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Genetic deletion of somatostatin receptor 1 alters somatostatinergic transmission in the mouse retina

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Abstract

In the mammalian retina, sparse amacrine cells contain somatostatin-14 (SRIF) which acts at multiple levels of neuronal circuitry through distinct SRIF receptors ($sst_{1–5}$). Among them, the sst_1 receptor has been localised to SRIF-containing amacrine cells in the rat and rabbit retina. Little is known about sst_1 receptor localisation and function in the mouse retina.

We have addressed this question in the retina of mice with deletion of sst_1 receptors (sst_1 KO mice). In the retina of wild type (WT) mice, sst_1 receptors are localised to SRIF-containing amacrine cells, whereas in the retina of sst_1 KO mice, sst_1 receptors are absent. sst_1 receptor loss causes a significant increase in retinal levels of SRIF, whereas it does not affect SRIF messenger RNA indicating that sst_1 receptors play a role in limiting retinal SRIF at the post-transcriptional level. As another consequence of sst_1 receptor loss, levels of expression of sst_2 receptors are significantly higher than in control retinas.

Together, these findings provide the first demonstration of prominent compensatory regulation in the mouse retina as a consequence of a distinct SRIF receptor deletion. The fact that in the absence of the sst_1 receptor, retinal SRIF increases in concomitance with an increase in sst_2 receptors suggests that SRIF may regulate sst_2 receptor expression and that this regulatory process is controlled upstream by the sst_1 receptor. This finding can be important in the design of drugs affecting SRIF function, not only in the retina, but also elsewhere in the brain.

Keywords: Somatostatin receptor 1 null mutation; Retinal cells; Somatostatin levels; Somatostatin receptor 2 expression; Compensatory events

1. Introduction

Somatostatin-14 (somatotropin release-inhibiting factor, SRIF) is a regulatory peptide produced throughout the central nervous system and in most major peripheral organs. It exerts its functions through the activation of distinct G-protein-coupled SRIF subtype receptors designated $sst_{1–5}$ (Barnett, 2003, for review).

SRIF and its receptors are found in the retina. In particular, sparse-occurring SRIF-immunoreactive neurons are present in the innermost inner nuclear layer (INL) and in the ganglion cell layer (GCL) of the mammalian retina (Bagnoli et al., 2003, for review). Those in the INL have been identified as amacrine cells, whereas those in the GCL are either displaced amacrine or ganglion cells. In the mouse retina, SRIF immunoreactivity (IR) has been recently localised to sparse-occurring amacrine cells present both in the proximal INL of the entire retina and in the GCL of the ventral retina (Cristiani et al., 2002).

In spite of the low density of SRIF-containing somata, dense SRIF-positive processes are widely distributed to distinct laminae of the inner plexiform layer (IPL) of the entire retina, thus suggesting that SRIF may act at multiple levels of retinal circuitry (Bagnoli et al., 2003, for

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