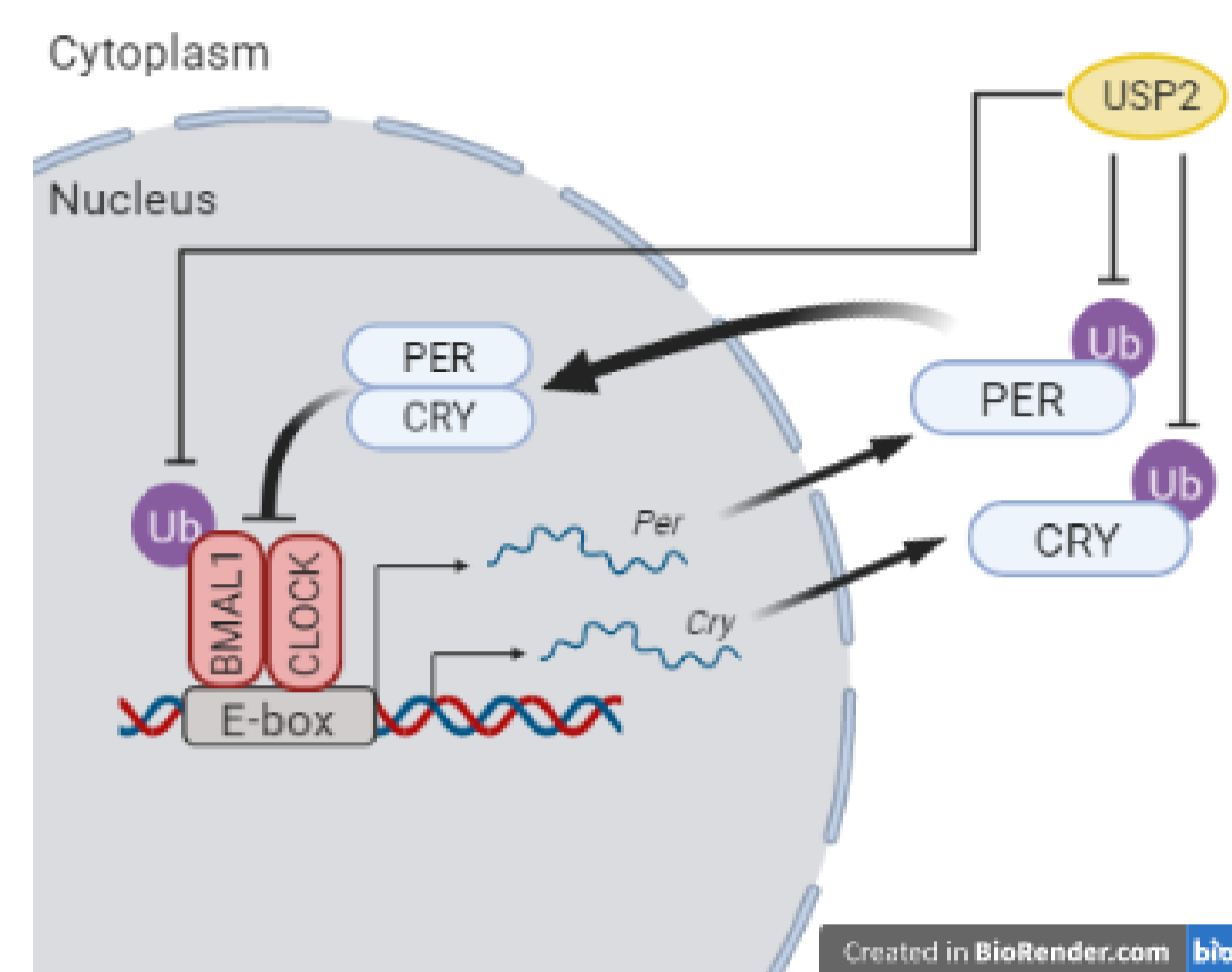


Altered entrainment to light and behavioral deficits in mice lacking the circadian deubiquitinase USP2

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Background



❖ Ubiquitin specific peptidase 2 (USP2) is a circadian deubiquitinase found in multiple brain regions, including the SCN, (the seat of the mammalian master clock, in the brain). The non-circadian functions of USP2 in the brain remain poorly understood.

❖ In the clock machinery, USP2 is known to interact with core clock proteins like BMAL1 [1], PER1 [2] and CRY1 [3].

Direction of Jetlag	WT	Usp2 KO
✈️ → 🌞	🔋	🔋
✈️ ← 🌞	🔋	🔋

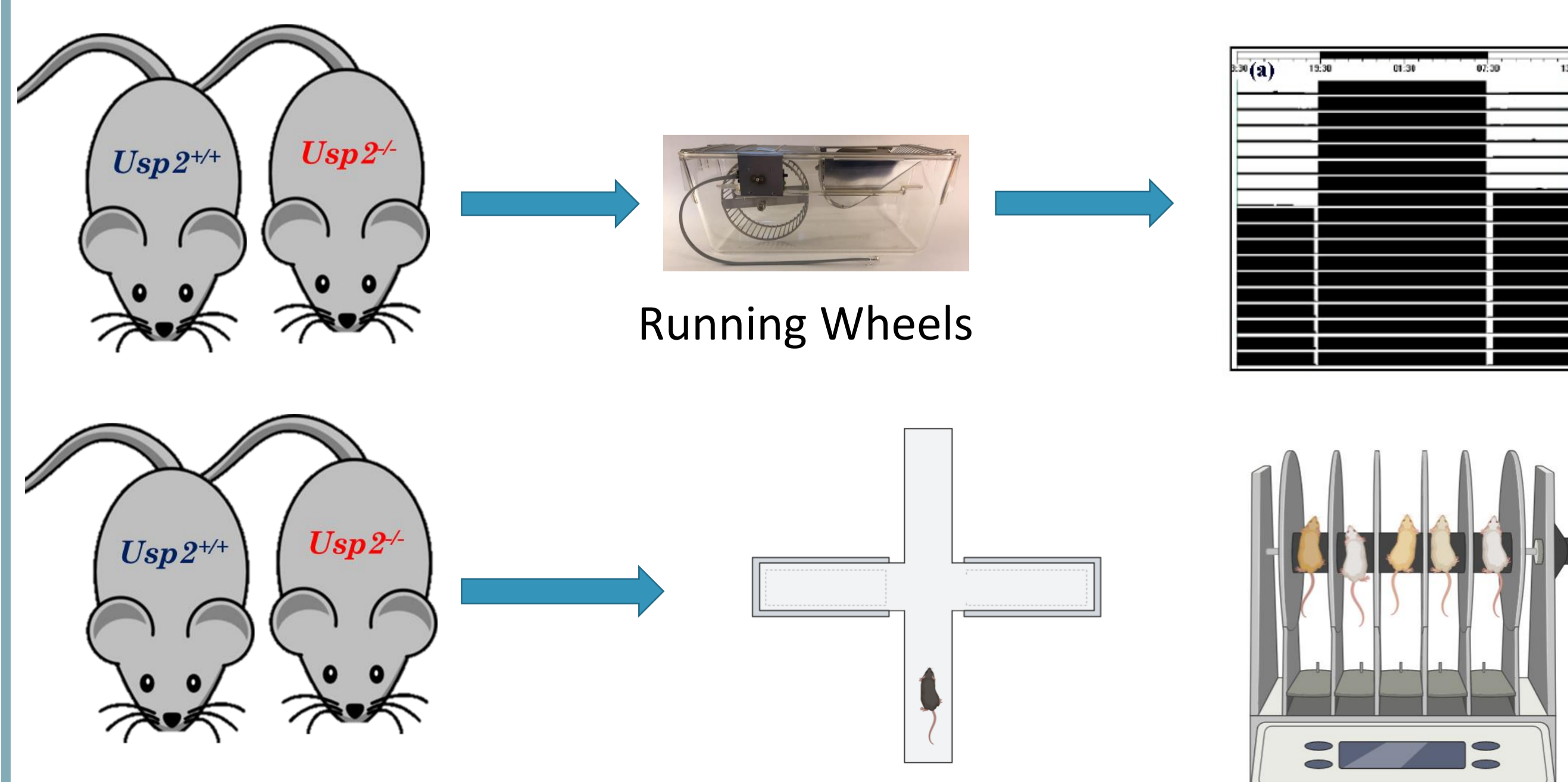
❖ Mice lacking USP2 show altered adaptation to light at abnormal times (Eg: Shift-work), hence implicating USP2 in the clock's response to light cues. [2].

❖ The pathways modulating USP2 action remain to be studied, both, in the circadian system as well as in modulating non-circadian behaviors.

Aim 1: To understand the role of USP2 in the circadian system.

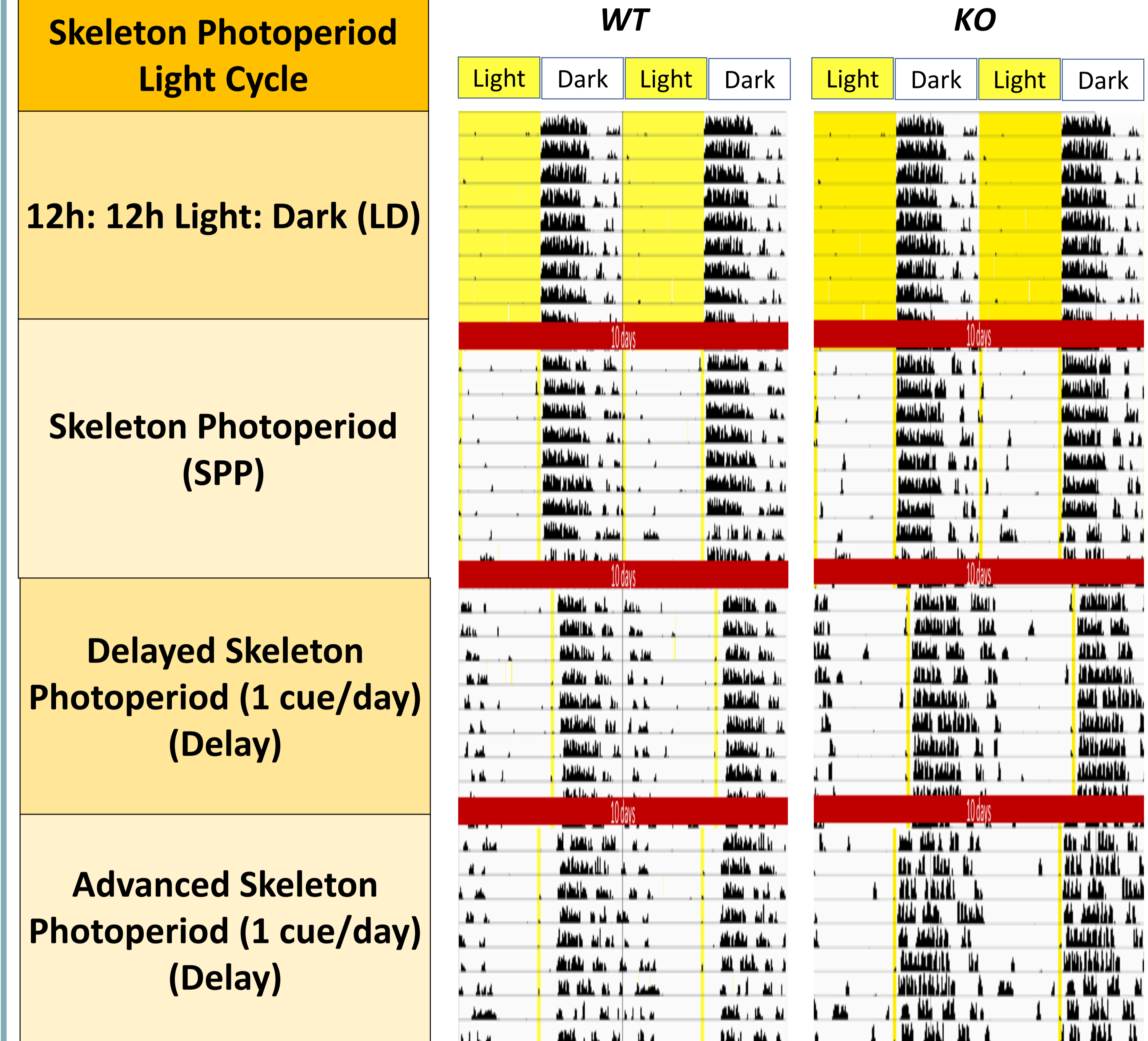
Aim 2: To understand non-circadian behaviors of Usp2 KO mice and their contribution to the observed circadian phenotypes

Methods



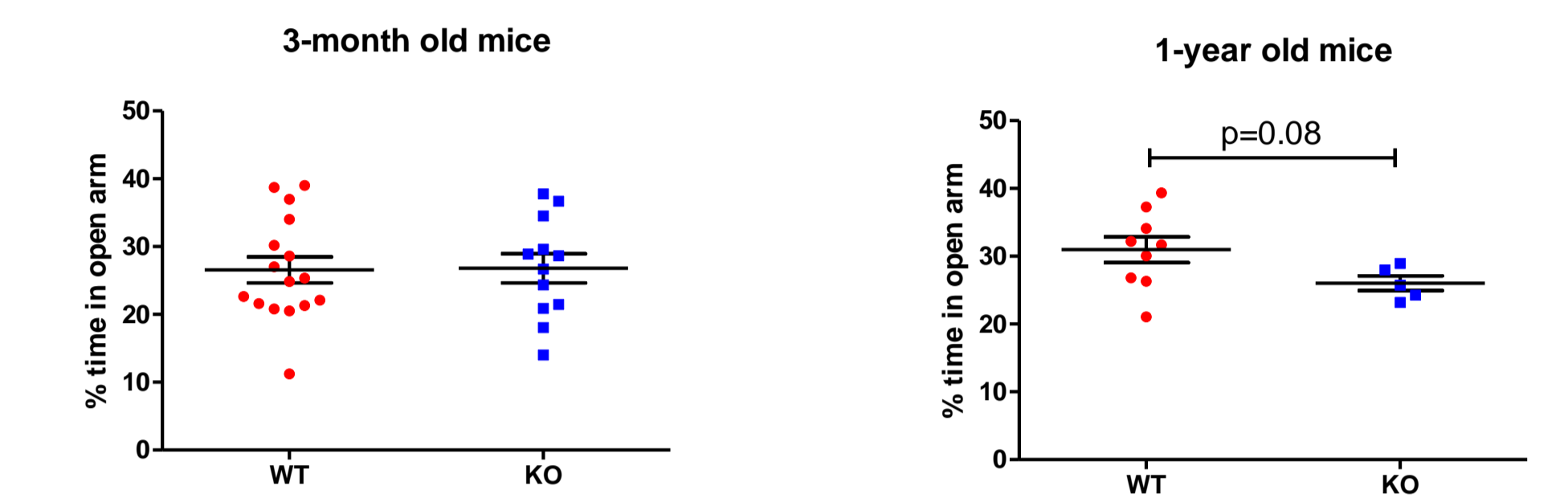
Results

Effect of light on behavioural activity in freely moving mice: Skeleton Photoperiod



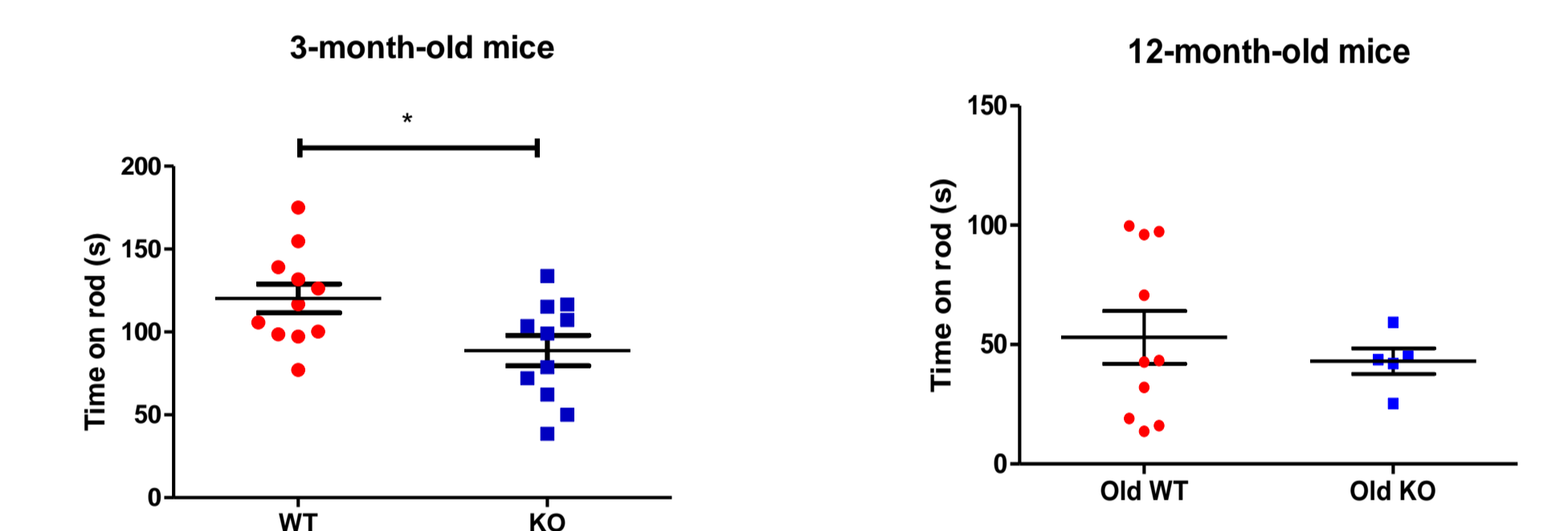
Role of USP2 in the brain

Elevated Plus Maze Assay



Older KO mice spend less time in the open arms, showing a trend towards increased anxiety-like phenotypes.

Rotarod Assay



Usp2 KO mice spend less time on the rotating cylinder, showing significantly decreased motor co-ordination

Behavioral tests with non-significant effects

Actimetry	Depression-like behavior	Motor-coordination	Spatial learning
Open Field test	Forced Swim test	Beam walking assay	Morris Water Maze

Summary & Future Directions

❖ Our preliminary results suggest an important role for USP2 in mediating entrainment of the SCN clock to external light cues, and in modulating non-circadian behaviours

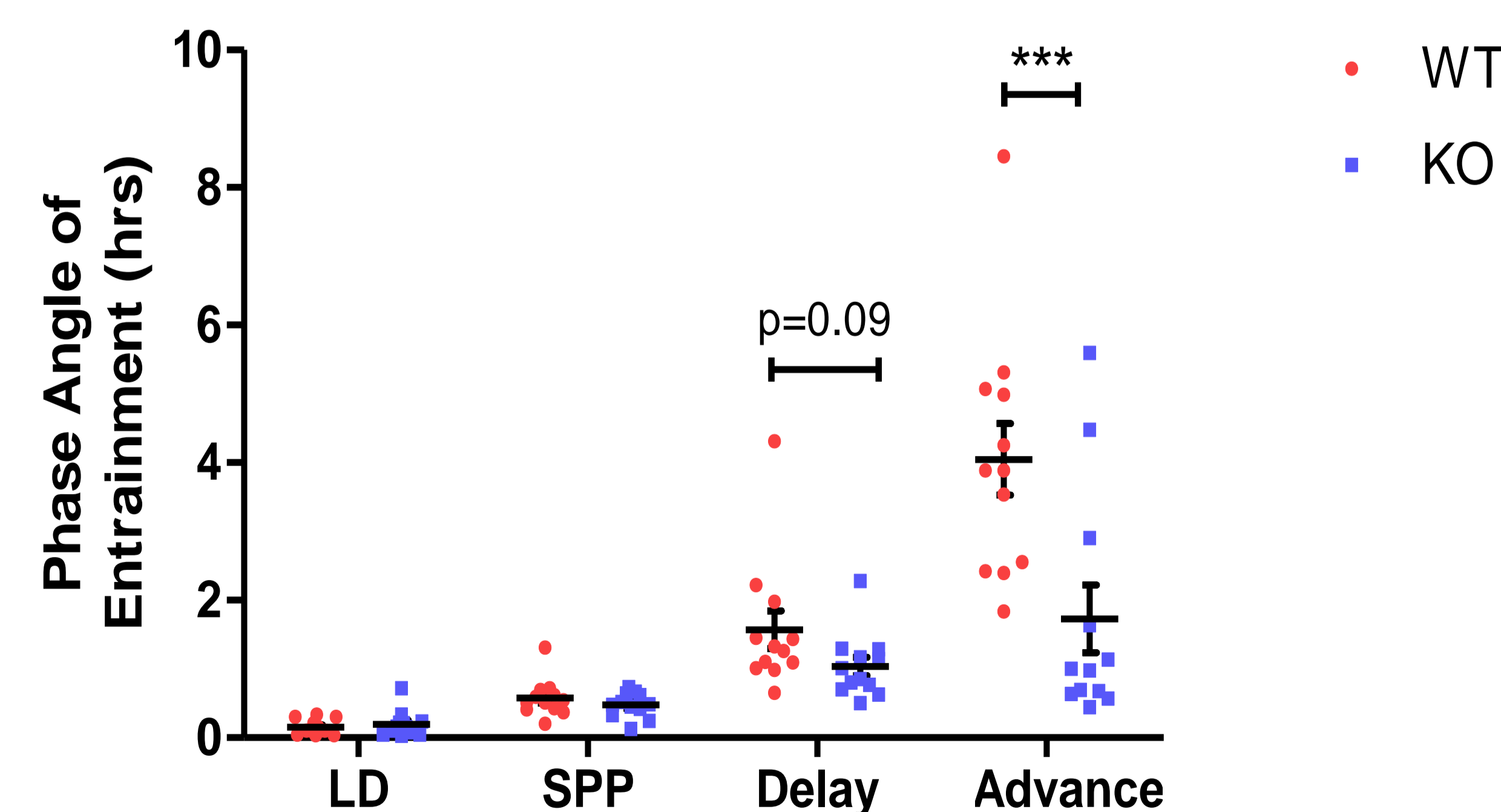
❖ Our findings assume importance in light of the circadian disruptions that result from modern lifestyle options such as jetlag and shift work. Studying the molecular basis of USP2 will allow us to understand these processes better.

References

[1]. Scoma et. al., *PLoS One*, 6(9) (2011); [2]. Yang et. al., *Biol Open*, 1(8) (2012); [3]. Tong et. al., *JBC*, 287(30) (2012)

Acknowledgements

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The KO of Usp2 seems to increase the ability of mice to entrain to light cues late in the subjective day (Even before nightfall!).