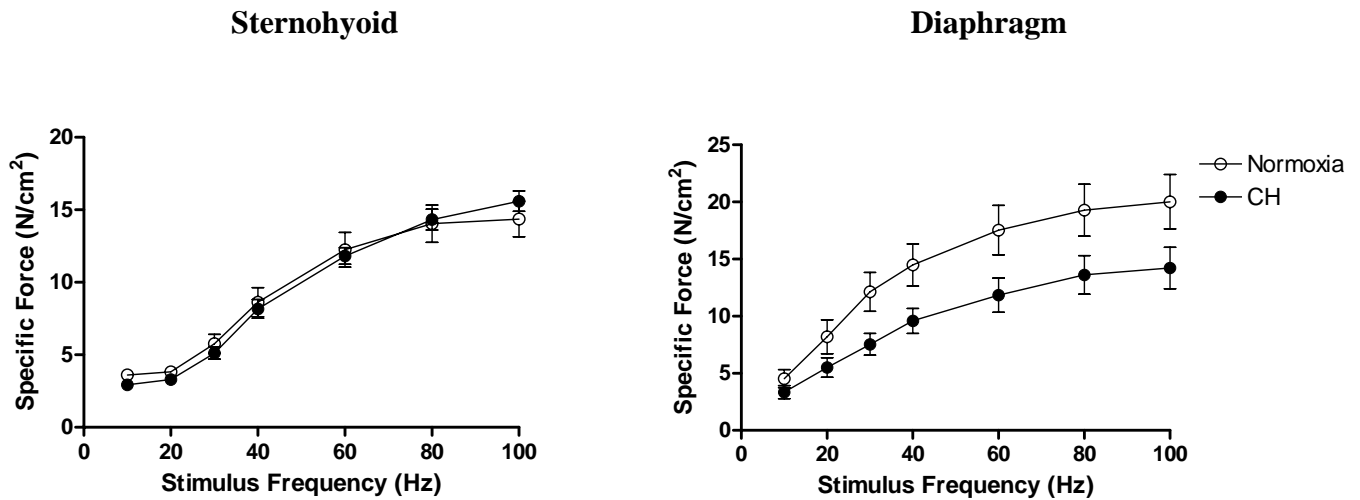


ONLINE DATA SUPPLEMENT
Figures and Tables

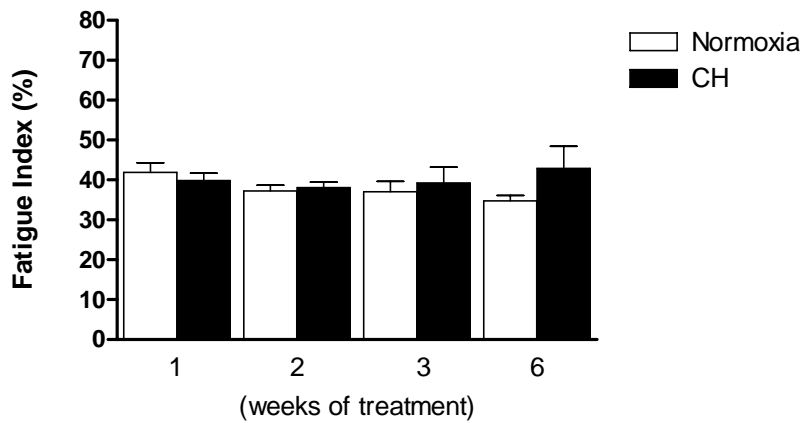
FIGURE 1: EFFECT OF CHRONIC HYPOXIA ON RESPIRATORY MUSCLE FORCE



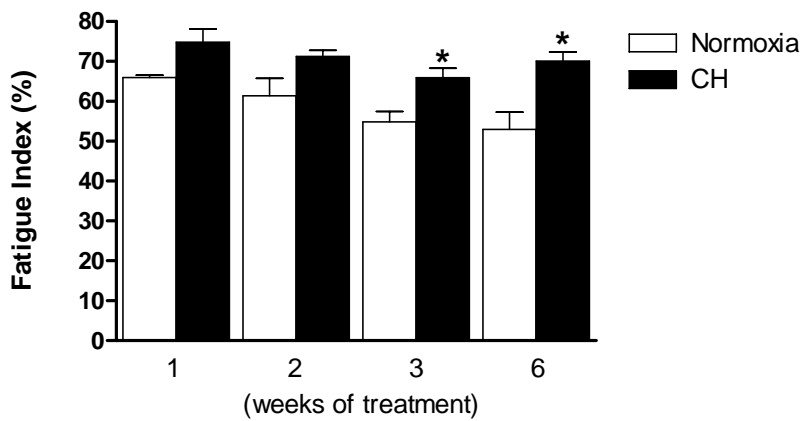
Values (mean \pm S.E.M.) for respiratory muscle force-frequency relationship in rats exposed to 6 weeks of normoxia or chronic hypoxia (CH). Two-way ANOVA for diaphragm force-frequency relationship revealed CH: $P=0.07$; Frequency: $P<0.001$; Interaction: $P=0.0006$ ($n=6$ for both groups).

FIGURE 2: EFFECT OF CHRONIC HYPOXIA ON RESPIRATORY MUSCLE FATIGUE INDEX

Sternohyoid



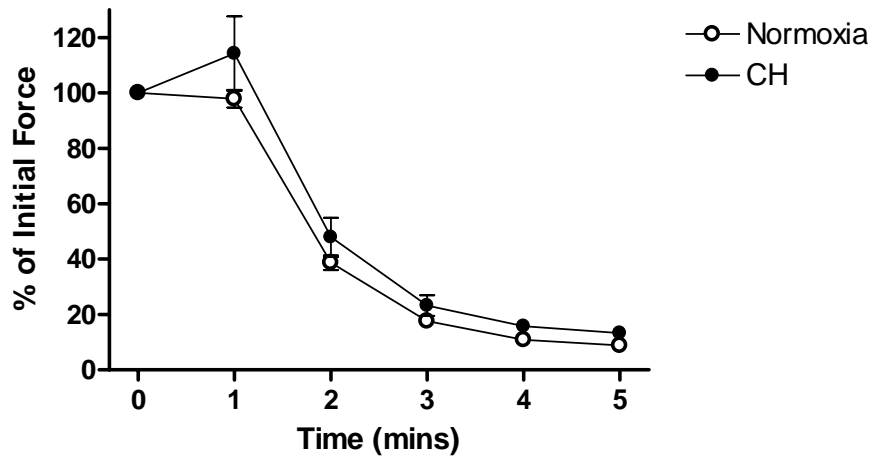
Diaphragm



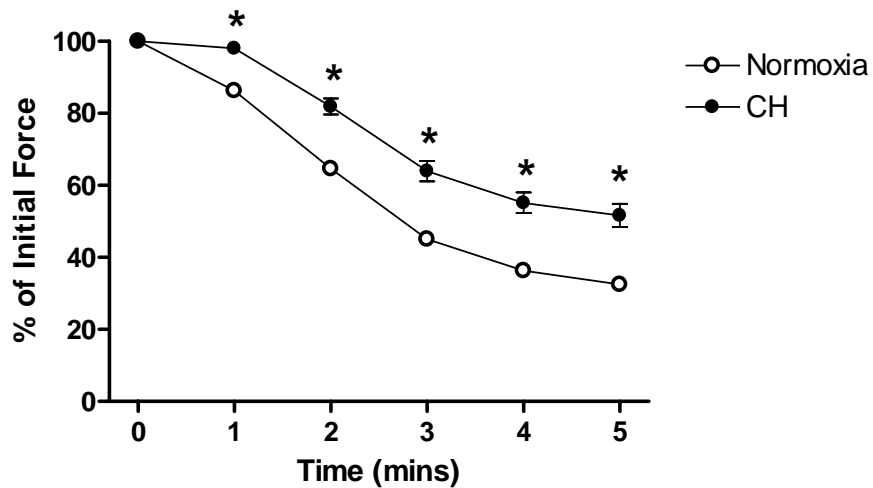
Values (mean \pm S.E.M.) for respiratory muscle fatigue index in rats exposed to 1-6 weeks of normoxia or chronic hypoxia (CH). * indicates significant difference from control (ANOVA, $P < 0.05$; $n = 6$ for both groups).

FIGURE 3: EFFECT OF CHRONIC HYPOXIA ON RESPIRATORY MUSCLE ENDURANCE

STERNOHYOID

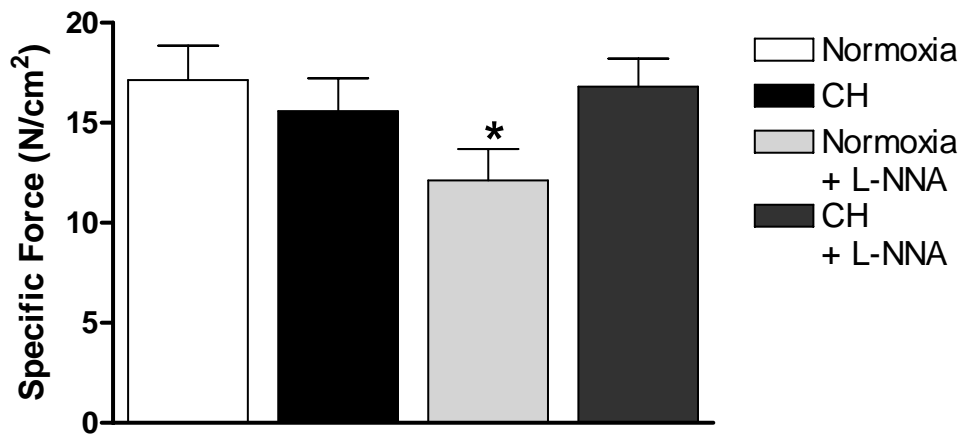


DIAPHRAGM



Values (mean \pm S.E.M.) for respiratory muscle endurance in rats exposed to 6 weeks of normoxia or chronic hypoxia (CH). Two-way ANOVA, CH: $P=0.0058$; Time: $P<0.0001$; Interaction: $P<0.0001$. * indicates significant difference from normoxia (n=6 for both groups).

**FIGURE 4: CHRONIC NOS INHIBITION DECREASES
NORMOXIC DIAPHRAGM FORCE**



Values (mean \pm S.E.M.) for diaphragm muscle peak tetanic force in normoxic and chronic hypoxic (CH) rats \pm chronic NOS inhibition (2mM L-NNA in the drinking water). * indicates significant difference from normoxia (ANOVA, $P < 0.05$, $n = 5-6$ per group).

TABLE 1: BODY MASS, HAEMATOCRIT AND RIGHT VENTRICULAR MASS

	Body Mass (g)	Haematocrit (%)	RVM (mg)	RVM/BM (mg/100g)
1 Week				
Normoxia	305.7 ± 7.4	39.3 ± 1.7	154.3 ± 7.4	50.4 ± 1.9
CH	*238.3 ± 5.0	*62.6 ± 1.9	*194.8 ± 8.9	*81.6 ± 3.0
2 Weeks				
Normoxia	302.3 ± 5.0	39.6 ± 1.1	157.8 ± 3.4	52.2 ± 0.9
CH	*229.7 ± 4.6	*70.1 ± 1.0	*204.7 ± 11.2	*89.1 ± 4.4
3 Weeks				
Normoxia	325.0 ± 10.3	45.0 ± 0.7	166.8 ± 3.6	51.6 ± 1.9
CH	*255.0 ± 8.3	*71.3 ± 1.0	*238.7 ± 18.9	*92.9 ± 4.4
6 Weeks				
Normoxia	369.8 ± 5.9	43.0 ± 2.6	164.7 ± 3.9	44.5 ± 0.6
CH	*277.5 ± 7.9	*75.1 ± 1.4	*251.3 ± 8.0	*90.7 ± 2.7

Definition of abbreviations: RVM = right ventricle mass; BM = body mass; CH = chronic hypoxia. Values are mean ± S.E.M.; n=6 per group. * indicates significant difference from corresponding control (normoxia) value (Student's *t* test, P<0.05).

TABLE 2: RESPIRATORY MUSCLE FORCE AND CONTRACTILE KINETICS

	Pt (N/cm²)	Po (N/cm²)	CT (ms)	HRT (ms)
STERNOHYOID				
1 Week				
Normoxia (n=6)	1.8 ± 0.1	9.6 ± 0.9	24.0 ± 1.9	18.3 ± 2.0
CH (n=6)	*2.5 ± 0.1	*13.1 ± 1.2	25.4 ± 1.3	21.1 ± 1.7
2 Weeks				
Normoxia (n=6)	2.6 ± 0.2	15.2 ± 1.4	20.3 ± 1.0	19.2 ± 1.4
CH (n=6)	3.1 ± 0.1	15.5 ± 1.9	21.6 ± 0.5	17.0 ± 1.4
3 Weeks				
Normoxia (n=5)	2.8 ± 0.4	16.2 ± 1.9	19.9 ± 0.5	16.9 ± 0.8
CH (n=6)	2.9 ± 0.3	14.5 ± 1.7	19.7 ± 1.0	17.9 ± 1.5
6 Weeks				
Normoxia (n=6)	3.3 ± 0.4	14.4 ± 1.2	18.9 ± 0.4	16.0 ± 1.0
CH (n=6)	2.5 ± 0.3	15.6 ± 0.7	18.8 ± 0.5	16.3 ± 1.1
DIAPHRAGM				
1 Week				
Normoxia (n=3)	2.8 ± 0.6	12.2 ± 3.0	30.6 ± 0.6	37.8 ± 3.7
CH (n=6)	3.6 ± 0.7	15.6 ± 1.7	*39.5 ± 2.4	*52.3 ± 2.5
2 Weeks				
Normoxia (n=6)	2.9 ± 0.4	14.2 ± 1.5	29.3 ± 1.2	49.5 ± 6.1
CH (n=6)	2.8 ± 0.3	14.5 ± 1.0	30.7 ± 1.1	36.9 ± 2.6

3 Weeks

Normoxia (n=5)	2.5 ± 0.3	17.0 ± 2.2	30.6 ± 0.5	44.0 ± 3.8
CH (n=6)	*4.0 ± 0.5	17.9 ± 3.3	30.4 ± 1.2	40.0 ± 1.4

6 Weeks

Normoxia (n=6)	4.0 ± 0.7	20.0 ± 2.3	32.2 ± 0.8	36.8 ± 3.0
CH (n=6)	2.8 ± 0.4	14.2 ± 1.8	31.2 ± 0.6	37.0 ± 3.2

Definition of abbreviations: Pt = single twitch tension; Po = peak tetanic tension; CT = contraction time; HRT = half relaxation time; CH = chronic hypoxia. Values are mean ± S.E.M. * indicates significant difference from corresponding control (normoxia) value (Student's *t* test, P<0.05).

TABLE 3: Na⁺ - K⁺ PUMP CONTENT

	Sternohyoid	Diaphragm	Soleus	EDL
Normoxia	317 ± 19	370 ± 7	278 ± 7	378 ± 10
CH	351 ± 32	*458 ± 12	277 ± 13	*420 ± 9
Normoxia + L-NNA	*253 ± 14	*317 ± 40	-	358 ± 15
CH + L-NNA	301 ± 13	360 ± 23	-	403 ± 14

Definition of abbreviations: CH = chronic hypoxia; L-NNA = N-nitro-L-arginine (NOS inhibitor): 2mM in the drinking water throughout gas treatments. Values are mean ± S.E.M. for Na⁺-K⁺ pump content (ouabain binding sites occupied pmol.g wet weight⁻¹) in respiratory and limb muscles (n=5-6 for all except n=3-5 for soleus). * indicates significant difference from normoxia (ANOVA, P<0.05).

TABLE 4: STERNOHYOID AND DIAPHRAGM MUSCLE CSA

	Type 1	Type 2A	Type 2X	Type 2B
STERNOHYOID				
Normoxia	993 ± 64	1192 ± 31	1999 ± 43	3792 ± 64
CH	891 ± 44	*1489 ± 52	*2235 ± 70	3834 ± 53
Normoxia + L-NNA	1064 ± 52	*1393 ± 59	1809 ± 63	4095 ± 70
CH + L-NNA	1047 ± 71	1121 ± 30	1776 ± 52	3523 ± 58
DIAPHRAGM				
Normoxia	1410 ± 38	1422 ± 26	2565 ± 80	5024 ± 177
CH	*1232 ± 25	1384 ± 23	*2040 ± 75	*3424 ± 85
Normoxia + L-NNA	1315 ± 29	*1635 ± 47	2505 ± 138	*4623 ± 325
CH + L-NNA	*1151 ± 27	1362 ± 35	*2152 ± 138	5325 ± 323

Definition of abbreviations: CSA = cross-sectional area; CH = chronic hypoxia; L-NNA = N-nitro-L-arginine (NOS inhibitor): 2mM in the drinking water throughout gas treatments. Values are mean ± S.E.M. for fibre CSA (μm^2); n=5-10 per group. * indicates significant difference from corresponding normoxia value (ANOVA, P<0.05).

TABLE 5: SOLEUS AND EDL MUSCLE CSA

	Type 1	Type 2A	Type 2X	Type 2B
SOLEUS				
Normoxia	3590 ± 63	4050 ± 143		
CH	3665 ± 86	*3350 ± 119		
Normoxia + L-NNA	3061 ± 76	*2548 ± 123		
CH + L-NNA	2738 ± 62	*2393 ± 81		
EDL				
Normoxia	1003 ± 70	1134 ± 41	1979 ± 92	1578 ± 54
CH	1094 ± 90	1190 ± 42	*1483 ± 105	1533 ± 60
Normoxia + L-NNA	*1281 ± 56	*1328 ± 30	1896 ± 94	*2829 ± 62
CH + L-NNA	1139 ± 45	1230 ± 31	*1616 ± 60	*2667 ± 91

Definition of abbreviations: CSA = cross-sectional area; CH = chronic hypoxia; L-NNA = N-nitro-L-arginine (NOS inhibitor); 2mM in the drinking water throughout gas treatments. Values are mean ± S.E.M. for fibre CSA (μm^2); n=4-6 per group. MHC fibre typing indicated no type 2X or type 2B fibres in soleus muscle. * indicates significant difference from corresponding normoxia value (ANOVA, $P < 0.05$).