Restoring light sensitivity in blind retinae using a photochromic AMPA receptor agonist

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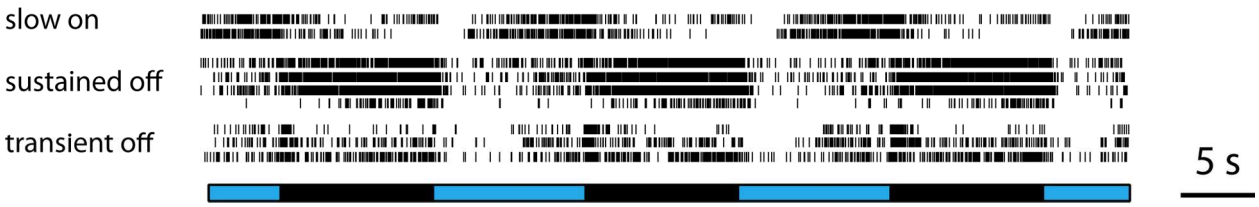
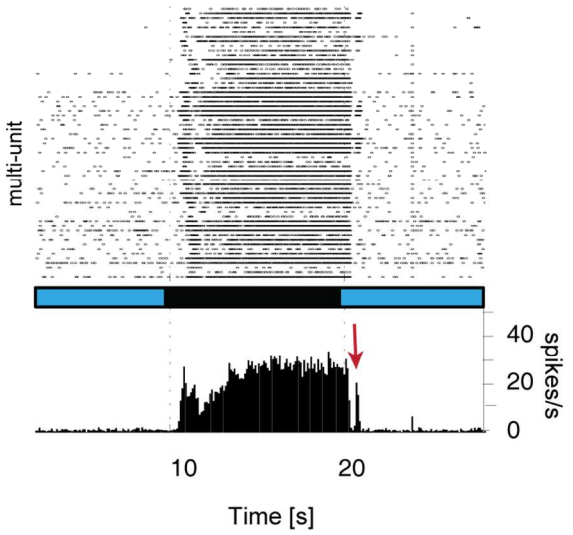
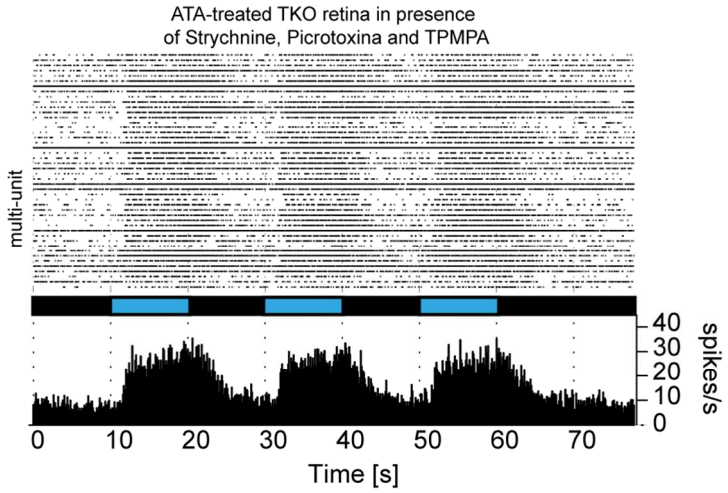
Supporting Information



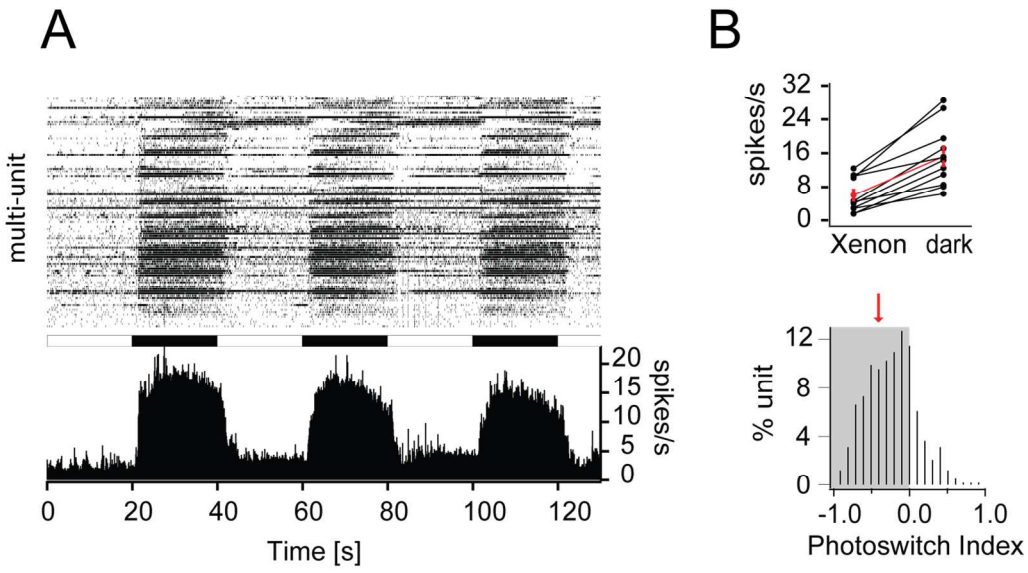
SI Figure 1 - ATA induces different light responses on single cell level. Raster plot of example RGCs showing slow on-light responses, sustained and transient off-light responses. The bar underneath the raster plot indicates the light stimulation protocol.



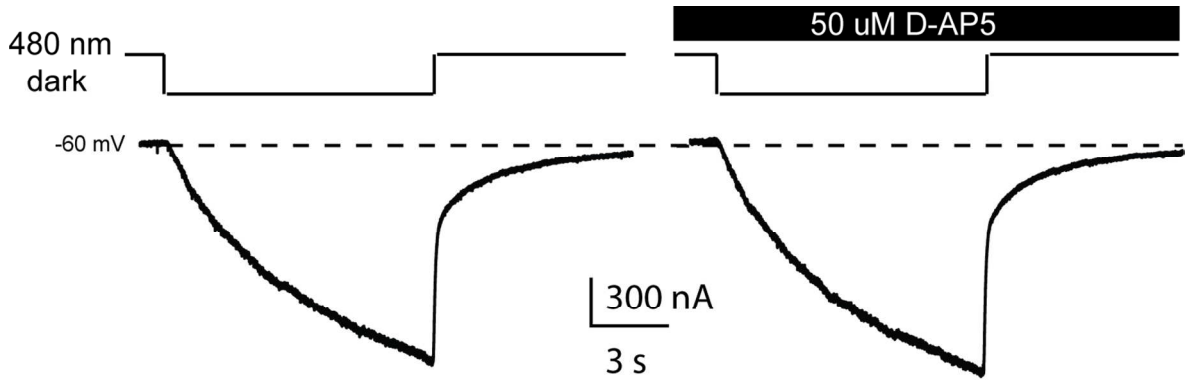
SI Figure 2 - ATA-mediated light responses show a small transient light-on response in presence of $CdCl_2$. Raster plot and histogram of MEA recording of ATA-treated TKO retina in presence of 500uM $CdCl_2$. Red arrow indicates transient light on-response seen in a few experiments performed in presence of $CdCl_2$.



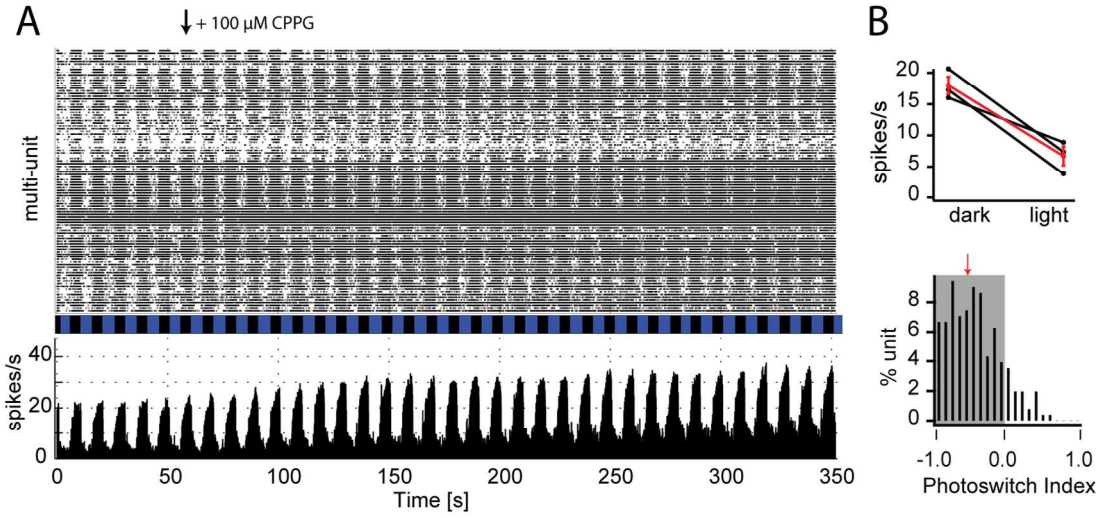
SI Figure 3 - ATA -mediated light responses invert in presence of pictrotoxin, strychnine and TPMPA. Raster plot and histogram of MEA recording of ATA-treated TKO retina in presence of strychnine (1 µM), picrotoxine (5 µM) and TPMPA (10 µM)



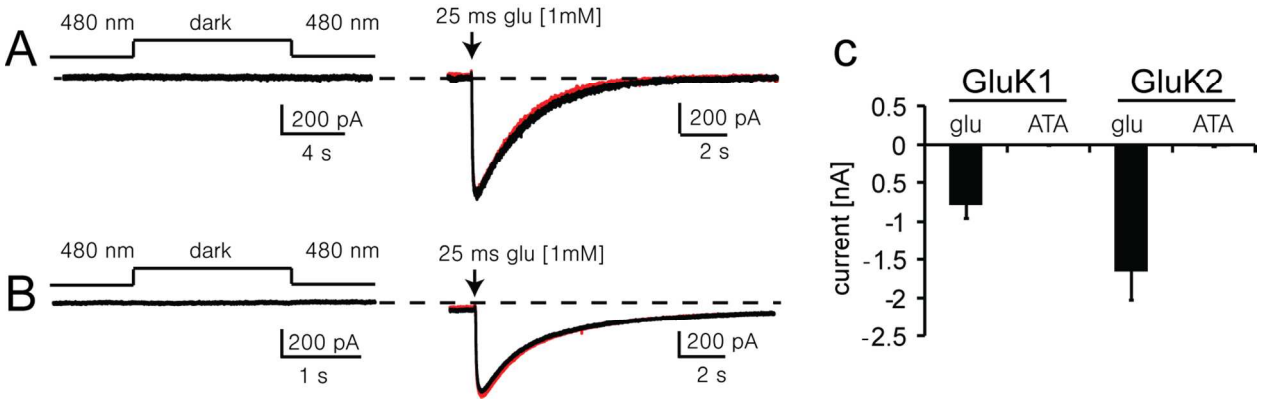
SI Figure 4 - ATA responses under white light illumination. (A) Raster plot and histogram of MEA recording of ATA-treated TKO retina with Xenon light stimulation. **(B)** Statistics of light responses in ATA-treated TKO retinae. (Top) Average spiking rate in darkness and with Xenon light (n=11 retinae, $p<0.01$). (Bottom) Distribution of photoswitch index for RGC populations (n=577 cells). The red arrow indicates the mean photoswitch index for all recorded cells (Photoswitch Index = -0.38 ± 0.038).



SI Figure 5 - Application of ATA in hippocampal neurons of acute murine brain slices. Example traces of ATA-application (25 µM). During illumination with 480 nm light, ATA has no effect on membrane currents. After turning light off large light-induced currents are recorded (> 1 µA), which were insensitive to the selective NMDA receptor antagonist D-AP5 (50 µM).



SI Figure 6 - ATA responses in presence of CPPG. (A) Raster plot and histogram of MEA recording of ATA-treated TKO retina during wash in of 100 µM CPPG. **(B)** Statistics of light responses in ATA-treated TKO retinae. (Top) Average spiking rate in darkness and with 480 nm light (n=3 retinae). (Bottom) Distribution of photoswitch index for RGC populations (n=255 cells). The red arrow indicates the mean photoswitch index for all recorded cells (Photoswitch Index = −0.54±0.09).



SI Figure 7 - Heterologous expression of (A) GluK1 and (B) GluK2 in HEK cells. ATA application (25 µM) to HEK cells was not able to induce light-mediated currents through kainate receptors (left). Control of expression level was performed by a 25 ms puff application with 1 mM glutamate (right). Experiments were performed in presence of Concanavalin A (300 mg/ml) to prevent desensitization. In black and in red are two consecutive puff applications shown. (c) Quantification of glutamate- and light-induced currents. Glutamate application result in GluK1-mediated currents of -0.79±0.17 nA, whereas light-induces currents were negligible (0.0024±0.0027 nA, n=4 cells). In HEK cells expressing GluK2 glutamate currents were -1.66±0.37 nA and light-induced currents -0.01±0.01 (n=5).