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## Behavioral assessment of visual acuity in a new multifactorial model of schizophrenia

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## Introduction

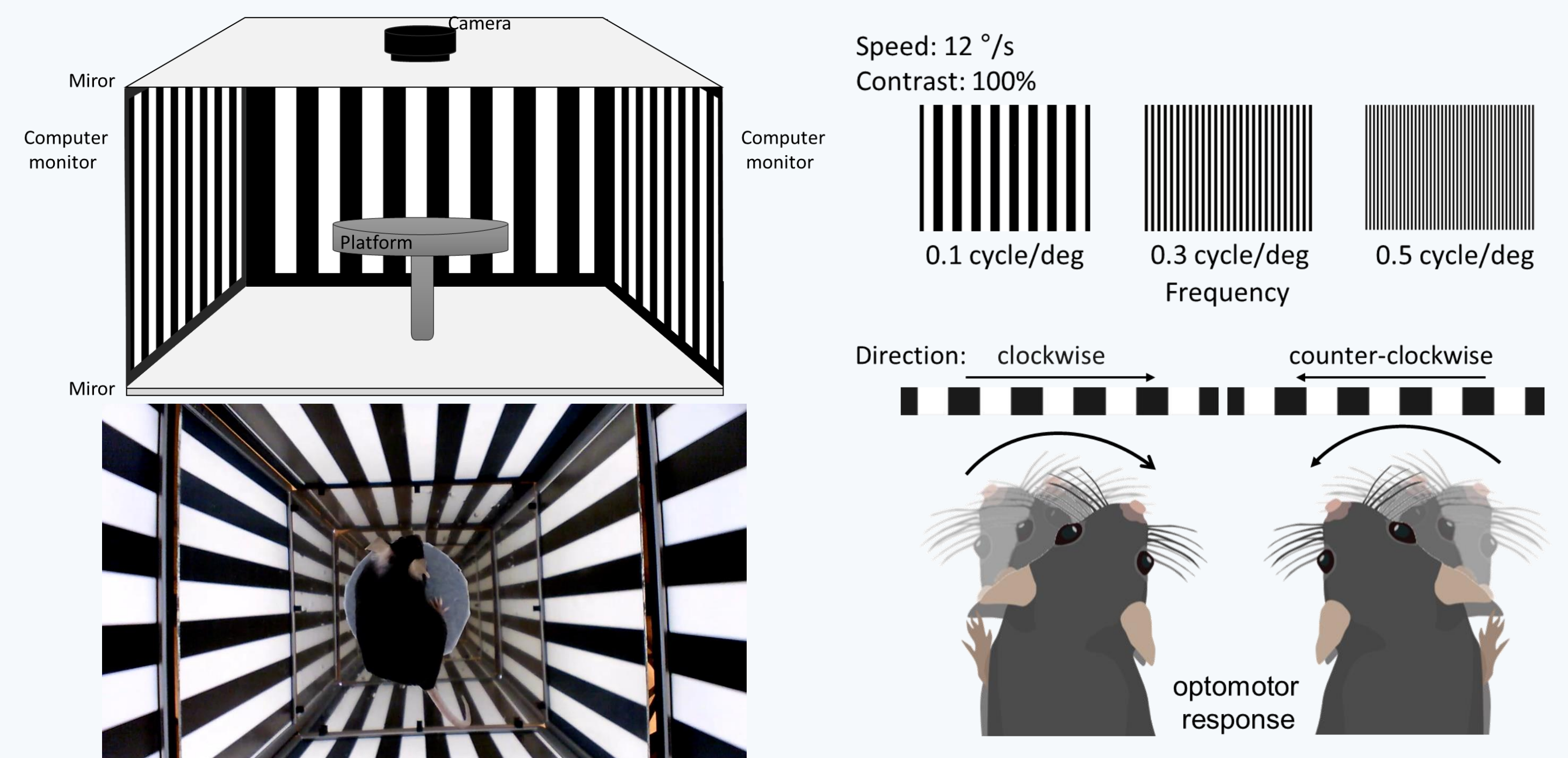
Most behavioral tests used to assess cognitive functions (touchscreen, object recognition...) in animal models, require normal vision functioning. However, vision which could be affected by genetic alteration or brain insult, is rarely assessed, possibly leading to misinterpretation.

We are currently studying a new animal model of schizophrenia constructed on the combination of two factors (2-hit) : a genetic factor (deletion of serine racemase altered glutamate transmission) and an environmental factor (maternal separation for 24h at post-natal day 9, early stress). Serine racemase synthesizes the NMDA receptor co-agonist, D-serine and is present not only in the brain but also in the retina (Stevens et al., 2003). Its absence in SRKO mice could disturb vision development. Moreover, the second factor, maternal separation, would have long-term effects on visual functions and the retina (Grigoruta et al., 2020).

Based on virtual optomotor system of Prusky et al. (2000), our aim was herein to do a longitudinal checking of optomotor response development between 4 and 10 weeks of age in 2-hit mice.

## Methods

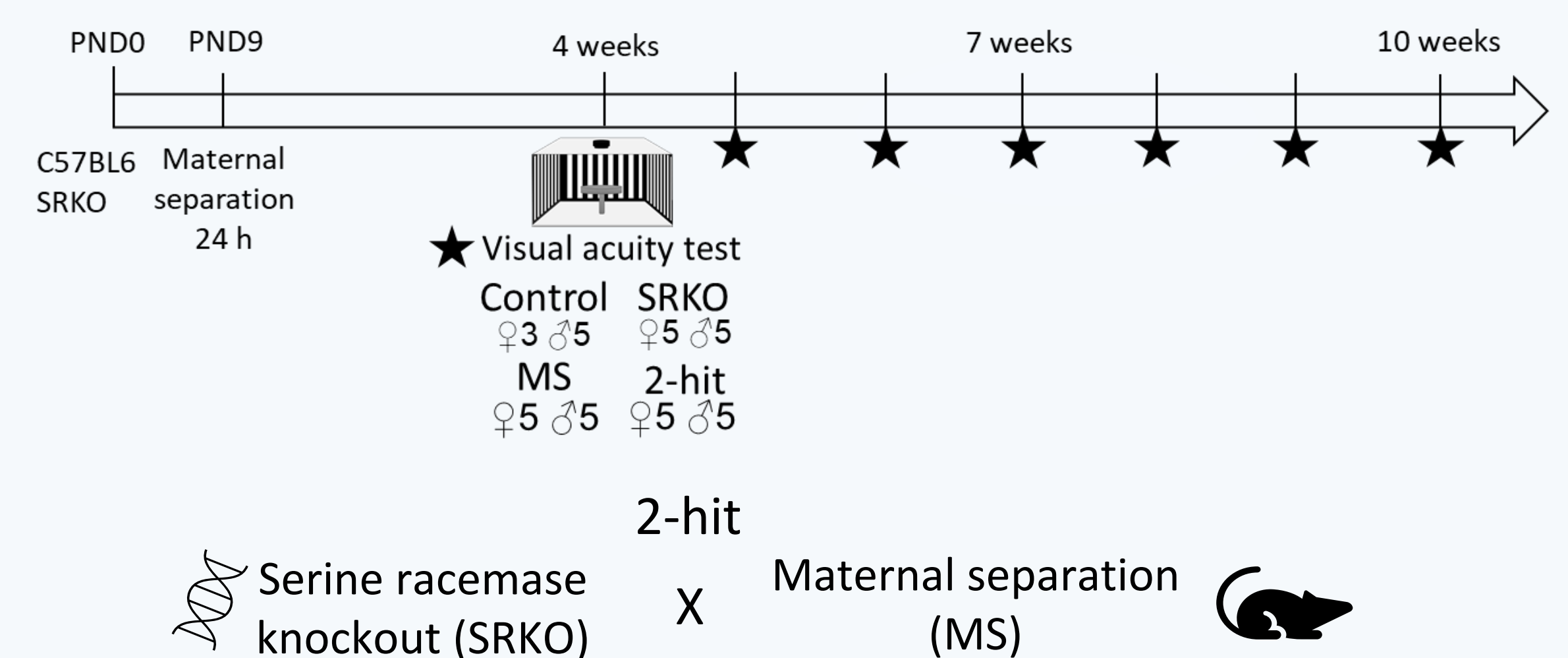
### Virtual optomotor system



**Optomotor response:** head movement in the direction of the movement of vertical black and white bars, without body moving.

**Visual acuity threshold:** the highest frequency (cycle/deg) where the optomotor movement is visible

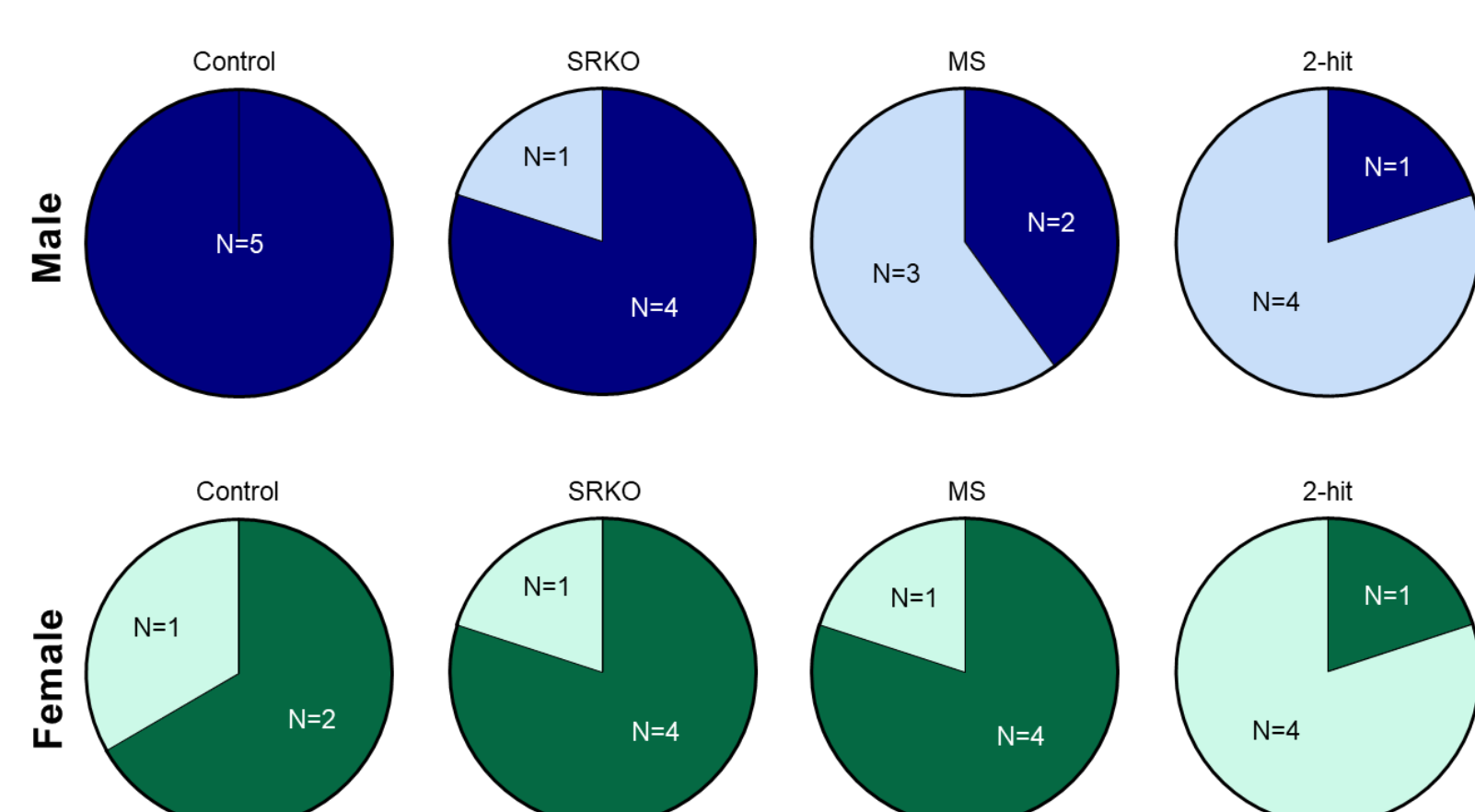
Longitudinal experiment to follow the evolution of visual acuity.



## Results

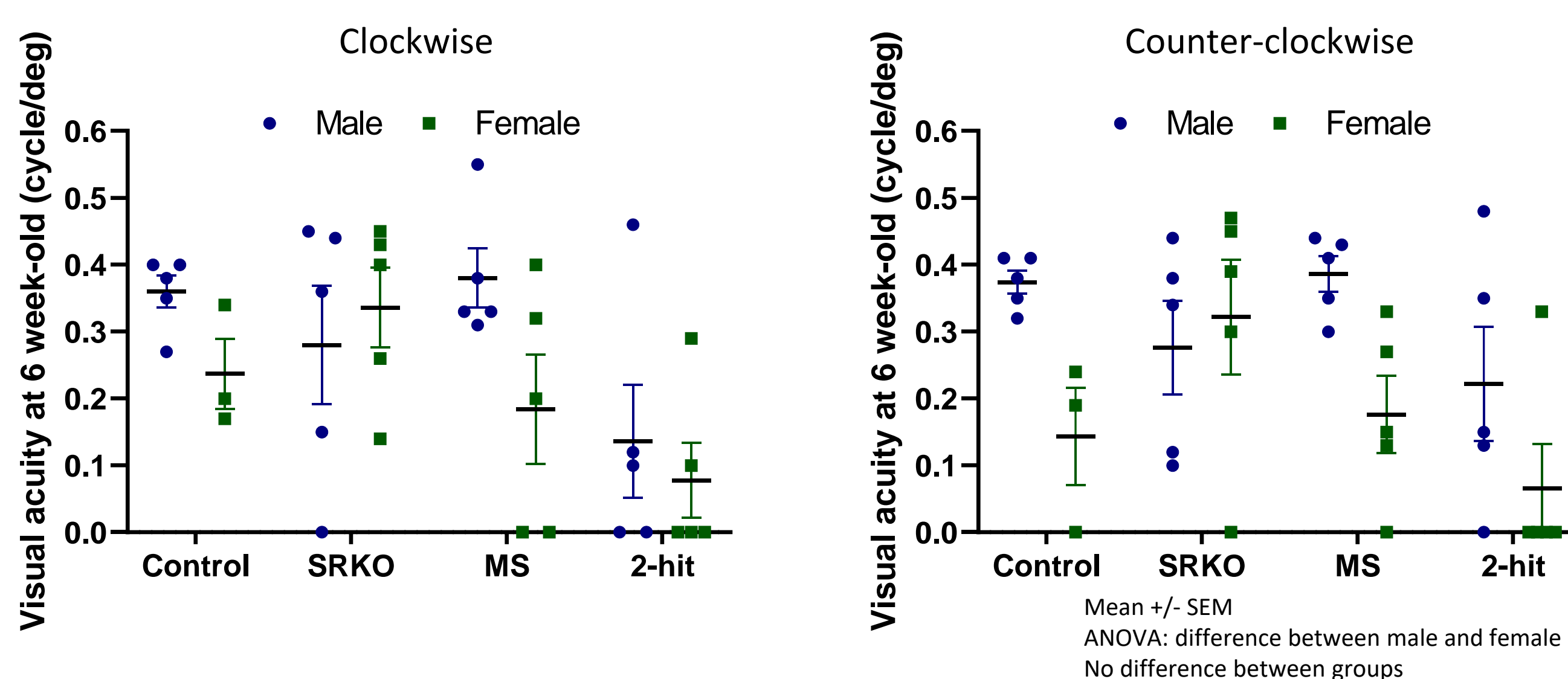
At 4 weeks of age, mice usually have a minimal visual acuity threshold of  $>0.1$  cycle/deg (Prusky et al. 2000)

Male Female  
■ ■  $<0.1$  cycle/deg  
■ ■  $>0.1$  cycle/deg



**Number of mice that validated the criterion.** Control male and female mice predominantly validated the criterion at 4 weeks, as do the SRKO male and female and MS female groups. However, in the 2-hit male and female groups, only one mouse passed the criterion.

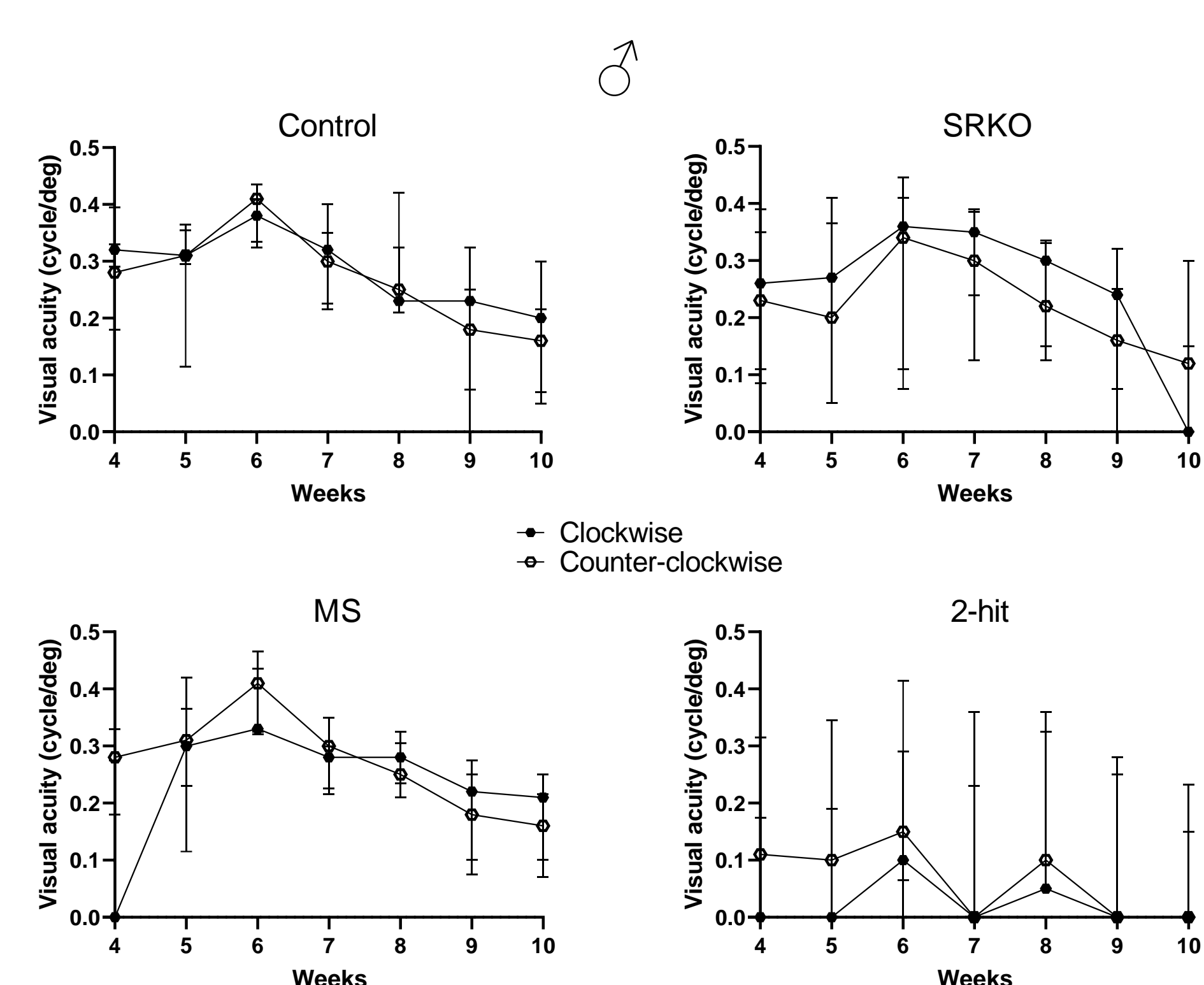
Maximal visual acuity is normally reached during mouse's 6 weeks (Prusky et al. 2000)



**Comparison of the visual acuity at 6 weeks.** The maximal visual acuity for male control and MS mice in both clockwise and counter-clockwise directions is around 0.35 cycle/deg corresponding to the normal vision in adult mice. SRKO female and male mice are a maximal visual acuity of 0.3 cycle/deg. In contrast control and MS female mice have a maximal visual acuity of 0.2 cycle/deg. The 2-hit male and female mice, in both directions, seem to have a deleterious visual acuity (about 0.1 cycle/deg for male mice in clockwise direction and 0.2 cycle/deg in counter-clockwise and lower than 0.1 cycle/deg for female 2-hit mice in both directions).

## Conclusion

The optomotor test was used to monitor the visual acuity of juvenile 2-hit mice. The results suggest that the combination of genetic and environmental factors has an impact on visual acuity. It will therefore be important to adapt the behavioral tests to be used to assess cognitive processes and avoid misinterpretation of measurements.



**Longitudinal tracking of visual acuity in male mice.**

In both control, SRKO and MS male mice an increase of visual acuity is observed until the maximal acuity at 6 weeks. After 7 weeks a decrease of visual capacity is found. For the 2-hit group, no improvement of visual acuity is found.

Median +/- interquartile range

**Longitudinal tracking of visual acuity in female mice.**

Control and MS mice present no improvement of the visual acuity. In SRKO group an increase of visual acuity is observed until the maximal acuity at 6 weeks. For the 2-hit group, no improvement of visual acuity is found.

Median +/- interquartile range

