



A proxy measure of striatal dopamine predicts individual differences in temporal precision

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Abstract

The perception of time is characterized by pronounced variability across individuals, with implications for a diverse array of psychological functions. The neurocognitive sources of this variability are poorly understood, but accumulating evidence suggests a role for inter-individual differences in striatal dopamine levels. Here we present a pre-registered study that tested the predictions that spontaneous eyeblink rates, which provide a proxy measure of striatal dopamine availability, would be associated with aberrant interval timing (lower temporal precision or overestimation bias). Neurotypical adults ($N = 69$) underwent resting state eye tracking and completed visual psychophysical interval timing and control tasks. Elevated spontaneous eyeblink rates were associated with poorer temporal precision but not with inter-individual differences in perceived duration or performance on the control task. These results signify a role for striatal dopamine in variability in human time perception and can help explain deficient temporal precision in psychiatric populations characterized by elevated dopamine levels.

Keywords Dopamine · Eye-tracking · Temporal cognition · Time perception · Schizophrenia

Introduction

Human adults display pronounced heterogeneity in interval timing (Wiener et al., 2014), which impacts a diverse array of basic and complex psychological functions from precise subsecond motor control to suprasedond cognitive decision making (Merchant & Georgopoulos, 2006; Sohn & Carlson, 2003). However, the neurocognitive factors underlying timing variability remain poorly understood.

Multiple strands of evidence implicate the striatal dopamine system in interval timing and timing heterogeneity (for reviews, see Agostino & Cheng, 2016; Coull et al., 2011). For example, psychiatric populations characterized by aberrant striatal dopamine profiles exhibit atypical timing (Allman & Meck, 2012). In schizophrenia, which is characterized by a hyper-responsive dopamine system (Howes et al.,

2015) and elevated striatal D2-receptor availability (Seeman, 2013), patients reliably display poorer temporal precision (variance of perceived intervals across trials) (Thoenes & Oberfeld, 2017; Ueda et al., 2018). One interpretation of these impairments is that elevated dopamine leads to the over-weighting of priors under uncertainty, which will produce a flattening of psychometric slopes and a corresponding reduction in temporal precision. In support of this proposal, a previous study found that controls and patients with schizophrenia exhibited timing migration effects towards context tone intervals (priors) drawn from low-variance (low uncertainty) distributions (Cassidy et al., 2018). Critically, unlike controls off amphetamine, patients and controls on amphetamine exhibited such timing performance even after the precision of priors was reduced in a high-variance (high uncertainty) context condition.

Conversely, striatal dopamine blockage may diminish signalling of a precise prior. Tomassini et al. (2016, 2019) presented participants with foreperiods between warning and go stimuli, when they were required to respond quickly and accurately. Foreperiod intervals were drawn from distributions with high or low means and variances. Critically, low-variance conditions yielded higher predictability of foreperiod offset (prior) and concomitantly improved

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response times and temporal precision. The administration of haloperidol reduced this advantage, independently of a motor impairment (Tomassini et al., 2016), suggesting that dopamine may mediate the ability to extract temporal expectations (priors) across trials.

Notably, some of these results do not align with the predictions of pacemaker-accumulator models of interval timing (Gibbon et al., 1997; Treisman & Brogan, 1992). In these models, dopamine is hypothesized to affect the speed of a putative internal clock consisting of a pacemaker emitting pulses and an accumulator collecting these pulses. A faster clock (higher dopamine) would be expected to generate more pulses resulting in duration overestimation and finer temporal resolution (superior precision). An abundance of pharmacological and animal research aligns with these predictions (for reviews, see Agostino & Cheng, 2016; Coull, Cheng, et al., 2011) but the evidence is not without controversy. Whereas the D2-receptor agonist quinpirole has been shown to attenuate temporal precision (Santi et al., 2001), another agonist pergolide improved temporal sensitivity (Rammsayer, 2009). Poorer temporal precision was also observed with the dopamine antagonist haloperidol (Coull et al., 2011), but not with sulpiride (Rammsayer, 1997). Moreover, the majority of pharmacological studies do not include appropriate control tasks (Buhusi & Meck, 2002; Maricq & Church, 1983; Rammsayer, 1989a, 1989b, 1997), suggesting that timing deficits may be mediated by non-timing cognitive effects (Coull, 2014; Rammsayer, 1997; Saedi et al., 2006).

Evidence for a role of dopamine in temporal accuracy (proximity of temporal estimates and stimulus intervals) is similarly mixed. Although some clinical evidence implicates dorsal striatum in temporal accuracy (Allman & Meck, 2012), the recent literature suggests only a weak tendency toward aberrant accuracy in schizophrenia (Thoennes & Oberfeld, 2017) and in Parkinson's disease (Terao et al., 2021), which are respectively characterized by elevated and diminished dopamine levels. By contrast, pharmacological modulation of dopamine synthesis reliably alters timing accuracy (Coull et al., 2011). For instance, rodents administered dopamine agonists exhibit leftward shifts of psychometric functions, suggesting subjective dilation of time, whereas the administration of antagonists is associated with rightward shifts reflecting temporal contraction (Buhusi & Meck, 2002; Maricq & Church, 1983; Matell et al., 2004). More recently, however, a study using optogenetics reported temporal dilation in response to attenuated midbrain dopamine levels (Soares et al., 2016; see Mikhael & Gershman, 2019, for a proposed reconciliation of these findings).

Free from pharmacological intervention, *baseline* striatal dopamine concentrations (and D2-receptor availability) fluctuate over the course of hours, albeit at much lower magnitude scales (Ferris et al., 2014). Whether the clinical

and pharmacological observations extend to the neurotypical baseline is not known. Previous research attributed poorer temporal precision to carriers of a genetic allele associated with reduced density of D2-receptors (Wiener et al., 2011, 2014). However, insofar as the prevalence of this allele is only ~20–27% in the general population (National Centre for Biotechnology Information, 2021), the relationship between baseline dopamine and temporal perception remains poorly understood.

A common feature of studies of the association between dopamine and interval timing is that they seldom extend to human neurotypical timing free from experimentally induced perturbation of dopaminergic activity, mostly due to the invasive nature of available methods (e.g., Kishida et al., 2016). Yet, such investigations would complement current understanding of timing mechanisms and provide a benchmark for studies with clinical populations. This issue has been addressed in investigations of the role of dopamine in cognition with the use of spontaneous eyeblink rates (EBRs) as a dopamine proxy (for a review, see Jongkees & Colzato, 2016), given its association with the availability of dorsostriatal D2-receptors (Elsworth et al., 1991; Groman et al., 2014; Karson, 1983; Kleven & Koek, 1996; Taylor et al., 1999; but see also Dang et al., 2017). We previously reported that EBRs covary with intra-individual fluctuations in perceived duration of auditory and visual intervals (Terhune et al., 2016), showing temporal dilation for trials following spontaneous eyeblinks, as would be expected from some pharmacological studies (Buhusi & Meck, 2002; Maricq & Church, 1983; Matell et al., 2004). By contrast, temporal precision did not statistically differ after blinks although we observed a trend for poorer precision in post-blink trials (Terhune et al., 2016).

This pre-registered study sought to expand upon previous observations by investigating how EBR relates to *inter*-individual variability in human neurotypical interval timing. Toward this end, neurotypical adults underwent resting state eye-tracking and completed a visual psychophysical timing task (temporal bisection) and a control task (color bisection) to assess the cognitive specificity of associations between EBR and perception. Drawing on our previous results (Terhune et al., 2016), we expected that EBR, with higher rates reflecting greater striatal dopamine receptor availability (Groman et al., 2014), would be associated with a relative tendency to overestimate stimulus intervals. Terhune et al. (2016) also observed consistent trends for poorer precision in post-blink trials. Based on their observations and the links between elevated dopamine and attenuated temporal precision in schizophrenia (Thoennes & Oberfeld, 2017), we hypothesized that EBR would be associated with poorer temporal precision. An alternative prediction, derived from the striatal beat

frequency model (Matell & Meck, 2004), is that EBR would be associated with superior temporal precision.

Methods

Participants

Seventy-five healthy adults (82.66% female, 17.33% male) between 18 and 45 years old ($M_{\text{Age}} = 23.07$ years, $SD = 4.22$) with at least 1 year of post-secondary education ($M = 3.43$, $SD = 2.21$) provided informed written consent to participate in this study in accordance with approval by a local departmental ethics committee. Participants were right-handed, had no history of neurological or psychiatric disorders, and had normal or corrected-to-normal vision. Sample size was estimated a priori on the basis of a pilot study using G*Power 3.1 (Faul et al., 2009), using the parameters of $r = .33$ (unpublished pilot data), $1 - \beta = .80$, $\alpha = .05$ (two-tailed), which resulted in a required sample size of 69 participants. We pre-specified a target sample size of 75 participants, in order to account for attrition. The study was preregistered prior to data collection on the Open Science Framework (<https://osf.io/fzdbv>).

Resting state eye-tracking

The detailed eye-tracking protocol has been described elsewhere (Terhune et al., 2016). Participants attended to a fixation cross at the center of a computer monitor whilst their resting state right eye movements were tracked using an EyeLink 1000 (SR Research, Ontario, Canada). Their head movements were minimized using a chinrest. The participant's gaze location was monitored in real-time by a trained experimenter on a separate monitor out of the participant's view. The data were monocularly sampled with the right eye at a rate of 500 Hz. A blink was defined as a period in which a pupil was not detected for three or more consecutive samples.

Temporal bisection task

Participants completed a visual temporal bisection task that entailed learning two anchor intervals (300 and 967 ms) in a training phase. In a subsequent testing phase, participants were presented with colored circles of varying intervals and judged whether they were closer in duration to the trained short or long anchor intervals. Trials consisted of a jittered interstimulus interval (blank screen) drawn from a truncated Poisson distribution (200–500 ms), a circle (2.7 cm, $\sim 2^\circ$ of visual field) that randomly flickered between blue and red at 60 Hz and varied in duration (300, 433, 567, 700, 833, or 967 ms), a second interstimulus interval (blank screen; 300

ms), and a two-alternative forced choice judgment prompt (S L or L S [S = short; L = long]) (see Fig. S1 in the Online Supplemental Materials (OSM)). There were six different color proportion sets at each stimulus interval, as detailed in *Color bisection task*. Participants responded by pressing one of two keys using their index and middle fingers.

Color bisection task

A color bisection task was administered to control for attention and working memory demands in the temporal bisection task (Coull, 2014). The stimulus set and trial sequence were identical to those in the temporal bisection task except the training phase, which involved training with two anchor colors (mostly-red: 22%, blue and mostly-blue: 78% blue) and the judgment prompt (B R or R B [B = blue, R = red]). At the prompt, participants judged whether the preceding flickering circle was closer to the previously learned blue or red anchor stimuli. Colors were drawn from six proportion sets of blue and red circles (22, 34, 45, 55, 66, or 78% blue). Each color stimulus included equal proportions of the six intervals in the temporal bisection task.

Procedure

Participants first underwent the resting state eye-tracking, which involved sitting at a desk with their head on a chinrest at ~ 55 cm distance from the monitor (34×57 cm) and ~ 40 cm distance from the eye-tracker camera. They first completed a 9-point calibration procedure and subsequently attended to a centrally presented fixation cross on the monitor for 8 min, during which their eye movements and pupil diameter were continuously recorded. The experimenter monitored the participant's eye movements on an external monitor outside of the participant's view. The room was kept dark during the eye-tracking recording and subsequent tasks.

Participants next completed the temporal and color bisection tasks with stimulus presentation implemented with Psychtoolbox (Brainard, 1997) in MATLAB v. 2018b (MathWorks, Natick, MA, USA). Task order and response key mappings (S L vs. L S and B R vs. R B) were both counter-balanced across participants. The training phases consisted of 20 trials, comprised of equal proportions of each anchor stimulus. Additional trials automatically followed if accuracy was below 80% until the 80% target was reached in the lattermost 20 trials or until the maximum training time of 6 min had passed. In the temporal bisection task, seven participants required more than 20 anchor trials in the training phase and four of them eventually achieved the performance target. In the color bisection task, four participants required additional anchor trials in the training phase, and two of them subsequently reached the performance target. The five

participants who did not reach the performance target completed both training phases with > 70% accuracy.

Participants subsequently completed three blocks of 76 trials of each task. Experimental blocks began with two reminders of each anchor stimulus (four trials); the remaining 72 trials included 16 repetitions of the four middle stimuli and four repetitions of each anchor stimulus. In both tasks, participants were instructed to focus on the center of the monitor and only use the interval or color information to guide their judgment and to avoid other strategies such as counting or humming. Participants subsequently completed two psychometric measures (hallucination-proneness and frequency of drug use) that will be reported independently.

Analyses

All analyses were performed in MATLAB. Eye-tracking data were used to compute the mean number of eyeblinks per minute (eyeblink rate; EBR). The EBR includes only the last 5 min of the recording as the first 3 min were discarded to account for adaptation to the room lighting. Task performance was assessed by computing the proportion of “long” [$p(\text{long})$] and “red” [$p(\text{red})$] responses at each stimulus level in the temporal and color bisection tasks, respectively. We fitted logistic functions to these values in individual participants using maximum likelihood estimation as implemented in the Palamedes toolbox (Kingdom & Prins, 2016) in order to estimate the alpha (bisection point [BP]) and beta (slope) parameters of the psychometric function (guess rates and lapse rates were set at 0). The fit of psychometric functions was assessed by computing a p -value for deviance ($p\text{Dev}$), based on 1,000 permutations. In each task, we estimated the bisection point (BP), which corresponds to the estimated stimulus level that is perceived as equidistant to the two anchor stimuli (lower values reflect relative overestimation of intervals [temporal bisection] and relative overestimation of redness [color bisection]). We additionally estimated the Weber fraction (WF), which is the difference limen proportional to the BP, with the former given as half of the difference between the intervals (or color proportions) corresponding to 75% and 25% of the $p(\text{long})$ (or $p(\text{red})$) response proportions on the fitted psychometric function (lower values reflect superior precision).

Two participants' eye-tracking data were not recorded due to technical errors involving the eye-tracker. We additionally excluded four participants in the temporal bisection task and six participants in the color bisection task due to poor fit of the psychometric functions, $p\text{Dev} < .05$. These exclusions resulted in final sample sizes of 69 and 67 for the temporal and color bisection tasks, respectively. EBRs were correlated with psychophysical parameters using the Robust Correlation toolbox in MATLAB (Pernet et al., 2013). Spearman correlations (r_s) and partial Spearman correlations (r_{ps}) were

used throughout due to violations of distribution normality or homoscedasticity. We report correlations pre- and post-multivariate outlier removal for completeness (the latter are reported in the OSM, section S6, *Bivariate outliers*). Correlations are supplemented with bias-corrected and accelerated confidence intervals using Bootstrapping (10,000 samples) (Efron, 1987). Correlations were compared across tasks by standardizing coefficients (Fisher z -transform; Myers & Sirois, 2014) and computing the Bootstrap 95% confidence intervals (CIs) of the correlation coefficient difference, with intervals non-overlapping with zero denoting significance.

For each correlation, we additionally report the Bayes factor (BF_{10}) quantifying the likelihood of the data under the experimental hypothesis H_1 relative to the likelihood of the data under the null hypothesis H_0 . The BF_{+0} and BF_{-0} denote the hypothesized positive and negative correlations, respectively. Conventionally, BF values greater than 3 and less than 1/3 denote moderate or greater evidence for H_1 and H_0 , respectively, whereas intermediate values indicate an ambiguous result (Wagenmakers et al., 2016). BFs were computed in JASP (JASP Team, 2019) with pre-specified default parameters of the H_1 and H_0 distributions (Wagenmakers et al., 2016), and their robustness was verified using a BF sensitivity analysis with different H_1 priors (section S2 in the OSF). When different priors yielded markedly different BF results, the ambiguity of the evidence was acknowledged.

Results

Our primary analyses tested the predictions that EBR would be selectively associated with performance in the temporal bisection task but not in the control (color bisection) task. In particular, we expected that higher EBR (reflecting elevated striatal dopamine receptor availability; Jongkees & Colzato, 2016) would be associated with higher WFs (reflecting poorer temporal precision) and shorter BPs (reflecting longer perceived duration) (see Fig. 1 for summary information of the data).

Eyeblink rate (EBR) and temporal precision

In support of our first prediction, EBR positively correlated with WFs in the temporal bisection task, $r_s = .28$ [Bootstrap 95% CI: .04, .49], $p = .019$ ($N = 69$) (see Fig. 2). This correlation is similarly reflected in Fig. 1 (bottom left), where the first tercile, comprising participants with the lowest EBR, displayed the steepest slopes, reflecting superior temporal precision. The BF_{+0} was 4.02, suggesting that these data were four times more likely to be observed under our hypothesis than the null hypothesis. By contrast, EBR did not significantly correlate with WFs in the control (color

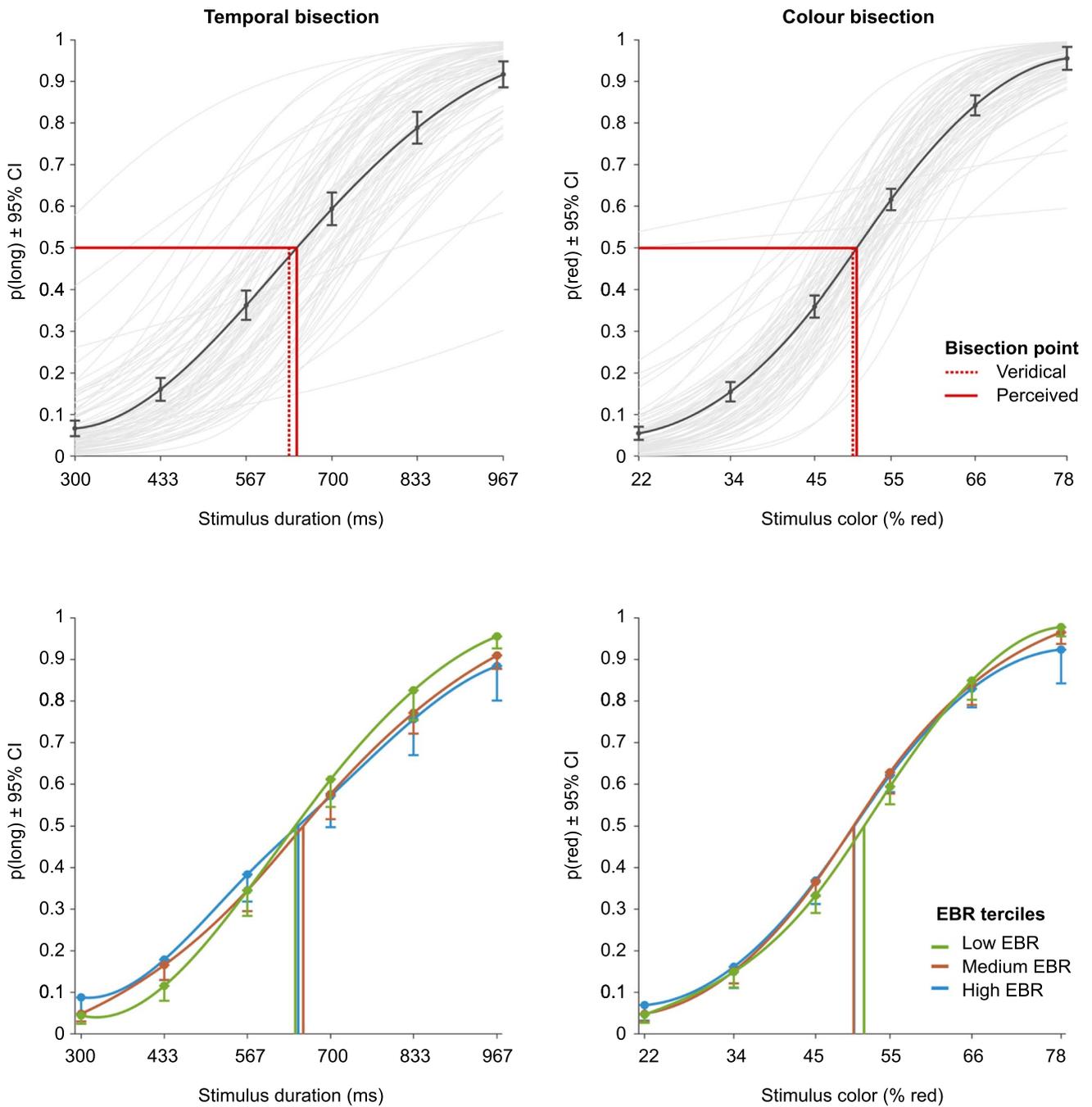


Fig. 1 PF models of task performance. The lines in saturated colors show spline-interpolated sample means of actual p(response) for each stimulus. **Top row:** The pale grey lines represent individual PFs for all participants and the vertical lines denote veridical and perceived bisection points (BPs). Circular markers and error bars denote sample

means and 95% bootstrapped confidence intervals for the proportions of long [p(long)] or red [p(red)] responses. **Bottom row:** Group PFs for low, medium, and high eyeblink rate (EBR) tertiles. To improve legibility of the overlapping error bars, only the lower limits are plotted

bisection) task, $r_s = .08 [-.17, .32]$, $p = .50$ ($N = 67$), with Bayesian evidence in favor of the null hypothesis, $BF_{+0} = .31$. The robustness of these results is supported by BF sensitivity analyses and the strength of evidence further increased after excluding bivariate outliers (see OSM). Finally, the

temporal specificity of this effect was corroborated by the correlation between temporal WFs and EBR being significantly greater than that between color WFs and EBRs, $r_{s(diff)} = .33$ [Bootstrap 95% CI: .05, .54], $t(62) = 2.52$, $p = .010$, $d_z = .32$.

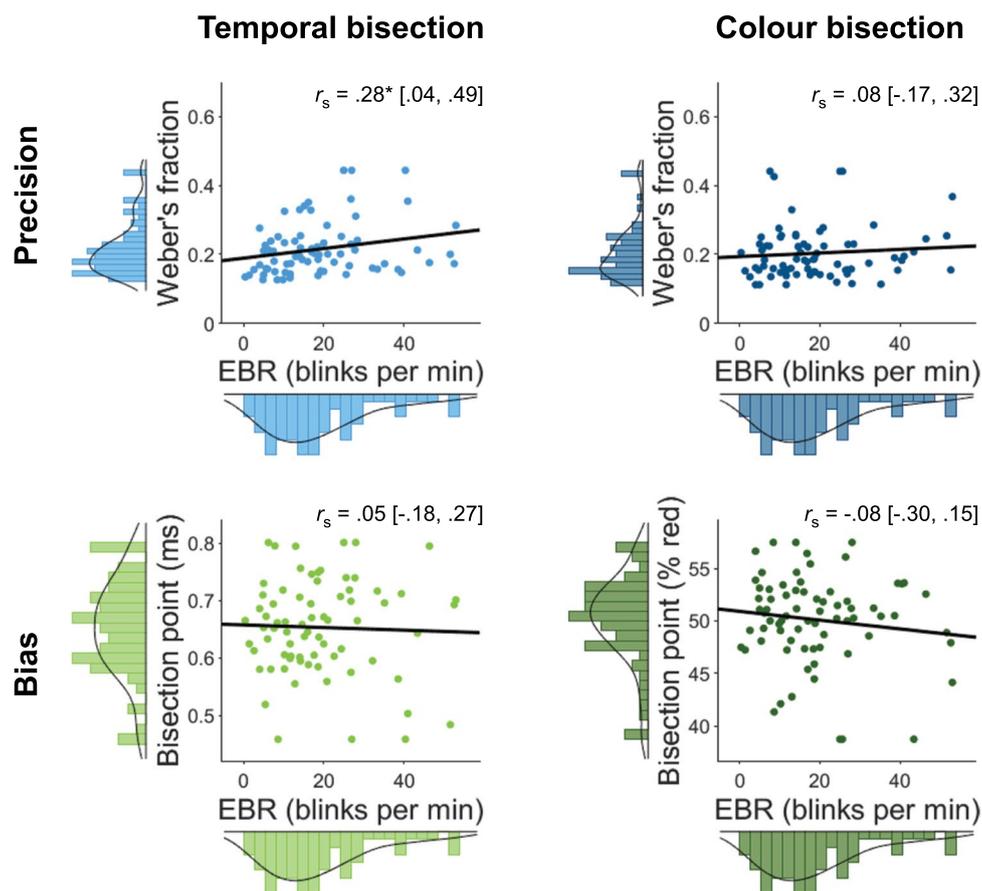


Fig. 2 Individual Weber fractions (WFs; blue) and bisection points (BPs; green) as a function of spontaneous eyeblink rate (EBR). Square brackets denote bootstrapped 95% confidence intervals. Plots

show original non-ranked data with winsorized outliers, and the least-squares line fit for visualization purposes. r_s = Spearman correlation. * $p < .05$

A series of unregistered correlational analyses were conducted to exclude alternative interpretations of the reported effects. Temporal and color WFs were positively correlated, $r_s = .31$ [.09, .51], $p = .011$ ($N = 65$), $BF_{+0} = 6.77$. A semi-partial Spearman correlation between temporal WFs and EBR (after partialling out shared variance between temporal and color WFs) was significant, $r_{ps} = .33$ [.05, .53], $p = .009$ ($N = 63$), $BF_{+0} = 9.62$. The association between temporal WFs and EBR similarly remained stable when partialling out the shared variance between BPs and WFs (see OSM). Conversely, the association between EBR and color WFs remained non-significant after controlling for temporal WFs, $r_{ps} = -.11$ [-.35, .13], $p = .39$ ($N = 63$), $BF_{+0} = .09$. Further, since larger WFs are associated with flatter psychometric function slopes and as such reflect increased task difficulty, we compared the WFs across tasks. We observed a non-significant difference with evidence for the null hypothesis, $t(74) = 1.21$, $p = .23$, $d_z = .14$, $BF_{10} = .26$, suggesting that the tasks were appropriately matched in difficulty.

Cumulatively, these results suggest that although temporal and color precision were associated, EBR is selectively

associated with poorer temporal precision, but not with color precision.

EBR and temporal bias

In contrast with our prediction, EBR did not significantly correlate with temporal BPs (Fig. 2), $r_s = .03$ [-.23, .29], $p = .78$ ($N = 69$), with clear evidence in favor of the null hypothesis, $BF_{-0} = .14$. The same held for color BPs, $r_s = -.12$ [-.36, .13], $p = .31$ ($N = 67$), albeit with more ambiguous Bayesian evidence, $BF_{-0} = .40$. The two correlations did not significantly differ, $r_{s(\text{diff})} = .04$ [Bootstrap 95% CI: -.31, .38], $t(62) = .34$, $p = .74$, $d_z = .04$.

BPs in the two tasks did not significantly correlate $r_s = .10$ [-.17, .35], $p = .43$ ($N = 65$), with evidence for the null hypothesis, $BF_{10} = .22$. Controlling for the influence of the other task did not change the association between EBR and temporal BPs, $r_{ps} = -.03$ [-.28, .23], $p = .80$ ($N = 63$), $BF_{-0} = .24$, or between EBR and color BPs, $r_{ps} = -.09$ [-.33, .15], $p = .49$ ($N = 63$), $BF_{-0} = .32$. Taken together, these results

suggest that EBR is unrelated to inter-individual variation in perceived duration.

EBR and response times

Although the color task allowed for dissociating non-specific memory effects, the decisional components of task performance were further modelled using hierarchical drift diffusion modelling (DDM; Ratcliff & McKoon, 2008; Wiecki et al., 2013). DDM was fitted to responses and response times to decompose the data into parameters reflecting the decision process (prior bias, speed of evidence accumulation, decision thresholds, and non-decisional perceptual and motor processes). We assessed the association between EBR and these parameters, and we observed non-significant results (see OSM).

Discussion

This study was motivated by the wealth of pharmacological and clinical data linking interval timing to striatal dopamine (Buhusi & Meck, 2002; Rammsayer, 1993; Thoenes & Oberfeld, 2017) but a corresponding dearth of evidence regarding the role of dopamine in baseline neurotypical temporal cognition. We found that elevated striatal D2-receptor availability, inferred non-invasively from spontaneous eyeblink rates (EBRs), was selectively associated with poorer temporal precision, but not overestimation or precision or bias in a difficulty- and stimulus-matched control task. Moreover, although temporal and color bisection tasks tax partially overlapping cognitive processes (Coull, 2014), the association between temporal precision and EBR was independent of color precision. These results expand upon research implicating dopamine systems in interval timing (Coull et al., 2011) by demonstrating a similar link without pharmacological intervention in healthy individuals.

Higher dopamine was previously suggested to drive increased reliance on expectations (priors) in interval timing (Cassidy et al., 2018). Cassidy et al. (2018) manipulated reliance on temporal priors in a temporal reproduction task in patients with schizophrenia and controls. They replicated the standard migration effect across groups (Jazayeri & Shadlen, 2010) and observed that timing performance in patients and controls on amphetamine was influenced even when priors became less reliable (Cassidy et al., 2018). On the basis of these results, we suggest that higher EBR in the present study was associated with overreliance on priors, particularly under uncertainty (stimulus intervals close to the middle interval). This led responses to drift closer to the prior (mean of the interval range), resulting in lower precision and higher WFs. This result appears to diverge from Terhune et al.'s (2016)

observation of *no* significant association between trial-by-trial blink patterns and temporal *precision*. However, that study did observe a trend in the direction of poorer precision in post-blink trials, which aligns with the present results.

This interpretation aligns with results demonstrating that schizophrenia is characterized by reduced temporal precision (Thoenes & Oberfeld, 2017), and elevated dopamine (Howes et al., 2015), D2-receptor availability (Seeman, 2013), and EBR (Adamson, 1995), as well as reduced temporal precision in its subclinical expression (schizotypy; Ferri et al., 2017). However, whilst models of schizophrenia acknowledge some role of general motivational processes, we show an effect specific to timing, as reflected by a significantly lower association between EBR and color precision. Further, we replicated our central result after adjusting for shared variance in precision in the two tasks.

An alternative interpretation of our results in line with the striatal beat-frequency model of timing (SBF; Matell & Meck, 2004) is that higher dopamine impairs coincidence detection by striatal spiny neurons (Buhusi & Meck, 2005; Urakubo et al., 2020), which would lead to a reduced precision regarding the interval onset or offset times (Paton & Buonomano, 2018). Whereas these conclusions are speculative, there are some indications supporting this possibility. Allman and Meck (2012) suggested that atypical stimulus onsets and cortical asynchronization may explain timing variability in schizophrenia, reflecting disturbed coincidence detection and starting (or ‘resetting’) of the striatal interval clock under the SBF model.

Insofar as the speed of a putative clock is hypothesized to increase with elevated D2-receptor activity (MacDonald & Meck, 2005), our results are inconsistent with this model's prediction that a higher clock speed, mediated by elevated dopamine, relates to improved temporal precision. The SBF model proposes that activation of striatal neurons reflects their sensitivity to a pattern of glutamatergic corticostriatal signals (MacDonald & Meck, 2005). There is evidence that dopamine, and D2-receptors specifically, play a role in the filtering of more active glutamatergic corticostriatal inputs (Bamford et al., 2004). Conversely, interval training has been shown to ‘blunt’ the effects of dopaminergic drugs and this ‘dopamine-insensitive’ state was reversed by administration of ketamine, an NMDA (glutamate) receptor antagonist (Cheng et al., 2007). Importantly, Cheng et al. (2007) highlighted that the transition to a dopamine-insensitive state was similar to general observations of striatal neurons becoming silent once a reward becomes predictable with training (Schultz, 1998). Similarly, Wang et al. (2020) recently suggested that the noise in corticostriatal circuits that underlies timing variability is subject to adjustments through reinforcement learning. This overlap between learning and timing may help to reconcile our seemingly discrepant results.

At first glance, our results demonstrating no association between temporal bias and EBR seem at odds with the previously reported association between trial-by-trial eyeblinks and the tendency to overestimate stimulus intervals (Terhune et al., 2016). Our results suggest that individual differences in striatal dopamine do not contribute to inter-individual variability in temporal bias, which is consistent with the available evidence from clinical populations characterized by dopamine dysregulation (Terao et al., 2021; Thoenes & Oberfeld, 2017; but see Ueda et al., 2018). Alternatively, given that the link between temporal accuracy and dopamine (D2) expression has typically been studied in conditions when dopamine availability markedly deviated from a neurotypical baseline, our data may demonstrate the null effect across much smaller inter-individual variations at baseline.

Some recent developments suggest that interval timing may not require internally driven mechanisms involving basal ganglia and that exteroceptive perceptual content alone may be the principal determinant of subjective time (Roseboom et al., 2019; Suárez-Pinilla et al., 2019). This model would not strictly preclude dopamine-mediated timing; it would, however, favor a more complex and indirect interpretation, for instance via dopamine-affected signaling within local circuits and global networks that impacts attention but also timing specifically (Coull et al., 2012; Nagano-Saito et al., 2008; Shafiei et al., 2019). Nevertheless, whereas sparse population coding, with neuronal populations activating in sequence over the course of the timed interval, was reported in regions such as orbitofrontal cortex and secondary motor cortex (Bakurin et al., 2017; Zhou et al., 2020), *striatal* activity exhibits the highest degree of sequentiality for the parsing of intervals by biologically constrained decoder networks, and therefore provides the most optimized set of signals to readout duration (Zhou et al., 2020).

EBR shows considerable promise as a non-invasive proxy of striatal dopamine in timing research if its limitations are acknowledged. Although the evidence shows it to be a viable proxy for D2-receptor availability (Groman et al., 2014; Jongkees & Colzato, 2016), it is nonetheless only an indirect measure and the strength of the association between EBR and D2-receptor availability will therefore modulate our findings. It remains poorly understood how stable this association is across the typical range as well as for more extreme high and low dopamine levels in human striatum as well as how stable it is across individuals and over time. Although we only recorded EBR at baseline prior to the completion of the perceptual tasks, previous research shows that EBR is stable over short time periods (> 1 h) (Barbato et al., 2000). Since Terhune et al. (2016) observed their effects in both sub- and suprasecond interval ranges, future studies should assess whether the current findings extend to suprasecond timing. Finally, our use of basic visual stimuli does not allow for an assessment of perceptual context in

the shaping of subjective timing in a manner that is enabled with the use of more ecologically valid stimuli (Roseboom et al., 2019; van Rijn, 2018).

To summarize, the association between EBR and interval timing was timing- and precision-specific, and thereby builds on research implicating dopamine in interval timing (Coull et al., 2011) and extends this to individual differences in the neurotypical population. Altogether, our results complement studies demonstrating associations between EBR and cognitive-perceptual functions subserved by dopamine systems (Jongkees & Colzato, 2016), and they attest to the utility of EBR as a proxy measure of dopamine in time perception research.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.3758/s13423-022-02077-1>.

Acknowledgements This paper is dedicated to the memory of Warren H. Meck.

Code availability Custom scripts are available at <https://osf.io/jxc3f>.

Authors' contributions All authors designed the research, LM collected the data, RS analyzed the data, RS and DBT drafted the manuscript, and all authors approved the final manuscript for submission.

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Data availability The data and materials are available at <https://osf.io/jxc3f>.

Declarations

Competing interests The authors have no relevant financial or non-financial interests to disclose.

Ethics approval Approval was obtained from the ethics committee of the Department of Psychology at Goldsmiths, University of London, UK. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent for publication Not applicable.

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Open practices statement The data and materials are available at <https://osf.io/jxc3f>. The study was preregistered (<https://osf.io/fzdbv>).

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