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Research Project: Trigeminal and melanopsin signals in brain trauma symptoms

Purpose and Approach

Tactile stimulation of the ophthalmic division of the trigeminal nerve elicits a blink reflex. There is evidence that variation in the intensity of this stimulus produces gradations in the properties of the blink response (Bixler 1967). This study will measure the blink reflex to puffs of air of varying intensities. This measurement will be made in two separate sessions. Our goal is to identify features of the blink response that vary systematically with stimulus intensity, and which show high test / re-test reliability across subjects between sessions.

Subjects

We will collect a complete dataset from 15 healthy subjects, ages 18-35, without a history of concussion in the previous 2 years. These subjects are selected, screened, and studied by the BlinkCNS company. At the time of the posting of this pre-registration document, data from 13 subjects has been collected, but not yet analyzed.

Subject Preparation

At the start of a data collection session, subjects will be acclimated to the experimental room. The operator will then review the experimental procedure with the subject and adjust the apparatus and chair for subject comfort. Subjects may hold onto the tripod to stabilize themselves if air puffs are startling to them.

Apparatus and Stimulus

Trigeminal responses are measured using a custom-modified EyeStat device, positioned over the eye of the seated subject. During an acquisition, the device delivers 8 air puffs to the lateral canthus, with the left or right eye selected randomly on each trial. The eye is illuminated with a ring of IR-LEDs that produce a corresponding ring of glint reflections on the tear film of the eye. A pair of high-speed IR cameras measure the timing of obscuration of the glints by the movement of the eyelid. Microphones adjacent to the lateral canthus detect the air puff and sync the timing of recorded response across trials. The mean properties of the blink response are obtained across the 8 trials in an acquisition. A testing session consists of 26 acquisitions, 5 each at 5 different puff pressures in counterbalanced order (Aguirre 2007), with the first acquisition discarded.

Air puff pressure is set on each acquisition to one of 5 specified pressure levels (3.5, 7, 15, 30, 60). The nominal pressure is set manually by the operator, and the actual, delivered pressure is recorded. Data will be analyzed using the measured, as opposed to nominal, pressure level.

Trial Design

Each session will include 26 acquisitions, following this trial sequence: 3, 3, 0, 2, 4, 4, 2, 0, 1, 3, 1, 1, 0, 4, 3, 2, 2, 3, 4, 1, 2, 1, 4, 0, 0, 3, where 0 = 3.5 PSI, 1 = 7.5 PSI, 2 = 15 PSI, 3 = 30 PSI, and 4 = 60 PSI. Subjects will have a brief moment to rest their eyes between each trial while the device processes the scan recording and the administrator manually adjusts the PSI via the knob on the regulator. Subjects will return for a second session 2-4 days after their first visit.

Data analysis

Analysis of raw IR video recordings will be performed by BlinkCNS. For each puff, the proprietary analysis code determines if a “valid” blink was recorded ipsilateral and / or contralateral to the stimulated eye. Each valid blink yields values for several features (e.g., onset latency, maximal lid velocity, total “area under the curve”). These values are derived for the ipsi and contra lid, and the average value across the valid blinks in a given acquisition are provided. The average value for each of the 25 retained acquisitions will be obtained for each subject / session. BlinkCNS will perform this first stage of data analysis.

For each blink feature, the data from each subject / session consist of 5 measurements each at each of 5 nominal stimulus intensities. After log-transforming the measured stimulus pressures, we will fit these data with a 3 parameter Hill function. The R-squared value of this fit will be retained. For a given feature, we will examine the rank-correlation across subjects of a parameter (e.g., slope) as measured in session 1 compared to session 2. We will identify the blink feature(s) that yield fit parameters that *a)* tend to have a high within-session R^2 , and *b)* have a high correlation of values between sessions. In addition to the measured blink features, we will also examine the number of valid blinks evoked on the ipsi and contra side as a function of puff pressure.

Exclusion Criteria

We will exclude subjects on the basis of poor quality blink reflex data. A given acquisition will be considered valid if at least 3 / 8 blinks ipsilateral to the stimulus are valid. A given session will be considered valid if at least 3 / 5 acquisitions are valid at each of the nominal stimulus intensities. We will exclude a subject if either of the two sessions are judged to be invalid. We will attempt to replace excluded subjects with newly recruited subjects to meet our recruitment goal of 15 total subjects.

We cease enrolling subjects and end the study on March 1, 2022 if we have not yet met our recruitment goal. In this instance, we will report our results given the subjects we have studied to that point.

References

Bixler, E.O., Bartlett, N.R. & Lansing, R.W. Latency of the blink reflex and stimulus intensity J. Perception & Psychophysics 2, 559–560 (1967). <https://doi.org/10.3758/BF03210267>