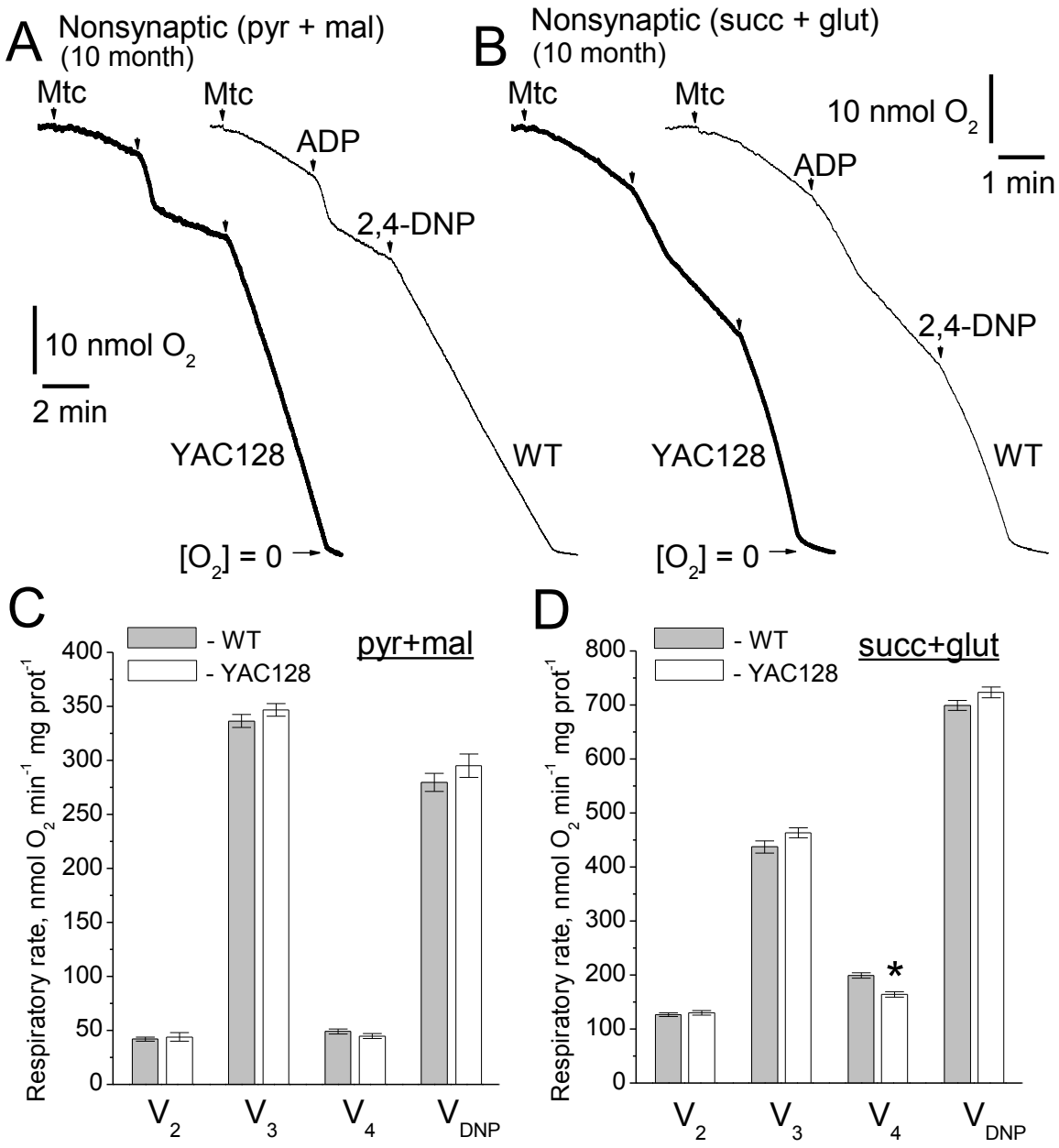
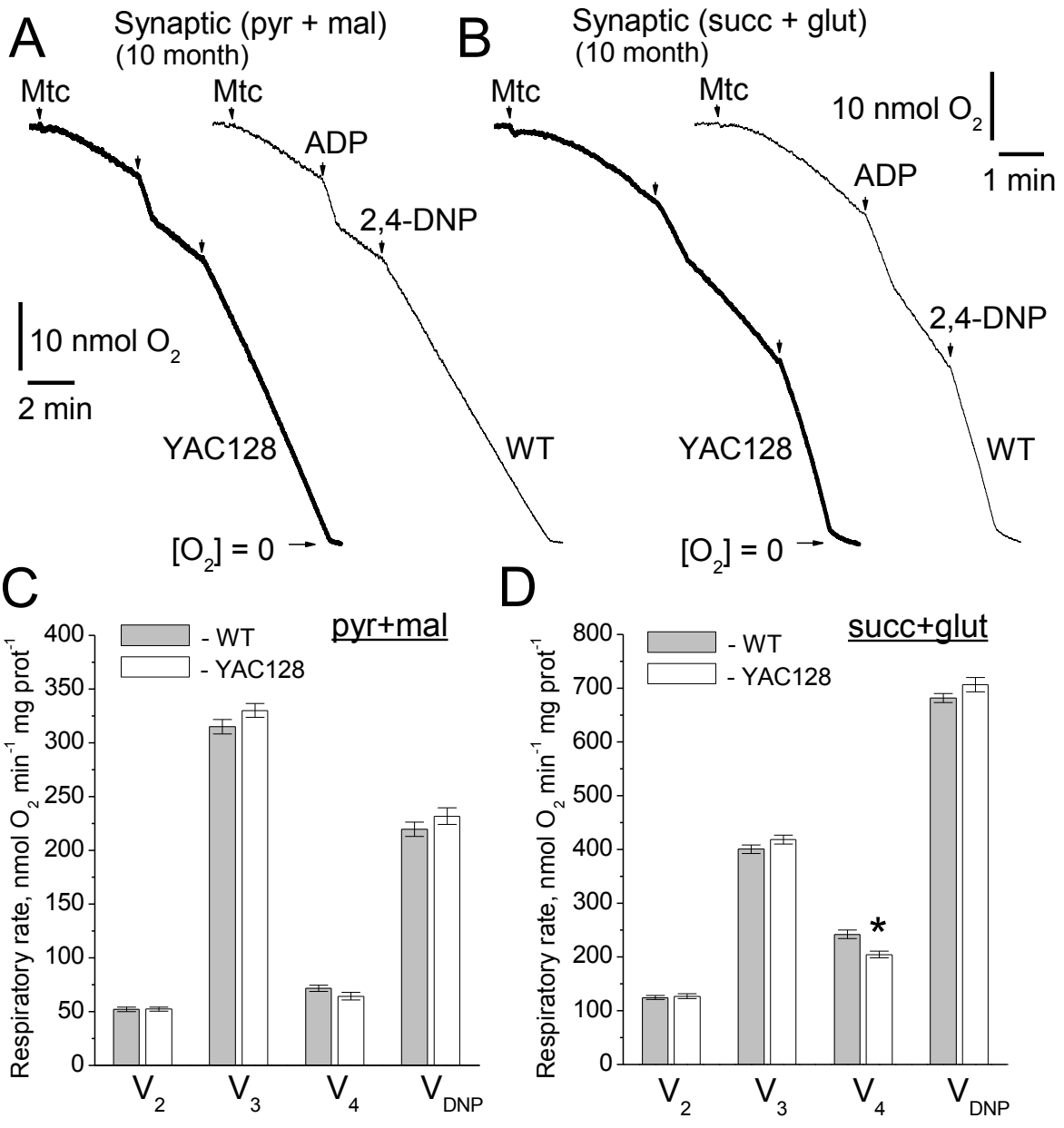
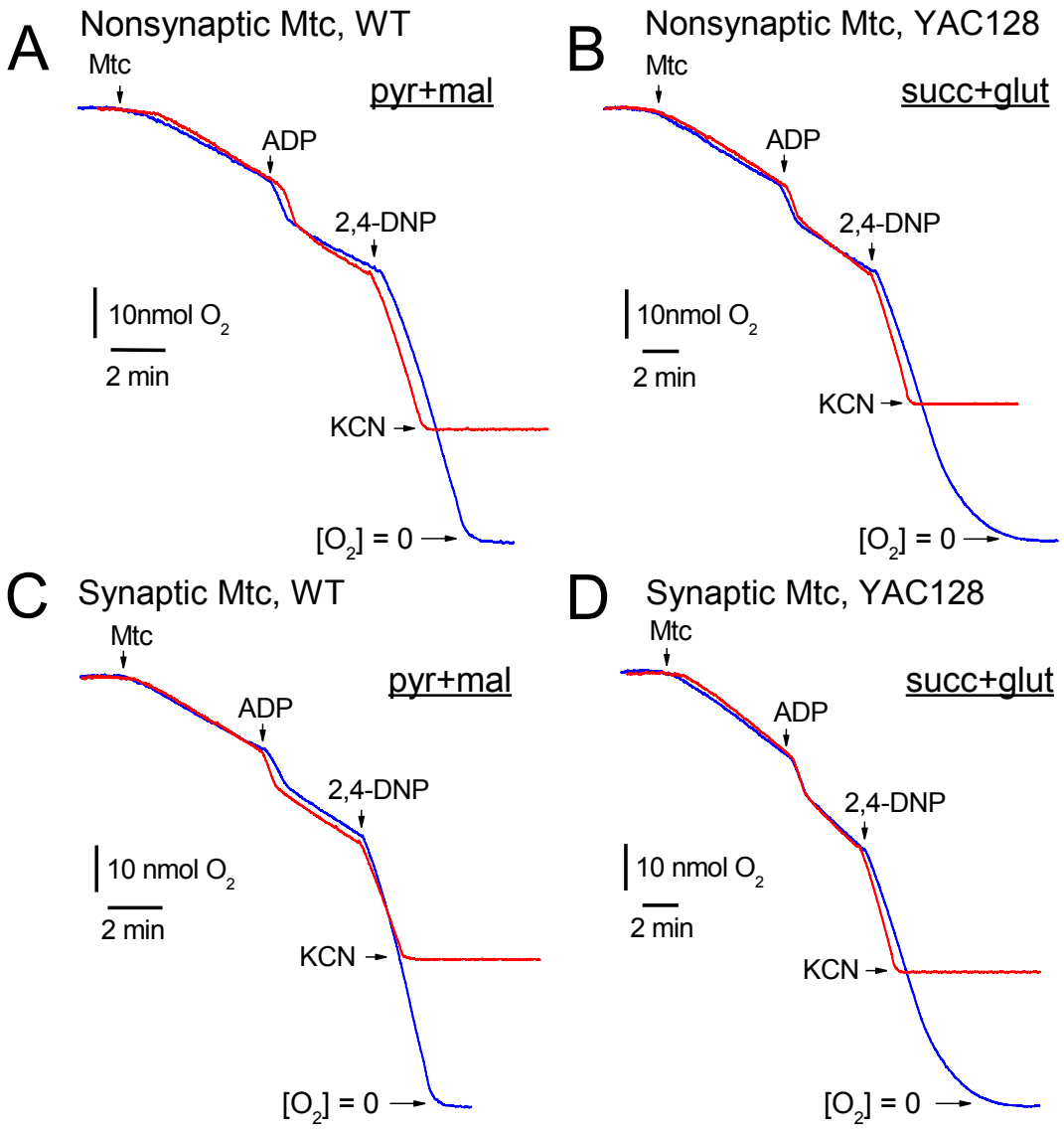
SUPPLEMENTAL MATERIALS



Suppl. Figure 1. Respiratory activity of nonsynaptic mitochondria isolated from 10-month old WT (thin traces) and YAC128 (thick traces) mice. In **A** and **B**, representative traces for mitochondrial O_2 consumption. Where indicated, mitochondria (Mtc), 200μM ADP, and 60μM 2,4-dinitophenol (2,4-DNP) were added. In **A**, incubation medium was supplemented with 3 mM pyruvate (pyr) and 1 mM malate (mal). In **B**, incubation medium contained 3 mM succinate (succ) and 3 mM glutamate (glut). In **C** and **D**, statistical analysis of respiratory rates. Data are mean±SEM *p<0.05 comparing V_4 respiratory rates of mitochondria from WT and YAC128 mice, N=7.

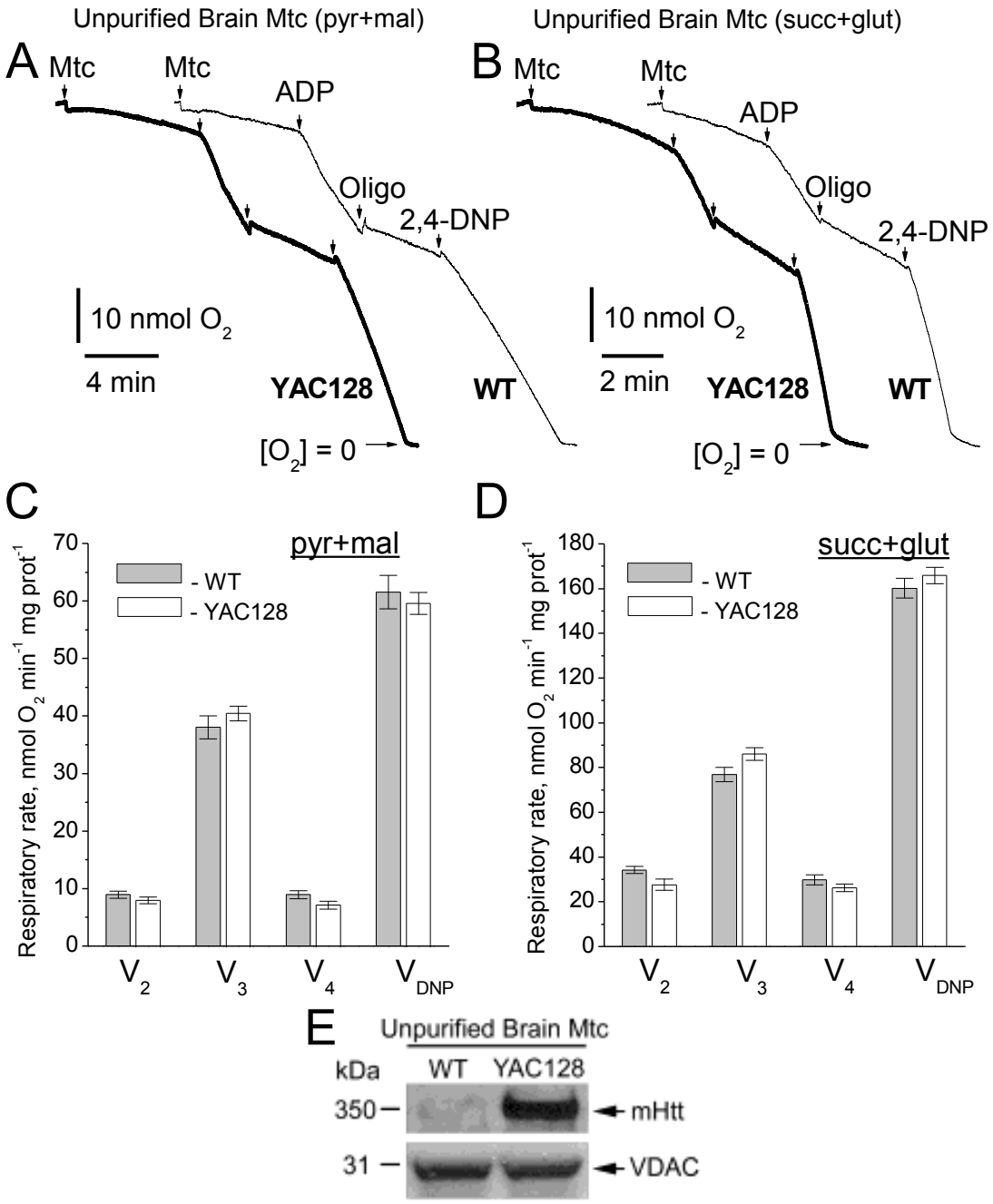


Suppl. Figure 2. Respiratory activity of synaptic mitochondria isolated from 10-month old WT (thin traces) and YAC128 (thick traces) mice. In **A** and **B**, representative traces for mitochondrial O_2 consumption. Where indicated, mitochondria (Mtc), 200μM ADP, and 60μM 2,4-dinitophenol (2,4-DNP) were added. In **A**, incubation medium was supplemented with 3 mM pyruvate (pyr) and 1 mM malate (mal). In **B**, incubation medium contained 3 mM succinate (succ) and 3 mM glutamate (glut). In **C** and **D**, statistical analysis of respiratory rates. Data are mean±SEM. *$p<0.05$ comparing V_4 respiratory rates of mitochondria from WT and YAC128 mice, N=7.

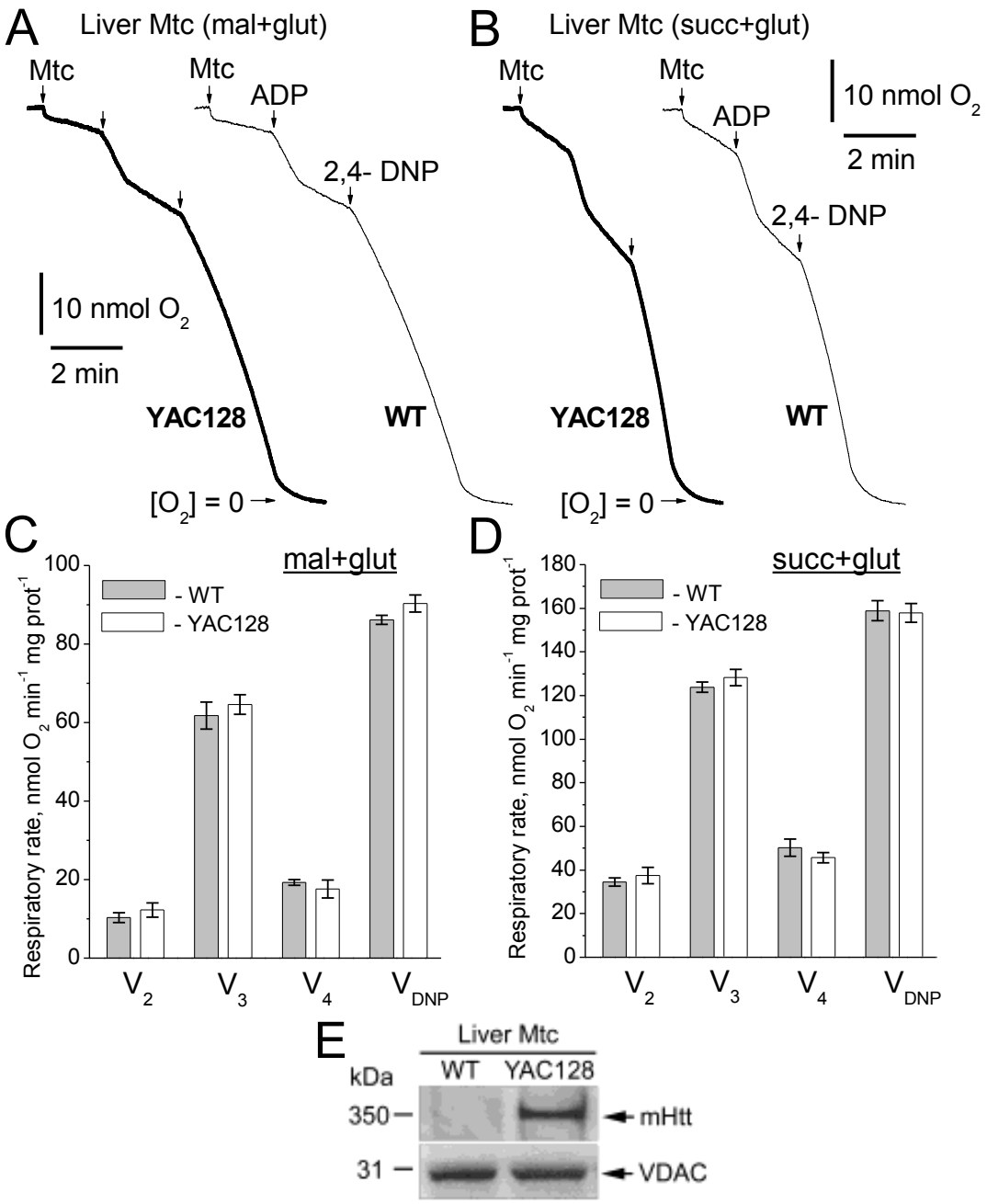


Suppl Fig 3.

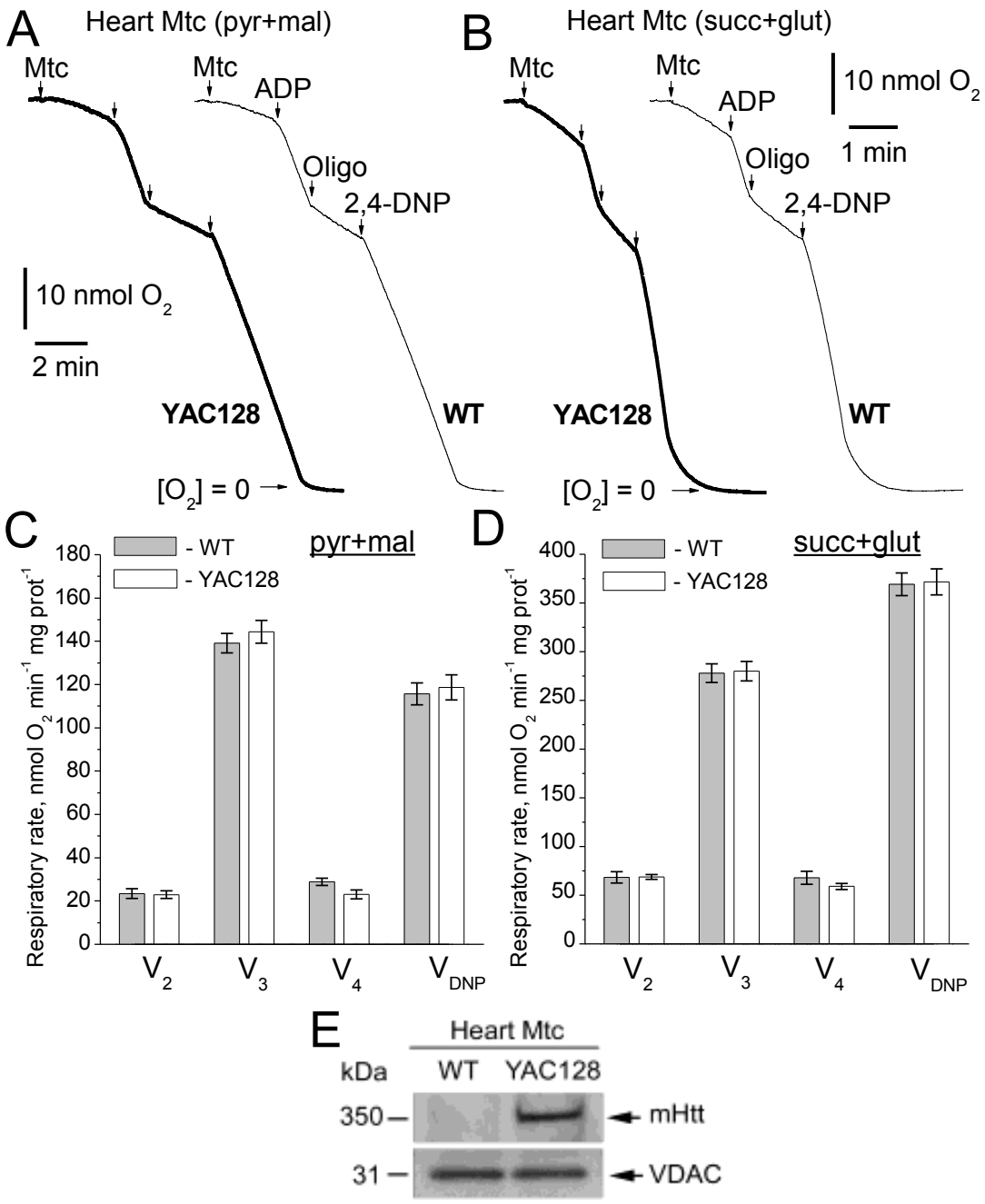
Suppl. Figure 3. KCN completely inhibits respiration of isolated brain mitochondria. In **A** and **B**, representative traces for mitochondrial O_2 consumption by nonsynaptic mitochondria from WT and YAC128 mice. In **C** and **D**, representative traces for mitochondrial O_2 consumption by synaptic mitochondria from WT and YAC128 mice. Where indicated, mitochondria (Mtc), 200μM ADP, 60μM 2,4-dinitophenol (2,4-DNP), and 5 mM KCN were added. In **A** and **C**, incubation medium was supplemented with 3 mM pyruvate (pyr) and 1 mM malate (mal). In **B** and **D**, incubation medium was supplemented with 3 mM succinate (succ) and 3 mM glutamate (glut).



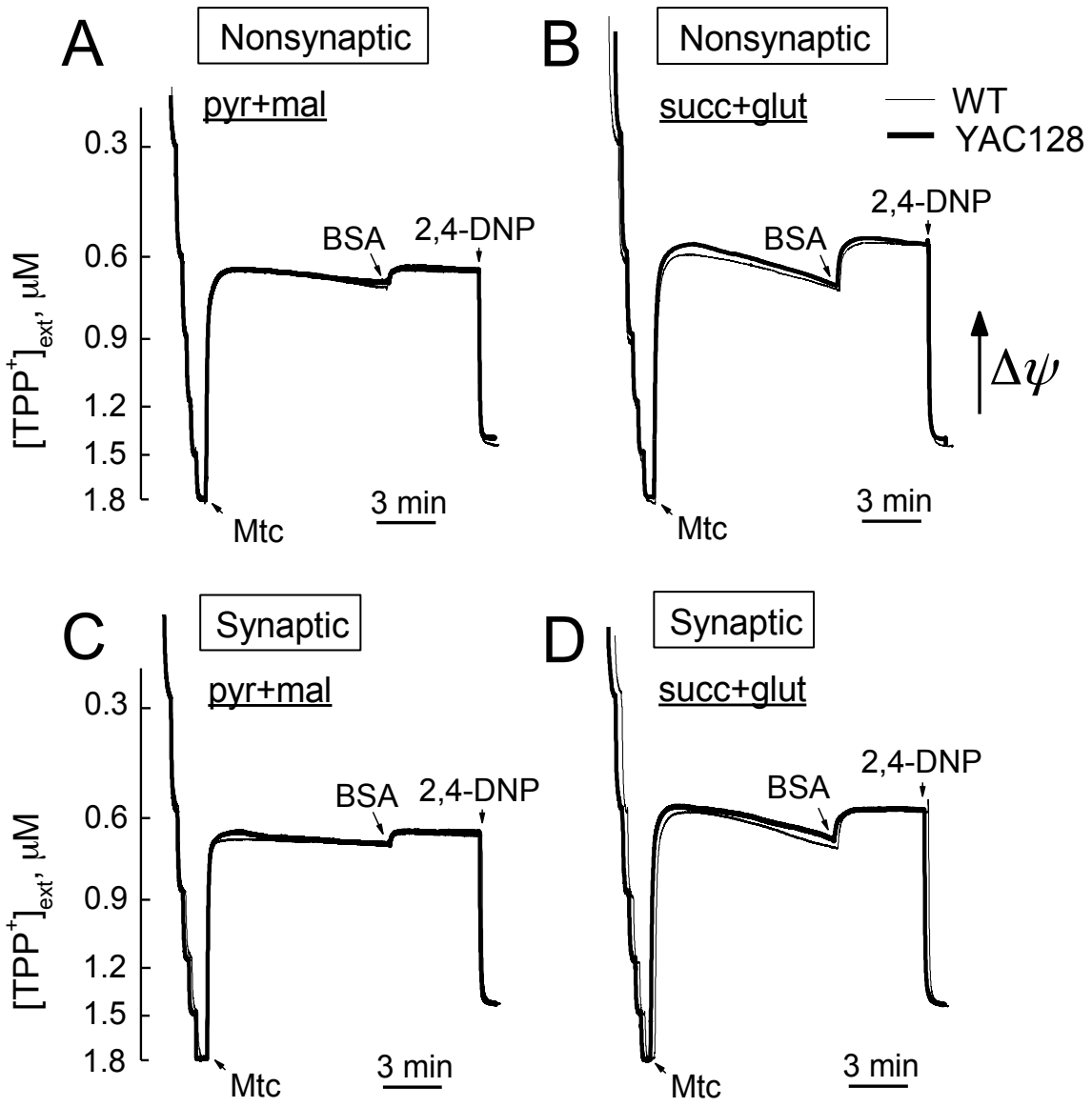
Suppl. Figure 4. Respiratory activity of unpurified brain mitochondria isolated from 2-month old WT (thin traces) and YAC128 (thick traces) mice. In **A** and **B**, representative traces for mitochondrial O_2 consumption. Where indicated, mitochondria (Mtc), 200μM ADP, 1μM oligomycin (to inhibit ATP synthase) and 60μM 2,4-dinitophenol (2,4-DNP) were added. In **A**, incubation medium was supplemented with 3 mM pyruvate (pyr) and 1 mM malate (mal). In **B**, incubation medium contained 3 mM succinate (succ) and 3 mM glutamate (glut). In **C** and **D**, statistical analysis of respiratory rates. Data are mean±SEM, N=7. **E,** Western blot, showing the presence of mHtt in unpurified brain mitochondria from YAC128 mice. VDAC was used as a loading control.



Suppl. Figure 5. Respiratory activity of liver mitochondria isolated from 2-month old WT (thin traces) and YAC128 (thick traces) mice. In **A** and **B**, representative traces for mitochondrial O_2 consumption. Where indicated, mitochondria (Mtc), 200μM ADP, and 60μM 2,4-dinitophenol (2,4-DNP) were added. In **A**, incubation medium was supplemented with 3 mM glutamate (glut) and 1 mM malate (mal). In **B**, incubation medium was with 3 mM succinate (succ) and 3 mM glutamate (glut). In **C** and **D**, statistical analysis of respiratory rates. Data are mean±SEM, N=6. **E,** Western blot, showing the presence of mHtt in liver mitochondria from YAC128 mice. VDAC was used as a loading control.



Suppl. Figure 6. Respiratory activity of heart mitochondria isolated from 2-month old WT (thin traces) and YAC128 (thick traces) mice. In **A** and **B**, representative traces for mitochondrial O_2 consumption. Where indicated, mitochondria (Mtc), 200μM ADP, 1μM oligomycin (to inhibit ATP synthase) and 60μM 2,4-dinitophenol (2,4-DNP) were added. In **A**, incubation medium was supplemented with 3 mM pyruvate (pyr) and 1 mM malate (mal). In **B**, incubation medium was with 3 mM succinate (succ) and 3 mM glutamate (glut). In **C** and **D**, statistical analysis of respiratory rates. Data are mean±SEM, N=6. **E,** Western blot, showing the presence of mHtt in heart mitochondria from YAC128 mice. VDAC was used as a loading control.



Suppl Fig 7.

Suppl. Figure 7. The effect of bovine serum albumin (BSA) on mitochondrial membrane potential in nonsynaptic (A, B) and synaptic (C, D) mitochondria isolated from 2-month old WT (thin traces) and YAC128 (thick traces) mice. Representative traces for TPP^+ accumulation indicating changes in mitochondrial membrane potential ($\Delta\psi$) in response to 0.1% BSA (free from fatty acids) and 60μM 2,4-dinitrophenol. In **A** and **C**, incubation medium was supplemented with 3 mM pyruvate (pyr) and 1 mM malate (mal). In **B** and **D**, incubation medium contained 3 mM succinate (succ) and 3 mM glutamate (glut).

Supplemental Table 1. **Calculation of a sample size using Power Analysis method**.

Respiration						
	Nonsynaptic Mtc			**Synaptic Mtc**		
	Pyruvate + Malate					
Effect size	10%	20%	30%	10%	20%	30%
V_3	29.7	59.4	89.1	30.8	61.6	92.4
SD	22.6	22.6	22.6	18.6	18.6	18.6
N=	10	4	3	7	3	3
V_{DNP}	21.8	43.6	65.4	20.6	41.2	61.8
SD	14.4	14.4	14.4	13.5	13.5	13.5
N=	8	4	3	8	4	3
	Nonsynaptic Mtc			**Synaptic Mtc**		
	Succinate + Glutamate					
Effect size	10%	20%	30%	10%	20%	30%
V_3	31.8	63.6	95.4	40.7	81.4	122.1
SD	23.5	23.5	23.5	22.8	22.8	22.8
N=	10	4	3	7	3	3
V_{DNP}	49.1	98.2	147.3	70.9	141.8	212.7
SD	25.1	25.1	25.1	43.9	43.9	43.9
N=	6	3	3	8	3	3
Membrane potential ($\Delta\psi$)						
	Nonsynaptic Mtc			**Synaptic Mtc**		
	Pyruvate + Malate					
Effect size	10%	20%	30%	10%	20%	30%
$\Delta\psi$	15.2	30.4	45.6	14.6	29.2	43.8
SD	6.8	6.8	6.8	7.9	7.9	7.9
N=	6	3	3	6	3	3
	Nonsynaptic Mtc			**Synaptic Mtc**		
	Succinate + Glutamate					
Effect size	10%	20%	30%	10%	20%	30%
$\Delta\psi$	16.6	33.2	49.8	15.7	31.4	47.1
SD	8.0	8.0	8.0	9.2	9.2	9.2
N=	6	3	3	7	3	3

Power analysis was performed using G*Force software version 3.1.9.2 (by Franz Faul, Universitat Kiel, Germany) to establish the sample size necessary to detect a 10 and 20% difference between mitochondria from WT and YAC128 mice. Based on this power analysis,

the number of experiments that gives an 80% likelihood (the accepted level in statistical analysis) of detecting 10% difference between two means at the significance level of α=0.05 is within the range of 6 to 10 experiments. The number of experiments suitable for statistical analysis was assumed to be 3 or higher. V_3, respiratory rate in the presence of 200μM ADP; V_{DNP}, respiratory rate in the presence of 60μM 2,4-DNP; $\Delta\psi$, mitochondrial membrane potential; SD, standard deviation. Where indicated, the incubation medium was supplemented either with 3 mM pyruvate plus 1 mM malate or with 3 mM succinate plus 3 mM glutamate.