Home cage activity monitoring reveals changes in circadian rhythm in the chakragati mouse model of aspects of schizophrenia.

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1 Introduction

The *chakragati* (*ckr*) mouse is a transgenic insertional mutant that has been proposed to model aspects of schizophrenia. The *ckr* mouse exhibits hyperactivity and circling that are reduced by antipsychotic drugs [1] together with a cluster of features reminiscent of aspects of the symptomatology of schizophrenia, including enlargement of the ventricles [2], impairment of social interactions [3], and deficits in pre-pulse inhibition of startle and latent inhibition [4]. Schizophrenia is associated with disruption of circadian rhythms and sleep. In this study, we investigated the behaviour of *ckr* mice across the circadian cycle by continuous home cage activity monitoring.

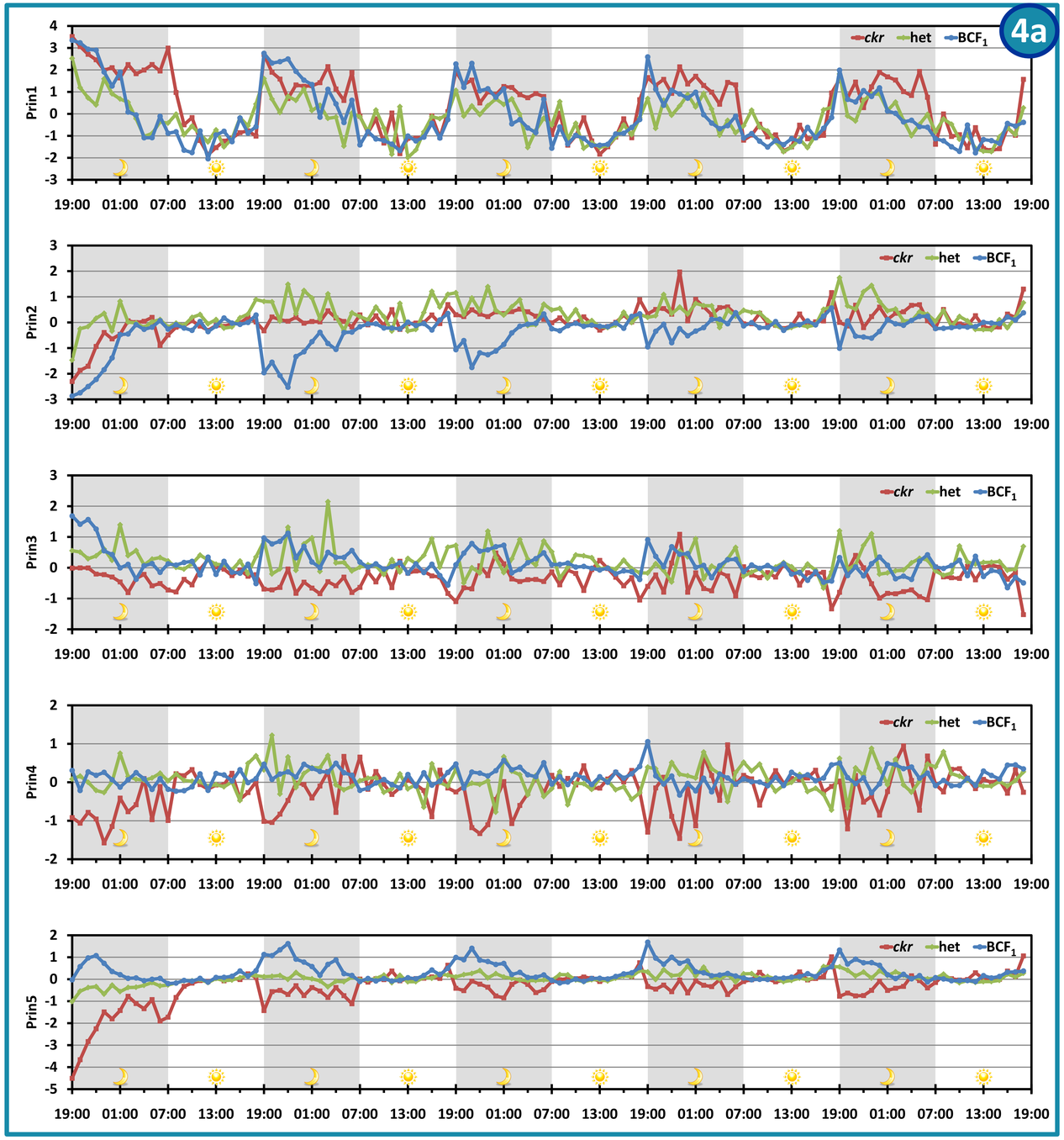
2 Methods

We investigated the behaviour of individually housed *ckr* mice homozygous for the transgenic insertional mutation, heterozygous mice and wildtype BCF_1 (C57BL/10Rospd x C3H/HeRos) mice across a 12 hour dark/12 hour light cycle over at least 5 days with a LABORAS homecage monitoring system. Time spent in locomotor activity, immobility, climbing, grooming, eating and drinking was analyzed for 1 hour epochs. The data were analyzed by principal components analysis (PCA) followed by MANOVA for repeated measures across time.

3 Results

PCA on correlations revealed five principal components with Eigenvalues above 0.5 that explained greater than 98% of the variation. Subsequent MANOVA confirmed that there were significant genotype differences for all 5 principal components. Four of the principal components also showed significant circadian rhythms.

4a



4b Principal components

	Weighting				
	Prin1	Prin2	Prin3	Prin4	Prin5
Locomotion	0.7804	-0.3083	0.0013	-0.0662	-0.5220
Immobility	-0.9643	-0.0121	0.1209	0.0006	0.0735
Climbing	0.4805	-0.6278	0.3721	0.1200	0.4703
Grooming	0.5696	0.3356	-0.4961	0.4916	0.2553
Eating	0.5033	0.3666	0.0209	-0.7347	0.2607
Drinking	0.2864	0.5410	0.7288	0.2944	-0.0851

5 Statistical analysis

Prin18	MANOVA	Genotype effect:	$F_{2,15}$=12.9231	P<0.0005
	Planned comparisons	*ckr* vs BCF_1:	$F_{1,15}$=13.3940	P<0.0023
		ckr vs het:	$F_{1,15}$=23.8719	P<0.0002
		BCF_1 vs het:	$F_{1,15}$=1.5033	P>0.2391
Prin2	MANOVA	Genotype effect:	$F_{2,15}$=8.7709	P<0.0030
	Planned comparisons	*ckr* vs BCF_1:	$F_{1,15}$=7.8998	P<0.0132
		ckr vs het:	$F_{1,15}$=1.6482	P>0.2187
		BCF_1 vs het:	$F_{1,15}$=16.7647	P<0.0010
Prin3	MANOVA	Genotype effect:	$F_{2,15}$=9.2988	P<0.0024
	Planned comparisons	*ckr* vs BCF_1:	$F_{1,15}$=11.9598	P<0.0035
		ckr vs het:	$F_{1,15}$=15.6845	P<0.0013
		BCF_1 vs het:	$F_{1,15}$=0.2521	P>0.6229
Prin4	MANOVA	Genotype effect:	$F_{2,15}$=4.7304	P<0.0255
	Planned comparisons	*ckr* vs BCF_1:	$F_{1,15}$=8.1335	P<0.0121
		ckr vs het:	$F_{1,15}$=5.8745	P<0.0285
		BCF_1 vs het:	$F_{1,15}$=0.1834	P>0.6746
Prin5	MANOVA	Genotype effect:	$F_{2,15}$=16.4765	P<0.0002
	Planned comparisons	*ckr* vs BCF_1:	$F_{1,15}$=32.6740	P<0.0001
		ckr vs het:	$F_{1,15}$=5.7629	P<0.0298
		BCF_1 vs het:	$F_{1,15}$=10.9927	P<0.0047

6 Conclusions

- *Ckr* mice show differences in the circadian rhythm of behaviours compared to heterozygous mice and wildtype BCF_1 mice.
- The *ckr* mouse model may be useful in screening for the ability of drugs to ameliorate abnormalities in circadian rhythm.

7 References

[1] Dawe et al. (2010) Neuroscience. 171(1):162-72.
[2] Torres et al. (2005) Dev Brain Res. 154(1):35-44.
[3] Torres et al. (2005) Brain Res. 1046(1-2):180-6.
[4] Verma et al. (2008) Neurosci Res. 60(3):281-8.