Histological evaluation of postnatal retinal development of senescence-accelerated OXYS rats

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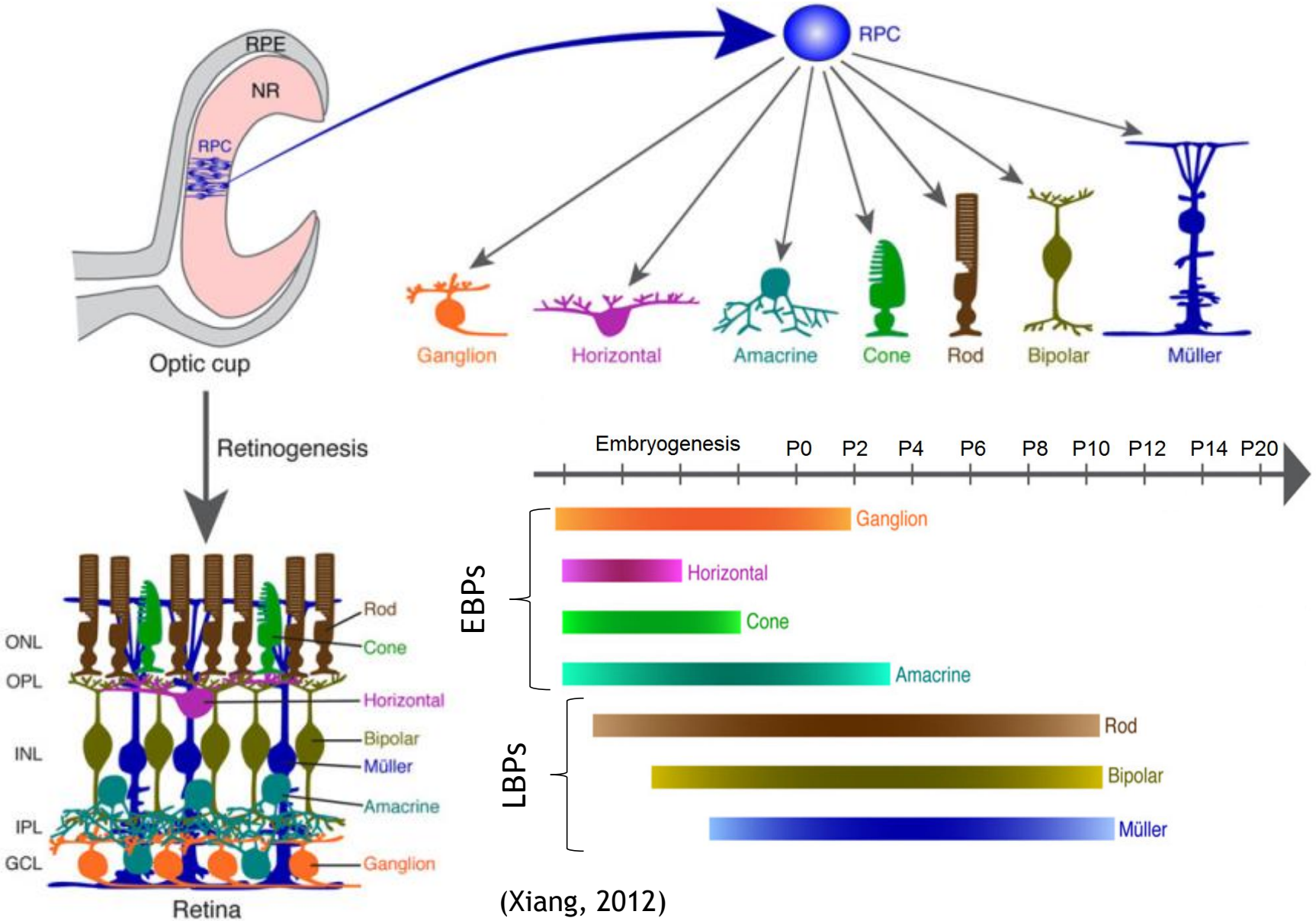
***De novo* neurogenesis in the adult mammalian retina very limited. Thereby the structural and functional features formed during the period of maturation and formation of retina can have long-term effects on the further ontogenesis of the tissue. However the mechanisms of these disorders remain unclear.**

Using model of premature aging OXYS rats we investigated the early histopathological changes during postnatal retinal neurogenesis. OXYS rats spontaneously develop a retinopathy similar to age-related macular degeneration (AMD).

Our results indicating an alteration of retinal formation in OXYS rats during the postnatal period which may contribute to the early development of their signs of neurodegeneration.

We hypothesize that the histological features presented in OXYS rats during postnatal neurogenesis could underlie the functional and structural alterations and can have long-term effects on the further ontogenesis of the tissue.

De novo neurogenesis in the adult mammalian retina very limited. Thereby the structural and functional features formed during the period of maturation and formation of retina can have long-term effects on the further ontogenesis of the tissue, however, the mechanisms of these disorders remain unclear.



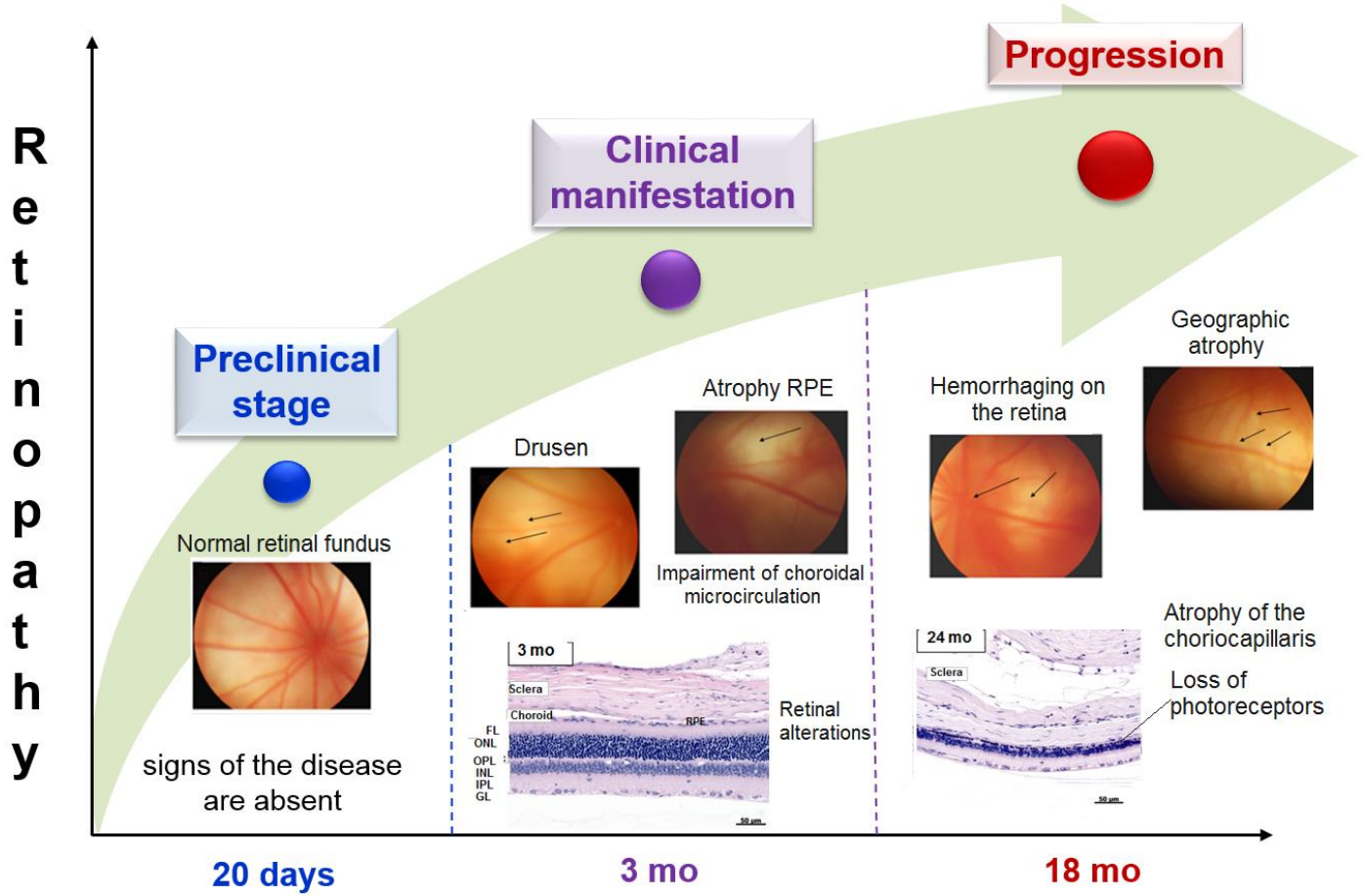
(Xiang, 2012)

The retinal neurons include cone and rod photoreceptors and horizontal, amacrine, bipolar, and ganglion cells.

Ganglion, horizontal, amacrine, and early-born cone photoreceptor cells originate froma common pool of intermediate progenitors (EBPs). Bipolar, Müller, and late-born photoreceptor cells share a pool of common intermediate progenitors (LBPs).

In rat and mouse EBPs arise from E10 to P4 and peak at E16, while LBPs appear from E13 to P10 and peak at P2. Retinogenesis is complete at P20 in rodents.

Senescence-accelerated OXYS rats develop retinopathy similar to age-related macular degeneration in human



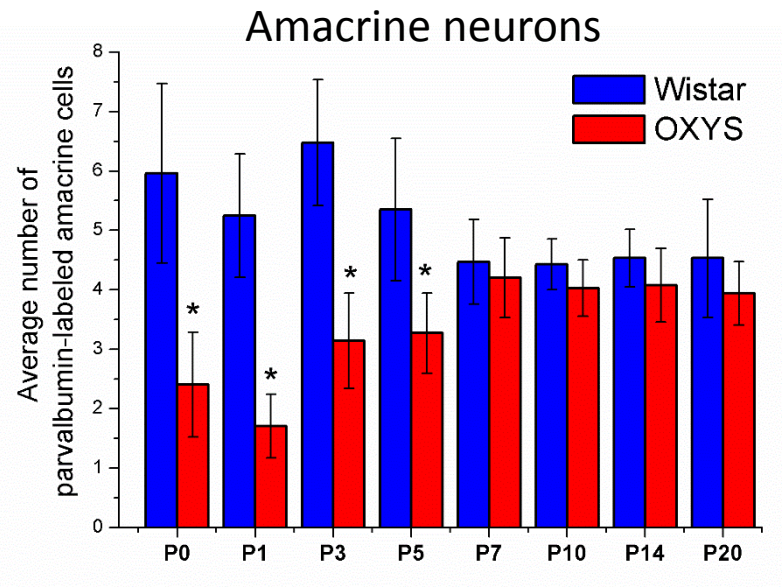
Telegina et al., 2015-2019;
Kozhevnikova et al; 2013-2019
Kolosova et al; 2002-2020

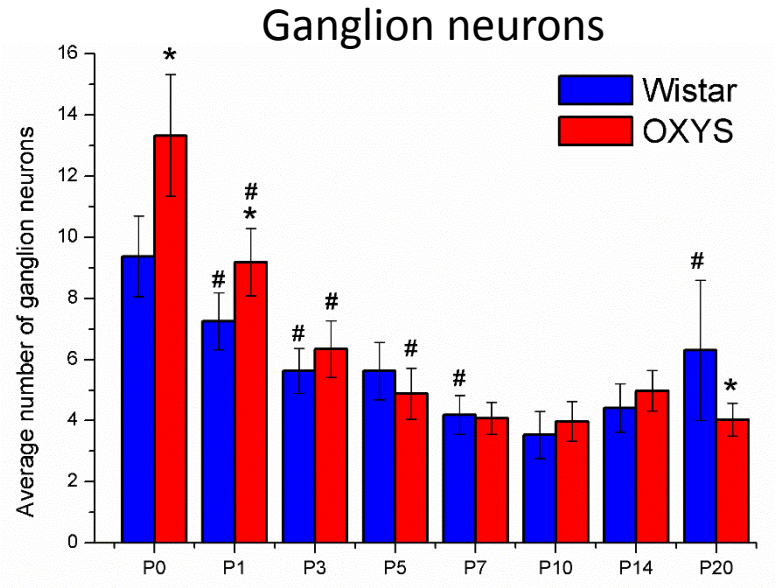
Retinopathy that develops in OXYS rats already at a young age corresponds to the dry atrophic form of AMD in humans.

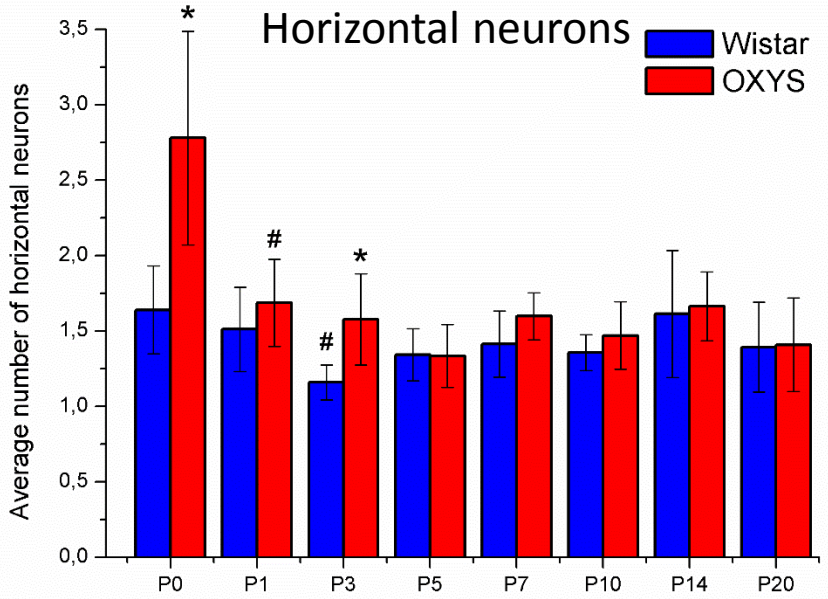
We aimed to give a detailed qualitative and quantitative description on the early histopathological changes in the postnatal development retina of OXYS and Wistar rats (as control).

We analyzed critical days of postnatal neurogenesis in retina:
P0, P1 – active neurogenesis of all neurons
P3 – neurogenesis of amacrine neurons is complete
P5 – the beginning of bipolar neurons differentiation
P7 – active apoptosis of neurons
P10 - neurogenesis of bipolar neurons and photoreceptors is complete
P14 – opening of eyes
P20 – retinogenesis is complete

OXYS rats are born with alterations of quantitative number of early-born progenitors: amacrine, ganglion and horizontal neurons







Data are presented as mean ± SD. *Significant differences between the strains; #significant differences from control animals of the same strain

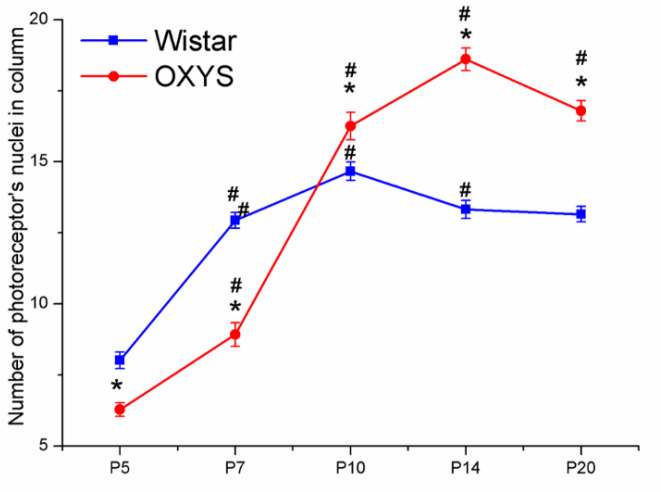
Quantitative analysis showed decreasing amacrine cells in OXYS rats as compared Wistar rats (control) at the age of P0, P1, P3 and P5.

At the age of P0 and P1, the number of ganglion neurons increased in OXYS rats as compared Wistar rats.

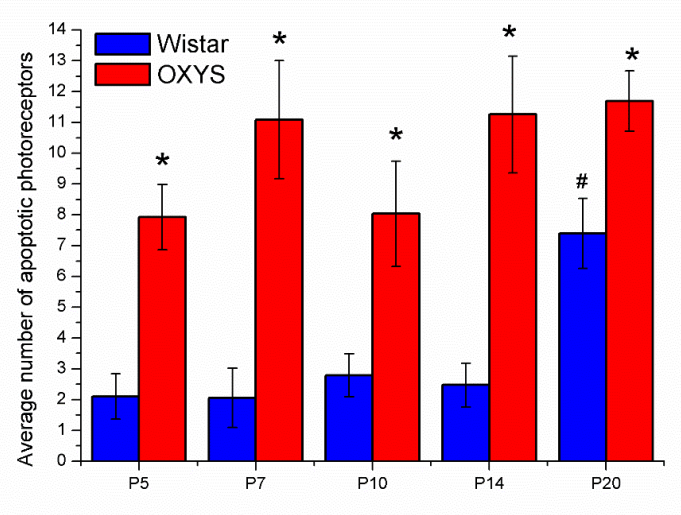
At the age of P0 and P3, the number of horizontal neurons increased in OXYS rats as compared Wistar rats

OXYS rats showed features of neurogenesis of late born progenitors: bipolar neurons and rod photoreceptors

Rod photoreceptors



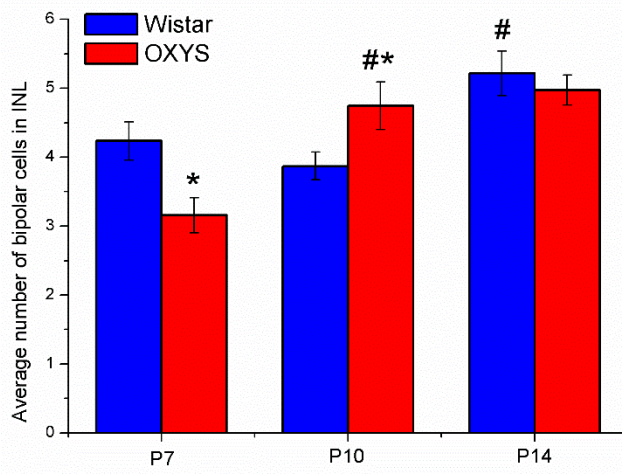
Apoptosis of photoreceptors



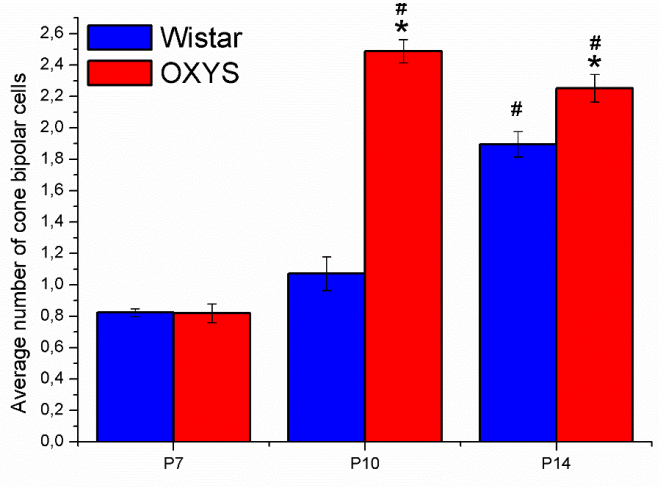
Quantitative analysis showed shift to neurogenesis of rod photoreceptors in later period in OXYS rats (as compared Wistar rats). Also we detected significant increasing photoreceptor's apoptosis in retina of OXYS rats.

Data are presented as mean ± SE. *Significant differences between the strains; #significant differences from control animals of the same strain

Pan-bipolar neurons



Cone bipolar neurons



We detected alterations of average number of pan bipolar and cone bipolar neurons in OXYS rats as compared Wistar rats. We proposed that this phenomenon associated with adaptive mechanisms.