SUPPLEMENTARY DATA

Supplementary Table 1. Animal characteristics and steady state and load-independent parameters of the left ventricular function in isolated perfused hearts from chow fed lean controls (CON) and mice fed a high fat diet (HFD) for 9 weeks.

	CON	**HFD**
	n=26	n=26
Body weight (g)	25.8 ± 0.3*	33.6 ± 0.6
Heart weight (mg)	130 ± 2	128 ± 2
Perirenal fat (mg)	149 ± 13	649 ± 51*
Plasma free fatty acids $_{fed}$ (mM)	0.34± 0.04	0.57±0.03
Plasma glucose $_{fasted}$ (mM)	9.2 ± 0.6	11.6 ± 0.2*
Aerobic capacity (ml $O_2/kg^{0.75}$)	47.0 ± 0.5	45.8 ± 0.4
Cardiac function	n=7	n=8
Aortic flow (ml/min)	11.2 ± 0.9	9.3 ± 0.7
Coronary flow (ml/min)	3.2 ± 1.1	2.9 ± 0.2
dP/dt_{max} (mmHg/sec)	4153 ± 269	4386 ± 177
dP/dt_{min} (mmHg/sec)	-3403 ± 239	-3485 ± 113
Tau glantz (msec)	20.2 ± 2.2	19.8 ± 1.0
EDPVR (mmHg/µl)	0.21 ± 0.02	0.26 ± 0.05
ESPVR (mmHg/µl)	0.69 ± 0.13	0.52 ± 0.08
PRSWi (mmHg)	31.6 ± 6.4	25.6 ± 2.7

The maximum positive and negative time derivative of LV pressure (dP/dt_{max} and dP/dt_{min}), left ventricular relaxation time constant (Tau). Hearts were paced at 7 Hz and steady state conditions were obtained at pre- and afterload of 8 and 50 mmHg, respectively). Load-independent functional parameters was obtained by a temporary preload reduction. EDPVR and ESPVR; is the slope of end-diastolic and end-systolic pressure-volume relationships. PRSWi; preload-recruitable stroke work index. Values are mean ± SEM, *$p<0.05$.

SUPPLEMENTARY DATA

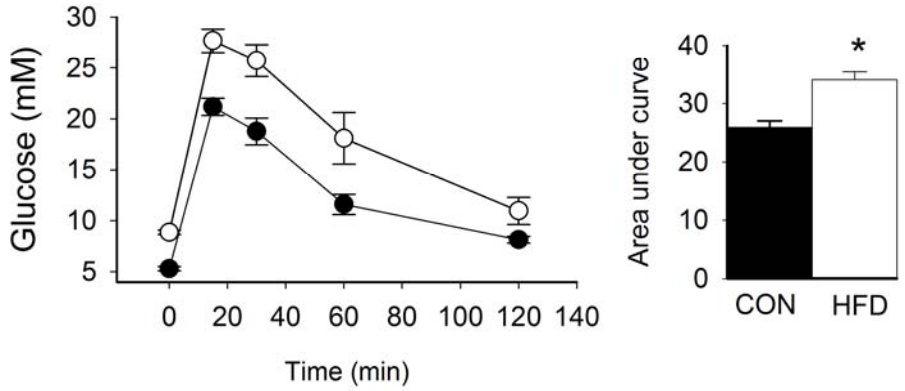
Supplementary Table 2. Left ventricular mRNA expression of selected genes from lean controls (CON) and diet-induced obese sedentary (DIO_{SED}), moderate intensity trained (DIO_{MIT}) and high intensity trained (DIO_{HIT}) mice.

	CON	**DIO_{SED}**	**DIO_{MIT}**	**DIO_{HIT}**
hk2	0.97 ± 0.03	1.00 ± 0.03	1.12 ± 0.04*	1.14 ± 0.03*
hif1α	1.00 ± 0.03	1.00 ± 0.03	1.03 ± 0.04	1.04 ± 0.04
mhcα	1.00 ± 0.02	1.00 ± 0.04	1.09 ± 0.03*	1.09 ± 0.02*
mhcβ	1.50 ± 0.20	1.00 ± 0.10	0.90 ± 0.02	0.88 ± 0.06
ucp3	1.02 ± 0.09	1.00 ± 0.07	1.31 ± 0.15	0.87 ± 0.08
mte1	0.75 ± 0.02*	1.00 ± 0.03	1.10 ± 0.05	1.02 ± 0.04
gpx3	0.83 ± 0.05	1.00 ± 0.07	1.15 ± 0.03	1.05 ± 0.03
cat	0.81 ± 0.02*	1.00 ± 0.03	1.08 ± 0.03	1.06 ± 0.03
timp1	1.12 ± 0.19	1.00 ± 0.14	1.17 ± 0.13	1.32 ± 0.17
bnp	0.93 ± 0.07	1.00 ± 0.12	0.94 ± 0.08	0.83 ± 0.08
anf	1.11 ± 0.19	1.00± 0.03	0.90± 0.13	0.94± 0.10
serca2	0.97 ± 0.02	1.00 ± 0.04	0.98± 0.02	0.99± 0.03
ryr2	0.89± 0.02*	1.00± 0.03	0.96± 0.02	1.02± 0.03

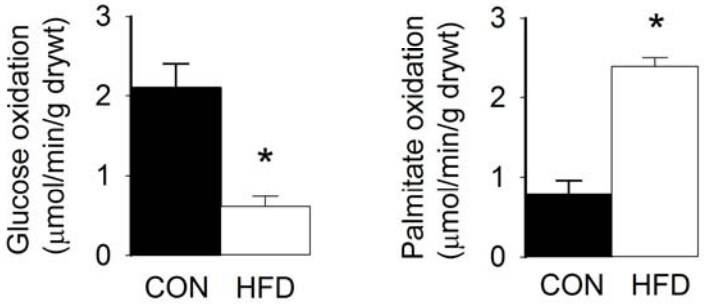
mRNA expression of the genes of interest was adjusted to the average of three housekeeping genes. For primer/probe sequences for housekeeping genes, mitochondrial thioesterase 1 (*mte1*), uncoupling protein 3 (*ucp3*): gluthadion peroxidase 3 (*gpx3*), catalase (*cat*), hexokinase2 (*hk2*), hypoxia-inducable factor 1 α (*hif α*), myosin heavy chain α (*mhcα*), tissue inhibitor of metallopeptidases 1 (*timp 1*), cardiac B-type natriuretic peptide (*bnp*), sarcoplasmic reticulum calcium ATPase 2 (*serca2*) see referance under. Forward and reverse primer and probe sequences (5'-3'): collagen III type α (*col III type1α*): forward: ACGTAGATGAATTGGGA-TGCAG, reverse: GGGTTGGGGCAGTCTAGTG, tissue inhibitor of metallopeptidase 1 (*timp1*): forward: GCAACTCGGACCTGGTCATAA T, reverse: CGGCCCGTGATGAGA-AACT, hexokinase (*hk2*): forward: GAAGGGGCTAGGAGCTACCA, reverse: CTCGGA-GCACACGGAAGTT, hypoxia-inducable factor 1 α (*hif α*): forward: GCACTAGACAA-AGTTCACCTGAGA, reverse: CGCTATCCACATCAAAGCAAA, atrial natriuretic peptide (*anp*) forward: CAC AGA TCT GAT GGA TTT CAA GA, reverse: CCT CAT CTT CTA CCG GCA TC ryanodine Receptor 2 (*ryr2*): forward: ATTATGAAGGTGGTGCCGTATCA, reverse: TTCCACTCCACGCGACTCTTA. Where probes are not specified, cyber green was used. Values are mean ± SEM, n=6-8 in each group, *$p<0.05$ *vs.* DIO_{SED}.

SUPPLEMENTARY DATA

Supplementary Figure 1. Glucose tolerance test and the area under curve calculations following intraperitoneal administration of glucose solution (1.3g/kg body weight) in chow fed lean control mice (CON, black circles) and mice fed a high fat diet (HFD, white circles) for 9 weeks. Values are mean ± SEM, n=6 in each group, *p<0.05.

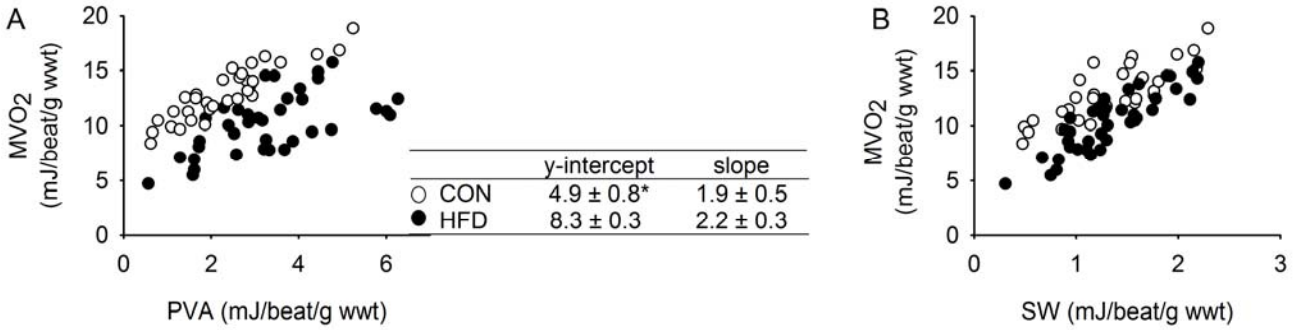


Supplementary Figure 2. Myocardial glucose and fatty acid oxidation rates measured in isolated perfused working hearts from chow fed lean control mice (CON, n=6) and mice fed a high fat diet (HFD, n=7) for 9 weeks. Values are mean ± SEM, *p<0.05.



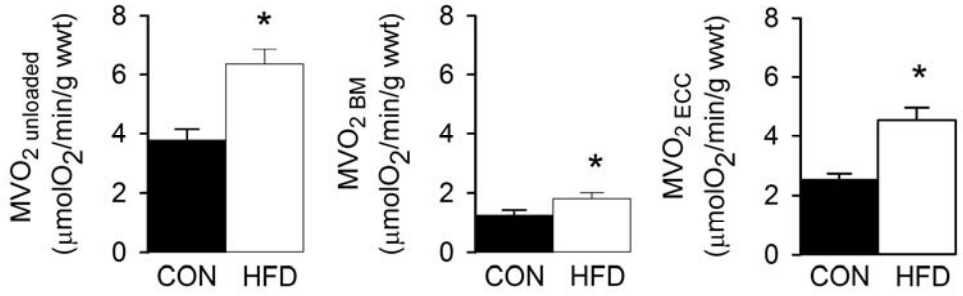
SUPPLEMENTARY DATA

Supplementary Figure 3. Individual values of myocardial oxygen consumption (MVO_2) and total mechanical energy (assessed as pressure-volume area, PVA, panel A) and stroke work (SW, panel B) in isolated working hearts from chow fed lean control mice (CON, black circles) and mice fed high fat diet (HFD, white circles) for 9 weeks at different workloads (preload: 4-10 mmHg, afterload: 40-50mmHg). The table below gives the y-intercept and the slope of the PVA-MVO_2 relationships. Values are mean ± SEM, n=5 in each group, *p<0.05.



	y-intercept	slope
○ CON	4.9 ± 0.8*	1.9 ± 0.5
● HFD	8.3 ± 0.3	2.2 ± 0.3

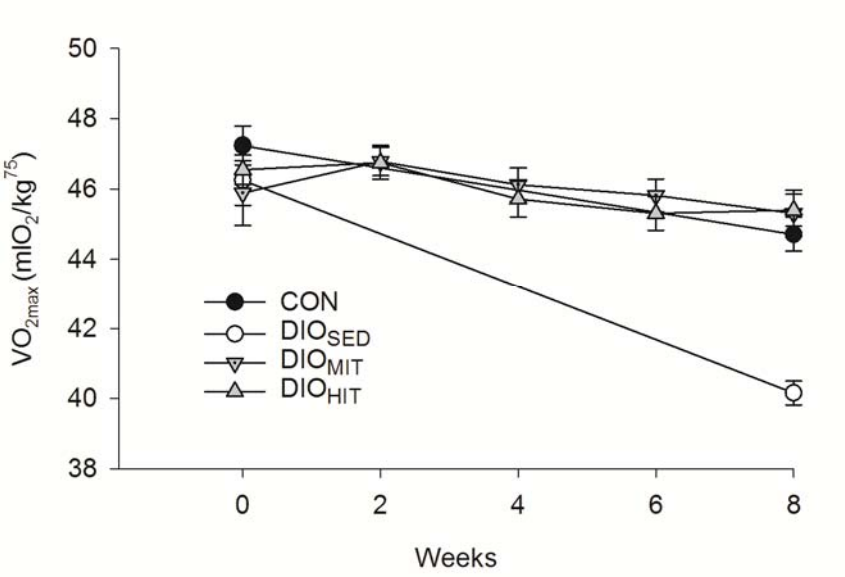
Supplementary Figure 4. Myocardial oxygen consumption (MVO_2) in retrograde perfused unloaded hearts, paced at 7Hz from chow fed lean control mice (CON, n=7) and mice fed a high fat diet (HFD, n=8) for 9 weeks before ($MVO_{2unloaded}$) and after electrical arrest (MVO_{2BM}). MVO_2 for excitation-contraction coupling (MVO_{2ECC}) is defined as the difference between $MVO_{2unloaded}$ and MVO_{2BM}. Values are mean ± SEM, *p<0.05.



SUPPLEMENTARY DATA

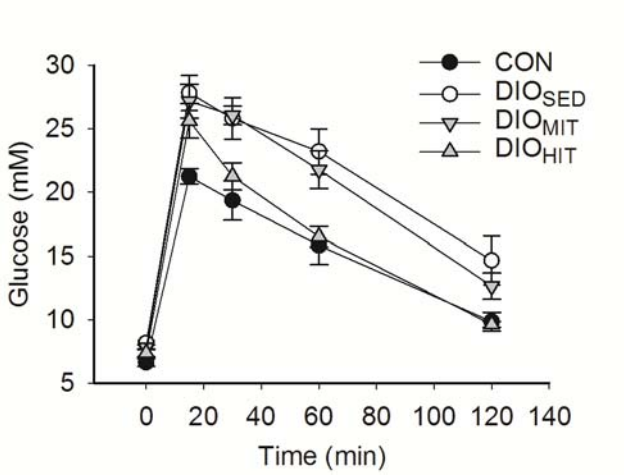
Supplementary Figure 5. Body weight development in chow fed lean control mice (CON, n=15) and diet-induced obese (DIO, n=35) mice. After 8-9 weeks DIO mice were divided into 3 groups and the diet was changed from high fat diet (60% kcal from fat) to a palatable western diet (35% kcal from fat, 27% fructose) and exercise protocols started. Sedentary (DIO_{SED}, n=15), moderate intensity trained (DIO_{MIT}, n=10) and high intensity interval trained mice (DIO_{HIT}, n=10). Values are mean ± SEM.

Supplementary Figure 6. Whole body maximal oxygen consumption (VO_{2max}) in lean (CON, n=15) and diet-induced obese sedentary (DIO_{SED}, n=15), moderate intensity trained (DIO_{MIT}, n=10) and high intensity interval trained mice (DIO_{HIT}, n=10) during the exercise period. Values are mean ± SEM.

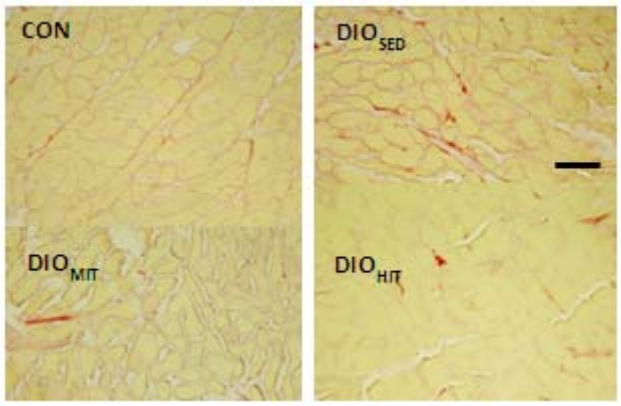


SUPPLEMENTARY DATA

Supplementary Figure 7. Glucose tolerance test and the area under curve calculations following an intraperitoneal administration of glucose solution (1.3g/kg body weight) in control (CON) and diet-induced obese sedentary (DIO_{SED}), moderate intensity trained (DIO_{MIT}) and high intensity interval trained mice (DIO_{HIT}). Values are meane ± SEM, n=8 in each group, *p<0.05 *vs.* DIO_{SED}.



Supplementary Figure 8. Representative pictures of Sirius red stained cardiac section (scale bar: 50µm) from lean control (CON) and diet-induced obese sedentary (DIO_{SED}), moderate intensity trained (DIO_{MIT}) and high intensity interval trained (DIO_{HIT},) mice.



SUPPLEMENTARY DATA

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3. Hafstad,AD, Boardman,NT, Lund,J, Hagve,M, Khalid,AM, Wisloff,U, Larsen,TS, Aasum,E. High intensity interval training alters substrate utilization and reduces oxygen consumption in the heart. J Appl Physiol 2011:111:1235-1241