A biphasic temporal pattern in pupil size around perceptual switches in binocular rivalry

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Abstract

In binocular rivalry, two incompatible inputs are presented separately to the two eyes, causing subjects to alternate between two perceptual interpretations. These percept switches engage a large frontoparietal network, accompanied by large pupil dilations. It is unclear whether these measured functional MRI (fMRI) and pupil responses relate to neural processing causing the switches, or constitute the brain's response to the switches. The temporal dynamics with which subjects switch between the two interpretations are determined by catecholaminergic neuromodulatory systems and these dynamics should be reflected in pupil size. We simultaneously recorded pupil dilation and fMRI during binocular rivalry, and show a biphasic pupil response around the time of a percept switch. The strength of a transient pupil dilation after the behavioral response reflects the temporal predictability of the switch. We also find a marked pupil constriction before the behavioral response. Surprisingly, the amplitude of this constriction predicts the duration of the subsequent percept several seconds in advance, implying that the pupil can be used as a proxy for two different neural mechanisms underpinning perceptual dynamics in ambiguous perception. Together with concurrent fMRI recordings, these results allow us to disambiguate between competing computational accounts of the ongoing inference process that shapes the dynamics of bistable perception.

Keywords: binocular rivalry; bistable perception; pupillometry; fMRI; neuromodulation

Introduction

In multistable perception, an observer is presented with a stimulus that can be interpreted in multiple, mutually exclusive ways (percepts). Observers switch between different interpretations over time, even though sensory input remains constant. This poses an interesting corner case for theories of perceptual inference, because it suggests that even when the evidence for two concurrent states of the world is identical, the interpretation of this evidence dynamically changes. These phenomenological reappraisals of sensory information are thought to be due to a change only of an observer's internal brain state (Brascamp, Sterzer, Blake, & Knapen, 2018). What drives this brain state? How are perceptual switches represented in the brain, and how can we separate it from neural mechanisms involved in the formulation of a behavioral response?

Pupillometry offers a non-invasive proxy to the brain state of a subject and has been related to neuromodulatory systems originating in the brain stem (Aston-Jones & Cohen, 2005; de Gee et al., 2017), that are known to regulate the stability of a global brain state. Previous work using pupillometry during bistable perception has shown that the pupil tends to strongly dilate in response to a percept switch (Einhäuser, Stout, Koch, & Carter, 2008; Kloosterman, Meindertsma, van Loon, et al., 2015).

Some studies using pupillometry suggests that the pupil dilation is mostly a *result* of percept switches. For example, Kloosterman, Meindertsma, van Loon, et al. (2015) manipulated the predictability of the timing of on-screen simulacrums of switches (termed 'replay') by sampling them from distributions with different mean *hazard rates*. A hazard rate quantifies how likely an event is to happen immediately, given that it did not occur yet. Larger hazard rates indicate greater predictability and less surprise. Kloosterman, Meindertsma, van Loon, et al. (2015) found that the pupil dilation after a reported switch scaled inversely with the predictability of the timing of the switch. This finding fits well with neuroimaging studies that showed that some fronto-parietal brain activations during perceptual switches in bistable perception are related to a cascade of cognitive processes induced by the percept switches, such as the detection and reporting of the switches, rather than the percept switches themselves (Brascamp, Blake, & Knapen, 2015; Brascamp et al., 2018).

But can the pupil also be used to also probe the brain mechanisms that *lead up to* the perceptual switch? A recent study by Pfeffer et al. (2018) showed that a pharmacological manipulation of catecholaminergic (dopaminergic and noradrenergic) systems, but not cholinergic systems, manipulated the rate at which subjects switch between percepts. Specifically, the noradrenaline reuptake inhibitor atomoxetine increased the rate at which subjects switches between percepts. Furthermore, Pfeffer et al. showed, by computational modeling and electrophysiological measurements, that this can be explained by a change in the ratio of excitatory and inhibitory activity in cortical areas. It is hypothesized that the variability in catecholaminergic tone should be reflected in pupil size (de Gee et al., 2017).

In sum, past research suggests that pupil size fluctuations, accompanied by activations in fronto-parietal networks could potentially be associated with at least two separate underlying processes during bistable perception:

1. The adaptation of cortical excitability and thereby the stability of a dominant percept (Pfeffer et al., 2018), i.e. the underlying conditions which cause an increase of the switches. These fluctuations should *precede* reported switches.

2. A cascade of cognitive processes that derive from the switch, such as surprise and the reporting of the percept (Kloosterman, Meindertsma, van Loon, et al., 2015; Brascamp et al., 2015, 2018), i.e. the *result* of the switches which should follow them.

In our present study, we recorded pupil dilation and functional MRI (fMRI) during binocular rivalry, a form of bistable perception where two incompatible stimuli are presented to the two eyes (see Figure 1), in an attempt to dissociate the substrates of these two distinct processes in the pupil and BOLD response. Here, we only report results regarding pupil size. We used a general linear model (Friston et al., 1998; de Hollander & Knapen, 2018) to deconvolve the pupil responses around the report of percept switches and to relate these to the two putative processes described above, using two behavioral measures: (1) subsequent stable percept durations, which are related to cortical excitability (Pfeffer et al., 2018) and (2) hazard rates of the onset of the modeled switches, which are a measure of the temporal predictability these switches (Kloosterman, Meindertsma, van Loon, et al., 2015).

We find that the mean pupil dilation time course around the report of a percept switch has a biphasic nature, where the pupil is relatively constricted already 2-3 seconds before the report of the switch, after which the pupil dilates again around the time of report. Furthermore, we show that (1) the magnitude of the pupil constriction before switch report is predictive of the subsequent full perceptual dominance duration, approximately 3 seconds into the future, and (2) the dilation just

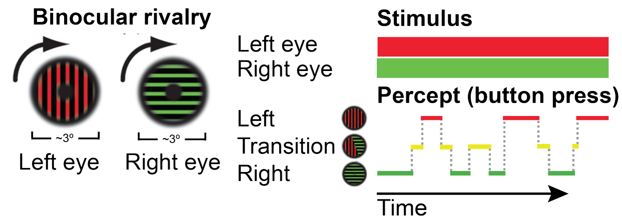

Figure 1: Illustration of the experimental paradigm. During one trial block, subjects were presented with a red and green rotating grating in the left and right eye, respectively. Even though the stimulus input to the two eyes was constant, the subjects reported their percepts as either the grating in left eye (red), right eye (green), i.e. a stable percept, or the start of a perceptual transition (yellow) between two, i.e. percept switch.

after the time of report is negatively related to the predictability (hazard rate) of the timing of the percept switch (a conceptual replication of Kloosterman, Meindertsma, Hillebrand, et al., 2015, for ambiguous, endogenously controlled bistable perception) .

Results

Deconvolution was performed using a general linear model (GLM), accounting for blinks and microsaccades, as well as percept switches which were indicated by the subjects through a button press. Percept switches that were preceded by a blink within 1.5 seconds, and thus might be triggered by that blink rather than endogenous perceptual processing, were modeled separately as a nuisance regressor. Fourier sets were used to deconvolve the pupil size time course between 3 seconds before and 3 second after the report of the percept switch and to correlate them to behavioral measures.

The deconvolved time courses show that the pupil constricts already 2-3 seconds before the subject reports a percept switch. Crucially, the more the pupil is constricted compared to baseline, the shorter the duration of the next perceptual dominance state. The deconvolved time course also shows that the pupil dilates during and just after the report of the percept switch. This dilation is negatively correlated with the hazard rate of the previous trial. In other words, the more predictable the timing of a percept switch was, the smaller was the resulting pupil dilation (see also Figure 2).

Discussion

In this study, we investigated the temporal dynamics of pupil dilation during binocular rivalry where subjects had to indicate switches of percept between the inputs of the two eyes. Our results show that pupil size shows a biphasic response, with a decrease in size before and increase in size after the report of a percept switch during binocular rivalry. These two distinct phases around a perceptual switch were related to two specific processes: (1) the modulation of the rate at which percept switches take place and (2) monitoring of unexpected

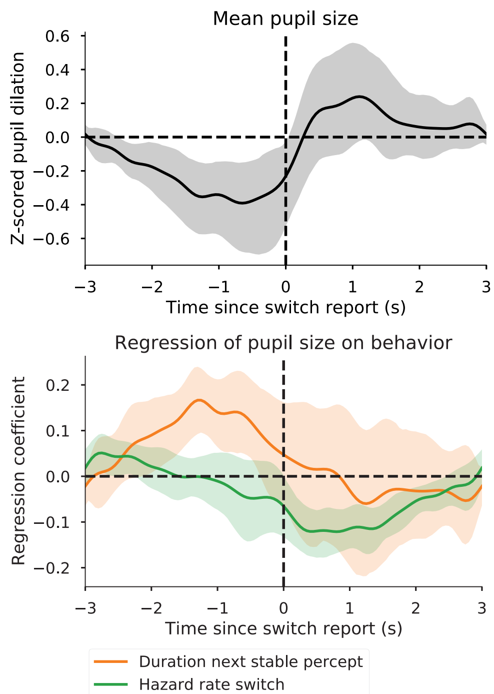

Figure 2: (Upper panel) mean pupil size across time and regression slopes of the percept duration. (Lower panel) the hazard rate of the reported switch timing on the pupil size across time. Shaded areas report bootstrapped 99% confidence intervals across subjects. The mean pupil size shows a slow decrease before the switch is reported. The time-resolved regression slopes show that pupil size before the report is predictive of the duration of the next stable percept. The pupil size after the report is predictive of the hazard rate (measure of predictability) of the reported switch.

perceptual changes, operatinalised as the predicatbility of the onset of a switch.

Our work shows that the pupil response during binocular rivalry can give insight into its complex temporal dynamics, which can be studied using linear deconvolution approaches. Deconvolution allows us to relate pupil size to behavioral measures-of-interest in a time-resolved manner, showing that different parts of its time course are correlated with different underlying processes.

Future work will include results in the fMRI data that were collected simultaneously, with a focus on brainstem regions that contain the nuclei that are the source of many neuromodulatory signals (de Gee et al., 2017), the frontoparietal network that shows heightened activity after a perceptual switch report (Brascamp et al., 2018), as well as retinotopically-defined cortical areas. The high temporal resolution of the fMRI data that were collected (TR <1 s) might aid in providing insight into the complex temporal dynamics during bistable perception.

Methods

Experimental paradigm

Nine subjects were scanned during 4 - 6 runs of 11.6 minutes each. Stimuli consisted of a red grating in the left eye and an orthogonal grating in the right eye (or vice versa). Both gratings were turning clockwise or counter-clockwise. Each run contained four blocks, corresponding to the four possible stimulus presentations (two factors: clockwise/counter-clockwise and red stimulus in the left eye/red stimulus in the right eye). Subjects had to report via a button box whether they were observing a red grating, green rating, or a mixed percept (see Figure 1).

Physiological measurements

MRI Functional MRI data were collected using a 3 Tesla Philips Achieva scanner at the Spinoza Center of the University of Amsterdam. The functional sequence was a Gradient-Recalled Echo (GRE) EPI (Echo-planar imaging) sequence, with an in-plane resolution of 1.88 mm and 3 mm thick slices (FOV: 184 x 231 mm). The total number of slices was 17, covering the entire occipital cortex, the inferior frontal cortex, the most dorsal part of the brainstem, as well as all of the midbrain. The repetition time (TR) was 0.971 seconds.

Pupil data Pupil data were collected using a customized Eyelink system inside the scanner at a sampling rate of 1000 Hz. Data were preprocessed and further analyzed following the protocol reported by Knapen et al. (2016). Eye blinks and artefacts were interpolated and the signal was temporally filtered (low-pass filter at 4 Hz, high pass filter at 0.02 Hz). Blinks and microsaccades were detected using customized Eyelink software (Knapen et al., 2016).

Analysis

Behavior For the behavioral analysis, we focused on the durations of 'full percepts'. That is, intervals between which the subject indicates he/she perceives a stable, unambiguous percept. To calculate the hazard rate of the onset of switches to a mixed or different percept, we fitted a Wald distribution to the time intervals between the onset and offsets of full percepts, using a maximum likelihood approach. This distribution fitted reasonably well and allowed for calculating analytical hazard rates for every percept switch (see Figure 3).

Deconvolution using Fourier sets For the analysis of the pupil time series, we used a GLM approach, where impulse functions on the onsets of the the perceptual events (indicated by the subject with a button press) are convolved with as set of basis functions (Friston et al., 1998). The basis functions consisted of a limited set of 24 sine and cosine functions plus an intercept. Such Fourier sets can model a large possible array of smooth time courses with a relatively limited set of regressors. The linear deconvolution using Fourier sets is implemented in the open-source Python package *response_fytter* (de Hollander & Knapen, 2018).

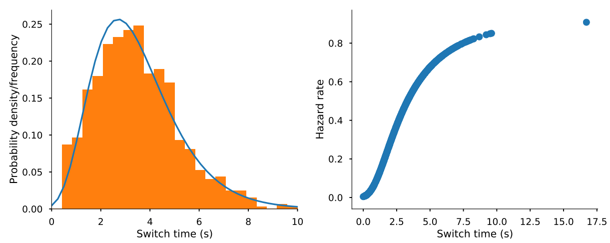

Figure 3: (Left) Empirical between-percept intervals of a representative subject. Overlaid is the probability density of a fitted Wald distribution. (Right) resulting hazard rate for each percept duration.

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