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Dopamine and reward-related vigor in younger and older adults

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ABSTRACT

Vigor reflects how motivated people are to respond to stimuli. We previously showed that, on average, humans are more vigorous when a higher rate of reward is available, and that this relationship is modulated by the dopamine precursor levodopa. Dopamine signaling and probabilistic reward learning deteriorate across the adult life span, and thus, the relationship between vigor and reward may also change in aging. We tested this assertion and assessed whether it correlates with D1 dopamine receptor availability, measured using Positron Emission Tomography. We registered response times of 30 older and 30 younger participants during an oddball discrimination task where rewards varied systematically between trials. The average reward rate had a similar impact on vigor in both age groups. There was a weak positive association between ventral striatal dopamine receptor availability and the effect of average reward rate on response time. Overall, the effect of reward on response vigor was similar in younger and older adults, and weakly correlated with dopamine D1 receptor availability.

1. Introduction

We all pursue rewards. We do this by optimizing our choices and the vigor with which we carry out those choices. Despite its central role in behavior, the mechanism behind vigor is not well understood compared to the mechanism behind value-based choice. A key finding is that vigor - defined as the inverse latency of response – is influenced by how much reward is received, on average, over time (Beierholm et al., 2013; Guitart-Masip et al., 2011; Otto and Daw, 2019; Yoon et al., 2018). This is formalized in a theoretical model (Niv et al., 2007), in which vigor is computed as a compromise between the energy cost of responding quickly and the opportunity cost of missing out on potential rewards by responding slowly (Niv et al., 2007, 2005).

Individuals vary widely in how they respond to rewards (Santesso et al., 2008). For example, patients with Parkinson's disease show disrupted effort-based reward responses (Le Heron et al., 2018). A key source of variation in healthy individuals is age. Aging leads to structural changes in the dopamine system: age-related loss of dopamine neurons occurs within reward-processing areas such as the substantia nigra and ventral tegmentum (Fearnley and Lees, 1991; Vaillancourt et al., 2013). Loss of dopamine neurons over the lifespan is associated with functional changes such as cognitive deficits (Bäckman et al., 2010; Düzel et al., 2010a). Older adults are worse at probabilistic reward learning than younger adults (de Boer et al., 2017; Eppinger et al., 2011; Mell et al., 2005), and advancing age is associated with changes in reward anticipation in frontal regions (de Boer et al., 2017). Administration of the dopamine precursor L-DOPA improves performance in a probabilistic reward task in older people by restoring reward prediction-error signaling and facilitating the expression of reward anticipation (Chowdhury et al., 2013). Further, a meta-analysis of 95 studies imaging PET function showed a large negative effect of age on dopamine function, more so on D1 than D2 receptors (Karrer et al., 2017) This indicates that aging leads to structural changes in dopamine-rich areas and a decrease in dopamine function. For average reward rate to influence response

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vigor, the average reward needs to be represented in the brain. If aging is associated with a decreased ability to anticipate rewards, one would expect that response vigor in older adults is less sensitive to changes in the average reward rate. Vigor is an important element of reward behavior because it reflects a dynamic cost-benefit analysis of expending energy to gain a reward. However, to our knowledge, no study has explored whether the relationship between reward and vigor is affected in normal aging. We examined this relationship and predicted that older people would show attenuated modulation of response vigor by the average rate of reward compared to younger people.

Niv et al.'s (2007) vigor model asserted that tonic dopamine levels in the nucleus accumbens signal the average rate of reward. Recent work has built on this notion and claims that dopamine-associated alterations in vigor reflect the expected value of effort (Zénon et al., 2016). In line with these claims, dopamine has been linked to response vigor, alongside other elements of reward-related behavior (Beierholm et al., 2013; Berridge and Robinson, 1998; Lex and Hauber, 2008; McClure et al., 2003; Mohebi et al., 2019; Montague et al., 1996; Parkinson et al., 2002; Salamone and Correa, 2002; Schultz et al., 1997; Taylor and Robbins, 1986; Ungerstedt, 1971). For example, our previous work has shown that the administration of a dopamine agonist increases the magnitude of the relationship between average reward rate and vigor (Beierholm et al., 2013). However, a correlation between endogenous dopamine receptor availability and reward-related vigor has not been explored. Based on our previous work showing that administration of a dopamine agonist increases reward-related vigor (Beierholm et al., 2013), we also reasoned that the effect of reward on vigor would be associated with endogenous dopamine D1 receptor availability as measured using Positron Emission Tomography (PET). Specifically, we predicted that higher D1 receptor availability in the striatum would be associated with a stronger invigorating effect on the average reward rate. We operationalized vigor by performance on an oddball discrimination task with individualized response time thresholds, where 30 younger and 30 older participants identify the 'odd one out' from three symbols. We measured the effect of systematically varying the average reward rate over the task and use a formalized reinforcement learning model to quantify the impact of average reward rate on response vigor, with the prediction that a higher average reward rate would increase response vigor.

2. Materials & Methods

2.1. Participants

Data were collected as part of a study examining the relationship between D1 receptor availability and value-based decision-making in healthy older and younger participants (de Boer et al., 2019, 2017; Garzón et al., 2021). 30 older participants aged 66–75 years and 30 younger participants aged 19–32 years were recruited through local newspaper advertisements in Umea, Sweden, and provided written informed consent before commencing the study. Ethical approval was obtained from the Regional Ethical Review Board. Participants were paid 2000 SEK (∼$225) for participation. The health of all potential participants was assessed before recruitment by a questionnaire administered by the research nurse. The questionnaire enquired about past and present neurologic or psychiatric conditions, head trauma, diabetes mellitus, arterial hypertension that required more than two medications, addiction to alcohol or other drugs, and bad eyesight. Year of birth was recorded for all participants (70.6 +/- 2.92 years and 24 +/-3.46 years for older and younger participants respectively). Reported sex was also recorded (12 and 18 females among the older and younger participants respectively). Years of education were also recorded: 13.2 +/-3.54 years and 14.7 +/- 1.96 years for older and younger participants, respectively.

Sample size was calculated based on 2 previous studies (Chowdhury et al., 2013; Rieckmann et al., 2011). Chowdhury et al. (2013) found a behavioral difference on the same task that we used between younger and older participants of similar age ranges (Cohen's d = 0.57, pooled SD = 0.99). Based on this effect size, in order to obtain 70% power on a 1-tailed t-test of a behavioral difference between 2 samples, 30 participants were needed in each group. Due to the financial constraints of collecting PET data, we could not reach a higher power. Rieckmann et al. (2011) found differences between age groups in PET D1 receptor density for frontal and parietal (Cohen's d = 3, pooled SD = 0.04) and striatal ROIs (Cohen's d = 1.60, pooled SD = 0.21). Based on this effect size, 10 participants were needed in each group to obtain 90% power on a 2-tailed independent samples t-test.

2.2. Response threshold task

Participants completed a shortened version of the main task to tailor their individual response time threshold. They completed 40 trials with an average response time threshold of 500 ms and a range between 400 and 600 ms. The 70th percentile of the response time for trials in which the participant responded correctly was taken as their response time threshold for the main task.

2.3. Vigor task

The experiment used a well-described paradigm (Beierholm et al., 2013; Guitart-Masip et al., 2011). Fig. 1A depicts a single trial. Participants selected the "odd one out" from a set of 3 symbols. At the beginning of a trial, the potential payout of that trial (Rt) was presented visually as a number from 0 to 100 Krona, which varied according to a prespecified function that was designed to vary across trials to avoid correlation with the linear trend of gradual improvement in performance over time (Fig. 1B). After a variable interval (750–1250 ms), participants were asked to identify the "odd one out" from a set of 3 figures presented on the screen, within a response threshold which was determined by the response threshold task described above. This individually titrated threshold differs from previous versions of the task whereby the threshold was fixed at 500 ms for 80% of the trials and 400 ms for 20% of the trials (Beierholm et al., 2013; Guitart-Masip et al., 2011). We titrated thresholds in order to ensure that any differences in performance were not due to a discrepancy between older and younger participants in how easy they found the task, but rather ensure that we were testing for a true difference in motivational vigor. A blank screen presented for 500 ms was followed by a screen informing participants of the outcome of that trial, and another blank screen. There was a total of 430 trials. The magnitude of the potential reward varied pseudorandomly from trial to trial (Fig. 1B). This sequence was kept identical between participants.

2.4. PET image acquisition and analysis

PET images were acquired using a Discovery 690 PET/CT (General Electric, WI, USA), at the Department of Nuclear Medicine, Norrland's University Hospital in Umeå, Sweden. We injected participants with a bolus of 200 MBq [11C] SCH 23390 timed with the start of a 55-minutes dynamic acquisition (9 frames x 2 minutes, 3 frames x 3 minutes, 3 frames x 4, 20 minutes, 3 frames x 5 minutes). PET and fMRI scanning were planned 2 days apart. Due to a technical problem with the PET scanner, 12 participants

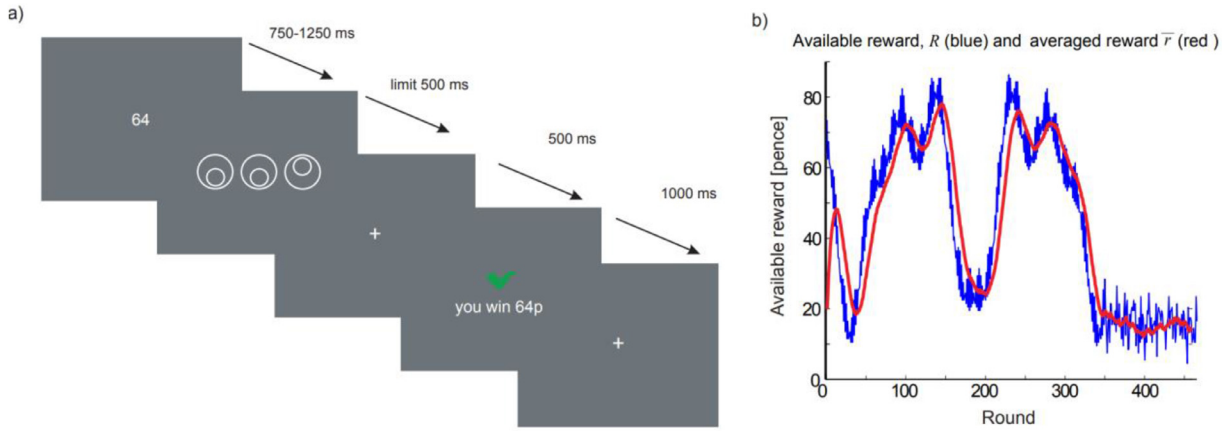

Fig. 1. (A) Time-series of a single trial from the main task. Participants are presented with the potential reward for 750-1250 ms, and then asked to identify the odd-one-out within an individually tailored threshold. After a 500 ms pause, participants are presented with their received award. (B) Experimentally manipulated available reward (blue) and averaged reward as calculated by the computational model based on a well-documented Rescorla-Wagner reinforcement learning rule (red) magnitude in pence (Y axis) varied by trial (X axis).

were scanned at a longer delay apart (range 4–44 days apart; for older participants 4 +/- 5.86 days; for younger participants 5.9 +/- 9.95 days). PET data were analyzed in a standard ROI-based protocol using in-house developed software (imlook4d version 3.5, https://dicom-port.com/product/imlook4d/) and we focused on 3 ROIs: cortex; dorsal striatum; and ventral striatum, because the striatum is densely innervated by dopaminergic neurons. To obtain ROI binding potentials, the PET time series were co-registered to the individual T1-weighted images and ROI images. The average time activity curves were extracted across all voxels within each ROI and we calculated binding potential by applying the Logan method (Logan et al., 1990) to each ROI time activity curve using the cerebellum as reference tissue. See SI Appendix, Fig. S3 of our previous study for the time–activity curves (TACs) and BPND values for young and old participants (de Boer et al., 2019). Binding potentials for all ROIs were averaged across hemispheres. As in previous work (Raz et al., 2004), we computed the β coefficient for the correlation between age and binding potential in each ROI and regressed out the effect of age on binding potential by calculating the effect of age on BPND and correcting for this effect:

$$BP_{ND(adj)}(\text{participant, ROI}) = BP_{ND}(\text{participant, ROI}) + \beta_{age(ROI)} * \text{age(participant)},$$

This is similar to regressing out age. To reduce collinearity between the binding potential values and age, we carried out PCA on the resulting PET binding potential values.

The binding potential values in different ROIs were highly correlated ($r > 0.5$; $p < 0.001$ in all ROIs). To obtain hypothetically different sources of variance in DA D1 receptor availability, we performed a PCA on the age-adjusted binding potential data, by first using PCA to extract principal components and then maximizing each component accounted for with an orthogonal varimax rotation. These analyses were performed in R, with the function principal (psych package). The number of components to retain was determined by performing a Cng test on the eigenvalues, done with the R package nFactors (function nCng) (Gorsuch, 2014). Cng involves computing the slopes between the eigenvalues in the scree plot. The point at which the greatest change in slope is observed is the cutoff point for the number of components (Gorsuch, 2014).

Due to the limited spatial resolution of PET, the accuracy of quantitative measurements of dopamine receptor availability is influenced by partial volume averaging of gray matter with other tissues such as white matter or CSF. This effect is increased in the presence of cortical atrophy such as typically observed in normal aging. Therefore, there is the risk that our results are influenced by differences in partial volume effects between younger and older participants. To control for this possibility, we included a measure of the gray matter volume of our ROIs in the statistical models. Total gray matter volume of our ROIs was calculated by summing the probabilities of each voxel included in each considered ROI being classified as a gray matter after segmenting the T1 images into gray matter maps. The total reflects the number of gray matter voxels within each considered ROI. Including this measure did not change the results.

2.5. Statistical analysis

2.5.1. Behavioral performance

In the raw data, we tested for differences between older and younger participants in behavioral performance on the task, such as response time and number of errors, using independent t-tests. We also tested for a speed-accuracy trade-off and whether this differed between older and younger participants, using stepwise multiple linear regression; the dependent variable was average response time and the predictor variables were number of correct responses, age group, and the interaction between these variables.

2.5.2. Computational model

We fitted a log-normal distribution to each individual's response time (RT) data. To allow participants time to get used to the task, the first 20 trials were not analyzed, in line with our previous studies using this task (Guitart-Masip 2011; Beierholm, 2013). Trials with no behavioral response were not analyzed.

We performed a linear regression across all participants on the log-normalized RTs, which replicated the previously described regression (Beierholm et al., 2013), using the following regressors:

The averaged reward ($\bar{r}_t$) signal is given by $\bar{r}_t = \bar{r}_{t-1} + \alpha(r_{t-1} - \bar{r}_{t-1})$ where r_{t-1} is the reward obtained on the preceding trial. This update rule is equivalent to the Rescorla-Wagner reinforcement learning rule extensively used in reinforcement learning to calculate the average reward. The learning rate α was a free parameter of a random effects model fitted to each participant's responses using the same algorithm as in Beierholm et al., 2013 (see below). The learning rate could range between 0 (no learning, relying completely on the available reward) and 1 (relying completely on the reward obtained in the previous trial).

Available reward: available reward on a given trial

Stimulus repetition: whether the stimulus was repeated in the previous trial

Linear trend: a linear term to account for fatigue or learning

Too late: a binary variable indicating whether the participant was too late on the previous trial

ISI: the pretrial interval while waiting for the stimulus to be presented

A constant term

The averaged reward signal was our regressor of interest, and the other regressors were included as nuisance variables, which could influence response times but were unrelated to our hypothesis. We performed a variant of linear regression on the transformed response time data using Expectation-Maximization, while simultaneously fitting the individual learning rates, α, implemented in MATLAB (Mathworks).

The model diverges from a regular linear model for linear regression in also having individualized learning rates α. We applied a top-level, Gaussian, prior $N(\mu_{prior}, \Sigma_{prior})$ for the β parameters (the load on the regressors) and the learning rates α, in effect making it a random effects model. We used a Bayesian Expectation-Maximization method, fitting the values of μ_{prior} and Σ_{prior} using regular linear regression as the inner loop for maximizing the likelihood with respect to β. For each participant i we made a Laplace approximation about this maximum to realize an approximately normally distributed likelihood proportional to $N(\mu^i_{like}, \sum^i_{like})$, which in the E-step was multiplied by the prior $N(\mu_{prior}, \Sigma_{prior})$ and normalized to create the posterior estimate of each β value $N(\mu^i_{post}, \Sigma^i_{post})$ In the M-step the parameters for the prior were optimized (this can be done analytically). The successive Expectation and Maximization steps were repeated until convergence, signified by a change in estimated variables between two E-steps being less than 0.001. For more details on this method, see (Beierholm et al., 2013).

2.5.3. Correlation between model parameters and PET measure of D1 receptor availability

Next, we tested for a correlation between PET D1 receptor density and the average reward rate beta from the linear regression model. For this purpose, we used the data from a factor analysis (see PET data analysis) for cortical, dorsal striatal, and ventral striatal regions. We used stepwise linear regression to test whether PET D1 receptor densities, group, and the interaction between PET D1 receptor density and group predicted the average reward rate beta. In this model, we also included the total number of gray matter voxels in the T1 image for cortical, ventral striatal, and dorsal striatal ROIs, as a control for total gray matter volume.

To assess how strongly data support the research hypothesis (Dienes and Mclatchie, 2018), Bayes factor$_{10}$ in favor of the alternative (non-null) hypothesis with a prior width of 0.5 was computed for all statistics using jasp (https://jasp-stats.org/).

To assess the association between PET D1 dopamine density and trial-by-trial average reward rate, we fitted a multilevel (mixed-effects) regression that predicted response times from the interaction between the participant-level measure of dopamine affinity for the three ROIs (cortical, dorsal striatal, and ventral striatal) and the trial-level measure of average reward rate, calculated using the learning rate obtained for each participant in the main analysis, as well as the interaction with a group (see supplementary materials for model syntax and https://osf.io/uegy7/ for the data), using R's brms package (Bürkner, 2017) to fit the mixed-effects regression model in a Bayesian framework, replicating previous similar work (Byrne et al., 2020). We also included the same predictors as in the linear regression (available reward; stimulus repetition; linear trend; too late; ISI). As well as including interaction terms, we also included total gray matter volume of each ROI (cortical, dorsal striatal, and ventral striatal) as nuisance covariates and random slopes for each participant. Each predictor was determined to be significantly different from zero if zero was not included in the 95% CI.

3. Results

3.1. Behavioral performance

Table 1 summarizes the behavioral data. Results indicated that older participants generally responded slower than younger participants, with significantly longer response threshold and response time. Although there was no difference in the number of correct responses between older and younger participants, the old made significantly fewer 'hits' (responding correctly and within the response threshold). Older participants also had more 'misses' (responding later than the threshold) and in these trials older participants exhibited a greater 'overshoot', responding further out of the response threshold.

A stepwise multiple linear regression on the average response times revealed that the group x number of correct trials interaction was a significant predictor of average response time, which indicated a group difference in speed-accuracy trade-off (Table 2). Whereas older participants that responded slower made more correct responses, no such association was observed in younger participants. The stepwise regression revealed that the predictors group and number of correct trials were excluded from the model. This interaction was driven by the fact that older participants exhibited a speed-accuracy trade-off, whereas younger participants did not.

3.2. Computational model

Table 3 shows the results of the model and Fig. 2 portrays a summary of beta values and statistics between age groups.

One-sample t-tests indicated no difference between older and younger participants in learning rate, suggesting that both groups had similar sensitivity to reward and equivalent estimates of average reward rate. The value of the learning rate across groups ($\alpha = 0.18$) was slightly higher than the learning rate obtained from the same modeling technique in a previous experiment, which ranged from $\alpha = 0.11$ to 0.15 (Beierholm et al., 2013).

Looking across all participants, as average reward rate increased, response time decreased. This demonstrates a positive association between average reward rate and response vigor, which replicates our previous findings in younger participants using the same task, with different response time thresholds (Beierholm et al., 2013; Guitart-Masip et al., 2011). Greater available reward on a given trial was associated with increased response time across participants, suggesting that people slowed down when there was more reward at stake (Starns and Ratcliff, 2010). There was no age-related difference in the impact of available reward on response vigor even though older participants showed a speed-accuracy trade-off. Repetition of the location of the oddball from the preceding trial was associated with participants speeding up, in line with repetition-based priming (Roberts and Bruce, 1989). The effect of the trial, namely the linear trend variable included in the linear regression model, caused participants to speed up, probably as they became more familiar with the task. The effects of the repetition of the oddball and the linear trend also replicate our previous findings (Beierholm et al., 2013; Guitart-Masip et al., 2011).

Comparing betas from the overall model between older and younger participants, the average reward rate beta was associated

Table 1
Performance on the task by age group. All behavioral performances are reported as averages (SD in brackets).

	All (n = 60)	Older adults (n = 30)	Younger adults (n = 30)	*p* (old vs. young)	BF_{10}
Response threshold, ms	576.43 (110.79)	671.63 (65.84)	481.23 (43.47)	<0.001	7.84e + 15
Response time, ms	499.57 (88.51)	574.44 (56.98)	424.69 (33.04)	<0.001	6.46e + 14
Correct regardless of response time, %	91.86 (5.79)	92.24 (5.81)	91.48 (5.84)	0.62	0.29
Hit (responded correctly & within response threshold), %	72.44 (13.16)	68.33 (14.38)	76.54 (10.53)	0.02	3.54
Miss (responded too late), %	19.42 (10.19)	23.91(11.4)	14.94 (6.31)	<0.001	69.53
Overshoot on miss trials, ms	71.85 (78.89)	98.19 (105.33)	45.49 (11.39)	0.01	5.37

Table 2
Speed-accuracy trade-off. Results of a stepwise linear regression showing that the group x number of correct responses interaction predicted average response time.

Stepwise multiple linear regression	B	*SE* B	*β*	*p*	BF_{10}
Constant	424.86	8.45		<0.001	
Group x number of correct trials	0.38	0.03	0.85	<0.001	6.35e + 14

Table 3
Beta weights for each regressor and individual learning rate (α), for each participant group.

Cohort	Measure	Average reward	Available reward	Stimulus repetition	Linear trend	Too late	ISI	Mean α
All (n = 60)	*p*	<0.001	0.017	<0.001	<0.001	0.49	0.67	
	Mean β	-0.07	0.032	-0.15	-0.12	-0.004	0.002	0.18
	BF_{10}	71.53	2.19	1.16e + 20	6.59e + 14	0.18	0.15	
Older adults (n = 30)	*p*	0.01	0.03	<0.001	<0.001	0.2	0.19	
	Mean β	-0.08	0.045	-0.18	-0.11	0.01	0.01	0.19
	BF_{10}	6.92	1.7	7.74e + 12	118511.5	0.42	0.44	
Younger adults (n = 30)	*p*	0.024	0.26	<0.001	<0.001	0.018	0.44	
	Mean β	-0.062	0.02	-0.11	-0.12	-0.02	-0.004	0.18
	BF_{10}	2.19	0.36	5.97e + 7	3.73e + 9	2.79	0.26	
Older adults vs. younger adults	*p*	0.71	0.36	<0.001	0.59	0.01	0.14	0.82
	BF_{10}	0.28	0.38	100.38	0.29	4.7	0.68	0.27

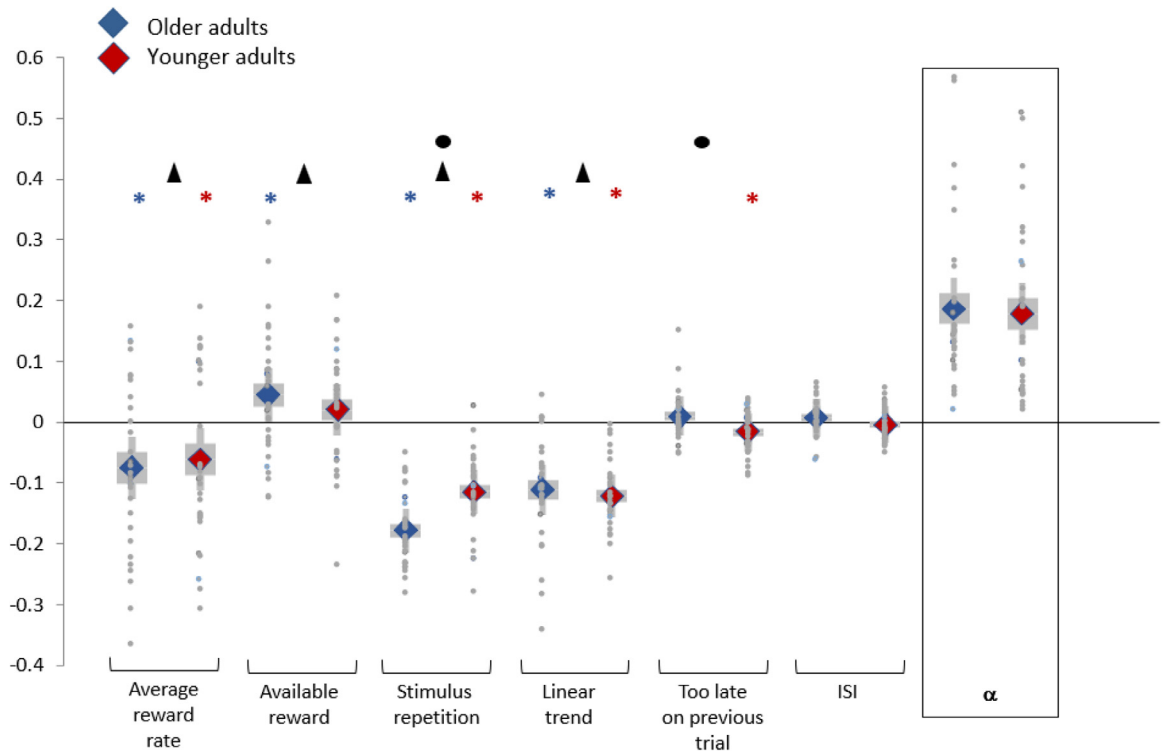

Fig. 2. A linear regression generated beta weights for each regressor (*,significantly different from zero within-group; ▲, significantly different from zero across participants; •, significant difference between-group).

Table 4
Association between PET D1 receptor density in ventral striatum and average reward beta.

	B	*SE* B	β	p	BF_{10}
Constant	-0.06	0.02		0.001	
PET D1 ventral striatal	0.04	0.02	0.27	0.045	1

with speeding up in both older and younger participants and there was no significant difference between groups, indicating that average reward rate modulated response vigor similarly across age, although the effect in younger participants was weaker ($BF_{10} = 2.19$), compared to the older group ($BF_{10} = 6.92$). There were some differences in the model between older and younger participants. Higher available reward on a given trial was associated with slowing in older, but not younger, participants, although this group difference did not approach conventional significance. Although stimulus repetition was associated with shorter response times in both older and younger participants, suggesting that both groups were primed by the previous trial, this association was significantly stronger in older participants. Both groups showed practice effects, reflected in speeding up in response to the linear trend. Whereas responding too late in a previous trial was associated with shorter response times in younger participants, this was not true for older participants.

3.3. Correlation between model parameters and PET measure of D1 receptor availability

Because we observed no difference between older and younger participants in terms of the relationship between average reward rate and vigor, for analysis of the relationship between average reward rate beta and PET D1 receptor density we treated the two groups as a single dataset. We carried out a stepwise linear regression using our 3 a priori factors reflecting the regional variance of D1 receptor availability (age-corrected cortical, dorsal striatal, and ventral striatal PET D1 receptor density), the total number of gray matter voxels in the T1 image for cortical, ventral striatal and dorsal striatal ROIs, as a control for total gray matter volume, group, and the interaction between D1 receptor availability and group as predictors of average reward rate beta. The regression revealed that the PET D1 cortical and dorsal striatal factors were excluded from the model and the ventral striatal factor was retained in the model (Table 4). A Bayesian linear regression was then carried out using the ventral striatal factor as a predictor of average reward rate beta.

Ventral striatal D1 dopamine receptor availability correlated with the average reward rate, indicating that higher receptor availability was positively associated with the relationship between average reward rate and response time (Fig. 3). The stepwise regression excluded the predictor variables a total number of gray matter voxels for cortical, ventral striatal, and dorsal striatal ROIs, group and the group x D1 ventral striatum receptor availability interaction from the model, indicating that there was no influence on total gray matter volume on responses and that the association between PET D1 ventral striatal receptor availability and the average reward rate beta did not differ between older and younger participants.

The multilevel mixed-effects regression showed that the interaction between the participant-level measure of ventral striatal D1 dopamine receptor availability and trial-level measure of average reward rate predicted trial-by-trial response times (Supplementary Table 1). Further mixed-effects regressions including the interaction with group were nonsignificant, indicating again that the interaction between PET D1 ventral striatal receptor availability and the average reward rate beta did not have a different effect between older and younger participants.

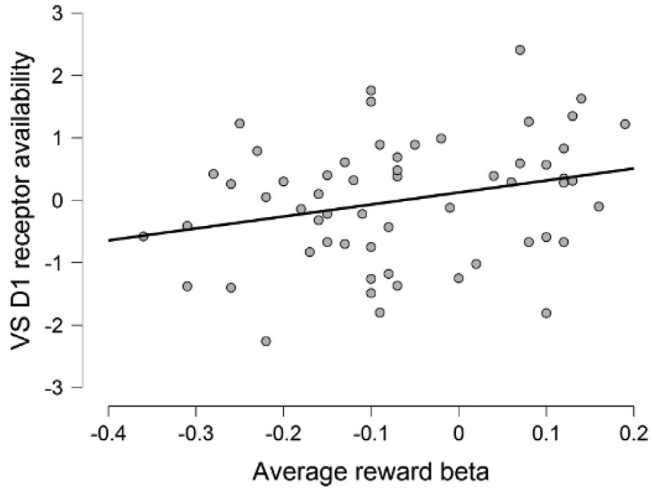

Fig. 3. Association between D1 receptor density in ventral striatum and average reward beta, across participants ($p = 0.045$, $B = 0.04$, $\beta = 0.27$, $BF_{10} = 1$).

4. Discussion

Our results demonstrate that participants emitted more vigorous motor responses to obtain a reward when the average reward rate was higher, and this response was similar between older and younger groups. This effect was weakly associated with D1 receptor availability in the ventral striatum.

The invigorating effect of average reward rate is in agreement with previous work (Beierholm et al., 2013; Guitart-Masip et al., 2011; Niv et al., 2007; Otto and Daw, 2019; Shadmehr et al., 2019) and with models of reward-related vigor (Lemon, 1991; Niv et al., 2007; Shadmehr et al., 2019). We speculated that average reward rate may decrease the effect on vigor in older participants because age-related decline in dopamine structure and function relates to decreased performance in probabilistic reward-learning tasks (de Boer et al., 2017; Eppinger et al., 2011; Mell et al., 2005) and individual levels of vigor vary across a population (Bargary et al., 2017; Choi et al., 2014; Reppert et al., 2018; Shadmehr et al., 2019). However, in our study, the invigorating effect of average reward rate was present in both older participants and younger participants, even to a slightly higher degree in older participants. This result suggests that given the appropriate reward, age-related changes in cognitive processing do not have a detrimental influence on motivational vigor. This is in line with recent research which indicates that motivational incentives improve cognitive task performance in both older and younger adults, suggesting that age-related reductions in motivation can be ameliorated with incentives (Yee et al., 2019). Further, contrary to what one would expect considering the well documented age-related dopamine decline, older adults do not display a straightforward decline in motivation with age; in fact, older individuals are actually more motivated to obtain rewards immediately than younger adults, as reflected by a study which showed that older adults are more likely to choose options that provided shorter time delays (Seaman et al., 2016) as well as a study showing that older adults are less motivated by extrinsic but more motivated by intrinsic reward (Inceoglu et al., 2012). However, we should also consider the possibility that older research participants in previous cognitive studies, including ours, come from the high end of the distribution over dopamine integrity and are therefore high performing in relation to the av-

erage participant of the same age in the population. This could potentially explain the lack of differences in motivation between younger and older participants. Future longitudinal studies should be able to address the question of whether there is an age-related decline in motivation associated with normal aging.

How could our findings be understood in light of the well-documented age-related changes in other reward-related activities (de Boer et al., 2017; Eppinger et al., 2011; Mell et al., 2005), and considering that dopamine functioning decreases in aging (Bäckman et al., 2010; Düzel et al., 2010a). One important factor may be that we used a tailored response threshold in this study. Because older participants are generally slower than younger participants, as is the case in our sample, the tailored response threshold may have made the task easier for older participants than if a global threshold had been used. It is possible that previous observations of reduced reward processing in older participants are at least partly due to the generally slower processing speed making decision-making within standard task parameters more difficult (Baron and Mattila, 1989; Cerella and Hale, 1994; Kerchner et al., 2012). The fact that our task was adjusted to suit both older and younger participants could have facilitated performance in older participants and magnified the relationship between average reward rate and vigor so that it matched that of younger participants. This means that, despite general decreases in behavioral vigor (Bohannon, 1997; Irving et al., 2006) and reward behavior (de Boer et al., 2017; Eppinger et al., 2011; Mell et al., 2005), older people may show equally strong invigoration by average reward rate as younger people, given the right conditions. Another possible explanation is that our task instructions to 'respond as quickly and accurately as possible' influenced their behavior. One study showed that - although slower than their younger counterparts - when provided with instructions to emphasize speed, older people will speed up (Starns and Ratcliff, 2010). Further, older participants use faster strategies when provided with monetary incentives (Touron et al., 2007). Perhaps our task instructions pushed older people to speed up in response to rewards. This is supported by our result that older participants exhibited a speed-accuracy trade-off, whereas younger participants did not. Thus, older people may have been triggered by the instructions to prioritize speed over accuracy. This hints at a possible dissociation between age-related changes in D1 dopamine function and reward-related vigor under certain conditions, when limitations on performance are removed, or when given explicit instructions to respond to reward with speed. Also, some brain regions involved in motivation such as the ventral striatum show relatively more preservation of D2 receptors with age when accounting for partial volume effects than other brain regions (Seaman et al., 2019), suggesting that motivation (and by extension, reward-related vigor) could be preserved in older people. Future research should fully dissociate the average reward rate over the experiment from any trial-by-trial incentive, to test whether vigor degrades in older participants in this context. Future studies should also dissociate the effect of effort cost from average reward rate, to independently examine how the two variables change in younger compared to older participants. However, it is important to highlight that our results demonstrate that older adults can show reward-related invigoration to a level comparable to younger adults. Even in the case that the lack of behavioral differences was due to the speed/accuracy trade-off, our results would falsify our hypothesis that older adults would show attenuated reward-related invigoration.

Finally, it is possible that our sample size of 60 participants, though adequate to detect the effect of average reward rate on vigor across and within-participant groups, was simply too limited to detect subtle differences in the average reward rate between older and younger participants.

Independent of reward-related vigor, older participants overall had a higher response time threshold, demonstrating an age related decrease in behavioral vigor as previously reported in older adults (Bohannon, 1997; Irving et al., 2006). Furthermore, older adults made fewer 'hits' and were slower on 'miss' trials compared to younger participants. It is well-established that processing speed slows down in aging (Baron and Mattila, 1989; Cerella and Hale, 1994; Kerchner et al., 2012)., The decreased performance in older participants is in line with previous work indicating that older people exhibit decreased cognitive performance; this is linked to neural variability in subcortical regions and dopamine losses (Guitart-masip et al., 2016).

Across participants, average learning rate was 0.18, which is slightly higher than in our previous work (0.11; (Beierholm et al., 2013). There was no difference between younger and older participants in this parameter, indicating that in our paradigm, older or younger age did not influence how quickly people learned new information.

The available reward on a given trial was a significant predictor of behavior across groups; participants slowed down when more reward was available. This is in contrast to results from monetary incentive delay tasks (Wittman et al., 2005), but in line with the results of previous studies using variations of the current task (Beierholm et al., 2013; Griffiths and Beierholm, 2017; Guitart-Masip et al., 2011). It is of note that available rewards slowed down older, but not younger participants. This pattern could be attributed to a speed-accuracy trade-off where participants slowed down to avoid error in anticipation of a greater potential reward. Indeed, older participants are known to prioritize accuracy over speed (Starns and Ratcliff, 2010). For example, despite having noisier sensory representations, older participants may maintain equal performance as younger participants by slowing down (Jones et al., 2019). Our results indicate a general sacrifice of speed for accuracy across older participants because older participants obtained a similar number of correct responses as younger participants. They also exhibited a slower response time and a greater overshoot when responding too late. Further, on a participant-by-participant basis, the speed-accuracy trade-off was present only in older participants. As demonstrated by the negative beta weight for the 'too late' regressor in Table 3, younger participants rather became faster if they were too late on a previous trial, suggesting they emphasized response speeding based on previous errors. Further, a second level comparison between young and old uncovered a significant difference in the betas for this regressor for young and old (see Table 3). In line with this assertion, younger participants are known to adjust their performance based on feedback (Starns and Ratcliff, 2010). Alternatively, this error-based speeding could be attributed to the frustration associated with reward loss (Eben et al., 2020; Verbruggen et al., 2017).

Our prediction that the effect of average reward rate on response vigor would correlate with dopamine D1 receptor availability was motivated by several lines of identifying an association between changes in reward responses and dopamine function over the lifespan (Chowdhury et al., 2013; de Boer et al., 2017; Guitart-masip et al., 2016). Models of vigor implicate tonic dopamine in the nucleus accumbens (Niv et al., 2007; Otto and Daw, 2019), supported by the observation that dopamine manipulations modulate vigor (Aberman and Salamone, 1999; Correa et al., 2002; Evenden and Robbins, 1983; Guitart-Masip et al., 2012; Lex and Hauber, 2008; Ljungberg and Enquist, 1987; Mingote et al., 2005; Niv et al., 2007; Salamone et al., 2001; Salamone and Correa, 2002, 2012a; Sokolowski et al., 1998; Taylor and Robbins, 1986; Salamone and Correa, 2012b) and that willingness to exert effort (Treadway et al., 2009) is associated with the degree of amphetamine-induced dopamine release in the striatum

and prefrontal cortex (Treadway et al., 2012). Whilst our previous pharmacological study showed a link between dopamine manipulation and reward-related vigor (Beierholm et al., 2013), and an fMRI study revealed that the relationship between average reward rate and response vigor is associated with activity in the midbrain (Rigoli et al., 2016), the current results indicate evidence for an association between the computationally-derived relationship between average reward rate and vigor with an endogenous measure of D1 dopamine receptor availability. We found a significant positive association, which indicates that the more D1 receptor availability, the greater the response time to more reward, which is the opposite of what might be expected. One possible explanation for the current results may stem from the fact that we measured D1 receptors. Although both D1 and D2 receptors are involved in reinforcement learning (Calaminus and Hauber, 2007), these receptors have different effects on reward-related behavior (Jenni et al., 2017; Lex and Hauber, 2008). D1 receptors expressed in the direct striatal pathway are associated with reinforcement of reward actions, so actions are more likely to be repeated in the same circumstances (D'Aquila, 2010; Sutton and Beninger, 1999). A recent study showed that dopamine medication reduces noninstrumental reward-related vigor in Parkinson's Disease patients (Grogan et al., 2020). This indicates that the relationship between dopamine and reward-related vigor is complex. Although this study did not delineate D1 and D2 receptors, it is feasible that D1 and D2 receptors modulate reward-related vigor differently. Hence, D1 receptors may be associated with a decrease in reward-related vigor. Previous work that indicates that dopamine is associated with reward-related vigor (Beierholm et al., 2013; Niv et al., 2007) could reflect the action on D2 receptors. Indeed, D2 receptors expressed in the indirect pathway are involved in regulating response vigor as shown in pharmacological studies (Augustin et al., 2020; Collins and Frank, 2014). Following this line of reasoning, we may have been more likely to see that greater D2 receptor availability was associated with shorter response times as predicted. It is also possible that a dynamic measure of tonic dopamine release using cyclic voltammetry (Oh et al., 2018) would be more sensitive to detect a relationship between response vigor and online average reward rate which might reveal an association with D2 receptors over D1 receptors.

We did not see a difference in the association between motivational vigor and D1 receptor availability between older and younger individuals. Our results indicate that although aging is associated with both structural and functional decline of the dopamine system (as previously reported in the current data set (de Boer et al., 2019, 2017)), cognitive functioning in the form of reward-related invigoration is preserved. For example, age-related loss of dopamine neurons occurs within reward- processing areas such as the substantia nigra and ventral tegmentum (Fearnley and Lees, 1991; Vaillancourt et al., 2013) and this loss could contribute to the deficits in probabilistic reward learning (Bäckman et al., 2010; Düzel et al., 2010b). Aging decreases dopamine function, more so on D1 than D2 receptors (Karrer et al., 2017). Despite all these alterations, when the appropriate reward incentive is offered, and the task is manageable, reward related invigoration is maintained. Although the association between dopamine neuromodulation and vigor is well established in the literature (see Niv et al., 2007; Salomone et al., 2012) and that we have previously shown this association using the task in this paper (Beierholm, 2013) our data suggest that reward-related invigoration is not only modulated by dopamine and that other neural factors may contribute to its modulation.

To summarize, our results indicate that the invigorating effect of average reward rate as measured here does not differ between older and younger individuals, despite a decrease in overall task performance in older adults. For the first time, we investigate an association with endogenous D1 receptor availability in this context. Our results indicate weak evidence for a relationship between the modulation of response vigor by average reward rate and D1 receptor availability.

Verification

The work described has not been published previously, it is not under consideration for publication elsewhere, its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder.

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Declaration of Competing Interest

None.

CRediT authorship contribution statement

Emily J Hird: Formal analysis, Writing – original draft, Writing – review & editing, Visualization. **Ulrik Beierholm:** Conceptualization, Methodology, Formal analysis, Writing – review & editing, Supervision. **Lieke De Boer:** Data curation, Formal analysis. **Jan Axelsson:** Methodology, Writing – review & editing. **Marc Guitart-Masip:** Conceptualization, Methodology, Writing – review & editing, Supervision, Funding acquisition.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neurobiolaging.2022.06.003.

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