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Retino-retinal projection in juvenile and young adult rats and mice

F.M. Nadal-Nicolás [a, b, 1], F.J. Valiente-Soriano [a, b, 1], M. Salinas-Navarro [a, b], M. Jiménez-López [a, b], M. Vidal-Sanz [a, b, *], M. Agudo-Barriuso [a, b, *]

[a] Instituto Murciano de Investigación Biosanitaria Hospital Virgen de la Arrixaca (IMIB-Virgen de la Arrixaca), Murcia, Spain
[b] Departamento de Oftalmología, Facultad de Medicina, Universidad de Murcia, Murcia, Spain

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ABSTRACT

Identification of retino-retinal projecting RGCs (ret-ret RGCs) has been accomplished by tracing RGCs in one retina after intravitreal injection of different tracers in the other eye. In mammals, rabbit and rat, ret-ret RGCs are scarce and more abundant in newborn than in adult animals. To our knowledge, ret-ret RGCs have not been studied in mice. Here we purpose to revisit the presence of ret-ret RGCs in juvenile and young adult rats and mice by using retrograde tracers applied to the contralateral optic nerve instead of intravitreally. In P20 (juvenile) and P60 (young adult) animals, the left optic nerve was intraorbitally transected and Fluorogold (rats) or its analogue OHSt (mice) were applied onto its distal stump. P20 animals were sacrificed 3 (mice) or 5 (rats) days later and adult animals at 5 (mice) or 7 (rats) days. Right retinas were dissected as flat-mounts and double immunodetected for Brn3a and melanopsin. Ret-ret RGCs were those with tracer accumulation in their somas. Out of them some expressed Brn3a and/or melanopsin, while other were negative for both markers. In young adult rats, we found 2 ret-ret RGCs displaced to the inner nuclear layer. In both species, ret-ret RGCs are quite scarce and found predominantly in the nasal retina. In juvenile animals there are significantly more ret-ret RGCs (9 ± 3, rats, 13 ± 3 mice) than in young adult ones (5 ± 6 rats, 7 ± 3 mice). Finally, juvenile and young adult mice have more ret-ret RGCs than rats.

Visual information, sensed by photoreceptors and conveyed to retinal ganglion cells (RGCs), and circadian information, directly perceived by the intrinsically photosensitive type of RGCs (ipRGCs), travel from the retina through the optic nerve, formed by the RGC axons, to the image forming and non-image forming target territories in the brain.

In rats and mice, RGCs project massively to the contralateral superior colliculi, (Dräger and Olsen, 1980; Lund, 1965; Lund et al., 1980; Nadal-Nicolás et al., 2014; Salinas-Navarro et al., 2009) but also send collaterals to the lateral geniculate nucleus, intergeniculate nucleus, the dorsal, lateral and medial terminal nuclei, the olivary pretectal nuclei and the supraquiasmatic nuclei (reviewed in Sefton et al., 2004).

RGCs projecting from one retina to the other have been described in anuran (Bohn and Stelzner, 1979, 1981a, 1981b, 1981c; Tennant et al., 1993; Toth and Straznicky, 1989), chicken (Halfter, 1987; Thanos, 1999) and mammals (Bunt and Lund, 1981; Lam et al., 1982; Müller and Holländer, 1988). To date, retino-retinal projecting RGCs (ret-ret RGCs) have been identified by intravitreal injection of different tracers and formulations in one eye and analysis of traced RGCs in the contralateral retina, with the exception of a very recent report in pigmented rats where they apply the tracer onto the contralateral optic nerve (ON) (Avellaneda-Chevrier et al., 2015).

In mammals, rabbit and rat, ret-ret RGCs are few and mainly located in the nasal retina. They are, however, more abundant in newborn than in adult animals. In fact, Müller and Holländer (1988) identified ret-ret RGCs in all newborn rat retinas, but not in all adult retinas. To our knowledge, ret-ret RGCs have not been studied in mice.

Thus, we have revisited the retino-retinal projection in juvenile and young adult rats and mice. We have applied the tracer onto the optic nerve instead of intravitreally and studied whether ret-ret RGCs express the RGC markers Brn3a and/or melanopsin. Brn3a is a transcription factor expressed by all RGCs except ipRGCs and half of the ipsilateral projection (Nadal-Nicolás et al., 2012), and

* Corresponding authors. Dpto de Oftalmología, Facultad de Medicina, Campus Espinardo, Universidad de Murcia, 30100 Murcia, Spain.
E-mail addresses: manuel.vidal@um.es (M. Vidal-Sanz), martabar@um.es (M. Agudo-Barriuso).
[1] Joint first authors.

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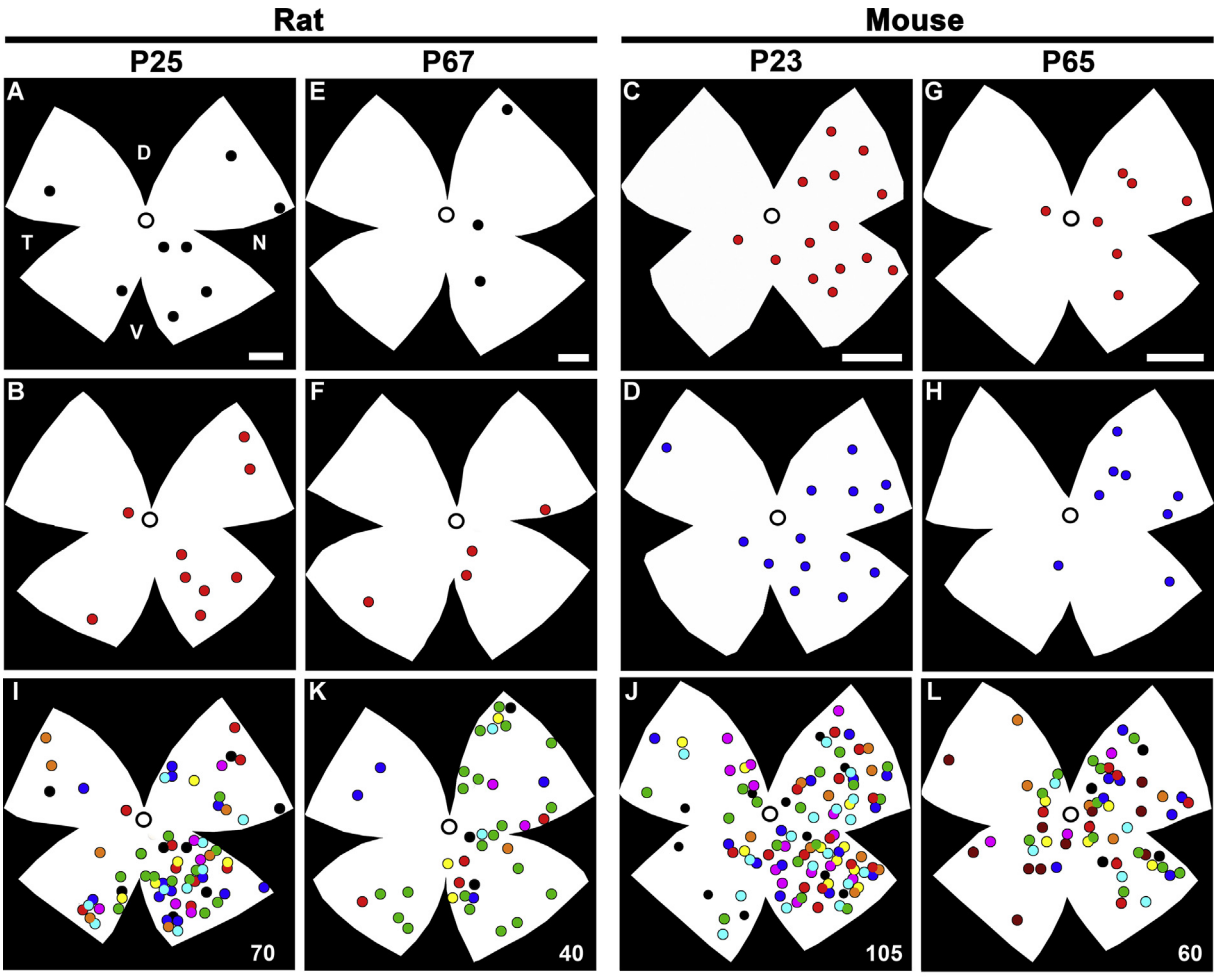

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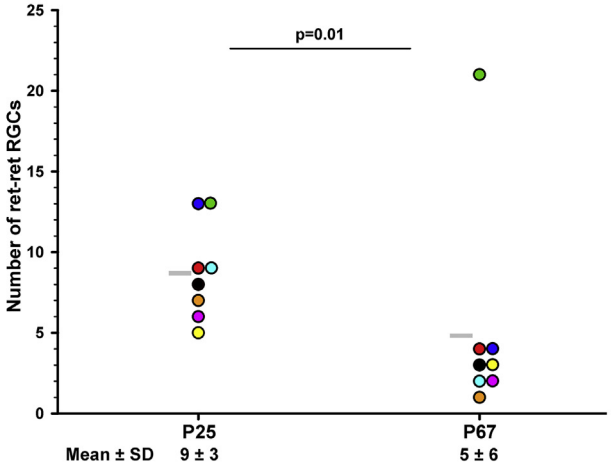

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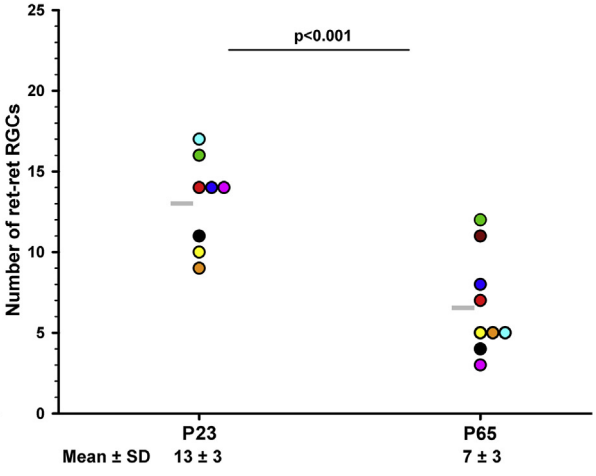

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P25		P67
50% (35)	Brn3a+ Mel-	85% (34)
41% (29)	Brn3a- Mel-	5% (2)
9% (6)	Brn3a- Mel+	10% (4)
0% (0)	Brn3a+ Mel+	0% (0)
0% (0)	Displaced	5% (2)

P

P23		P65
84% (88)	Brn3a+ Mel-	88% (53)
10% (10)	Brn3a- Mel-	8% (5)
6% (6)	Brn3a- Mel+	2% (1)
1% (1)	Brn3a+ Mel+	2% (1)
0% (0)	Displaced	0% (0)