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Time dilates after spontaneous blinking

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Accumulating evidence from pharmacology, neuroimaging, and genetics indicates that striatal dopamine influences time perception [1–5]. Despite these converging results, it is not known whether endogenous variations in dopamine underlie transient fluctuations in our perception of time. Here, we exploited the finding that striatal dopamine release is associated with an increase in spontaneous eye blink rate [6–8] to examine the relationship between intra-individual fluctuations in dopamine and interval timing. In two studies, participants overestimated visual subsecond and suprasecond and auditory subsecond intervals if they had blinked on the previous trial. These results are consistent with the hypothesis that transient fluctuations in striatal dopamine contribute to intra-individual variability in time perception.

Dopamine has been repeatedly linked to individual differences in time perception in the milliseconds to seconds range (interval timing) [2,4,5]. Dopamine agonists and antagonists produce relative overestimation and underestimation of temporal intervals, as reflected in leftward and rightward shifts of psychometric functions fitted to psychophysical data [1,3,9]. Convergent evidence from functional neuroimaging suggests that temporary dopamine depletion through a pharmacological manipulation reduces interval timing accuracy through attenuation in timing-specific activation in striatum [2]. Further research has implicated genetic polymorphisms associated with alterations in striatal and prefrontal dopamine with inter-individual differences in interval timing and brain morphometry in regions widely associated with timing [4].

The cumulative evidence for a role of dopamine in interval timing, however, does not offer any information regarding whether endogenous fluctuations in dopamine contribute to *intra*-individual differences in timing, namely why our perception of time varies from one moment to the next. Although intra-individual variability in interval timing has been almost wholly neglected, it undoubtedly influences performance variability in a variety of contexts requiring precise timing of the environment and it is closely intertwined with transient fluctuations in conscious states [10]. Relating dopamine to interval timing at the intra-individual level will more firmly clarify how dopamine modulates time perception. That is, if striatal dopamine phasically modulates perceived duration, then transient fluctuations in dopamine should shape intra-individual fluctuations in interval timing [3].

Spontaneous eye blinking provides an opportunity to test this hypothesis. Eye blink rate has long been associated with dopaminergic activity and is widely used as a biomarker of striatal dopamine receptor availability [6–8]. As is the case with time perception, spontaneous blinking is altered in clinical conditions characterized by aberrant dopamine levels, including Parkinson's

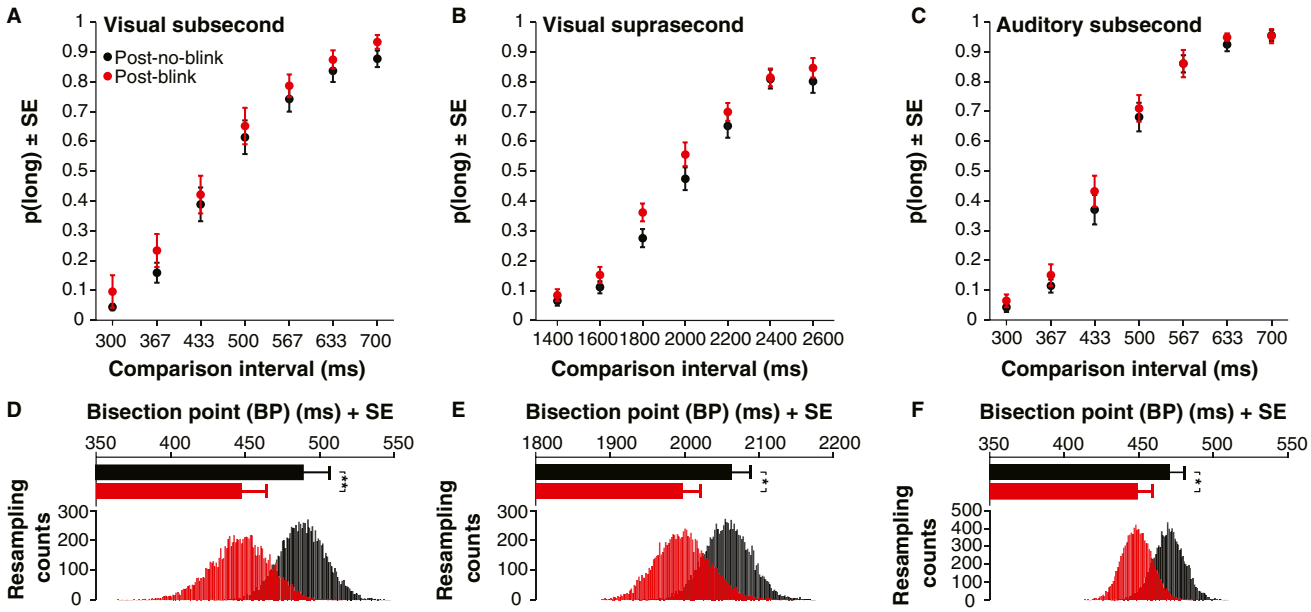

Figure 1. Interval timing as a function of spontaneous blinking.
(A–C) Proportion of long responses [p(long)] in trials in which the participant did not blink (post-no-blink, black) and did blink (post-blink, red) on the previous trial in (A) the visual subsecond temporal bisection task, (B) the visual suprasecond task, and (C) the auditory subsecond task. (D–F) Bisection points (BPs) (lower values reflect relative overestimation of comparison intervals) and bootstrap resampling counts (10,000 resamples) of mean BPs as a function of trial type in (D) the visual subsecond task, (E) the visual suprasecond task, and (F) the auditory subsecond task. $^{*}p < 0.05$, $^{**}p < 0.01$.

disease and schizophrenia, and it is responsive to pharmacological manipulations targeting dopamine [8,9]. Further evidence specifically links spontaneous blinking to D_2 receptor availability in the nigrostriatal dopamine pathway [6,8], which projects from substantia nigra to the caudate and putamen (dorsal striatum). This complements data pointing to a specific role of D_2 receptors in this pathway in the modulation of the speed of a putative internal clock [1]. Here we tested the prediction that participants would exhibit a leftward shift of psychophysical functions fitted to timing data, reflecting a relative overestimation of intervals, if they had blinked on the previous trial.

Participants completed visual subsecond (300–700 ms) and suprasecond (1400–2600 ms) temporal bisection tasks (Study 1) or an auditory subsecond (300–700 ms) temporal bisection task (Study 2) whilst having their spontaneous blinks recorded by an eye tracker (for methodological details, see Supplemental Information). In each task, trials were coded as to whether participants blinked or not in the inter-stimulus interval preceding the judgment prompt in the *previous* trial (Figure S1A). We fitted post-no-blink and post-blink trials with psychometric functions and computed each participant's bisection point (BP). The BP is the temporal interval that is perceived to be equidistant to the shortest and longest comparison intervals in the task and provides a measure of the perceived duration of comparison intervals (Figure S1B).

As predicted, participants exhibited a leftward shift of psychometric functions on post-blink trials relative to post-no-blink trials in all three tasks (Figure 1A–C). This was reflected in a smaller BP (reflecting relative overestimation) in post-blink than post-no-blink trials in the visual subsecond task, $t(20) = 2.44$, $p_{perm} = 0.008$, representing a difference of approximately one-half of a standard deviation, Cohen's $d = 0.53$ (bootstrap 95% CIs: 0.29, 0.88). This effect was also observed in the visual suprasecond task, $t(27) = 2.50$, $p_{perm} = 0.019$, $d = 0.47$ (0.10, 1.00), and in the auditory subsecond task, $t(26) = 2.17$, $p_{perm} = 0.017$, $d = 0.42$ (0.18, 0.68). The latter effectively rules out the possibility that the observed post-blink temporal dilation is driven by blink-induced changes in visual attention or visual processing (see Supplemental Information). The tendency to overestimate comparison intervals in post-blink trials was present at each temporal interval in all three tasks and the leftward shift of psychometric functions, reflecting lower BPs, is readily apparent in the bootstrap resampling distributions of BPs (Figure 1D–F). Further analyses revealed that these effects remained when controlling for a number of potential confounding variables; in addition, participants did not differ in temporal precision between post-blink and post-no-blink trials in any of the tasks (see Supplemental Information).

We observed that spontaneous eye blinking, demonstrated to be a reliable biomarker of striatal dopamine receptor availability [6–8], was associated with a tendency to overestimate both visual subsecond and suprasecond and auditory subsecond intervals. These results converge with a wealth of research showing that dopamine, particularly D_2 receptors in the nigrostriatal pathway, contributes to inter-individual differences in both subsecond and suprasecond interval timing [1–5]. The present work expands upon these studies by suggesting that endogenous fluctuations in striatal dopamine [6,8] phasically modulate perceived duration, resulting in transient intra-individual variations in time perception. Increased dopamine availability may produce overestimation of temporal intervals through an acceleration of a neural oscillator [1]. According to a dominant model of interval timing [1,3], this may occur through the modulation of the dopaminergic pulse that synchronizes the oscillations of cortical neurons at the onset of a to-be-timed stimulus. A transient increase in dopamine availability may speed up or magnify this pulse, resulting in earlier onset of the timing mechanism and thereby relative overestimation. Fluctuations in dopamine availability may underlie variance in the characteristics of this pulse and thereby introduce variability in perceived duration as computed by medium spiny neurons in striatum, which are hypothesized to be responsible for matching the duration of a comparison interval to intervals held in working memory [1,3]. Alternatively, it is plausible that the suggested association between striatal dopamine and interval timing is mediated by a change in temporal attention (see Supplemental Information).

SUPPLEMENTAL INFORMATION

Supplemental Information includes experimental procedures, further results and discussion, and two figures and can be found with this article online at http://dx.doi.org/10.1016/j.cub.2016.04.010.

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