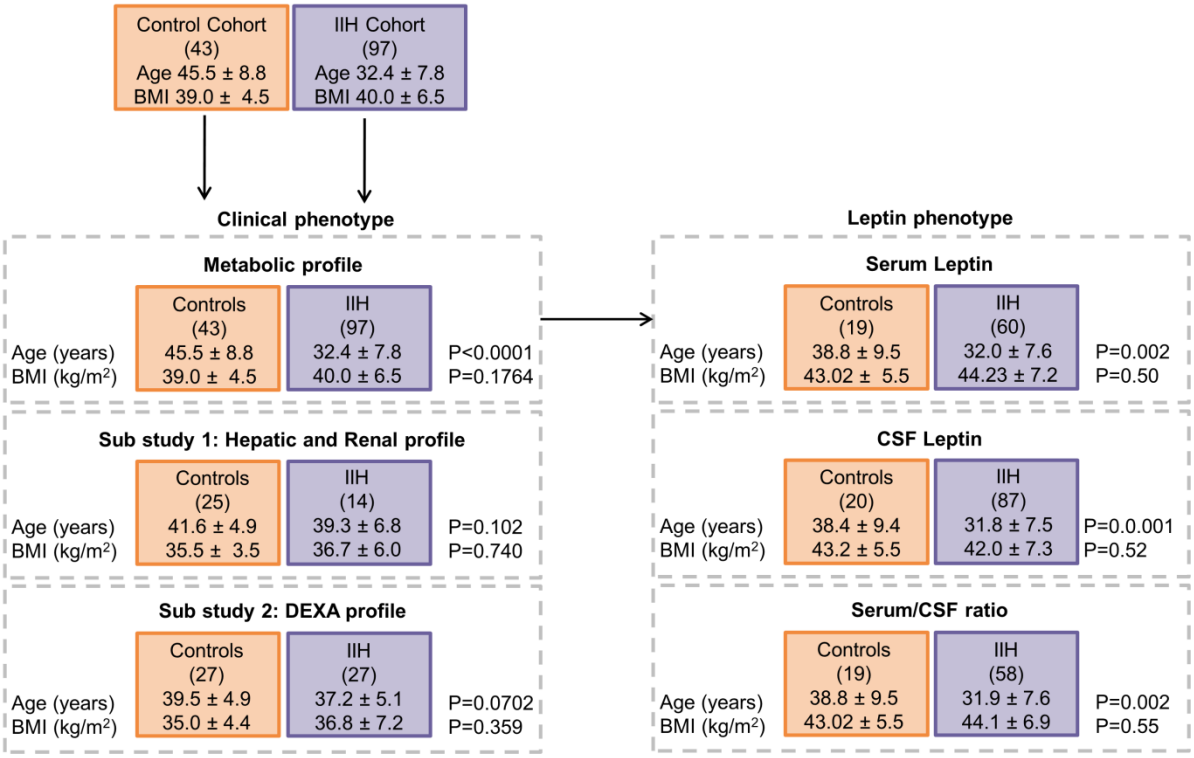

Figure S1 Consort diagram

Demographic characteristics for the control and IIH patients within the study and the sub-studies. Numbers in parentheses represent N for respective group. Data presented as mean±standard deviation. BMI= Body mass index.

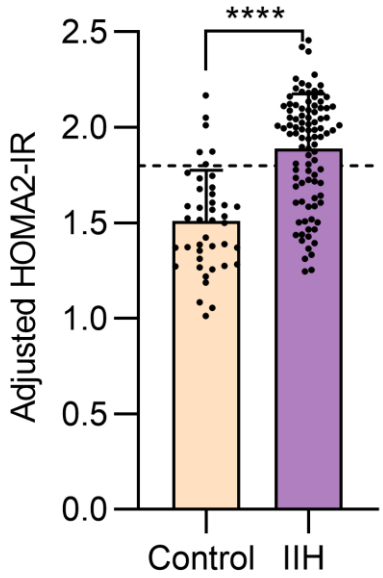

Figure S2) HOMA2-IR

Histograms of fasted HOMA2-IR adjusted for age and BMI via multiple regression analysis in control (n=43) and IIH patients (n=97). Dotted line represents threshold suggestive of type 2 diabetes mellitus.. N represents an individual patient. Data presented as mean±SD, ****=P<0.0001.

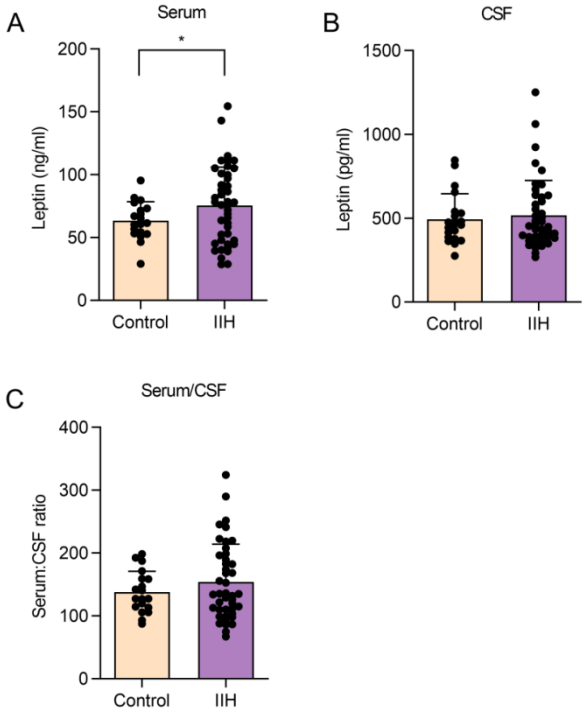

Figure S3) Leptin sensitivity analysis, relating to figure 3

A sex, BMI and age matched cohort of control and IIH patients were sub analysed for (**A**) serum, (**B**) CSF leptin and (**C**) serum/CSF leptin ratio. (D) Table of patient variables. Welch's for A, Mann-Whitney test for B and C. N=19 for control, N=43 for IIH. Data presented as mean±SD, *=P<0.05.

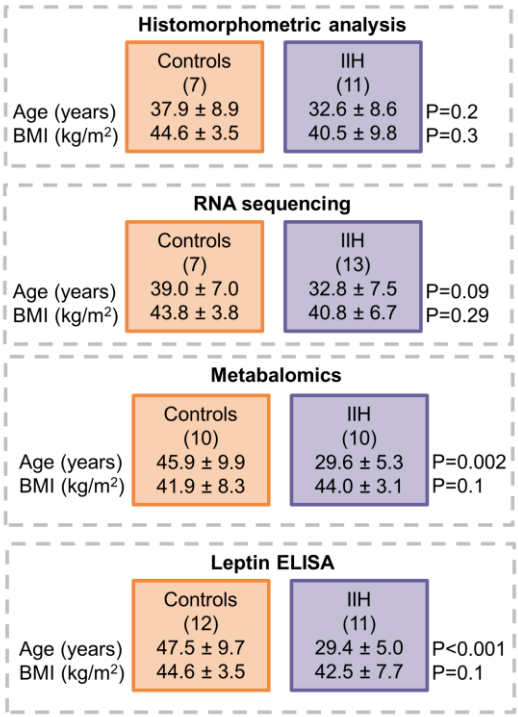

Figure S4) Adipose tissue group matching

Patient characteristics for adipose tissue experiments. Numbers in parentheses represent N for respective group. Data presented as mean±SD and T-tests.

	Subcutaneous			Omental		
µM/100mg	Control	IIH	P	Control	IIH	P
Acetate	232.7(176.8)	215.4(145.5)	0.81	286.8 (64.8)	166.5 (75.2)	0.0012*
Alanine	51.1 (20.8)	82.1 (43.0)	0.06	62.6 (28.7)	109.0 (73.4)	*0.052*
Arginine	202.8 (62.4)	215.8(117.7)	0.76	246.9 (72.2)	238.3 (88.4)	0.81
Formate	57.6 (47.9)	72.5 (52.9)	*0.35*	56.1 (28.5)	53.9 (34.7)	*0.73*
Glucose (mM)	3.7 (1.6)	3.6 (1.2)	0.86	4.1 (1.1)	3.6 (1.5)	0.43
Glutamate	N/A			146.5 (63.0)	150.6 (69.0)	*0.79*
Glutamine	551.5(287.2)	509.7(253.5)	0.73	679.6(241.7)	719.6(233.7)	0.71
Glutathione	13.2 (6.6)	22.9 (17.6)	*0.12*	20.9 (13.3)	16.7 (5.6)	*0.57*
Glycerol	339.0 (97.9)	305.7 (90.8)	0.44	296.1 (38.5)	274.1 (87.4)	*0.16*
Glycine	105.5 (44.6)	117.3 (47.7)	0.57	132.8 (36.3)	148.5 (68.2)	0.53
Histidine	41.9 (21.3)	36.4 (13.1)	0.49	38.9 (10.3)	43.5 (10.0)	0.32
Isoleucine	121.0 (46.6)	116.1 (42.8)	0.81	130.9 (30.3)	124.4 (25.0)	0.6
Lactate (mM)	616.2(409.3)	660.5(330.1)	*0.48*	0.85 (0.33)	1.59 (1.97)	*0.48*
Leucine	139.8 (53.8)	133.3 (48.3)	0.78	144.3 (35.6)	138.3 (26.9)	0.67
Lysine	134.1 (60.4)	151.1 (55.8)	0.52	162.1 (51.10	172.1 (43.0)	0.64
Methionine	34.1 (17.5)	29.7 (17.6)	0.58	34.1 (9.4)	41.3 (11.2)	0.13
Methylsuccinate	5.1 (3.7)	4.3 (2.4)	*0.85*	4.9 (2.8)	7.1 (5.1)	*0.49*
Phenylalanine	60.0 (27.4)	58.5 (19.7)	0.89	65.1 (18.7)	72.5 (15.7)	0.34
Proline	56.1 (38.2)	60.1 (30.7)	0.39	74.5 (24.9)	83.1 (23.4)	0.43
Pyroglutamate	191.6 (89.3)	184.2(132.1)	0.88	190.0 (84.4)	181.9 (86.3)	0.83
Pyruvate	9.5 (8.7)	21.3 (29.4)	*0.79*	4.5 (7.1)	23.6 (16.7)	*0.003**
Sarcosine	6.7 (2.6)	6.4 (2.9)	0.81	5.4 (1.4)	6.7 (2.6)	0.22
Succinate	N/A			13.5 (4.6)	18.2 (8.4)	0.14
Threonine	149.4 (57.7)	166.9 (70.0)	*0.48*	188.3 (44.5)	196.1 (60.4)	0.74
Tryptophan	10.6 (4.6)	11.3 (2.9)	0.66	12.3 (3.5)	13.8 (3.4)	0.34
Tyrosine	71.4 (30.4)	75.9 (28.7)	0.74	87.4 (23.4)	95.0 (21.4)	0.46
Valine	144.6 (52.5)	142.3 (50.9)	0.92	159.3 (38.3)	157.1 (31.1)	0.89
myo-Inositol	162.0 (74.1)	171.4 (86.7)	0.79	130.7 (59.0)	147.2 (86.7)	*0.91*
Sn-glycero-3-PC	94.0 (26.9)	95.9 (54.8)	0.79	83.9 (27.5)	77.3 (22.6)	0.56

Ratios	Control	IIH	P	Control	IIH	P
Lactate/Pyruvate	140.6(154.9)	155.2(160.3)	*0.85*	544.9(380.7)	145.0(199.9)	*0.015**

Table S1) Adipose tissue metabolite concentration

Concentration of tissue explant metabolite concentration in adipose explants from paired OM and SC adipose tissue from IIH and control patients as determined by NMR. Statistical significance is denoted by *, where $p<0.05$ is considered significant. Numbers marked in *Italics*= Mann-Whitney U-test, unmarked = unpaired T-test. Data presented as mean±SD.

	Subcutaneous			Omental		
ΔμM/100mg	Control	IIH	P	Control	IIH	P
Acetate	596.6 (336.8)	532.5 (250.5)	0.63	800.9(414.6)	335.4(176.4)	0.004*
Adenosine	-2.8 (0.4)	-1.9 (0.8)	0.012*	N/A		
Alanine	87.1 (84.8)	141.6 (84.3)	0.16	67.9 (43.9)	102.8(53.4)	0.14
Arabinose	-32.2 (5.2)	-23.1 (22.9)	*0.23*	N/A		
Arginine	-70.9 (90.9)	-90.4 (90.6)	*0.31*	-227.0 (274.7)	-58.4 (265.9)	*0.18*
Asparagine	2.8 (18.3)	-1.5 (19.0)	0.60	0.1 (6.3)	8.3 (10.8)	*0.31*
Aspartate	-23.9 (15.7)	-29.2 (15.6)	0.45	-23.6 (14.0)	-24.7 (5.3)	0.82
Choline	-5.2 (13.4)	-7.4 (14.3)	*0.27*	-6.5 (17.0)	0.3 (3.4)	0.76
Cysteine	19.6 (27.3)	30.1 (52.9)	0.58	12.9 (23.6)	10.0 (21.1)	0.18
Cystine	0.9 (37.5)	5.2 (61.7)	0.78	-42.6 (31.9)	-2.8 (21.5)	0.005*
Formate	34.6 (21.1)	53.5 (41.0)	*0.31*	40.5 (18.2)	40.3 (21.5)	0.98
Glucose (ΔmM)	-0.625 (376.8)	-1.015 (0.840)	0.22	-0.35 (1.2)	-0.27 (0.91)	0.85
Glutamate	1.7 (72.6)	-2.4 (35.5)	0.54	1.3 (64.0)	-10.2 (45.8)	*0.85*
Glutamine	-8.1 (467.9)	34.9 (28.6)	0.94	-86.8 (380.4)	105.3 (203)	0.18
Glycerol	84.5 (37.0)	157.3 (62.6)	0.005*	79.4 (33.5)	128.7 (45.6)	0.016*
Glycine	56.2 (40.3)	41.7 (52.5)	*0.19*	39.6 (34.1)	47.2 (28.5)	0.6
Histidine	39.8 (16.1)	33.8 (10.1)	0.33	28.9 (9.9)	33.9 (14.9)	0.40
Hypoxanthine	0.3 (10.4)	3.8 (9.6)	0.45	3.5 (7.2)	-2.9 (6.5)	0.055
Inosine	1.1 (2.8)	-0.2 (1.1)	*0.59*	N/A		
Isoleucine	25.3 (48.3)	-30.5 (25.2)	*0.002* *	-9.7 (41.6)	-29.2 (71.8)	0.48
Lactate (ΔmM)	1.4 (0.6)	1.5 (0.5)	0.35	1.8 (1.5)	1.8 (0.9)	*0.29*
Leucine	22.6 (54.3)	-38.0 (40.8)	0.011*	3.8 (55.9)	-9.8 (78.6)	0.66
Lysine	29.4 (139.1)	-8.4 (64.5)	0.97	17.6(159.7)	9.7 (50.5)	*0.24*
Methionine	-0.5 (15.1)	-8.9 (8.3)	*0.16*	-3.2 (12.4)	-1.7 (10.2)	*0.54*
Niacinamide	15.8 (4.1)	12.9 (3.5)	0.12	16.3 (6.9)	11.9 (2.4)	0.08
Phenylalanine	26.5 (19.6)	21.5 (17.9)	0.56	22.8 (10.6)	19.7 (13.5)	0.57
Proline	-11.2 (44.1)	38.8 (178.2)	*0.73*	-54.1 (56.8)	13.9 (36.4)	0.007*
Pyroglutamate	-123.3 (300.2)	-242.3 (244.0)	0.34	-160.9 (196.3)	-172.2 (252.3)	0.91
Pyruvate	-332.5 (128.2)	-188.9 (329.2)	*0.24*	-344.0 (107)	-226.1 (100)	0.02*
Serine	-129.8 (42.0)	-102.4 (79.5)	0.34	-120.7 (82.5)	-90.5 (91.5)	0.46
Threonine	119.6 (56.3)	77.6 (58.6)	*0.19*	106.1(82.2)	69.1 (51.6)	0.25
Tryptophan	0.5 (4.0)	-1.5 (2.8)	*0.63*	-4.5 (4.6)	-1.4 (1.9)	0.07
Tyrosine	54.9 (34.3)	39.0 (23.7)	*0.43*	48.2 (17.5)	52.0 (10.9)	*0.18*
Valine	103.2 (63.9)	52.8 (49.3)	*0.04**	83.6 (52.8)	66.0 (43.7)	0.43

Table S2) Conditioned media metabolite exchange

Conditioned media metabolites as assessed by NMR in paired omental and subcutaneous adipose tissue explants from IIH and control patients, where values are relative to a non-adipose incubated blank. Statistical significance is denoted by *, where $p<0.05$ is considered significant. Numbers marked in *Italics*= Mann-Whitney U-test, unmarked = unpaired T-test. Data presented as mean±SD.