The effect of retinal GABA Depletion by Allylglycine on mouse retinal ganglion cell responses to light
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Introduction

The inhibitory neurotransmitter GABA (γ-aminobutyric acid) is metabolized by glutamic acid decarboxylase (GAD) which exists in two isoforms in the mature CNS, GAD65 and GAD67. Allylglycine, a glycine derivative, is a nonspecific inhibitor of both GAD isoforms. Prolonged exposure to allylglycine can therefore deplete the tissue of endogenous GABA over time (Orlowski et al., 1977; Chabrol et al., 2012). Here we applied Allylglycine (ALLYL) in vitro over several hours to gradually deplete GABA in the adult mouse retina and compared the effects of GABA depletion on retinal ganglion cells (RGCs) receptive fields with those obtained by simultaneously blocking all GABAergic receptors (type A, B and C).

Methods

Full-array recordings were performed at a sampling frequency of 7.06 kHz. For light stimulation (mean luminance 1.73 µW/cm²) we used diffuse full field stimulation (0.5 Hz, 30 trials), and a checkerboard stimulus where blocks are shifted randomly in space at fixed time steps (Pampolina et al., CNS 2015). we computed a custom built high-resolution photostimulation system based on a DLP video projector (Texas Instruments, USA). We used diffuse full field stimulation (0.5 Hz, 30 trials), square wave gratings (2200 µm half cycle, 590 um/arc, 8 directions, 5 different contrasts, 10 trials) and a checkerboard stimulus where blocks are shifted randomly in space at fixed time steps (Pampolina et al., CNS 2015).

Results

Time course of GABA green expression at the onset of the experiment (top left) and up to 8 hours later in normal ACSF. After 8 hours in ALLYL (bottom), the only remaining cells still expressing GABA are the Starburst amacrine cells, co-expressing CHAT (red).

Effect of GABA depletion on responses to shifted white noise stimuli for receptive field mapping. In both cases there is a significant increase in diameters (Mann Whitney test). The plot shows medians with interquartile ranges.

Summary

Pharmacological depletion of endogenous retinal GABA reveals interesting changes in:
- motion sensitivity
- contrast sensitivity
- receptive field properties

and suggest that in addition to activating its three classical types of receptors, GABA may have some additional trophic roles that influence how RGCs respond to light.

These preliminary experiments provide useful insights into the role of synaptic inhibition in visual processing and this subject deserves further investigation.