

AUTHORS

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Commercial Relationships Disclosure (Abstract): Steven Hughes: Commercial Relationship: Code N (No Commercial Relationship) | Russell Foster: Commercial Relationship: Code N (No Commercial Relationship) | Stuart Peirson: Commercial Relationship: Code N (No Commercial Relationship) | Mark Hankiins: Commercial Relationship: Code N (No Commercial Relationship)

Study Group:

ABSTRACT

TITLE: Inhibitory effects of fluoxetine on photosensitive retinal ganglion cells

ABSTRACT BODY:

Purpose: Selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine (Prozac) are widely used for the treatment of depression. Common side effects of fluoxetine include blurred vision and increased pupil dilation, often leading to angle-closure glaucoma. However, the mechanisms underlying the effects of fluoxetine on visual function and pupil constriction are not well understood. Photosensitive retinal ganglion cells (pRGCs) play a pivotal role in controlling levels of pupil constriction. We have therefore investigated the effect of fluoxetine and other classes of antidepressants on pRGC function and melanopsin driven light responses.

Methods: Multi-electrode array (MEA) recordings were performed on retina explants from *rd1* mice lacking rods and cones, before and after the application of antidepressant drugs. Retina were maintained at 34°C, and perfused with AMES media bubbled with 95% O₂, 5% CO₂. Melanopsin driven light responses were measured as changes in spike firing rate following stimulation with 480nm light.

Results: Fluoxetine suppresses spontaneous spike firing and reduces the duration of pRGC light responses in a dose dependant manner, leading to a complete loss of melanopsin driven responses. The tricyclic antidepressant Clomipramine mimics the effect of fluoxetine, yet application of serotonin itself, or application of Citalopram, a potent and highly selective SSRI that exerts lesser effects on noradrenalin and dopamine uptake compared to fluoxetine, have only minimal effects on pRGC function. These data suggest that the effects of fluoxetine may not be dependent on serotonin, but rather due to off-target effects on other neurotransmitters. Fluoxetine also directly inhibits TREK-1 ion channels, which are expressed by pRGCs. The small molecule inhibitor of TREK-1, Spadin, was found to suppress spike firing and reduced the magnitude of pRGC light responses elicited to bright light stimuli, but did not fully replicate the effects of fluoxetine.

Conclusions: Our data show a direct effect of SSRI's and other classes of antidepressants on retina function and melanopsin expressing pRGCs. Our data suggest that fluoxetine may regulate pRGC function by multiple mechanisms, likely involving dopamine, cAMP and TREK-1 ion channels. These data offer a possible mechanism to explain the side effects of fluoxetine on pupil dilation and resulting susceptibility to angle-closure glaucoma.

(No Image Selected)

Layman Abstract (optional): Provide a 50-200 word description of your work that non-scientists can understand.

Describe the big picture and the implications of your findings, not the study itself and the associated details.: Here we show that commonly prescribed anti-depressant drugs can negatively impact the function of the retina. Prozac reduces the activity of a specialised set of light sensing cells within the retina that control pupil constriction and entrainment to day night cycles. These data potentially provide a mechanism to explain a range of common side effects associated with these drugs, including increased pupil dilation, blurred vision and disruptions of sleep patterns.

DETAILS

PRESENTATION TYPE: #1 Poster, #2 Paper

CURRENT REVIEWING CODE: 2600 intrinsically photoreceptive ganglion cell structure and function - VN

CURRENT SECTION: Visual Neuroscience

KEYWORDS: 224 ganglion cells, 366 photoreceptors, 200 drug toxicity/drug effects.

Clinical Trial Registration (Abstract): No

Other Registry Site (Abstract):

Registration Number (Abstract):

Date Trial was Registered (MM/DD/YYYY) (Abstract):

Date Trial Began (MM/DD/YYYY) (Abstract):

Grant Support (Abstract): Yes

Support Detail (Abstract): BBSRC

TRAVEL GRANTS and AWARDS APPLICATIONS

AWARDS: