2k brief Diabetes
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High-resolution respirometry: Diabetes

Time-restricted feeding during the inactive phase abolishes the daily rhythm in mitochondrial respiration in rat skeletal muscle

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OXPHOS capacity, uncoupled respiration and succinate/rotenone-linked respiration lower in the *soleus* muscle from rats that were time-restricted fed (TRF) during the light (inactive) phase, compared to rats with a normal *ad libitum* diet

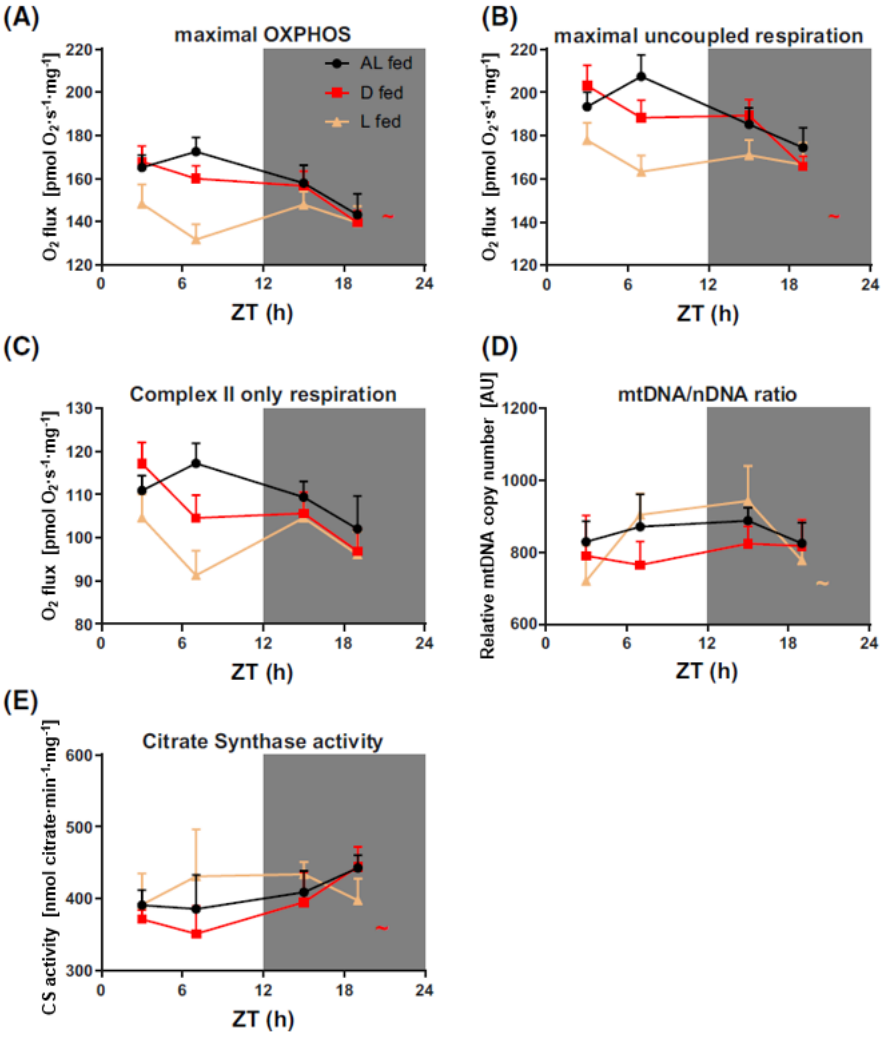

Figure 1. Daily profiles of the different mitochondrial respiration states and the mitochondrial abundance (mtDNA/nDNA ratio). **(A)** Maximal oxidative phosphorylation (OXPHOS; with pyruvate, glutamate, malate, and succinate). **(B)** Maximal uncoupled respiration (with FCCP). **(C)** Complex II only respiration (with succinate/rotenone). **(D)** Mitochondrial abundance (mtDNA/nDNA ratio). **(E)** Citrate synthase activity; Three technical replicates were measured for each biological replicate. *N* = 6 - 8 per experimental group per time point. Table 1 summarizes the main statistical findings for the mitochondrial respiration states and mtDNA/nDNA ratio. Color- coded "~" indicates that the (metabolic) parameter is significantly rhythmic for that TRF group as determined by JTK_Cycle ($p < .05$) ZT: Zeitgeber time points, AL fed: *ad libitum*, D fed: dark fed, L fed: Light fed.

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Table 1. Summary of the two- way ANOVA of oxidative phosphorylation (OXPHOS) capacity, maximal uncoupled respiration, succinate/rotenone- linked respiration, mtDNA/nDNA ratio, and CS activity.

	Two-way ANOVA *p* values			Post-hoc differences for effect of time		
Step	ZT	TRF	TRF post-hoc test	TRF group	One-way ANOVA (ZT)	JTK_Cycle
OXPHOS capacity (Figure 2A)	**0.011**	**0.002**	L < AL & D	AL	0.084	0.192
				D	**0.026**	0.091
				L	0.367	0.999
Uncoupled respiration (Figure 2B)	**0.008**	**0.001**	L < AL & D	AL	0.072	0.120
				D	**0.019**	0.091
				L	0.604	0.999
Succinate/rotenone (Figure 2C)	**0.030**	**0.015**	L < AL	AL	0.241	0.368
				D	0.072	0.322
				L	0.247	0.999
mtDNA/nDNA ratio (Figure 2D)	0.594	0.128	–	AL	0.885	0.999
				D	0.942	0.999
				L	0.172	**0.020**
Citrate synthase activity (Figure 2E)	0.680	0.626		AL	0.643	0.102
				D	0.185	**0.041**
				L	0.123	0.444

Note: Post hoc differences between groups are displayed. For the effect of time both one-way ANOVAs and cosinor analyses using JTK_Cycle were used as post-hoc test. No significant interactions (*ZT* × *TRF*) were found. Bold values correspond to *p*-values <.05.

Mistimed eating in relation to circadian rhythms, as often found during shift-work, disrupts mitochondrial function and reduces respiratory rates and metabolic flexibility, which could contribute to type-2 diabetes mellitus.

Reference: de Goede P, Wüst RCI, Schomakers BV, Denis S, Vaz FM, Pras-Raves ML, van Weeghel M, Yi CX, Kalsbeek A, Houtkooper RH (2022) Time-restricted feeding during the inactive phase abolishes the daily rhythm in mitochondrial respiration in rat skeletal muscle. https://doi.org/10.1096/fj.202100707R

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