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Research Project: Flicker photophobia as an experience of inefficient coding

Purpose and Approach

We will use a delayed estimation procedure to measure bias and precision in representation of the temporal frequency of a flickering stimulus. The participant will monitor a spatially uniform field of light. On each of many trials a 2 second “reference” flicker will be presented, followed by a 2 second delay. A second, continuous flicker (with the frequency randomly selected) is then presented and the participant is asked to adjust the frequency of the flicker using the left and right arrows on a keyboard to best match the reference. Data will be collected at two background light intensities (high and low photopic) crossed with two modulation directions (light flux and L–M). The goal is to test for differences in the bias and precision of these delayed estimates between the conditions.

Subjects

We will collect a complete dataset from 5 healthy participants, ages 18-40. Participants will meet these criteria:

1) Classified by the POEM (Kaiser et al., 2019; and as updated in the POEM analysis code as of the date of this pre-registration) to be “headache-free”.
2) Score less than 10 on a light sensitivity survey (Bullock 2018).
3) Have an Allodynia Symptom Checklist (ASC) score (Lipton et al, 2007) of less than 5.

Exclusion criteria for all subjects include:

- An answer of “yes” to the question “Do you have ongoing symptoms from a recent concussion?”
- An answer of “yes” to the question “Are you currently receiving treatment for a disease of the eye?”
- A color vision impairment defined as scoring below 17 on the first 21 plates of the Ishihara test.
- A best corrected visual acuity (BCVA) below 20/25 for the dominant eye.
- A history of generalized epilepsy.

It is possible that we will identify other exclusion criteria as we screen subjects for the study. If subjects are excluded for reasons identified prior to their participation in data collection, we will simply add these reasons to the list of exclusion criteria and not consider this a deviation from the protocol.

We will identify the dominant eye of the subject using a “telescope tube” test. Testing will be conducted using the dominant eye; the fellow eye will be patched. Subjects will be permitted to listen to music played from their smart phone speaker during the testing session, but not text-based audio (e.g., podcasts, audiobooks).

Subject Preparation

At the start of a data collection session, subjects will be acclimated to the experimental room. The room will be configured either in a high or low light state prior to the arrival of the participant. We will measure and report the luminous intensity present in the room at the subject location. The operator will then review the experimental procedure with the subject and adjust the apparatus and chair for subject comfort.

Apparatus, stimulus, data collection

All of the stimuli will be generated with a digital light synthesis engine (CombiLED) under computer control. The stimuli will be presented through a custom-made eyepiece with a circular, uniform field of 27.5° diameter. The subject will view the stimulus with their natural pupil. Visual stimuli are tailored to an individual observer's age, taking their predicted lens density and predicted pupil size into account (which in turn is based upon age, luminance of the stimulus background, and stimulus area). The background level of the stimulus is adjusted by passing the light through either a 0.5 or 3.5 log neutral density filter. The achieved luminance of the stimulus background will vary slightly by subject, but will be roughly 1-10 cd/m2 at the low light level and ~3000-4000 cd/m2 at the high light level. The chromatic content of the background may also vary slightly between observers and light levels as this shift is needed to provide the desired contrast levels. Ultimately, the nominal, targeted contrast upon the post-receptoral mechanisms will be set to 7.5% on L–M, and 33% on LMS.

Subjects will be studied in each of 6 sessions of ~1 hour in duration; more than one session may take place on a single day as long as there is a break of more than 15 minutes between sessions. A session is conducted at a single background light level, with the order of light levels alternated across sessions. Each session is composed of 10 blocks. Each block measures one post-receptoral direction (L–M or light flux), with the direction alternating across blocks. Each block presents 20 delayed estimation trials.

The reference flicker frequency within a trial is drawn from a uniform (log) distribution of values between 1 and 32 Hz. The initial frequency of the stimulus presented after the delay is drawn from a uniform distribution of ±7 dB around the reference frequency. Subjects receive feedback after each trial, with either a positive "beep" sound if their response is within 1.5 dB of the reference frequency. Responses outside of this range will receive the auditory feedback of "too fast" or "too slow" spoken by a computer voice. The subject is paid a bonus (of up to $10) based upon the proportion of "good" responses that they make during a session.

Data analysis and primary hypothesis testing

Data will be analyzed within subject, grouped across sessions and blocks into each of the four stimulus conditions (high and low light level, crossed with L–M and light flux post-receptoral directions). The data from each condition will be considered within a log-log plot across trials of the estimated flicker frequency vs. the reference flicker frequency. We will fit these data with a linear (in the log space) function, constrained to have an intercept at ~0 and obtain the slope. The slope measures bias in estimation. After removing this linear component we will measure the variance in the residual estimated frequencies. This variance is a measure of precision. We will obtain 95% confidence intervals for these measures by bootstrapping across trials. We will test if bias and / or precision differs by more than the 95% confidence interval between high and low light levels, and between the L–M and light flux directions.

Data Exclusion Criteria and handling errors in data collection

Device
If the testing apparatus fails temporarily (due to e.g., software crash) and it is possible to resume testing, then we will discard the single block during which the failure occurred, repeat this block, and then continue to complete the session. If the failure occurs between sessions, then the study can continue as originally planned after recovering from the failure.

There may be failures of the testing apparatus that cannot be resolved within a few minutes. If so we will discard all the data collected during this session, and we will invite the subject to return to re-collect data for the session.

Subject
If a subject leaves the study prior to the completion of six sessions of data collection, we will discontinue their participation in the study and exclude all of their collected data.

If a subject needs to briefly stop data collection during a session, we will treat that circumstance in the same manner as a brief equipment failure that interrupts collection of data during a block.

If a subject needs to stop data collection during a session and is unable to continue we will discard all data from that session and attempt to re-collect the session on a subsequent day. If the subject discontinues a second session we will discontinue their participation in the study.

Given the range of flicker frequencies presented during the estimation phase of each trial (±7 dB) and the range of flicker frequency estimation values that are coded as “good” (±1.5), chance performance in the experiment should be ~21%. If an observer registers performance of <25% on each of their first two sessions, then we will discontinue their participation in the study.

The operator may observe subject behavior during the session that prompts concern that the collected data will be of low quality (e.g., excessive movement and fidgeting or sleepiness). The operator will discuss these observations with the study team, and data for a subject may be excluded from the study on this basis, as long as the decision is made prior to examination of the data.

If subjects are discontinued, we will recruit additional subjects in an effort to meet our pre-specified study numbers.