iScience, Volume *24*

Supplemental information

Time-restricted feeding rescues high-fat-diet-induced hippocampal impairment

Jennifer A. Davis, Jodi R. Paul, Stefani D. Yates, Elam J. Cutts, Lori L. McMahon, Jennifer S. Pollock, David M. Pollock, Shannon M. Bailey, and Karen L. Gamble

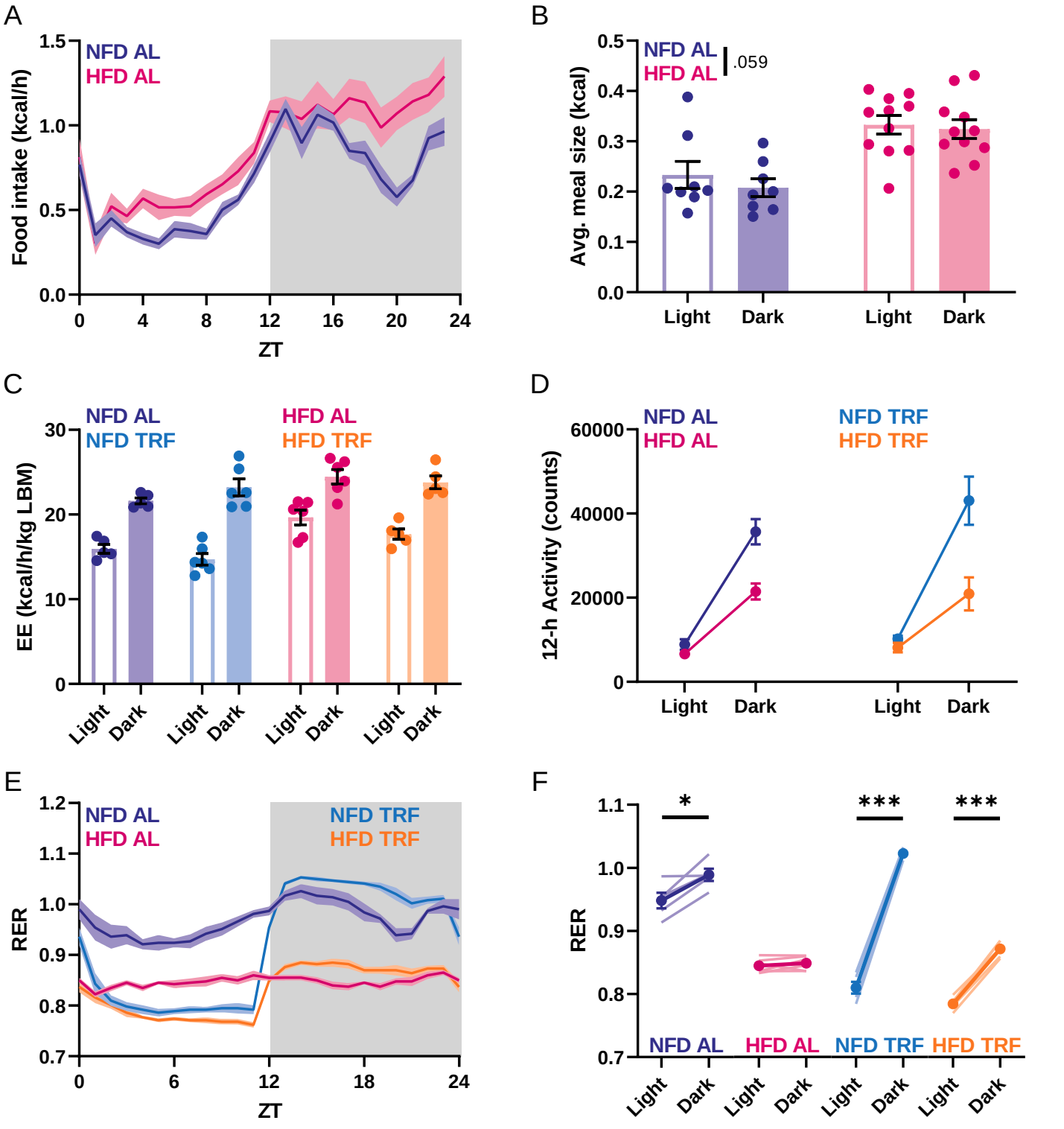
A
NFD AL
HFD AL
Food intake (kcal/h)
1.5
1.0
0.5
0.0
0
4
8
12
16
20
24
ZT
B
NFD AL
HFD AL
.059
Avg. meal size (kcal)
0.5
0.4
0.3
0.2
0.1
0.0
Light
Dark
Light
Dark
C
NFD AL
NFD TRF
HFD AL
HFD TRF
EE (kcal/h/kg LBM)
30
20
10
0
Light
Dark
Light
Dark
Light
Dark
Light
Dark
D
NFD AL
HFD AL
NFD TRF
HFD TRF
12-h Activity (counts)
60000
40000
20000
0
Light
Dark
Light
Dark
E
NFD AL
HFD AL
NFD TRF
HFD TRF
RER
1.2
1.1
1.0
0.9
0.8
0.7
0
6
12
18
24
ZT
F
*
***
***
RER
1.1
1.0
0.9
0.8
0.7
NFD AL
HFD AL
NFD TRF
HFD TRF
Light
Dark
Light
Dark
Light
Dark
Light
Dark

Figure S1. Metabolic and activity rhythms across feeding groups, Related to Figure 1.
(A) Averaged hourly caloric intake for NFD AL and HFD AL groups across a typical 24-hour cycle. The solid line is the average, and the shaded surrounding region is the SEM (n = 10-11 mice per group).
(B) Average meal size in kcal for NFD AL and HFD AL groups during the light and dark phase. HFD AL mice had a trend towards larger meals compared to NFD AL at both times of day (two-way ANOVA, effect of Diet, $F_{1,19} = 4.05$, $p = 0.059$, n = 10-11 mice per group).
(C) Light and dark energy expenditure (EE) measured in the CLAMS. Data was first normalized to lean body mass to account for the differences in fat mass in the HFD groups. In the NFD group, EE depended on both time of day and feeding schedule (three-way ANVOA, Time x Feeding Schedule interaction, $F_{1,9} = 21.50$, $p = 0.001$). The night phase EE was higher than the day phase in both AL and TRF groups, with a larger increase in the TRF group. EE for animals in the HFD groups also depended on both time of day and feeding schedule (Time x Feeding Schedule interaction, $F_{1,9} = 5.645$, $p = 0.042$). HFD-fed animals also had higher EE at night compared to day, with a more pronounced change in the TRF group. N = 5-6 mice per group.
(D) Activity levels of mice in the CLAMS. Activity depended on diet and light (three-way ANOVA, Diet x Time of Day interaction, $F_{1,18} = 17.833$, $p = 0.001$, n = 5-6 mice per group). All groups had higher activity during the dark phase, as expected for nocturnal animals. However, the HFD-fed animals in both feeding schedules had lower activity than the NFD-fed animals, and this is not rescued by TRF.
(E) Averaged RER traces from animals in all 4 groups (n = 5-6 mice per group). The solid line is the average, and the shaded surrounding region is the SEM.
(F) Averaged light vs dark RER for animals in all 4 groups (n = 5-6 mice per group). There was a significant 3-way interaction (three-way ANOVA, Time of Day x Diet x Feeing Schedule $F_{1,17} = 38.964$, $p < 0.001$). Pos-hoc pairwise comparisons revealed NFD AL animals have higher RER in the dark phase (*$p = 0.02$) whereas the HFD AL animals do not ($p = 0.393$). The TRF increased the strength of the RER rhythm in the NFD TRF group, with these animals now showing much lower RER during the light phase compared to the dark phase (***$p < 0.001$). The TRF rescued the rhythmicity in the HFD TRF group, these animals now have significantly higher RER in the dark phase compared to the light (***$p < 0.001$).
Data are plotted as Mean ± SEM with individual data points visible where possible (dots or shaded lines).