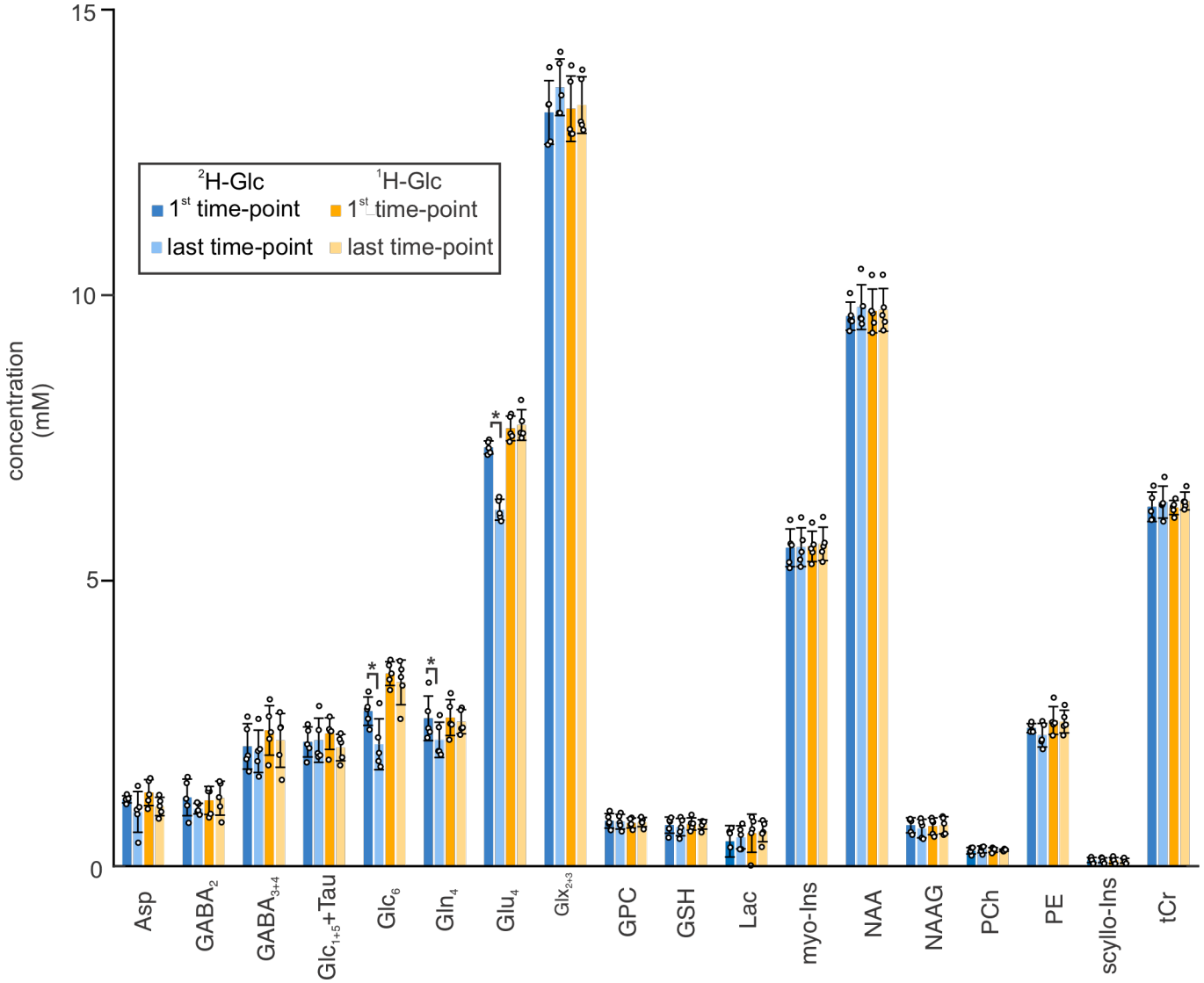
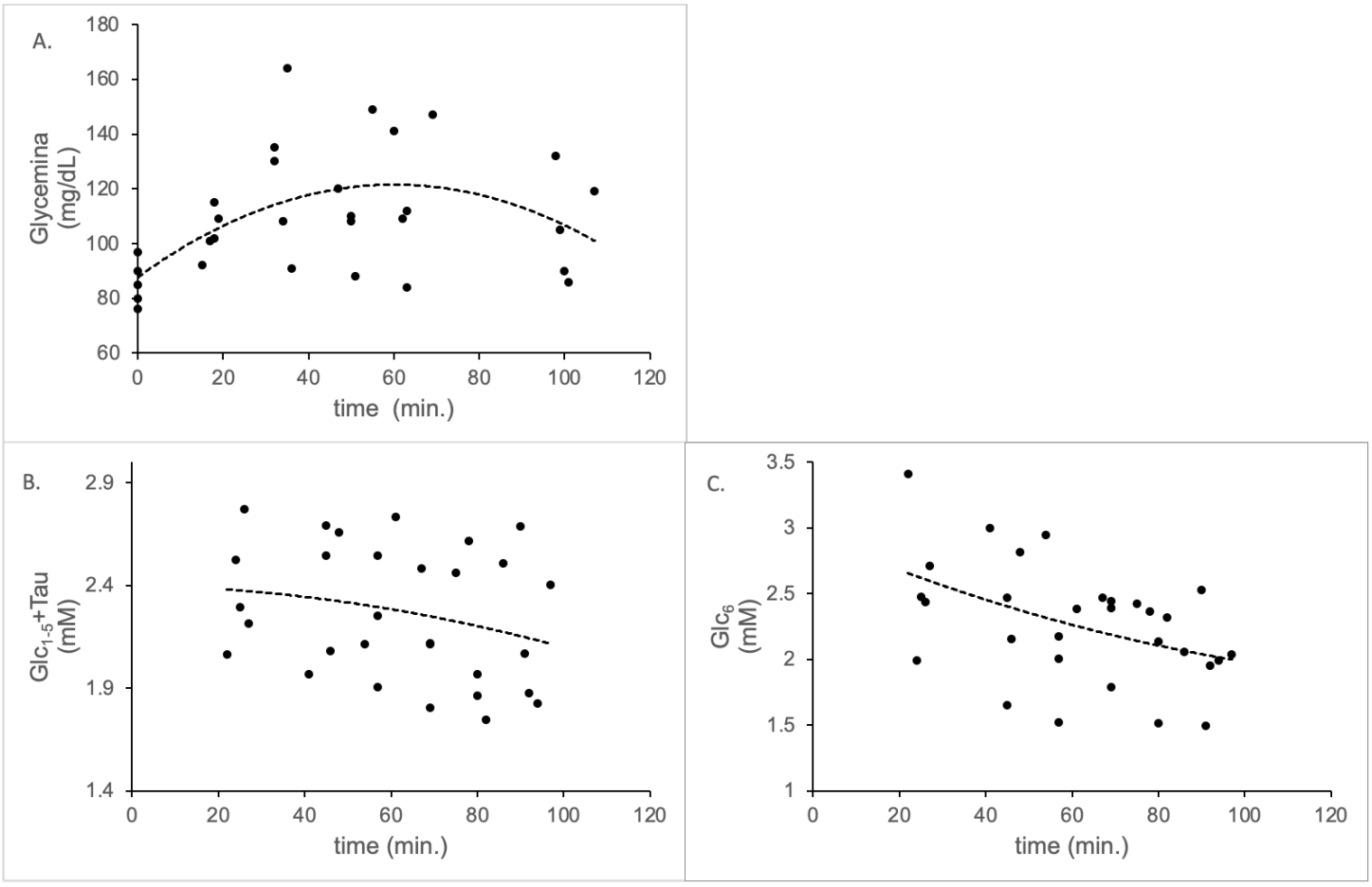
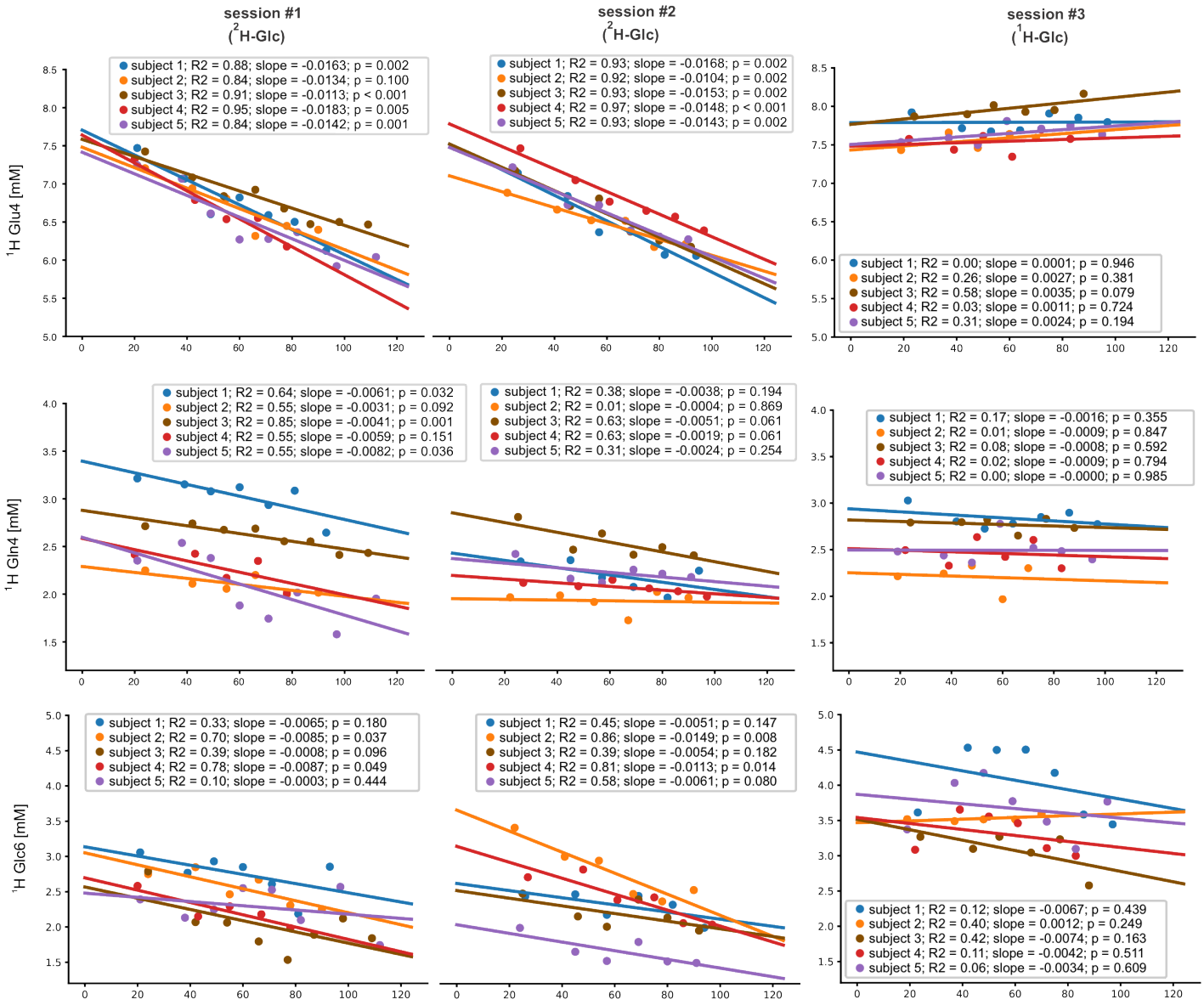


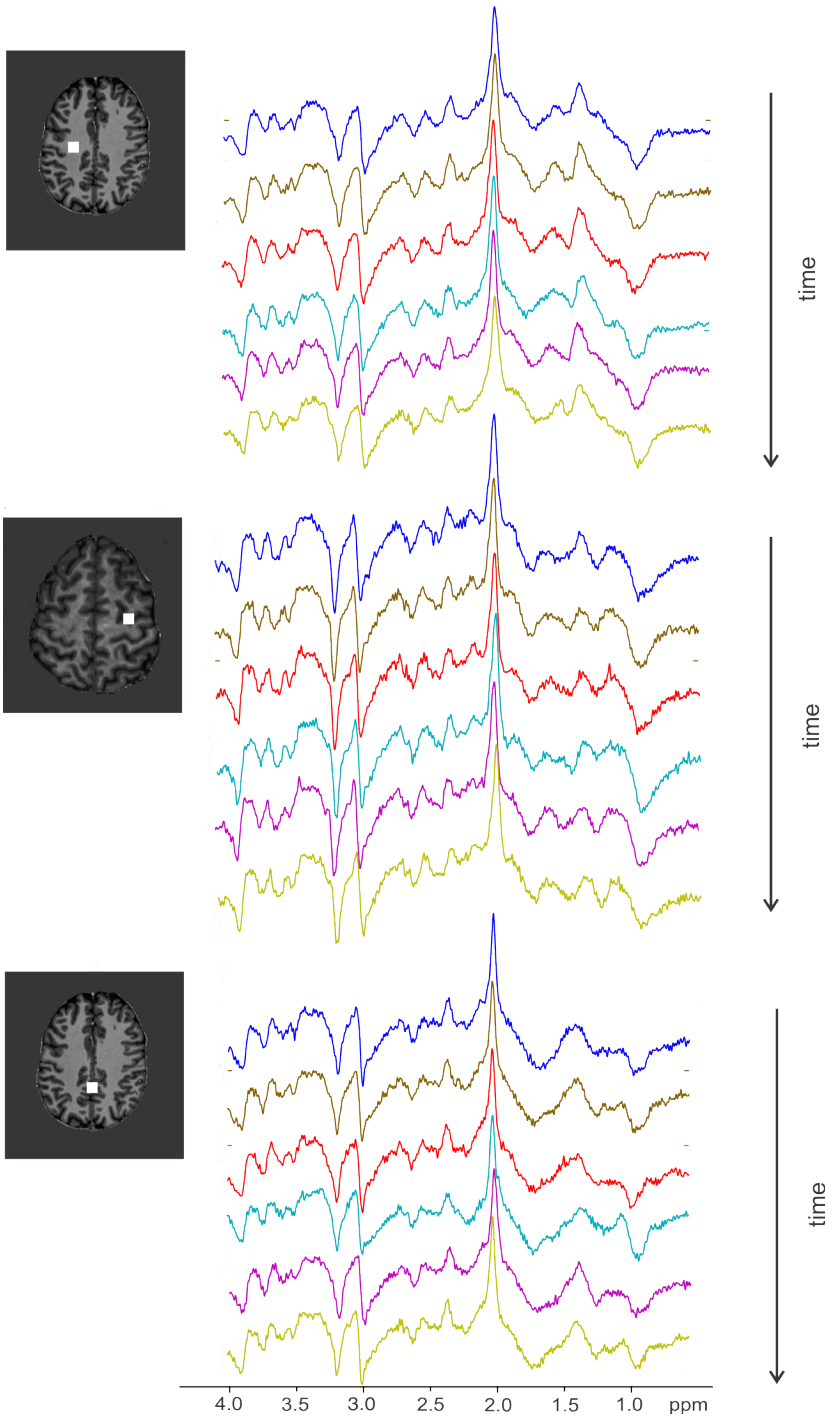
Supplementary Fig.1 | Quantification of SV-MR spectra obtained in posterior cingulate with single-voxel proton MRS. Bar diagrams demonstrate means (errors bars represent standard error of the mean) of concentration comparisons quantified from the first and last time-point spectra following ^{2}H-Glc and ^{1}H-Glc administration for 5 healthy volunteers. Peaks that originated from the specific carbon position undergoing deuteration, namely, the 6th carbon position for Glc (Glc$_6$) the 4th carbon position for Glu (Glu$_4$) and Gln (Gln$_4$) and the 2nd carbon position for GABA (GABA$_2$), were separated. Concentrations were compared with a standard, two-tailed, paired t-test between the first and last time-point within the ^{2}H-Glc and ^{1}H-Glc sessions. Concentration differences in Glc$_6$ ($p = 0.0086$), Gln$_4$ ($p = 0.0029$) and Glu$_4$ ($p = 0.0003$, no correction for multiple comparisons) appeared significant and reflect continuous concentration decrease over time, whereas all other metabolites were stable.



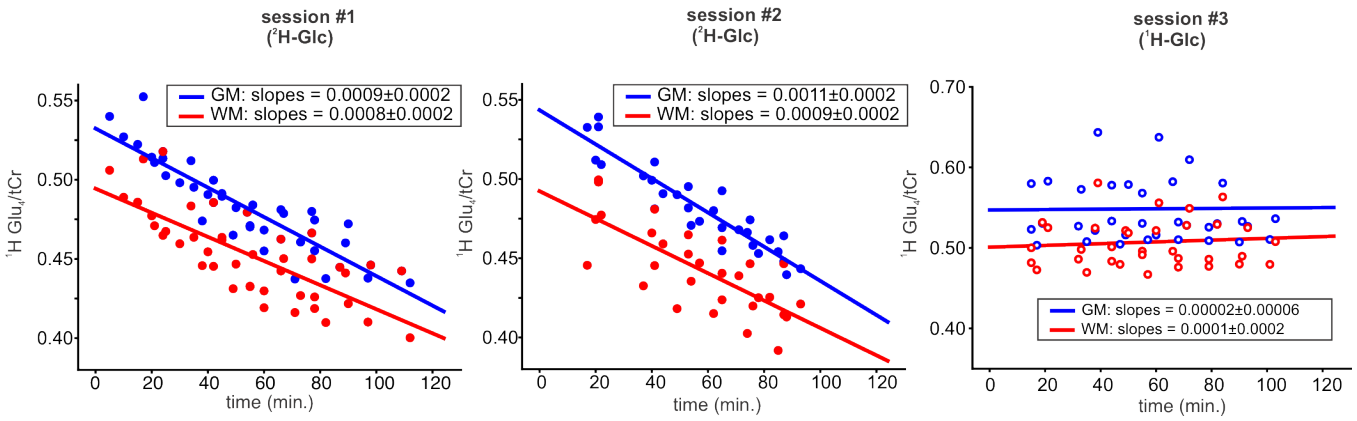
Supplementary Fig. 2 l Glycemia (panel A) and the separated glucose spectra components $Glc_{1\text{-}5+Tau}$ (panel B) and Glc_6 (panel C) measured in the brain. The values were measured in the session #2, after ^{2}H-Glc oral administration in 5 volunteers. The glycemic time-course reflects prolonged mild hyperglycemia as expected after oral administration of glucose load. While the $Glc_{1\text{-}5}$ is the non-deuterated part of the glucose molecule and according to LCModel strongly correlates with Tau, Glc_6 stands for the deuterated part of Glc and could be analyzed separately. Glc_6 time-course shows decrease reflecting the continuous ^{2}H-Glc supply into the brain.



Supplementary Fig. 3 | Linear fits of time-courses measured in 5 subjects in 3 sessions. While session number #1 and #2 were measured after oral administration of deuterated glucose, the session number #3 was conducted as a control experiment after administration of normal dextrose (non-deuterated Glc). Data were fitted with linear regression. The significance of the slopes was assessed by two-tailed test. P-values were not corrected for multiple comparisons.



Supplementary Fig. 4 l Example of spectra time-series obtained from one individual in the white matter, in the posterior cingulate and precentral gyrus using 3D-^{1}H-MRSI.



Supplementary Fig. 5 | Repeatability of ^{1}H-MRSI fits. The time-courses from averaged regional maps were linearly fitted. The session #1 and #2 were scanned after 2H-Glc ingestion, data in session #3 were acquired after 1H-Glc ingestion as a control condition.

Metabolite	Posterior cingulum						Whole gray matter						Whole white matter					
	conc.	CV	Δconc.		Δconc.		conc.	CV	Δconc.		Δconc.		conc.	CV	Δconc.		Δconc.	
	(mean±SD) (/tCr)	(mean±SD) (%)	(mean±SD) (%)	p-value	(mean±SD) (%)	p-value	(mean±SD) (/tCr)	(mean±SD) (%)	(mean±SD) (%)	p-value	(mean±SD) (%)	p-value	(mean±SD) (/tCr)	(mean±SD) (%)	(mean±SD) (%)	p-value	(mean±SD) (%)	p-value
Asp	1.29±0.23	15.0±6.2	19.4±27.6	0.2002	17.1±18.0	0.11	0.44±0.02	6.2±8.0	−5.9±6.4	0.107	−3.4±1.8	0.01	0.47±0.03	3.9±2.4	1.6±1.5	0.0848	−2.3±4.7	0.36
GABA	–	–	–	–	–	–	0.23±0.02	2.9±1.7	−3.0±4.4	0.215	−5.1±7.4	0.20	0.23±0.01	2.8±1.1	−2.2±4.8	0.3675	−3.9±7.1	0.26
$GABA_2$	1.15±0.25	9.8±1.9	11.9±21.4	0.1909	−3.6±15.6	0.60	–	–	–	–	–	–	–	–	–	–	–	–
$GABA_{3+4}$	2.38±0.43	14.1±7.5	−2.9±16.8	0.5735	−6.1±19.7	0.44	–	–	–	–	–	–	–	–	–	–	–	–
Glc_{1-5}+Tau	2.32±0.28	12±4.3	−1.3±11.8	0.8136	9.2±17.4	0.22	–	–	–	–	–	–	–	–	–	–	–	–
Glc_{1-5}	1.06±0.23	23.9±9.6	1.0±24.4	0.8801	16.8±34.4	0.22	–	–	–	–	–	–	–	–	–	–	–	–
Glc_6	3.37±0.21	8.2±4.3	21.8±10.3	**0.0086***	4.5±10.8	0.38												
Gln	–	–	–	–	–	–	0.30±0.03	6.3±4.1	−4.8±7.9	0.288	−3.1±8.5	0.46	0.30±0.02	5.5±3.1	0.3±6.2	0.8439	−9.4±8.8	0.07
Gln_{2+3}	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Gln_4	2.60±0.31	4.5±1.6	14.4±3.7	**0.0029***	2.4±4.4	0.25	–	–	–	–	–	–	–	–	–	–	–	–
Glu_{2+3}	–	–	–	–	–	–	0.72±0.04	2.3±2.6	−5.1±2.6	0.012	−4.2±6.7	0.23	0.71±0.02	2.7±2.7	−5.1±2.3	0.0068	−3.9±6.8	0.28
Glu_4	7.67±0.22	1.4±0.1	14.9±2.8	**0.0003***	−0.8±2.2	0.49	0.54±0.04	1.7±1.8	13.4±3.5	**0.001***	−0.7±1.3	0.35	0.50±0.03	1.6±1.5	14.0±2.9	**0.0007***	−2.4±3.8	0.24
Glx_{2+3}	13.26±0.57	1.1±0.1	−3.4±3.0	0.0651	−0.5±0.7	0.19	–	–	–	–	–	–	–	–	–	–	–	–
GPC	0.76±0.09	4.3±1.0	1.9±3.8	0.3373	−2.4±4.0	0.30	–	–	–	–	–	–	–	–	–	–	–	–
GSH	0.74±0.11	8.0±4.4	4.8±7.7	0.2804	0.3±10.0	0.85	–	–	–	–	–	–	–	–	–	–	–	–
myo-Ins	5.60±0.27	1.0±0.2	−0.2±1.6	0.7935	−0.8±1.1	0.20	0.82±0.05	2.3±0.9	−0.1±2.7	0.931	−0.6±2.7	0.65	0.84±0.07	2.2±0.6	−0.4±2.6	0.7662	−0.7±3.8	0.74
Lac	0.61±0.27	23.0±23.2	−11.1±24.7	0.3110	−18.6±54.1	0.95	–	–	–	–	–	–	–	–	–	–	–	–
NAA	9.72±0.38	1.1±0.7	−1.6±2.3	0.1861	−0.2±0.7	0.55	–	–	–	–	–	–	–	–	–	–	–	–
NAAG	0.70±0.15	8.2±3.2	8.8±7.4	0.0527	−2.7±5.8	0.34	–	–	–	–	–	–	–	–	–	–	–	–
PCh	0.28±0.04	12.0±3.5	−9.1±8.1	0.0676	−0.6±19.0	0.86	–	–	–	–	–	–	–	–	–	–	–	–
PE	2.55±0.24	3.6±1.2	5.2±7.8	0.2085	0.4±6.8	0.82	–	–	–	–	–	–	–	–	–	–	–	–
scyllo-Ins	0.10±0.05	12.7±6.3	2.4±14.1	0.6303	1.4±18.6	0.54	–	–	–	–	–	–	–	–	–	–	–	–
Tau	1.26±0.15	3.9±0.3	−3.5±5.6	0.2474	2.1±4.0	0.26	0.35±0.02	4.2±1.2	−5.9±5.6	0.077	−1.2±6.2	0.69	0.38±0.03	3.6±1.5	−3.4±9.7	0.4758	−3.0±7.2	0.39
tCh	1.04±0.06	1.8±0.6	−1.0±4.5	0.6782	−1.2±3.9	0.53	0.33±0.02	0.9±0.8	−2.3±1.8	0.050	−0.5±1.9	0.60	0.35±0.23	1.0±0.6	−1.7±1.8	0.1051	−0.9±2.1	0.43
tCr	6.28±0.12	1.3±0.5	−1.3±2.4	0.2870	−1.8±1.5	0.05	1.00±0.00	–	–	–	–	–	1.00±0.00	–	–	–	–	–
tNAA	10.42±0.49	1.2±0.7	−1.0±2.3	0.4015	−0.3±0.5	0.19	1.47±0.08	1.9±2.5	1.1±3.9	0.575	−1.2±2.2	0.30	1.59±0.06	1.7±2.2	1.4±3.2	0.4114	−0.3±2.1	0.78

Supplementary Table 1 | Metabolite concentration estimates, stability, and temporal changes with and without deuterated glucose all healthy volunteers (N = 5). Data are calculated from concentrations quantified in μmol/g for single-voxel ^{1}H-MRS and referenced to total creatine (tCr) for 3D-^{1}H-MRSI. The regional means from the gray and white matter voxels were used to calculate between-subject averages in metabolite concentrations. The average concentrations and their respective coefficients of variations were measured immediately after ^{1}H-Glc administration (the first time-point). The within-session differences were calculated by subtracting the concentrations of the first and last data point, and their statistical significance was assessed via a standard, two-tailed, paired t-test (separately for ^{2}H-Glc and ^{1}H-Glc scans). The asterisks indicate statistical significance after correction for multiple comparisons with the false discovery rate method, which limited the likelihood of false positives to 7% (single-voxel data) and 3% (MRSI data).