1. Provisional title
Objective and subjective assessment of spectral sensitivity in physiological responses to bright light in humans

2. Authors and affiliations
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3. Field and keywords
Vision science, perception, human neuroscience, psychophysiology, light sensitivity, visual discomfort, spectral sensitivity, pupillometry, facial electromyography, photoreceptor mechanisms

4. Research question(s) and/or theory
Which photoreceptor mechanisms underlie objective and subjective sensitivity to bright light in humans?

5. Hypotheses (where applicable)
Confirmatory CH_1: We hypothesize that the spectral sensitivity of light-adapted pupil responses (pupil constriction, post-illumination pupil response) is best fit by melanopsin.
Confirmatory CH_2: We hypothesize that the spectral sensitivity of EMG-measured facial responses (frowning, squinting, blinking) is best fit by melanopsin.
Exploratory EH_1: We hypothesize that the spectral sensitivity of scale-measured subjective sensations (visual discomfort, facial sensations, lacrimation) is best fit by melanopsin.

6. Study design and methods
We will recruit 24 healthy volunteers aged 18-35 years (to minimize differences in lens transmittance) for our within-subjects laboratory study. During the four 2.5-hour experimental sessions, light pulses from six narrowband wavelengths delivered through a spectrally tunable LED-based light engine (445, 475, 505, 545, 640 nm) under homogenous, full-field stimulation at a fixed quantal radiance will be shown to participants in a counterbalanced sequence, including a blank, "dark" stimulus. Pupillometry and facial electromyography data will be recorded continuously (60 Hz for pupillometry, 2048 Hz for the EMG) during the trial, and subjective sensations (visual discomfort, facial sensations, lacrimation and associated confidence ratings) reported. Prior to the sequence, participants undergo a 10-min darkness adaptation period, followed by 36 trials of light stimulation, with each cycle consisting of 30 s of light exposure followed by 30 s of refractory darkness to examine post-illumination pupil responses. The power obtained with the sample size will be determined using Bayes Factor Design Analysis.

7. Key analyses that will test the hypotheses and/or answer the research question(s)
For CH_1, CH_2, EH_1, we will follow a parallel analytic strategy to determine the spectral sensitivity of each response modality. At each wavelength for each participant, we will fit a four-parameter logistic regression to the radiance-response curve relative to the "dark" baseline. For each fitted curve at a given wavelength, we will then obtain the ED_{50} radiance values, and on the wavelength axis, fit the logarithmic spectral sensitivities of the human photosensitivities to the log-transformed inverted ED_{50} radiance values (representing sensitivity) using least-squares. For data quality control, we will examine whether the slopes of the logistic curves correspond to our hypotheses (i.e. the brighter the light, the stronger the response; or in the case of pupil diameter, the smaller the pupil).

8. Conclusions that will be drawn given different results
We hypothesize that across single-photoreceptor models (incorporating L, M, and S cones, rods and melanopsin each, i.e. the human photoreceptors), the melanopsin model will provide the best fit to the data. If this is not the case, it will be informative if other photoreceptors better describe the data. If no single-photoreceptor provides an acceptable fit, we will fit higher-level multiple-photoreceptor models using the Quick pooling model.

9. Key references
Kaiser, E. A., McAdams, H., Igdalova, A., Haggerty, E. B., Cucchiara, B. L., Brainard, D. H., & Aguirre, G. K. (2021). Reflexive eye closure in response to cone and melanopsin stimulation: a study of implicit measures of light sensitivity in migraine. *Neurology, 97*(17), e1672-e1680. https://doi.org/10.1212/WNL.0000000000012734
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Spitschan, M. (2019). Photoreceptor inputs to pupil control. *J Vis, 19*(9), 5. https://doi.org/10.1167/19.9.5
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