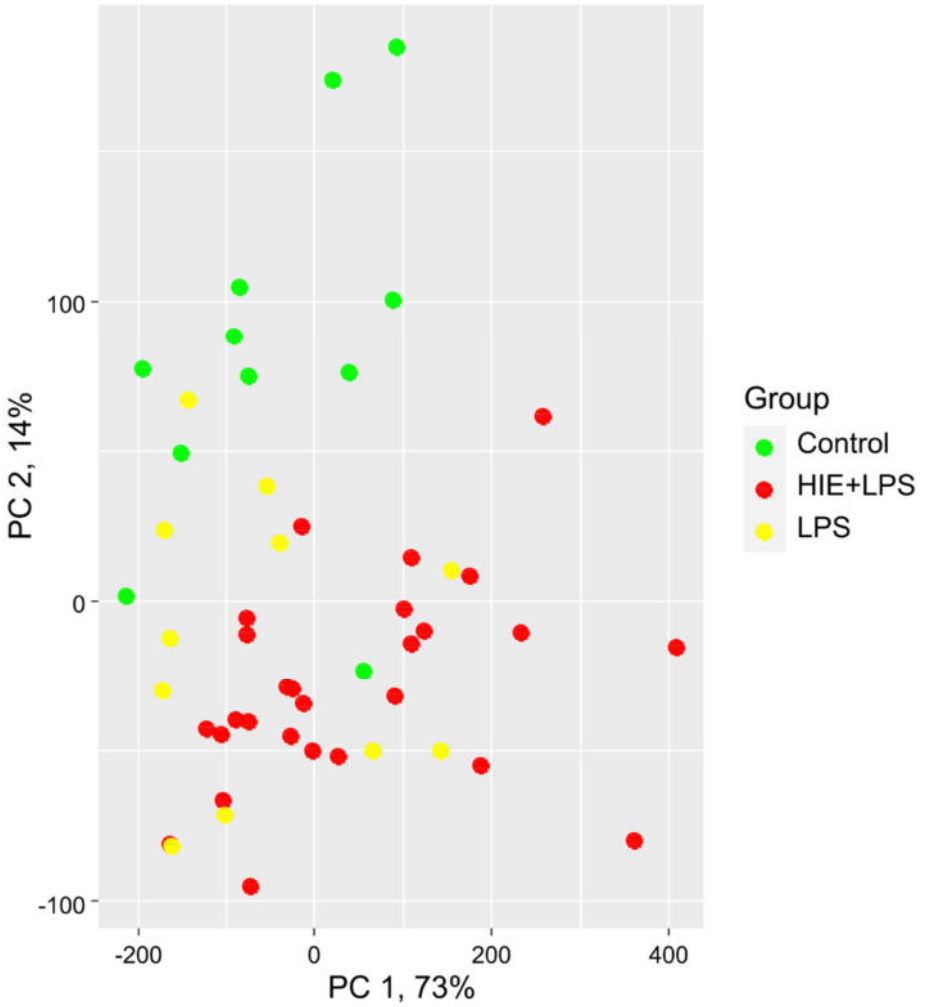

Figure S1. Principal component analysis (PCA) for the study of the effect inflammation influence on ischemia/hypoxia DBS metabolites, whose levels are statistically significantly different when comparing pairwise groups.

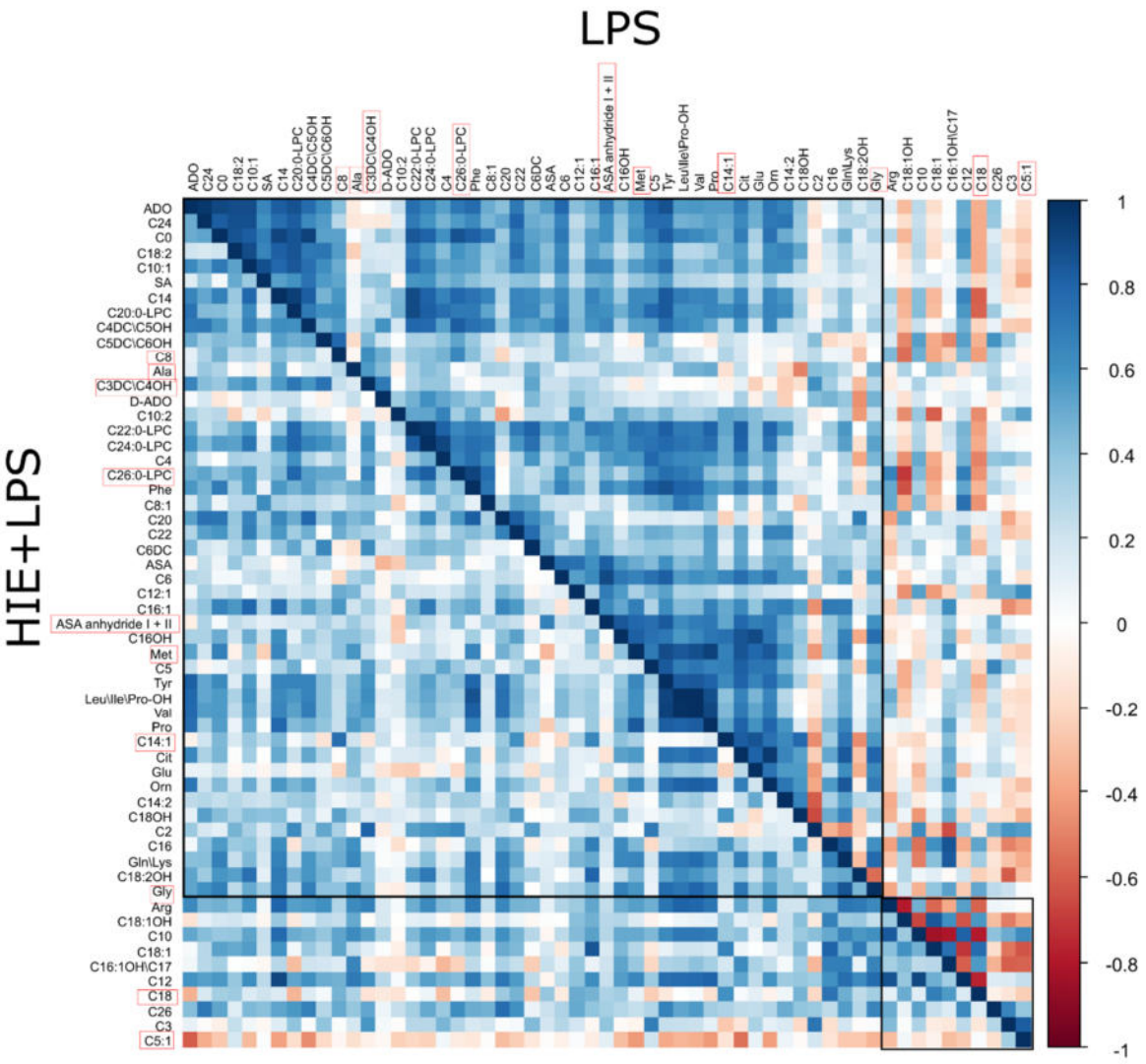

Figure S2. Comparison of correlations for the group with inflammation and the group with inflammation and hypoxia/ischemia. Compounds with a statistically significant difference in levels are highlighted in red, clusters of compounds are highlighted in black squares.

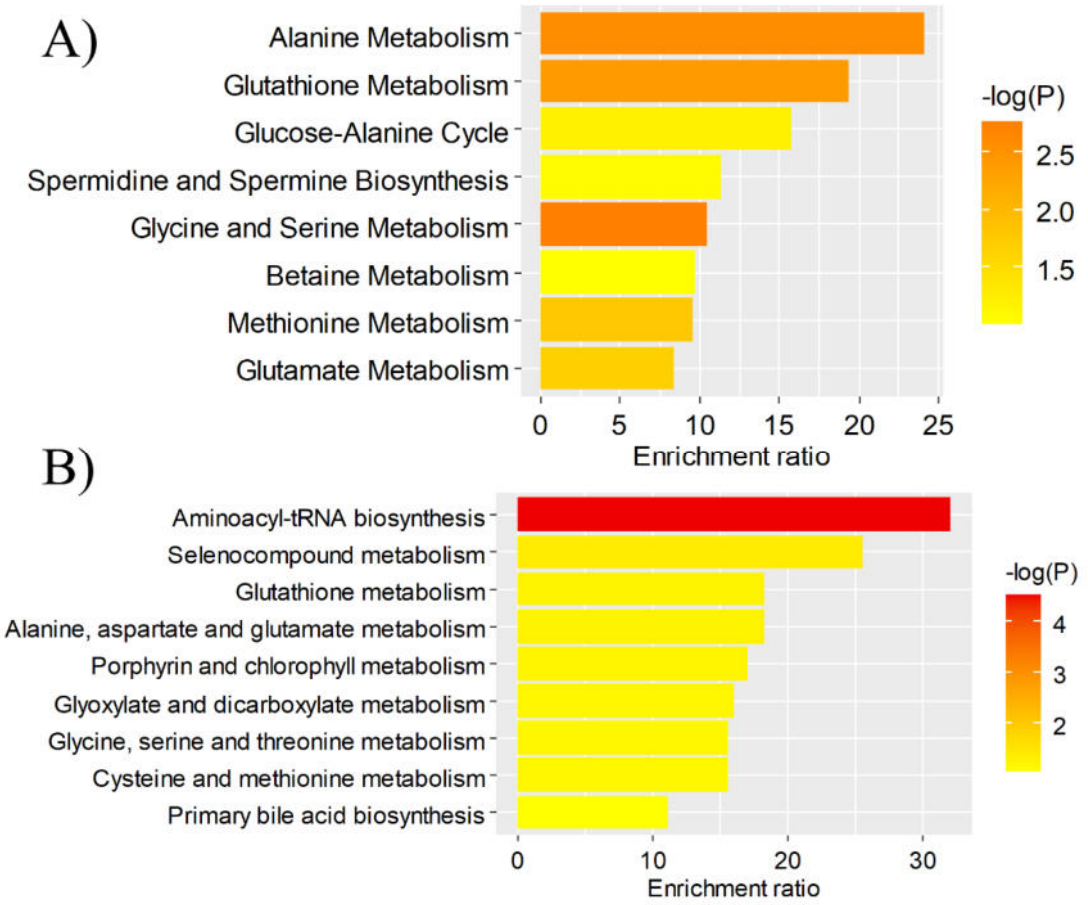

Figure S3. Enrichment levels of statistically significantly enriched pathways during ischemia/hypoxia against the inflammation according to a) the SMPDB library, b) the KEGG library.

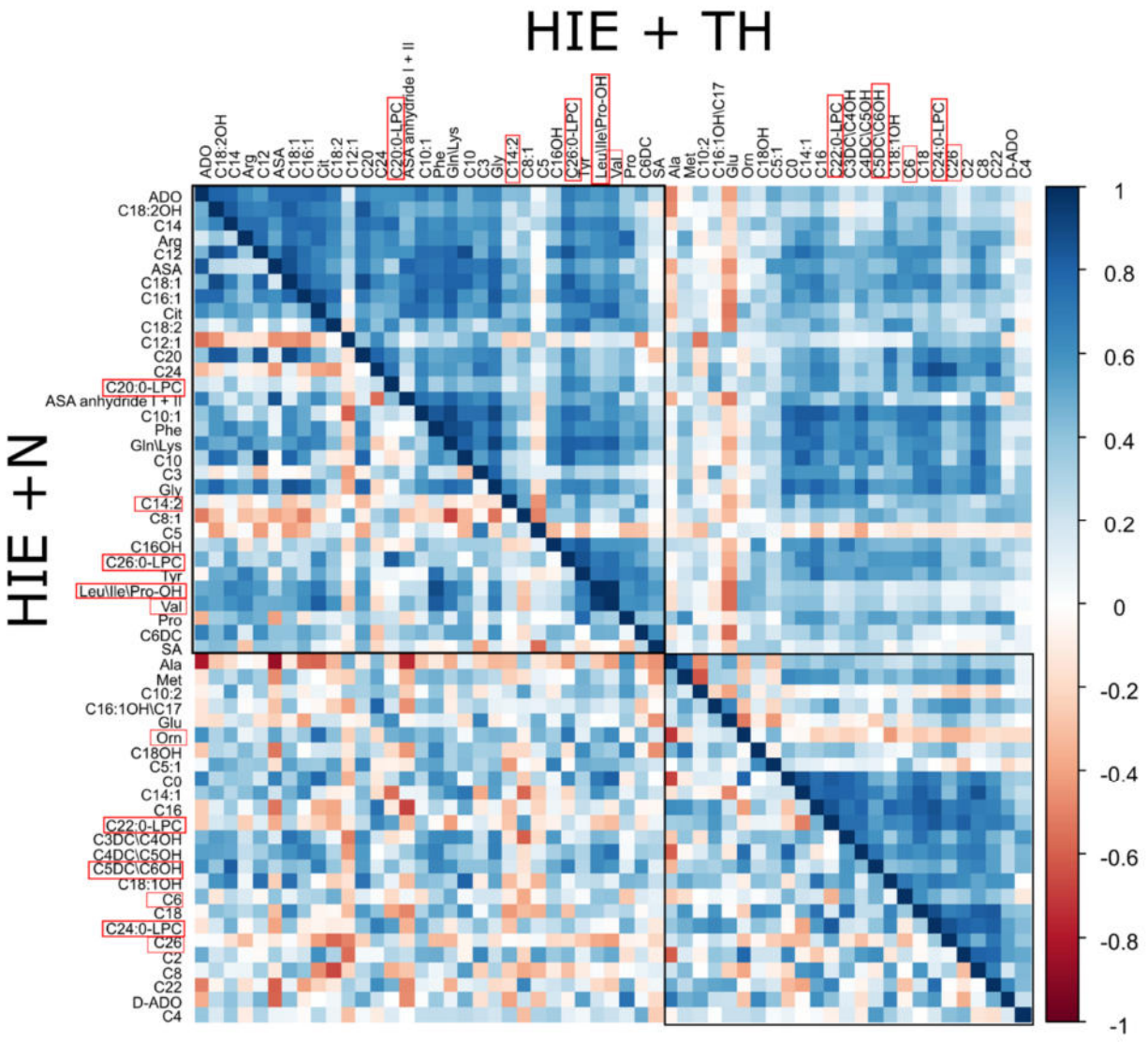

Figure S4. Comparison of correlations for the group with normothermia and the group with hypothermia after hypoxia/ischemia. Compounds with a statistically significant difference in levels are highlighted in red, clusters of compounds are highlighted in black squares.

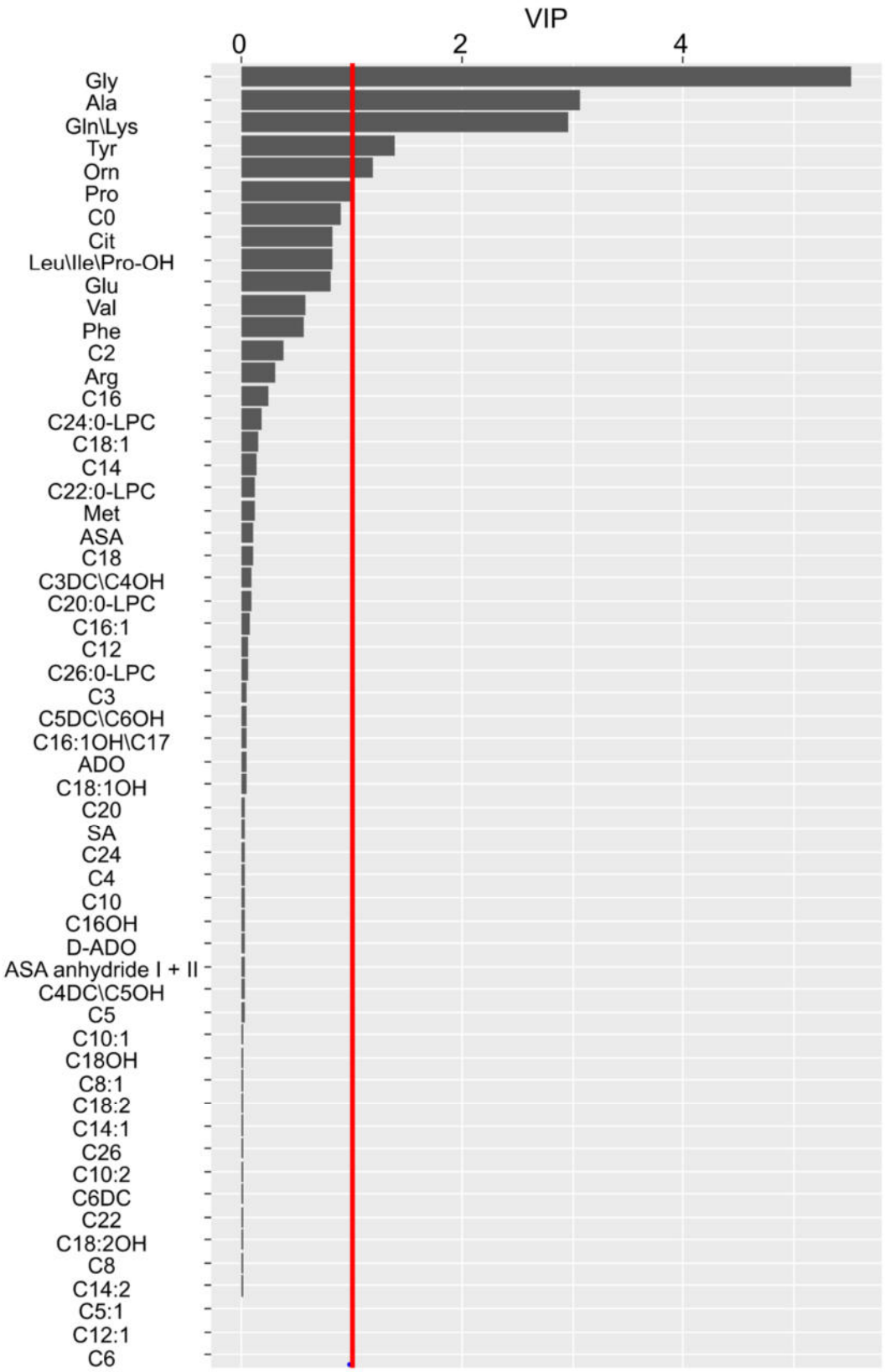

Figure S5. Distribution of variable projection values (VIP) in the OPLS-DA model for diagnosing hypoxia using a blood profile three hours after injury.

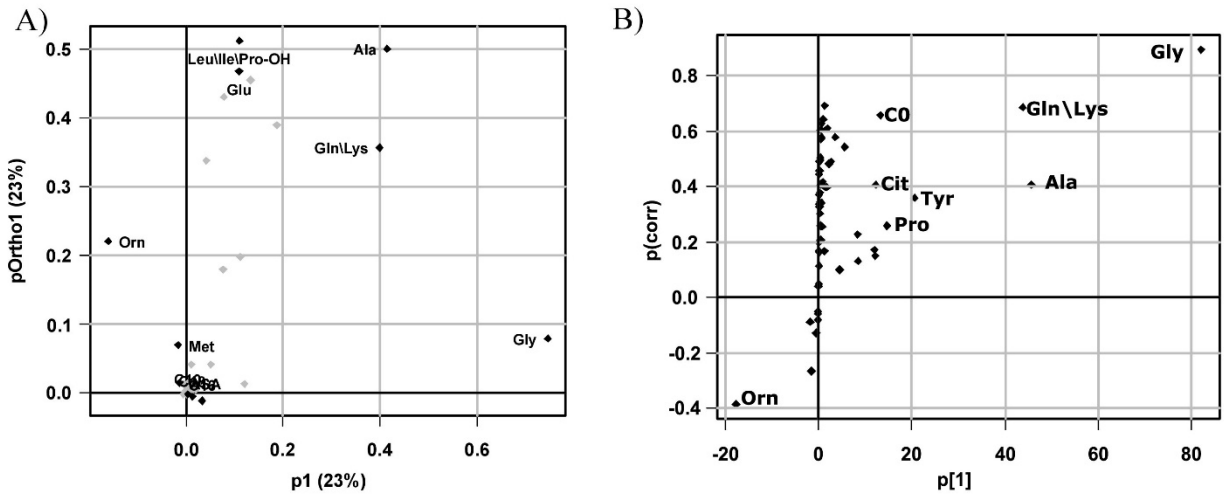

Figure S6. Loading plot a) and S-plot (b) of compounds, which are included in the OPLS model for hypoxia detection 3 hours after damage.

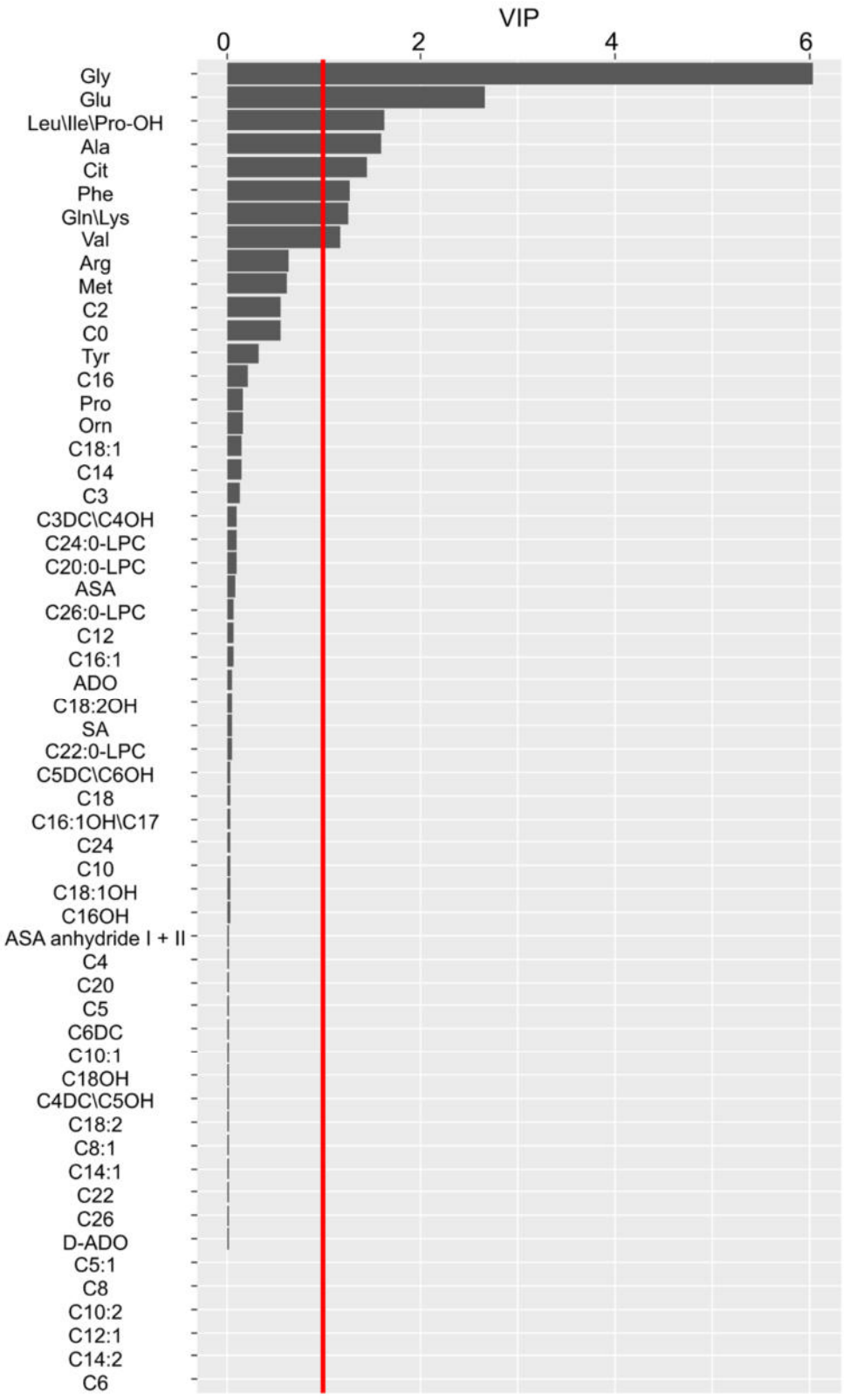

Рисунок S7. Distribution of variable projection values (VIP) in the OPLS-DA model for diagnosing hypoxia using a blood profile six hours after injury.

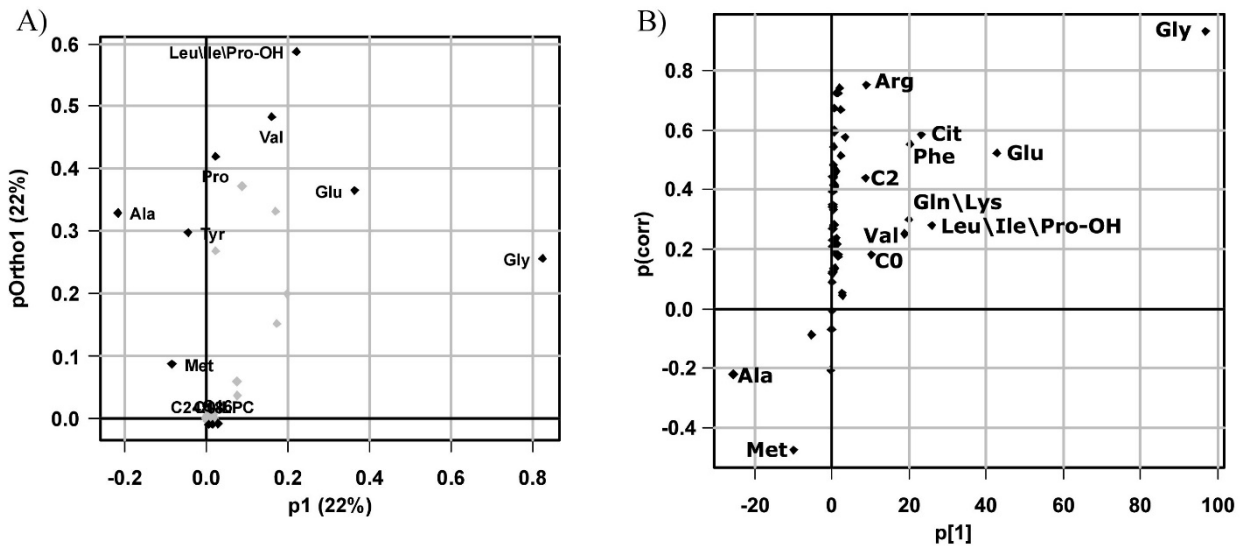

Figure S8. Loading plot a) and S-plot (b) of compounds, which are included in the OPLS model for hypoxia detection 6 hours after damage.

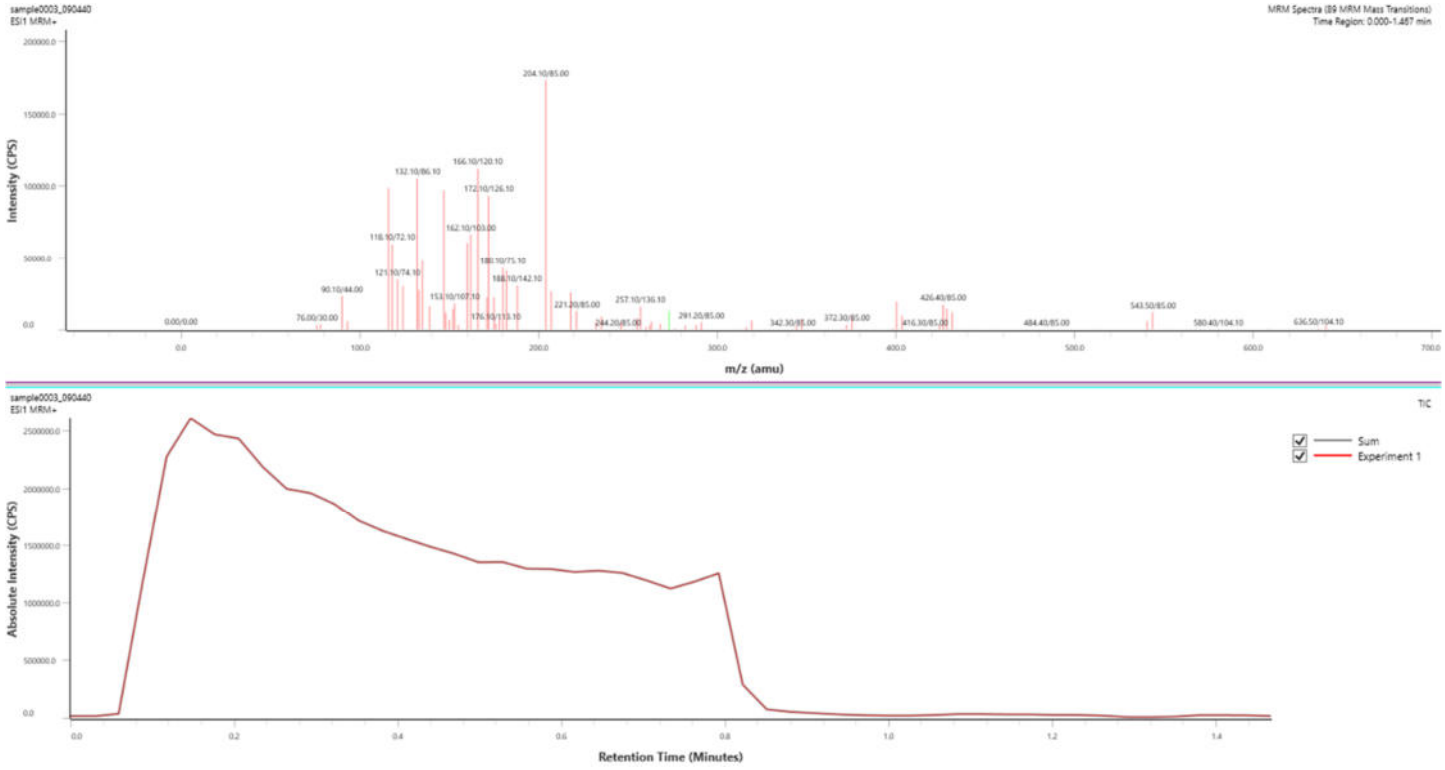

Figure S9. Example of a typical flow injection chromatogram obtained for a low quality control (LC) provided by NeoBase™ 2 Non-derivatized MSMS kit on the QSight 225MD tandem mass spectrometer.

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	3h	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	6h	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 S6. 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 S5. 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 S6. 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 S7. 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