

Table S1. Nucleotide sequences of primers used for PCR amplification in hypothalamus.

Gene	Forward primer (5' to 3')	Reverse primer (5' to 3')
<i>Bmal1</i>	GTAGATCAGAGGGCGACGGCTA	CTTGTCTGTAAAACCTGCCTGTGAC
<i>Cry1</i>	TGGAAGGTATGCGTGCCTC	TCCAGGAGAACCTCCTCACG
<i>Per2</i>	CGGACCTGGCTTCAGTTCAT	AGGATCCAAGAACGGCACAG
<i>Nampt</i>	CTCTTCACAAGAGACTGCCG	TTCATGGTCTTTCCCCCAG
<i>Ppia</i>	CTTCGAGCTGTTTGCAGACAA	AAGTCACCACCCTGGCACATG

Bmal1, hydrocarbon receptor nuclear translocator-like 1; *Cry1*, cryptochrome 1; *Nampt*, Nicotinamide Phosphoribosyltransferase; *Per2*, period 2; *Ppia*, Peptidylprolyl Isomerase A.

Table S2. Serum metabolites (Arbitrary units).

	L18-STD-VH (n=6)	L18-STD-GSPE (n=6)	L18-CAF-VH (n=6)	L18-CAF-GSPE (n=6)	L18	L6-STD-VH (n=6)	L6-STD-GSPE (n=6)	L6-CAF-VH (n=6)	L6-CAF-GSPE (n=6)	L6	CAF vs STD
METABOLITES	MEDIAN (IQR)	MEDIAN (IQR)	MEDIAN (IQR)	MEDIAN (IQR)	P-VALUE	MEDIAN (IQR)	MEDIAN (IQR)	MEDIAN (IQR)	MEDIAN (IQR)	P-VALUE	P-VALUE
2-HydroxyButyric acid	1.116 (0.874-1.217)	1.306 (0.999-1.709)	1.961 (1.372-2.155)	2.416 (2.008-3.351)	0.095	1.459 (0.895-3.036)	1.67 (1.325-1.999)	1.405 (0.952-1.737)	1.41 (1.077-2.749)	0.593	0.584
2-Hydroxyisobutyric acid	2.11 (2.001-2.297)	1.944 (1.798-2.547)	3.399 (2.997-4.409)aa	3.603 (3.443-3.711)aa	0.009	2.428 (2.165-3.148)	2.214 (2.084-2.288)	3.333 (3.03-4.083)	3.359 (2.955-3.489)	0.058	0.596
2-Hydroxyisovaleric acid	0.56 (0.503-0.596)	0.485 (0.411-0.635)	0.6 (0.445-0.687)	0.531 (0.481-0.572)	0.661	0.638 (0.534-0.734)	0.555 (0.425-0.673)	0.472 (0.443-0.519)	0.534 (0.474-0.572)	0.081	0.077
3-hydroxybutyric acid	13.207 (10.9-14.59)	14.365 (10.708-21.853)	15.972 (9.802-19.917)	14.222 (11.414-18.044)	0.391	20.158 (13.675-32.971)	17.76 (14.127-24.17)	10.173 (9.019-14.099)	10.415 (8.886-13.833)	0.547	0.829
3-Hydroxyisovaleric acid	0.465 (0.428-0.511)	0.47 (0.45-0.571)	0.46 (0.4-0.583)	0.493 (0.424-0.531)	0.985	0.552 (0.453-0.669)	0.477 (0.463-0.515)	0.434 (0.4-0.504)	0.438 (0.417-0.509)	0.08	0.255
3-Phosphoglyceric acid	0.034 (0.029-0.038)	0.029 (0.022-0.034)	0.048 (0.039-0.056)	0.048 (0.041-0.054)	0.064	0.035 (0.03-0.043)	0.035 (0.032-0.04)	0.034 (0.032-0.041)x	0.031 (0.028-0.038)	0.202	0.045
4-Hydroxybenzoic acid	0.104 (0.1-0.106)	0.104 (0.102-0.105)	0.103 (0.099-0.105)	0.105 (0.102-0.106)	0.419	0.103 (0.102-0.104)	0.104 (0.103-0.106)	0.102 (0.1-0.104)	0.102 (0.097-0.106)	0.774	0.857
4-hydroxyPhenyllactic acid	18.936 (14.946-36.319)	17.479 (12.284-25.008)	7.505 (2.901-9.057)aa	11.815 (9.026-13.967)€b	0.014	19.824 (3.534-28.675)	16.385 (13.276-17.492)	6.932 (4.908-7.705)	8.371 (7.355-10.211)€aa	0.042	0.105
4-Hydroxyproline	3.488 (2.458-3.729)	2.941 (2.475-4.022)	3.594 (2.819-4.926)	3.422 (2.921-4.478)	0.5	2.287 (2.167-2.533)+	2.435 (1.982-2.967)	2.982 (2.396-3.393)	2.485 (2.013-3.154)	0.769	0.027
Aconitic acid	0.051 (0.041-0.084)	0.054 (0.033-0.117)	0.154 (0.073-0.317)	0.074 (0.06-0.093)	0.373	0.052 (0.024-0.07)	0.034 (0.027-0.053)	0.087 (0.073-0.406)b	0.055 (0.042-0.074)€b	0.018	0.069
Alanine	16.385 (15.152-16.919)	16.884 (15.81-18.24)	17.821 (17.167-19.033)aa	16.571 (16.013-16.973)€	0.028	15.962 (14.955-17.133)	15.406 (14.533-16.171)	17.458 (16.541-20.436)b	17.19 (16.717-17.739)aa	0.004	0.006
alpha-ketoglutaric acid	2.25 (1.712-3.723)	1.951 (1.398-3.112)	2.27 (1.968-2.606)	2.405 (1.909-2.728)	0.718	2.359 (2.009-3.611)	2.512 (1.99-3.202)	1.825 (1.548-2.259)	1.706 (1.49-1.966)	0.492	0.745
alpha-tocopherol	0.043 (0.039-0.049)	0.039 (0.032-0.041)c	0.066 (0.053-0.068)a	0.056 (0.05-0.069)aa	0.001	0.029 (0.022-0.05)	0.034 (0.026-0.054)	0.074 (0.07-0.077)++	0.06 (0.052-0.07)	0.075	0.009
Aspartic	0.299 (0.223-0.418)	0.345 (0.283-0.384)	0.358 (0.281-0.407)	0.336 (0.325-0.347)	0.409	0.32 (0.278-0.43)	0.324 (0.284-0.389)	0.324 (0.285-0.363)	0.304 (0.299-0.347)	0.87	0.813
Cholesterol	11.455 (10.478-13.187)	9.564 (7.463-11.011)	12.476 (10.583-14.344)	11.793 (9.404-13.462)	0.101	10.482 (8.536-11.839)	9.569 (8.64-11.989)	13.437 (12.207-13.867)	12.14 (10.304-13.65)	0.188	0.373
Citric acid	32.587 (29.07-45.991)	32.052 (27.445-38.804)	36.627 (34-37.803)	32.683 (26.449-39.745)	0.52	37.319 (33.509-54.107)	35.811 (29.775-42.316)	25.074 (23.913-26.639)aa++	25.822 (22.242-28.263)a	0.003	0.016
d-Fructose	0.054 (0.043-0.075)	0.053 (0.036-0.065)	0.083 (0.059-0.109)aa	0.108 (0.095-0.132)aa	0.007	0.05 (0.035-0.074)	0.052 (0.047-0.077)	0.071 (0.053-0.096)	0.099 (0.09-0.115)caa	0.015	0.47
DL-2-Hydroxyglutaric acid	0.154 (0.127-0.224)	0.151 (0.134-0.187)	0.147 (0.129-0.165)	0.135 (0.127-0.164)	0.381	0.167 (0.15-0.199)	0.159 (0.145-0.169)	0.121 (0.108-0.136)a++	0.122 (0.116-0.139)a	0.003	0.02
d-Mannitol	0.068 (0.014-0.075)	0.051 (0.045-0.067)	0.015 (0.008-0.046)	0.011 (0.006-0.018)	0.059	0.037 (0.016-0.057)	0.036 (0.02-0.049)	0.01 (0.007-0.02)a	0.006 (0.005-0.014)ca	0.005	0.222
d-Mannonic acid	0.03 (0.024-0.038)	0.029 (0.026-0.035)	0.037 (0.035-0.045)	0.033 (0.028-0.036)	0.117	0.03 (0.025-0.035)	0.025 (0.023-0.029)	0.034 (0.027-0.039)	0.033 (0.03-0.037)	0.216	0.087
Dodecanoic acid	0.235 (0.219-0.272)	0.228 (0.222-0.269)	0.307 (0.245-0.455)	0.388 (0.295-0.461)	0.114	0.256 (0.226-0.28)	0.244 (0.213-0.296)	0.276 (0.253-0.306)	0.324 (0.295-0.369)ca	0.028	0.612
d-Sucrose	0.028 (0.013-0.059)	0.012 (0.007-0.025)	0.345 (0.152-	0.201 (0.12-0.332)aa	0.008	0.014 (0.006-0.036)	0.037 (0.015-0.349)	0.055 (0.051-	0.116 (0.053-0.181)	0.042	0.041

			0.477)aa					0.064)aa++				
<i>d-Threitol</i>	0.028 (0.025-0.03)	0.027 (0.024-0.029)	0.029 (0.025-0.036)	0.031 (0.03-0.035)	0.113	0.023 (0.022-0.026)	0.025 (0.023-0.026)	0.027 (0.025-0.029)	0.028 (0.026-0.031)	0.414	0.507	
<i>Ethanolamine</i>	0.496 (0.472-0.564)	0.555 (0.463-0.608)	0.525 (0.48-0.729)	0.513 (0.44-0.56)	0.456	0.55 (0.395-0.579)	0.587 (0.455-0.628)	0.543 (0.508-0.58)	0.547 (0.407-0.584)	0.455	0.625	
<i>Fructose-6-phosphate</i>	0.081 (0.068-0.272)	0.101 (0.048-0.142)	0.061 (0.041-0.086)	0.054 (0.038-0.066)	0.611	0.095 (0.057-0.193)	0.092 (0.071-0.109)	0.061 (0.054-0.112)	0.054 (0.047-0.061)	0.061	0.555	
<i>Fumaric acid</i>	1.04 (0.634-1.458)	0.775 (0.567-1.233)	0.846 (0.729-1.046)	0.816 (0.649-1.127)	0.72	0.995 (0.8-1.447)	0.902 (0.695-1.12)	0.622 (0.568-0.827)+	0.641 (0.572-0.759)	0.191	0.196	
<i>Galacturonic acid</i>	0.013 (0.011-0.016)	0.011 (0.01-0.017)	0.018 (0.018-0.021)a	0.021 (0.015-0.025)a	0.032	0.012 (0.011-0.013)	0.012 (0.01-0.014)	0.019 (0.016-0.022)aa	0.02 (0.017-0.025)aa	0.017	0.282	
<i>Glucose</i>	39.681 (36.993-41.692)	35.717 (33.906-37.901)	37.453 (32.53-37.92)	38.204 (36.749-39.582)	0.191	37.57 (34.76-42.263)	38.532 (35.612-41.266)	37.556 (34.842-40.092)	38.59 (36.543-40.286)	0.917	0.384	
<i>Glucose 6-phosphate</i>	0.039 (0.036-0.082)	0.035 (0.024-0.06)	0.033 (0.023-0.038)b	0.025 (0.016-0.034)	0.023	0.046 (0.027-0.057)	0.038 (0.036-0.052)	0.03 (0.025-0.052)	0.027 (0.023-0.03)	0.057	0.09	
<i>Glutamic acid</i>	6.613 (5.409-7.89)	6.696 (6.167-7.395)	7.523 (6.872-8.062)	7.051 (6.287-7.789)	0.833	7.32 (6.546-8.254)	7.156 (6.54-9.266)	6.691 (6.38-6.957)	6.355 (5.656-7.387)	0.529	0.577	
<i>Glutamine</i>	0.534 (0.433-0.855)	0.587 (0.457-1.663)	1.405 (0.747-3.522)	0.683 (0.55-0.909)	0.061	0.428 (0.27-1.203)	0.424 (0.294-0.492)	0.9 (0.727-6.487)b	0.654 (0.427-0.726)€b	0.003	0.004	
<i>Glyceraldehyde-3-phosphate</i>	0.005 (0.003-0.005)	0.005 (0.004-0.007)	0.004 (0.004-0.005)	0.004 (0.004-0.004)	0.086	0.006 (0.005-0.006)	0.005 (0.005-0.006)	0.004 (0.003-0.004)aa	0.004 (0.004-0.004)aa	0.007	0.083	
<i>Glyceric acid</i>	1.265 (0.794-1.849)	1.371 (0.76-1.521)	0.955 (0.861-1.054)	0.795 (0.714-1.368)	0.348	1.303 (0.624-2.434)	0.915 (0.649-1.547)	0.902 (0.746-1.46)	1.237 (0.939-1.47)	0.473	0.577	
<i>Glycerol</i>	0.671 (0.536-0.965)	0.861 (0.544-1.062)	1.106 (0.857-1.477)a	1.225 (1.132-1.562)a	0.001	0.834 (0.706-0.887)	0.954 (0.768-1.01)	1.118 (0.88-1.235)a	1.227 (1.088-1.414)aa	0.008	0.004	
<i>Glycerol-1-phosphate</i>	0.201 (0.165-0.275)	0.188 (0.154-0.221)	0.211 (0.165-0.266)	0.183 (0.147-0.199)	0.284	0.213 (0.162-0.275)	0.167 (0.143-0.258)	0.21 (0.183-0.278)	0.165 (0.144-0.214)	0.142	0.951	
<i>Glycine</i>	4.903 (4.716-5.021)	4.961 (4.726-5.151)	4.657 (4.276-4.934)	4.366 (4.133-4.547)	0.052	4.845 (4.725-5.139)	4.692 (4.611-4.801)	4.733 (4.685-5.176)	4.58 (4.297-4.933)	0.724	0.988	
<i>Glycolic acid</i>	0.097 (0.094-0.114)	0.109 (0.097-0.133)	0.135 (0.121-0.148)aa	0.116 (0.113-0.136)c	0.027	0.12 (0.097-0.146)	0.117 (0.109-0.125)	0.12 (0.115-0.134)	0.133 (0.127-0.137)	0.634	0.034	
<i>Heptanoic</i>	0.434 (0.406-0.49)	0.411 (0.395-0.464)	0.427 (0.382-0.465)	0.441 (0.402-0.539)	0.405	0.483 (0.4-0.5)	0.452 (0.432-0.468)	0.408 (0.376-0.447)	0.45 (0.434-0.492)	0.392	0.79	
<i>Hippuric acid</i>	0.342 (0.234-0.544)	0.631 (0.531-0.726)€	0.145 (0.121-0.287)a	0.106 (0.053-0.21)aa	0.001	0.451 (0.312-0.559)	0.482 (0.407-0.585)	0.107 (0.076-0.154)aax	0.077 (0.056-0.146)aa	0.004	0.006	
<i>Indole-3-propanoic acid</i>	1.343 (0.97-1.683)	1.528 (0.955-1.645)	1.088 (0.812-3.042)	0.911 (0.562-1.414)	0.701	1.101 (0.572-1.539)	0.953 (0.774-1.192)	0.861 (0.545-1.047)	0.6 (0.374-0.934)	0.176	0.602	
<i>Isoleucine</i>	4.477 (4.07-5.107)	4.47 (4.009-4.568)	4.355 (3.862-4.866)	4.198 (3.867-4.652)	0.563	4.364 (4.09-4.575)	3.938 (3.741-4.669)	4.236 (3.926-4.363)	4.252 (3.751-4.359)	0.483	0.378	
<i>Lactic acid</i>	75.808 (67.974-85.853)	76.14 (72.71-89.479)	85.463 (74.452-95.224)	75.406 (71.158-79.759)	0.226	79.845 (73.389-102.516)	77.012 (75.487-87.892)	75.961 (72.358-88.192)	77.382 (69.064-79.441)	0.4	0.255	
<i>Leucine</i>	7.4 (6.702-8.209)	7.387 (6.609-7.586)	7.18 (6.686-7.957)	7.124 (6.65-7.735)	0.919	6.999 (6.814-7.367)	6.524 (6.175-7.378)	7.022 (6.811-7.323)	7.044 (6.274-7.278)	0.664	0.901	
<i>Linoleic acid</i>	1.1 (0.504-1.703)	1.245 (0.686-1.628)	1.473 (0.975-2.1)	1.872 (1.269-2.806)	0.613	0.992 (0.767-2.113)	1.461 (1.248-1.808)	1.001 (0.927-1.129)	1.34 (1.091-1.709)	0.1	0.56	
<i>Malic acid</i>	0.587 (0.371-1.025)	0.501 (0.341-0.698)	0.567 (0.518-0.683)	0.602 (0.447-0.744)	0.217	0.539 (0.469-0.761)	0.503 (0.42-0.615)	0.406 (0.377-0.449)++	0.397 (0.348-0.469)	0.274	0.084	
<i>Maltose</i>	0.021 (0.016-0.041)	0.012 (0.008-0.014)€	0.008 (0.004-0.012)a	0.009 (0.005-0.011)	0.019	0.008 (0.007-0.012)+	0.009 (0.008-0.016)	0.009 (0.006-0.017)	0.008 (0.005-0.011)	0.232	0.009	
<i>Methionine</i>	3.496 (3.236-3.67)	3.443 (3.259-3.609)	3.139 (3.102-3.435)	3.189 (3.112-3.381)	0.166	3.372 (3.194-3.42)	3.292 (3.183-3.411)	3.439 (3.314-3.531)	3.285 (3.236-3.482)	0.348	0.272	
<i>myo-Inositol</i>	1.13 (0.923-1.209)	1.074 (0.784-1.174)	0.928 (0.897-1.066)	0.801 (0.733-1.016)	0.106	0.947 (0.816-1.124)	1.02 (0.908-1.092)	0.888 (0.773-1.052)	0.908 (0.804-1.077)	0.397	0.182	
<i>Oleic acid</i>	2.925 (1.2-4.668)	3.241 (1.188-4.486)	6.258 (4.026-10.184)	9.893 (5.664-13.354)	0.294	2.748 (2.071-4.622)	3.811 (2.815-6.342)	5.37 (5.074-5.81)	7.469 (5.014-10.02)	0.613	0.113	
<i>Ornithine</i>	2.685 (1.693-4.077)	2.208 (1.932-3.595)	2.284 (2.17-4.112)	1.709 (1.562-2.286)	0.268	2.401 (1.835-2.526)	1.713 (1.459-2.04)	2.185 (2.092-3.13)	1.777 (1.377-2.055)	0.208	0.78	
<i>Oxalic acid</i>	24.293 (21.582-26.714)	26.491 (25.029-27.684)	24.139 (23.125-29.799)	22.728 (20.231-23.998)	0.099	26.4 (21.505-36.416)	27.622 (24.27-36.927)	27.249 (25.882-29.611)	33.773 (29.3-37.54)	0.454	0.552	

<i>Oxoproline</i>	145.749 (136.603-166.354)	143.399 (132.564-167.096)	155.083 (123.075-183.659)	157.99 (142.17-165.27)	0.168	116.228 (105.816-175.582)	139.734 (122.876-145.385)	143.175 (111.038-179.911)	142.736 (121.332-153.167)	0.47	0.223
<i>Palmitic acid</i>	98.779 (77.763-108.3)	96.293 (75.619-106.847)	90.963 (73.175-105.392)	103.06 (84.162-113.351)	0.997	97.334 (84.965-118.958)	105.446 (98.11-114.62)	87.764 (81.965-91.883)	102.34 (75.426-107.523)	0.075	0.149
<i>Phenylalanine</i>	3.809 (3.607-4.009)	3.716 (3.456-3.877)	3.6 (3.516-4.176)	3.764 (3.616-3.831)	0.98	3.627 (3.538-3.706)	3.534 (3.428-3.698)	3.998 (3.873-4.051)aa	3.737 (3.589-3.909)€	0.001	0.076
<i>Phosphoric acid</i>	60.912 (57.252-67.868)	53.837 (51.97-57.999)€	50.315 (45.915-54.037)aa	49.091 (47.481-54.275)b	0.003	61.59 (59.219-70.695)	62.746 (60.781-67.589)	52.724 (47.416-56.343)	52.207 (49.76-56.746)	0.201	0.066
<i>Pipecolic acid</i>	0.096 (0.075-0.106)	0.088 (0.068-0.096)	0.054 (0.048-0.064)	0.06 (0.053-0.067)	0.134	0.09 (0.077-0.1)	0.083 (0.076-0.09)	0.054 (0.047-0.067)a	0.061 (0.054-0.073)a	0.01	0.068
<i>Proline</i>	26.014 (20.318-36.895)	26.863 (22.184-30.998)	45.239 (38.993-53.43)a	39.705 (35.115-40.687)caa	0.044	20.031 (13.587-27.608)	20.039 (17.055-23.79)	36.726 (35.376-38.474)aax	32.373 (29.917-35.205)€aa	0.0001	0.027
<i>Pyruvic acid</i>	24.766 (16.785-27.088)	19.627 (13.73-24.99)	27.456 (23.314-34.62)	29.068 (21.758-29.684)	0.082	19.781 (12.348-25.187)	21.118 (17.341-23.747)	26.343 (22.112-29.174)	19.131 (14.938-26.318)	0.838	0.269
<i>Serine</i>	9.355 (8.106-10.327)	9.605 (8.806-10.24)	13.718 (12.835-14.986)	13.062 (10.964-13.225)	0.509	9.04 (8.871-9.834)	9.033 (8.48-9.496)	13.246 (12.441-14.116)	12.433 (10.829-13.6)	0.115	0.854
<i>Succinic acid</i>	0.219 (0.185-0.321)	0.223 (0.194-0.243)	0.282 (0.268-0.292)b	0.224 (0.194-0.289)c	0.042	0.26 (0.218-0.29)	0.204 (0.179-0.257)	0.212 (0.184-0.243)++	0.24 (0.175-0.291)	0.454	0.055
<i>Taurine</i>	1.196 (1.092-2.008)	1.688 (1.173-2.916)	1.794 (1.373-2.587)	1.23 (1.041-1.535)	0.596	2.005 (0.923-4.912)	1.373 (1-2.538)	1.966 (1.695-2.372)	2.023 (1.636-2.278)	0.502	0.851
<i>Threonic acid</i>	0.443 (0.391-0.569)	0.466 (0.412-0.621)	0.701 (0.629-0.803)a	0.676 (0.622-0.737)aa	0.012	0.516 (0.39-0.791)	0.463 (0.422-0.494)	0.683 (0.636-0.775)	0.672 (0.632-0.74)	0.061	0.07
<i>Threonine</i>	6.486 (6.054-7.463)	6.719 (6.138-7.427)	7.405 (7.065-8.515)	7.307 (6.639-7.902)	0.24	6.716 (6.066-7.299)	6.529 (6.201-7.063)	7.87 (7.506-8.348)aa	7.826 (7.189-8.6)a	0.031	0.012
<i>Uric acid</i>	0.385 (0.353-0.423)	0.385 (0.345-0.423)	0.461 (0.411-0.505)	0.378 (0.355-0.464)	0.053	0.373 (0.305-0.437)	0.301 (0.273-0.533)	0.46 (0.432-0.522)	0.506 (0.476-0.665)	0.67	0.081
<i>Valine</i>	9.059 (8.376-10.22)	9.021 (8.137-9.48)	8.642 (7.902-9.741)	8.199 (7.647-8.887)	0.104	8.785 (8.143-9.291)	8.002 (7.697-9.028)	8.412 (8.152-8.577)	8.391 (7.495-8.672)	0.272	0.207
<i>Xylonic acid</i>	0.007 (0.006-0.008)	0.007 (0.006-0.012)	0.008 (0.007-0.013)	0.007 (0.005-0.008)	0.473	0.007 (0.007-0.012)	0.006 (0.005-0.008)	0.008 (0.007-0.01)	0.007 (0.006-0.008)	0.123	0.44

Data shown as Median (Interquartile Range) (IQR) in Arbitrary units. P-VALUE for L18 groups, L16 groups and STD vs CAF comparison was calculated by Kruskal-Wallis' test; a indicates significant differences between STD vs CAF; € indicates significant differences between VH vs GSPE; + indicates significant differences between L6-VH vs L18-VH groups by Mann-Whitney (a, € and + p ≤ 0.05; aa and ++ p ≤ 0.01). b Indicates tendency between STD vs CAF, c indicates tendency between VH vs GSPE conditions; x Indicates tendency between L6-VH vs L18-VH by Mann-Whitney (p =0.1-0.051).