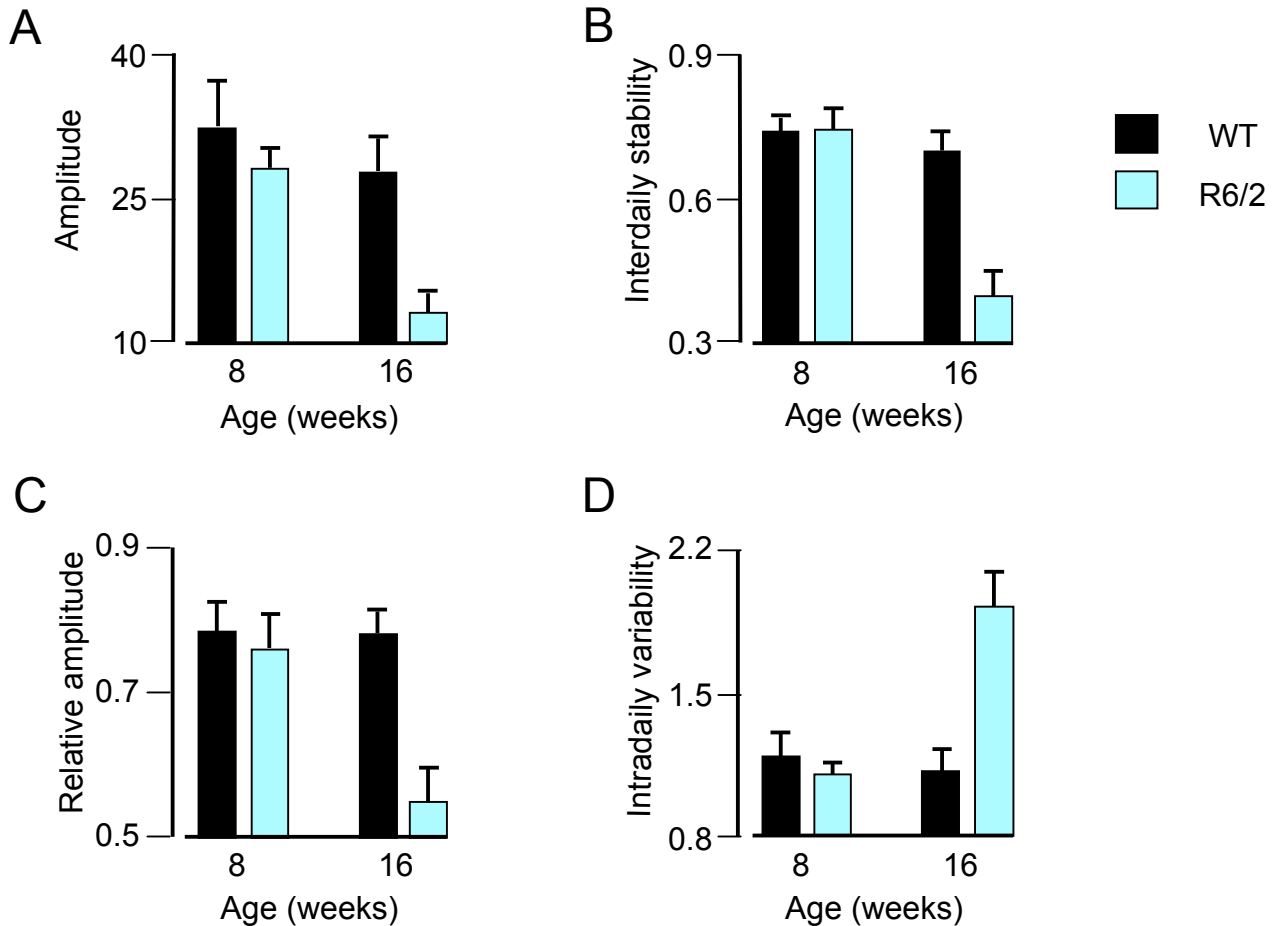


Supplementary Figure S1



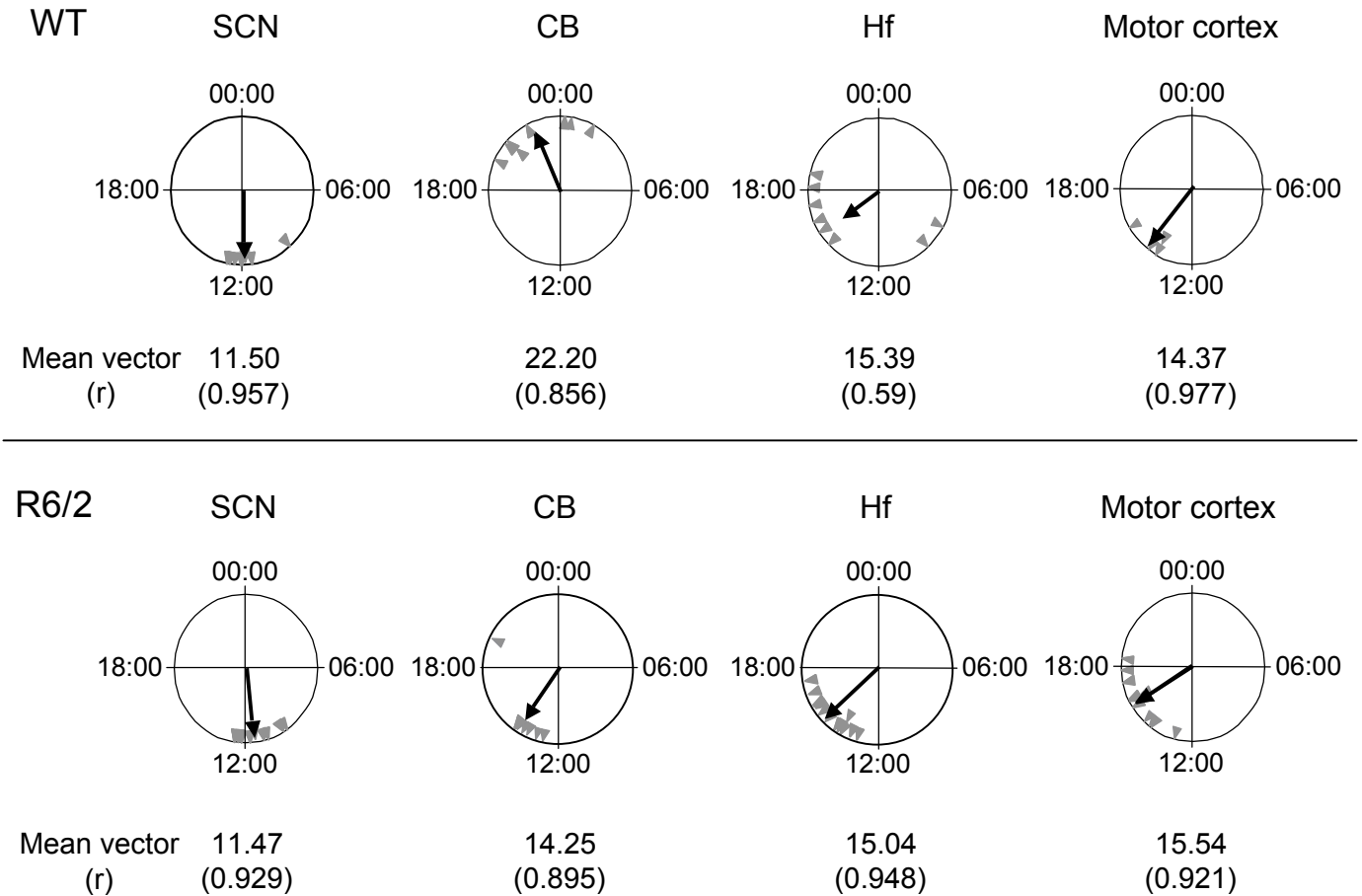
Non-parametric analyses revealed significant deterioration in the amplitude of activity (A), interdaily stability (B), peak/trough amplitude (C) and intradaily variability (D) of 16 week old R6/2 mice compared to R6/2 mice aged 8 weeks and to age-matched wild type (WT) control mice

Inter-daily stability is a measure of stability across days, while intra-daily variability reflects the relative consolidation/fractionation within days based on how many transitions occur between activity and rest. The rhythm amplitude reflects the difference in activity level between the ten most active and five least active hours in the day.

All R6/2 points at 16 weeks are significantly different from WT at 16 weeks and R6/2 at 8 weeks. Significance level is $p < 0.01$, except relative amplitude R6/2 16 weeks vs. R6/2 at 8 weeks which is $p < 0.05$.

Supplementary Figure S2

Distribution of phases of peak circadian expression of mPER2::LUC bioluminescence in brain explant cultures.

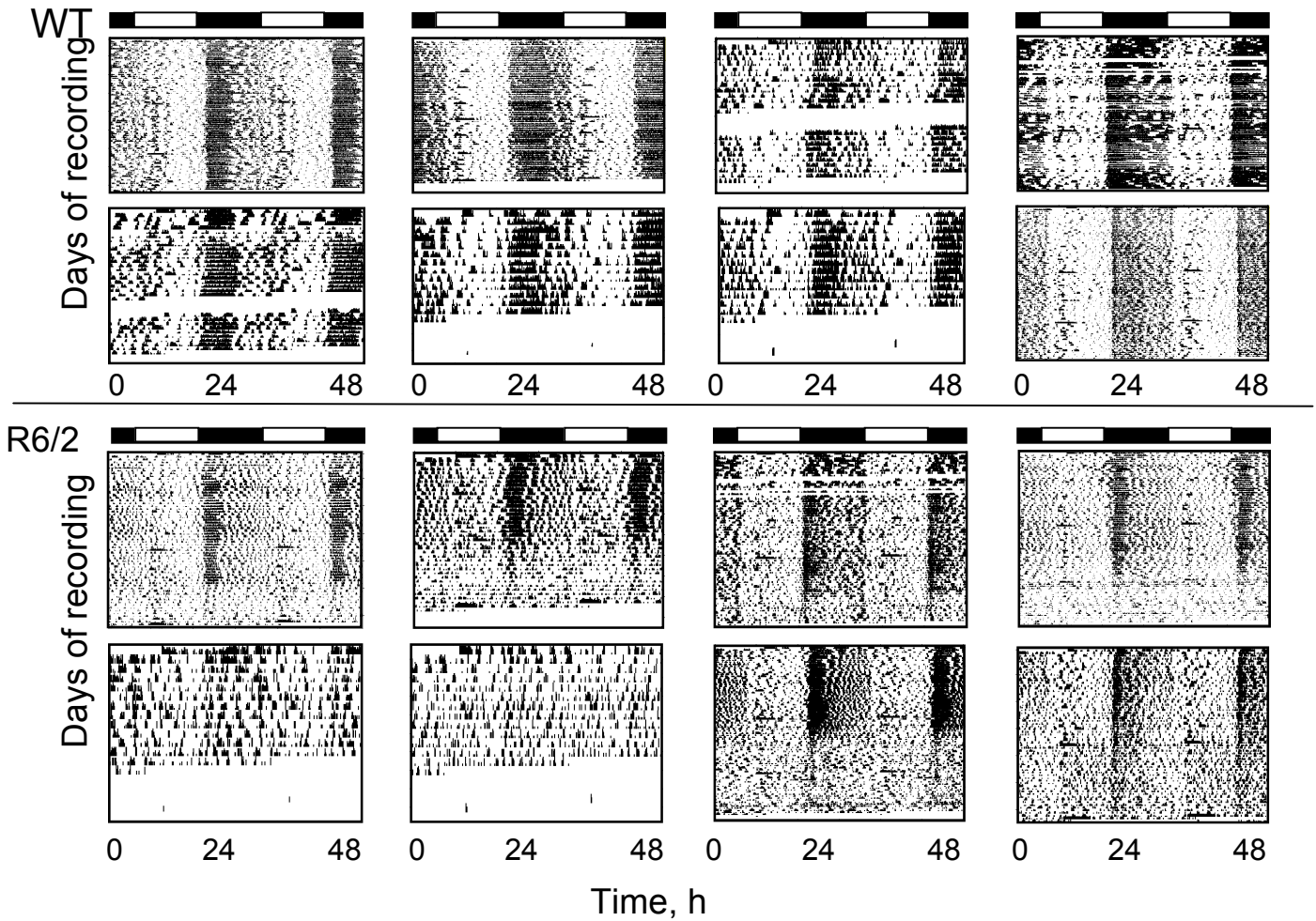


Rayleigh vector plots from WT (top row) and R6/2 (bottom row) tissue explants show the phase dispersal of the peak in mPER2::LUC expression for SCN, cerebellum (CB), hippocampal formation (Hf) and motor cortex explants (n= 4-12/group).

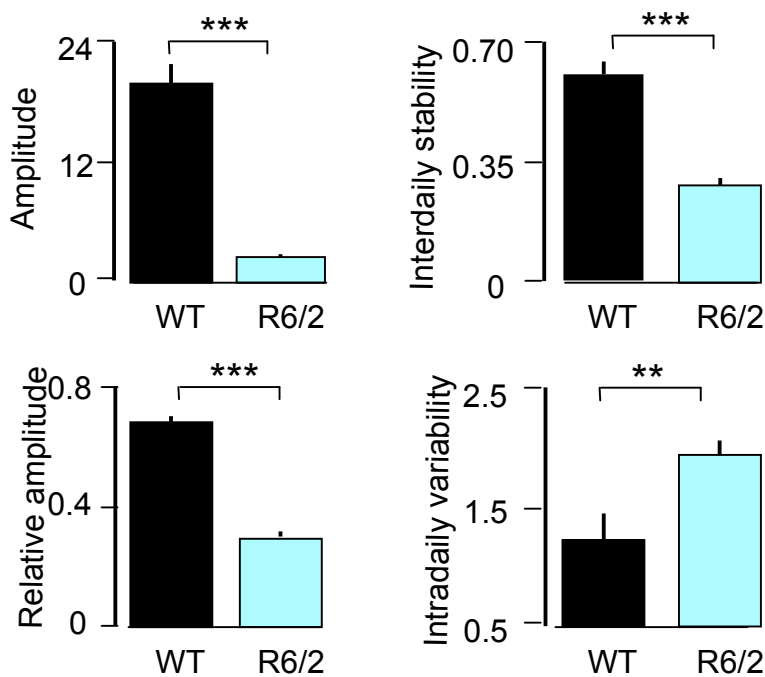
The arrowheads indicate phases of individual tissue explants and the black arrow represents the aggregate phase vector. The length of the arrow represents the strength of the mean vector (i.e. if they are all perfectly synchronised $r=1.0$ and arrow end touches the circle). The mean vector and length of the mean vector (indicating the strength of the clustering) for each tissue are shown underneath each vector plot. All tissues from both genotypes showed significant clustering ($p<0.01$) apart from the WT hippocampus ($p=0.057$). Peak phases were determined during the interval between 12 and 36 hours in culture.

Supplementary Figure S3a

Double plotted actograms show that the activity/rest profiles of R6/2 mice are disordered compared to WT mice



Supplementary Figure S3b



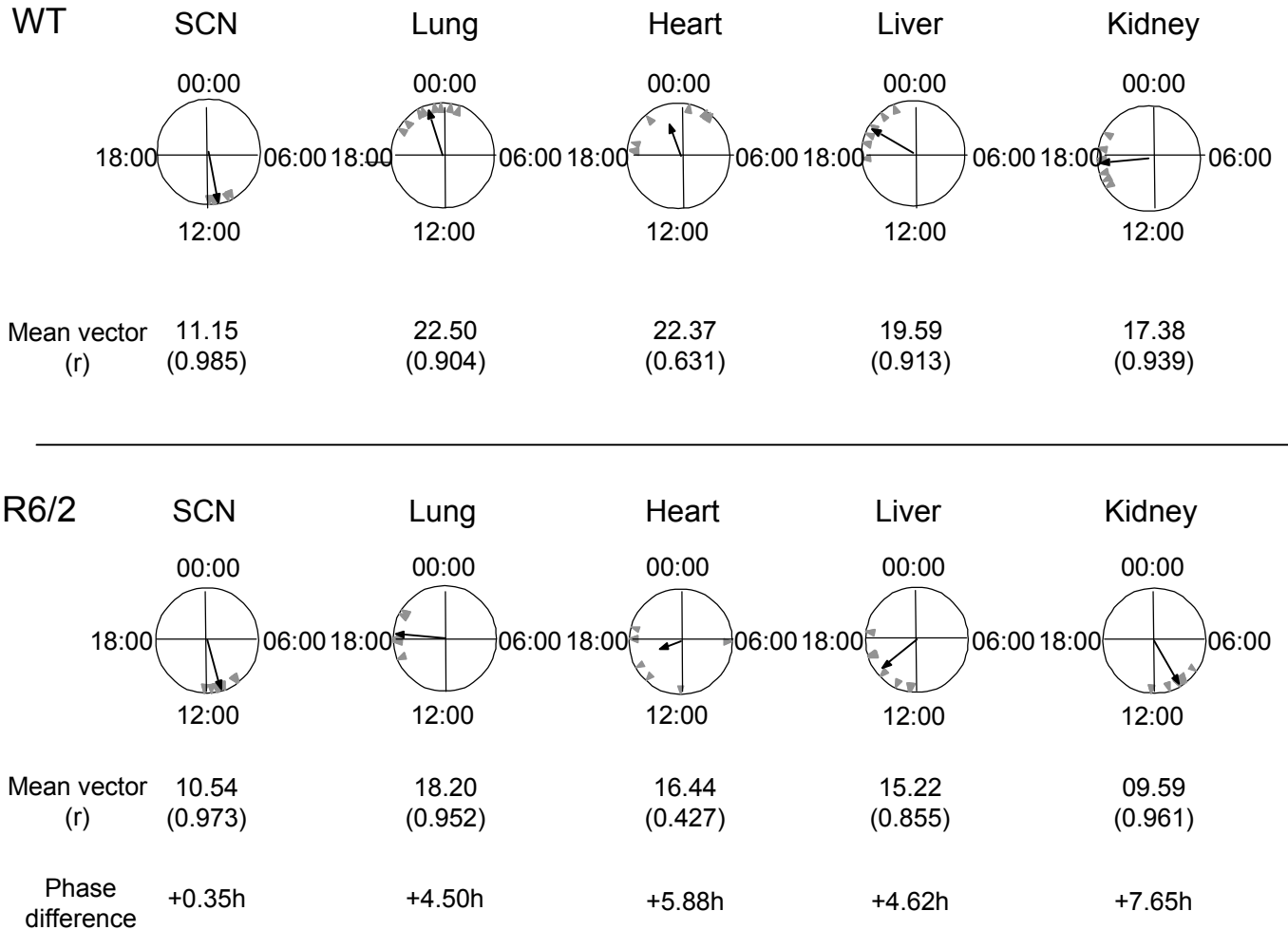
In the last week of recording, non-parametric analysis reveals the amplitude, interdaily stability, relative amplitude and intradaily variability in R6/2 mice are all significantly different from that seen in the WT littermates.

*** $p < 0.001$

** $p < 0.05$

Supplementary Figure S4

Distribution of phases of peak circadian expression of mPER2::LUC bioluminescence in SCN and peripheral tissues



Rayleigh vector plots from WT (top row) and R6/2 (bottom row) tissue explants show the phase dispersal of the peak in mPER2::LUC expression for SCN, lung, heart, liver and kidney explants (n= 6-8/group).

The arrowheads indicate phases of individual tissue explants and the black arrow represents the aggregate phase vector. The length of the arrow represents the strength of the mean vector. The mean vector and length of the mean vector (indicating the strength of the clustering) for each tissue are shown underneath each vector plot. All tissues from both genotypes showed significant clustering ($p < 0.01$; WT heart $p < 0.05$) apart from the R6/2 heart (n.s., $p = 0.29$). Peak phases were determined during the interval between 12 and 36 hours in culture. Phase differences shown are WT minus R6/2 phase.

Supplementary Table 1

Relative expression of core circadian clock genes (mean \pm SEM) in liver of mice subject to *ad libitum* or restricted feeding and sampled at ZT12 or ZT18 (n= 3- 8 per value).

a WT mice

Feeding regime	Time	Gene			
		<i>Per2</i>	<i>Cry1</i>	<i>Bmal1</i>	<i>Dbp</i>
<i>ad libitum</i>	ZT12	5.12 \pm 0.31	3.18 \pm 0.24	1.35 \pm 0.24	5.91 \pm 0.84
	ZT18	3.30 \pm 0.68	6.24 \pm 1.06	6.96 \pm 0.67	0.20 \pm 0.07
restricted	ZT12	5.05 \pm 0.48	6.08 \pm 0.38	5.42 \pm 0.88	0.30 \pm 0.17
	ZT18	1.00 \pm 0.65	4.53 \pm 1.27	7.98 \pm 0.44	0.09 \pm 0.05

2 –way ANOVA

Feeding effect	p<0.01	n.s.	p<0.01	p<0.01
Time effect	p<0.05	n.s.	p<0.01	p<0.01
Feed * Time	n.s.	p<0.05	p<0.05	p<0.01

b R6/2 mice

Feeding regime	Time	Gene			
		<i>Per2</i>	<i>Cry1</i>	<i>Bmal1</i>	<i>Dbp</i>
<i>ad libitum</i>	ZT12	6.90 \pm 0.56	3.18 \pm 0.43	1.34 \pm 0.47	2.66 \pm 0.82
	ZT18	3.04 \pm 0.71	5.52 \pm 0.37	6.69 \pm 0.38	0.16 \pm 0.02
restricted	ZT12	3.57 \pm 0.38	4.13 \pm 0.70	4.37 \pm 0.42	0.26 \pm 0.07
	ZT18	0.42 \pm 0.07	2.81 \pm 0.27	6.98 \pm 0.36	0.09 \pm 0.03

2 –way ANOVA

Feeding effect	p<0.01	n.s.	p<0.01	p<0.01
Time effect	p<0.01	n.s.	p<0.01	p<0.01
Feed * Time	n.s.	p<0.05	p<0.01	p<0.01