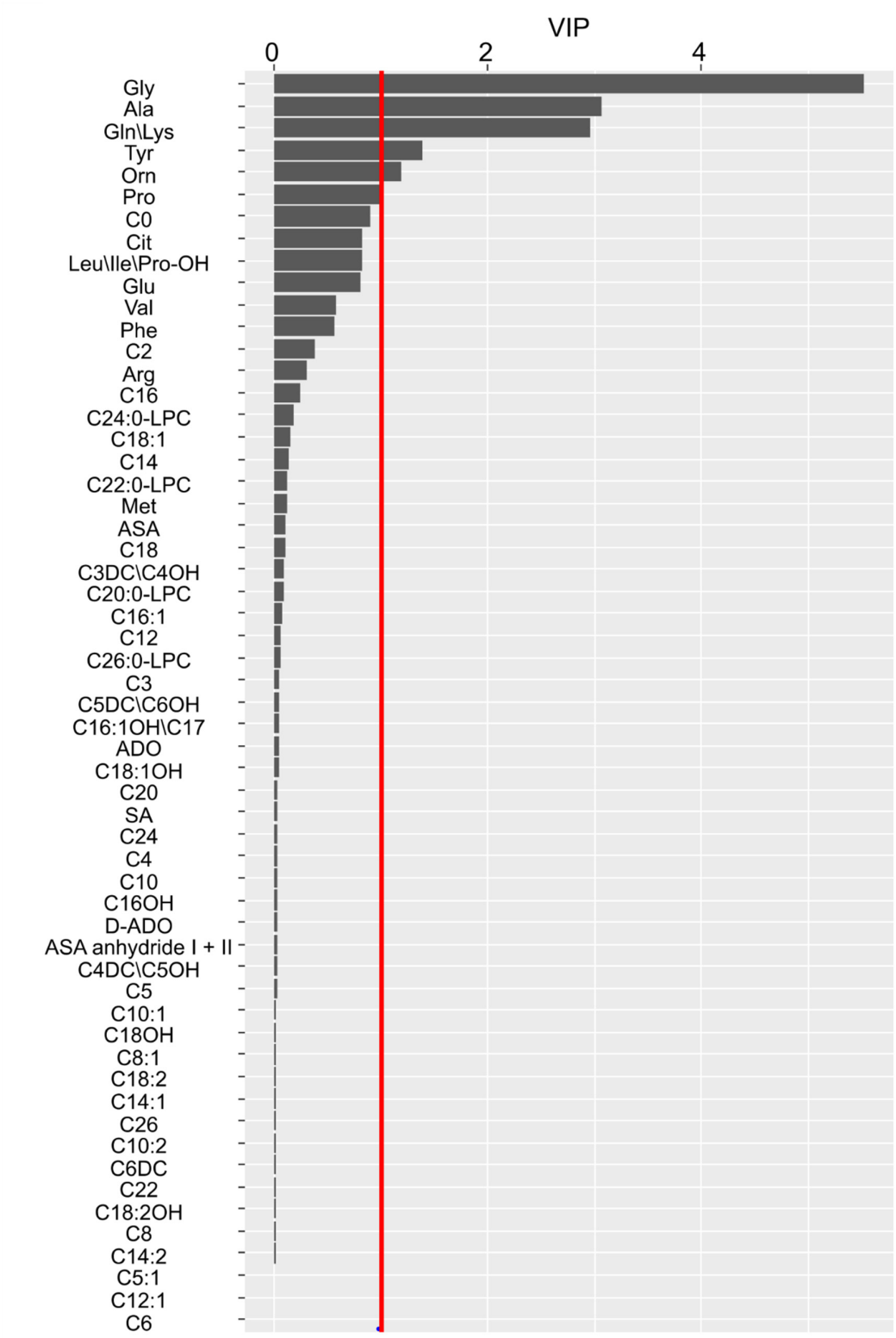

Figure S5. Distribution of variable projection values (VIP) in the OPLS-DA model for diagnosing hypoxia using a blood profile three hours after injury. The red line is threshold (VIP = 1) of more important metabolites.

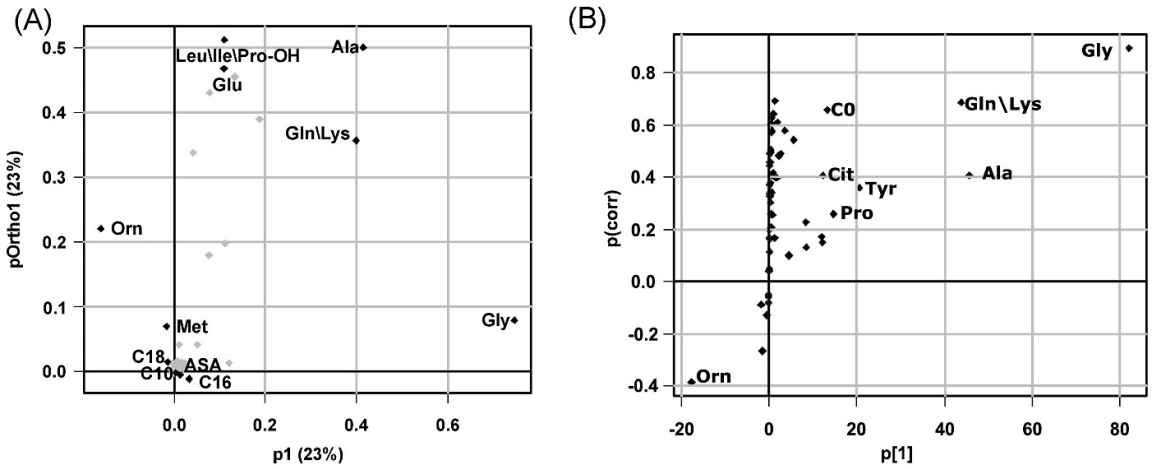

Figure S6. Loading plot (**A**) and S-plot (**B**) of compounds, which are included in the OPLS model for hypoxia detection 3 hours after damage.

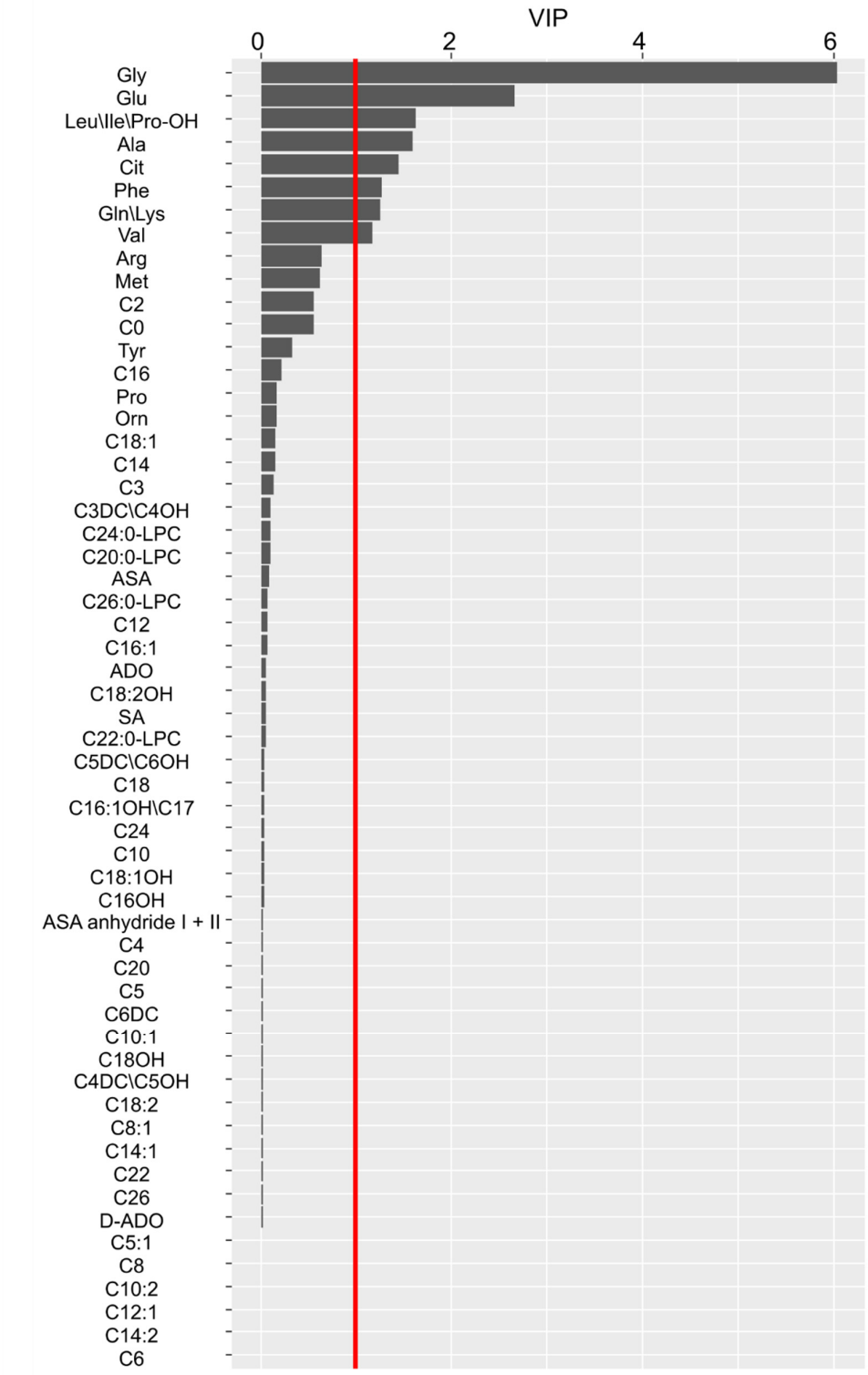

Figure S7. Distribution of variable projection values (VIP) in the OPLS-DA model for diagnosing hypoxia using a blood profile six hours after injury. The red line is threshold (VIP = 1) of more important metabolites.

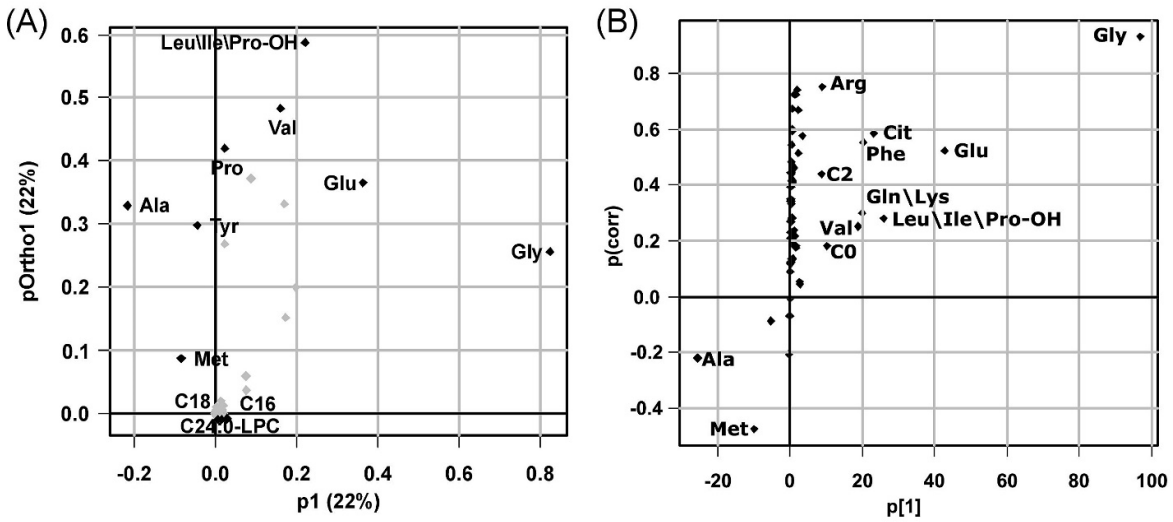

Figure S8. Loading plot (**A**) and S-plot (**B**) of compounds, which are included in the OPLS model for hypoxia detection 6 hours after damage.

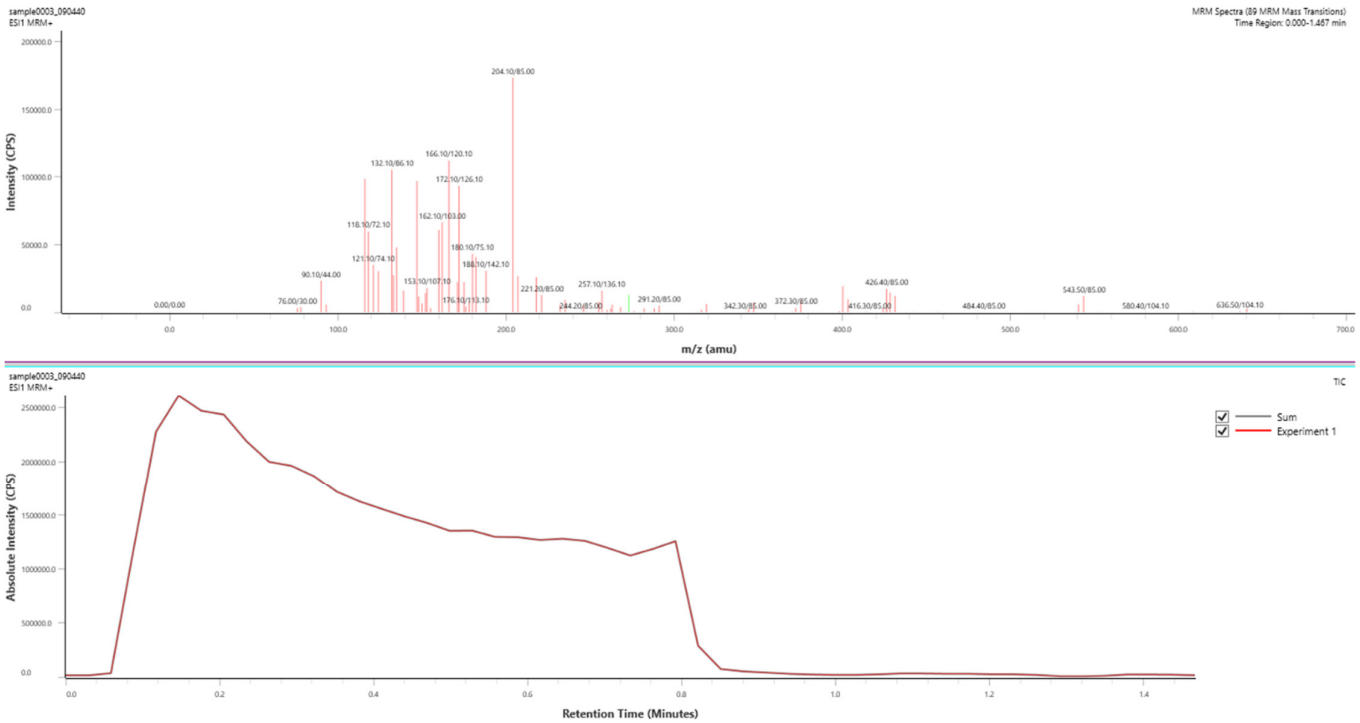

Figure S9. Example of a typical flow injection chromatogram obtained for a low quality control (LC) provided by NeoBase™ 2 Non-derivatized MSMS kit on the QSight 225MD tandem mass spectrometer.

Table S1. Differences in the molecular profile of blood 3 hours after hypoxia compared to control. Changes with FDR < 0.05 are marked bold.

Species	control	3 h	*p*	FDR	FC
Gly	**237(217;279)**	**359(322;384)**	**<0.001**	**0.004**	**1.51**
C3DC\C4OH	0.093(0.082;0.12)	0.15(0.12;0.16)	0.003	0.08	1.61
C5DC\C6OH	0.022(0.019;0.028)	0.034(0.026;0.042)	0.02	0.21	1.55
C10:2	0.002(0.002;0.0028)	0.004(0.003;0.004)	0.02	0.21	2.00
Gln\Lys	149(126;188)	202(187;211)	0.02	0.21	1.36
C26	0.004(0.004;0.005)	0.005(0.005;0.006)	0.02	0.21	1.25
C2	3.9(3.2;4.5)	4.3(4.1;5.6)	0.03	0.21	1.10
C18:2	0.005(0.0042;0.0068)	0.009(0.006;0.01)	0.03	0.21	1.80
C14	0.32(0.28;0.36)	0.42(0.35;0.44)	0.04	0.27	1.31
C24	0.034(0.03;0.035)	0.039(0.035;0.045)	0.05	0.27	1.15

Table S2. Differences in the molecular profile of blood 6 hours after hypoxia compared to control. Changes with FDR < 0.05 are marked bold.

Species	Control	6 h	*p*	FDR	FC
Gly	**237(217;279)**	**376(327;448)**	**<0.001**	**0.002**	**1.59**
C26	**0.004(0.004;0.005)**	**0.0075(0.0058;0.009)**	**<0.001**	**0.009**	**1.88**
Met	**20(18;22)**	**15(13;17)**	**0.002**	**0.03**	**0.75**
C3DC\C4OH	**0.093(0.082;0.12)**	**0.16(0.12;0.18)**	**0.002**	**0.03**	**1.72**
C3	**0.15(0.13;0.16)**	**0.22(0.18;0.28)**	**0.002**	**0.03**	**1.47**
C4	**0.042(0.04;0.048)**	**0.053(0.05;0.061)**	**0.004**	**0.04**	**1.26**
C18:2	**0.005(0.0042;0.0068)**	**0.008(0.007;0.009)**	**0.006**	**0.05**	**1.60**
C2	3.9(3.2;4.5)	5(4.6;5.8)	0.009	0.06	1.28
C5DC\C6OH	0.022(0.019;0.028)	0.031(0.029;0.038)	0.01	0.07	1.41
C24	0.034(0.03;0.035)	0.040(0.037;0.046)	0.01	0.07	1.18
C8:1	0.0075(0.0055;0.008)	0.012(0.0097;0.015)	0.01	0.07	1.60
C20	0.024(0.022;0.03)	0.032(0.029;0.039)	0.02	0.08	1.33
C5	0.03(0.025;0.037)	0.039(0.036;0.045)	0.02	0.11	1.30
SA	0.33(0.32;0.36)	0.37(0.35;0.38)	0.03	0.11	1.12
C10:2	0.002(0.002;0.0028)	0.0035(0.0028;0.0052)	0.03	0.13	1.75

Table S3. Pathways enriched with markers for a three-hour time period after ischemia/hypoxia relative to the control using the SMPDB and KEGG libraries, the number of compounds in them, the degree of enrichment, the number of markers in them, the probability of a random hit.

Library	Pathway	Total	Enrichment, Mean	Hits, Median	*p*, Mean
SMPDB	Ammonia Recycling	32	15.99	2	0.03
SMPDB	Beta Oxidation of Very Long Chain Fatty Acids	17	18.41	1	0.05
SMPDB	Alanine Metabolism	17	18.41	1	0.05
SMPDB	Carnitine Synthesis	22	23.26	2	0.02
KEGG	Glyoxylate and dicarboxylate metabolism	32	34.65	2	0.01
KEGG	Aminoacyl-tRNA biosynthesis	48	31.99	2	0.001
KEGG	Glutathione metabolism	28	24.36	1	0.04
KEGG	Porphyrin and chlorophyll metabolism	30	22.74	1	0.04
KEGG	Glycine, serine and threonine metabolism	33	20.67	1	0.049

Table S4. Pathways enriched with markers for a six-hour time period after ischemia/hypoxia relative to the control using the SMPDB and KEGG libraries, the number of compounds in them, the degree of enrichment, the number of markers in them, the probability of a random hit.

Library	Pathway	Total	Enrichment, Mean	Hits, Median	*p*, Mean
SMPDB	Oxidation of Branched Chain Fatty Acids	26	19.61	2	0.004
SMPDB	Methionine Metabolism	43	11.90	2	0.01
SMPDB	Glycine and Serine Metabolism	59	8.70	2	0.02
KEGG	Aminoacyl-tRNA biosynthesis	48	32.00	2	<0.001
KEGG	Glutathione metabolism	28	27.40	1	0.04
KEGG	Porphyrin and chlorophyll metabolism	30	25.58	1	0.04
KEGG	Glyoxylate and dicarboxylate metabolism	32	23.98	1	0.04
KEGG	Glycine, serine and threonine metabolism	33	23.26	1	0.04
KEGG	Cysteine and methionine metabolism	33	23.26	1	0.04

Table S5. Differences in the molecular profile of blood after hypothermic regimen compared to normothermic regimen in a rat model of hypoxic-ischemic injury.

Compounds	Normotermia	Hypotermia	*p*	FDR	FC
C22:0-LPC	1.5(1.3;1.7)	1.2(1.1;1.4)	0.006	0.20	0.80
C24:0-LPC	2.3(2.1;2.7)	1.9(1.8;2.2)	0.007	0.20	0.83
Orn	17(13;21)	25(20;41)	0.01	0.23	1.47
C26	0.007(0.0062;0.008)	0.006(0.005;0.007)	0.02	0.25	0.86
Val	110(104;124)	146(120;171)	0.02	0.25	1.33
C20:0-LPC	2.8(1.9;3.2)	2.1(1.7;2.5)	0.03	0.25	0.75
C26:0-LPC	0.49(0.42;0.52)	0.39(0.36;0.44)	0.04	0.25	0.80
C5DC\C6OH	0.043(0.034;0.048)	0.029(0.027;0.041)	0.04	0.25	0.67
Leu\Ile\Pro-OH	160(154;188)	209(177;229)	0.04	0.25	1.31
C6	0.004(0.003;0.005)	0.003(0.002;0.0032)	0.04	0.25	0.75
C14:2	0.007(0.0062;0.0087)	0.006(0.005;0.007)	0.05	0.25	0.86

Table S6. Parameters of the logistic regression model for the diagnosis of ischemia/hypoxia after 3 hours. Coefficient β, confidence interval CI β, Wald criteria Z, coefficient zero-probability P are provided.

Variable	β	CI β	Z	*p*
Intercept	-6.64	-14.06 - -2.52	-2.43	0.02
Glycine^2	$7.37*10^{-5}$	$3.01*10^{-5}$ - $1.56*10^{-4}$	2.49	0.01

Table S7. Parameters of the logistic regression model for the diagnosis of ischemia/hypoxia after 6 hours. Coefficient β, confidence interval CI β, Wald criteria Z, coefficient zero-probability P are provided

Variable	β	CI β	Z	*p*
Intercept	-9.13	-23.50 - -3.14	-1.96	0.05
Glycine^2	$9.54*10^{-5}$	$3.36*10^{-5}$ - $2.43*10^{-4}$	1.98	0.048

Table S8. MS parameters used for FIA-MS/MS analysis by NeoBase™ 2 Non-derivatized MSMS kit. For each compound, MRM transition (Q1 and Q3), entrance voltage, collision cell lens 2, collision energy, and dwell time are shown. IS - internal standard.

Compound	Q1	Q3	Entrance Voltage	Dwell Time	Collision Cell Lens 2	Collision Energy
Gly	76	30	30	15	-100	-50
Gly IS	78	32	30	15	-100	-50
Ala	90,1	44	30	15	-100	-50
Ala IS	93,1	47,1	30	15	-100	-50
Pro	116,1	70,1	30	15	-100	-50
Pro IS	121,1	74,1	30	15	-100	-50
Val	118,1	72,1	30	15	-100	-50
Val IS	124,1	77,1	30	15	-100	-50
Leu\Ile\Pro-OH	132,1	86,1	30	15	-100	-50
Leu\Ile\Pro-OH IS	135,1	89,1	30	15	-100	-50
Orn	133,1	70,1	30	15	-100	-50
Orn IS	139,1	76,1	30	15	-100	-50
Gln\Lys	147,1	84	30	15	-100	-50
Glu	148,1	84	30	15	-100	-50
Gln\Lys IS	152,1	88,1	30	15	-100	-50
Met	150,1	104,1	30	15	-100	-50
Met IS	153,1	107,1	30	15	-100	-50
SA	155,1	109,1	30	15	-100	-50
SA IS	160,1	114,1	30	15	-100	-50
Phe	166,1	120,1	30	15	-100	-50
Phe IS	172,1	126,1	30	15	-100	-50
Arg	175,1	70,1	30	15	-100	-50
Arg IS	180,1	75,1	30	15	-100	-50
Cit	176,1	113,1	30	15	-100	-50
Cit IS	178,1	115,1	30	15	-100	-50
Tyr	182,1	136,1	30	15	-100	-50
Tyr IS	188,1	142,1	30	15	-100	-50
D-ADO	252,1	136,1	30	15	-100	-50
D-ADO IS	257,1	136,1	30	15	-100	-50
ADO	268,1	136,1	30	15	-100	-50
ADO IS	273,1	136,1	30	15	-100	-50
ASA anhydride I + II	273,1	70,1	30	15	-100	-50
ASA	291,1	70,1	30	15	-100	-50
C0	162,1	103	30	15	-100	-50
C0 IS	171,2	103	30	15	-100	-50
C2	204,1	85	30	15	-100	-50
C2 IS	207,1	85	30	15	-100	-50
C3	218,1	85	30	15	-100	-50
C3 IS	221,2	85	30	15	-100	-50
C3DC\C4OH	248,1	85	30	15	-100	-50
C4	232,2	85	30	15	-100	-50
C4 IS	235,2	85	30	15	-100	-50

C5:1	244,2	85	30	15	-100	-50
C5	246,2	85	30	15	-100	-50
C4DC\C5OH	262,2	85	30	15	-100	-50
C5 IS	255,2	85	30	15	-100	-50
C6	260,2	85	30	15	-100	-50
C6 IS	263,2	85	30	15	-100	-50
C5DC\C6OH	276,2	85	30	15	-100	-50
C6DC	290,2	85	30	15	-100	-50
C5DC\C6OH IS	282,2	85	30	15	-100	-50
C8:1	286,2	85	30	15	-100	-50
C8	288,2	85	30	15	-100	-50
C8 IS	291,2	85	30	15	-100	-50
C10:2	312,2	85	30	15	-100	-50
C10:1	314,2	85	30	15	-100	-50
C10	316,2	85	30	15	-100	-50
C10 IS	319,3	85	30	15	-100	-50
C12:1	342,3	85	30	15	-100	-50
C12	344,3	85	30	15	-100	-50
C12 IS	347,3	85	30	15	-100	-50
C14:2	368,3	85	30	15	-100	-50
C14:1	370,3	85	30	15	-100	-50
C14	372,3	85	30	15	-100	-50
C14OH	388,3	85	30	15	-100	-50
C14 IS	375,3	85	30	15	-100	-50
C16:1	398,3	85	30	15	-100	-50
C16	400,3	85	30	15	-100	-50
C16:1OH\C17	414,3	85	30	15	-100	-50
C16OH	416,3	85	30	15	-100	-50
C16 IS	403,4	85	30	15	-100	-50
C18:2	424,3	85	30	15	-100	-50
C18:1	426,4	85	30	15	-100	-50
C18	428,4	85	30	15	-100	-50
C18:2OH	440,3	85	30	15	-100	-50
C18:1OH	442,4	85	30	15	-100	-50
C18OH	444,4	85	30	15	-100	-50
C18 IS	431,4	85	30	15	-100	-50
C20	456,4	85	30	15	-100	-50
C22	484,4	85	30	15	-100	-50
C24	512,5	85	30	15	-100	-50
C26	540,5	85	30	15	-100	-50
C26 IS	543,5	85	30	15	-100	-50
C20:0-LPC	552,4	104,1	30	15	-100	-50
C22:0-LPC	580,4	104,1	30	15	-100	-50
C24:0-LPC	608,5	104,1	30	15	-100	-50
C26:0-LPC	636,5	104,1	30	15	-100	-50
C26:0-LPC IS	640,5	104,1	30	15	-100	-50

Table S9. Results of mass-spectrometry analysis, include information about MRM transition, retention time, preprocession parametr, peak height and area, concentration in fmol/mkl, for serum metabolites and internal standards in study sample, quality control sample, low concentration sample and hight concentration sample. Containing in individual excel file.