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Dopamine Modulates the Efficiency of Sensory Evidence Accumulation During Perceptual Decision Making

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Abstract

Background: Perceptual decision making is the process through which available sensory information is gathered and processed to guide our choices. However, the neuropsychopharmacological basis of this important cognitive function is largely elusive. Yet, theoretical considerations suggest that the dopaminergic system may play an important role.
Methods: In a double-blind, randomized, placebo-controlled study design, we examined the effect of methylphenidate in 2 dosages (0.25 mg/kg and 0.5 mg/kg body weight) in separate groups of healthy young adults. We used a moving dots task in which the coherency of the direction of moving dots stimuli was manipulated in 3 levels (5%, 15%, and 35%). Drift diffusion modelling was applied to behavioral data to capture subprocesses of perceptual decision making.
Results: The findings show that only the drift rate (v), reflecting the efficiency of sensory evidence accumulation, but not the decision criterion threshold (a) or the duration of nondecisional processes (Ter), is affected by methylphenidate vs placebo administration. Compared with placebo, administering 0.25 mg/kg methylphenidate increased v, but only in the 35% coherence condition. Administering 0.5 mg/kg methylphenidate did not induce modulations.
Conclusions: The data suggest that dopamine selectively modulates the efficacy of evidence accumulation during perceptual decision making. This modulation depends on 2 factors: (1) the degree to which the dopaminergic system is modulated using methylphenidate (i.e., methylphenidate dosage) and (2) the signal-to-noise ratio of the visual information. Dopamine affects sensory evidence accumulation only when dopamine concentration is not shifted beyond an optimal level and the incoming information is less noisy.

Keywords: dopamine, drift diffusion model, perceptual decision making, pharmacology

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Significance Statement

Perceptual decision making is the process through which available sensory information is gathered and processed to guide our choices. Perceptual decision making can be further dissected into several subprocesses. Currently, it is unclear how neurotransmitter systems may affect these subprocesses. Here, we focus on the dopamine system in light of prior research on its role in regulating the fidelity of neural information processing. We show that using methylphenidate (MPH) as a pharmacological modulation of the dopamine system selectively modulates how efficient sensory evidence is accumulated to drive our decisions. However, this depends on the level of MPH and the quality of incoming sensory information. These results provide insights into the neuropharmacological basis that drive important aspects of human perception and decision making.

Introduction

The external environment is full of different sensory signals that could influence our behavior. Perceptual decision making is the process through which available sensory information is gathered and processed to guide our choices. Often sensory information is noisy; thus, prominent theories of perceptual decision making posit that sensory evidence needs to be accumulated (integrated) across multiple samples to arrive at a clearer perceptual representation, based on which choice or action can be taken (Ratcliff et al., 2009). Thus, when the brain processes sensory information, it needs to account for stimulus noise as well as inherent processing noise. Theoretical (Servan-Schreiber et al., 1990; Li et al., 2001; Ziegler et al., 2016) and empirical (Yousif et al., 2016; Ziegler et al., 2016) research has proposed dopaminergic modulation as a mechanism for regulating the signal-to-noise ratio (SNR) of neural information processing. Empirically, evidence from animal research shows that dopamine modulates persistent synaptic activity and enhances the SNR in the prefrontal cortex (Kroener et al., 2009). Furthermore, prefrontal dopamine signals have also been shown to regulate visual cortical signals (Noudoost and Moore, 2011). In humans, the availability of dopamine D1 receptors was found to be negatively correlated with intra-individual reaction time variability (MacDonald et al., 2012). Recently, it has also been shown that the dopamine receptor agonist pergolide improved visual cortical SNR and counteracted the impairing effect of inhibitory transcranial magnetic stimulation on visual perceptual learning (Yousif et al., 2016). To investigate dopamine's role in regulating sensory evidence integration during visual perception in humans, we combined pharmacological intervention of methylphenidate (MPH), a mixed dopamine/norepinephrine transporter blocker, with a perceptual decision task of visual motion in which we could systematically manipulate external sensory stimulus noise by the extent of motion coherence. Furthermore, since both theoretical (Li and Sikström, 2002) and empirical (Vijayraghavan et al., 2007; Cools and D'Esposito, 2011; Chowdhury et al., 2012) studies showed that dopamine's signal turning effect on cognition follows an inverted-U shaped function, with too little or excessive dopamine being suboptimal for performance, here we investigated effects of dopamine signaling at different dosages.

To explore effects of dopamine on subprocesses of perception decision making, we fitted drift diffusion models (DDM) to the behavioral data to derive estimates of parameters that reflect different aspects of the perceptual decision-making process (Wagenmakers et al., 2007, 2008; Ratcliff, 2014). The DDM assumes that a perceptual decision is a stochastic process that sequentially samples and accumulates sensory evidence for arriving at a perceptual decision (Winkel et al., 2012; Ratcliff, 2014; Stock et al., 2017). In DDM, the efficiency of sensory evidence accumulation is modeled by the drift rate (v) parameter, which strongly depends on the SNR of incoming sensory information (Ratcliff et al., 2009; Ratcliff, 2014). Given that MPH affects the dopaminergic system, which is known to be important to regulate the SNR, we hypothesize that modulation of the DA system by MPH affects efficiency of sensory evidence accumulation during perceptual decision making and may interact with environmental task factors affecting stimulus noise. Furthermore, during perceptual decision making it is also important to consider how much information is needed until one is certain to make a specific decision. Such decision criterion or threshold (Ratcliff and McKoon, 2008; Hoffmann and Beste, 2015) is captured by the boundary separation parameter (a). It has been hypothesized that the dopaminergic system may modulate the decision threshold (Winkel et al., 2012), since response selection processes are known to be modulated by the dopaminergic system (Willemssen et al., 2011; Schulz et al., 2012; Yildiz et al., 2013; Stock et al., 2014). Moreover, the threshold for action execution is likely to be modulated by the strength of the cortico-striatal synapse (Lo and Wang, 2006; Gold and Shadlen, 2007; Bogacz et al., 2010), which is known to be modulated by DA effects (Surmeier et al., 2007). Yet, a pharmacological manipulation using bromocriptine did not reveal modulatory effects, and it was argued that this could be due to the receptor specificity of bromocriptine (Winkel et al., 2012). In fronto-striatal circuits, the general dopamine level is strongly regulated by dopamine's presynaptic autoreceptor DAT, which removes dopamine from the synaptic cleft and is highly expressed in nigro-striatal and meso-corticolimbic pathways (Ciliax et al., 1999). MPH acts as a mixed dopamine/norepinephrine transporter blocker, thus increasing dopamine (norepinephrine) levels in fronto-striatal structures (Volkow et al., 1999; Skirrow et al., 2015). Since MPH is not specific for dopamine's postsynaptic receptor subsystems and generally plays an important role in striatal DA level regulation, it is possible that it might also modulate the boundary separation threshold (a).

We examine these hypotheses in a double-blind, randomized, placebo-controlled study in healthy adults in which we use a moving dots task to examine perceptual decision making. We examine the effects of MPH by administering 2 MPH dosages: 0.25 and 0.5 mg/kg body weight. As reviewed above, varying the dosage of MPH makes it possible to investigate how the above effects are scaled by variations in dopamine level. Since we examined healthy young adults with supposedly no dopamine system deficiencies, it is possible that the higher dosage shifts the dopamine system beyond the optimal level, which may then result in null treatment benefit or decreases in the efficiency of sensory evidence accumulation during perceptual decision making. Doing so, it will be possible to estimate boundary conditions of the dopamine system for subprocesses involved in perceptual decision making.

Materials and Methods

Participants

Fifty healthy young participants took part in this study. They were randomly assigned to 2 equally sized groups (n = 25 each) for the higher dosage level (mean age 25.5 y, 12 females) and the lower dosage level (mean age 22.9 y, 13 females). The dosages of MPH were 0.5 and 0.25 mg/kg for the higher and lower levels, respectively. Screenings before the first appointment ensured that participants were right-handed, had no regular drug and/or medication intake, and did not consume caffeine on the same days as the appointments. They were informed about the goals and procedure of this study and gave written consent. All participants received monetary compensation after the second appointment. The study was approved by the local Ethics Committee of TU Dresden, and the experiment was conducted according to the Helsinki Declaration of 1975. All subjects provided written informed consent.

MPH Administration

The study consisted of 2 appointments in one of which participants received a single dose of MPH. At the other appointment, participants were administered a placebo. The order of drug administration (MPH or placebo first) was counterbalanced across participants and gender, and the experimenter was blind to this order. The individual MPH dosage was calculated based on the participant's body weight at the beginning of the first appointment. The moving dots task started approximately 2 h after drug administration, which falls inside the time span when MPH is at maximum plasma concentration (Challman and Lipsky, 2000; Rösler et al., 2009). Prior to working on the task described in this publication, the participants spent 60 min performing 2 other tasks, the results of which have not been published so far.

Moving Dots Task

The experimental task was programmed using Java and presented on a 23.8-inch screen with resolution 1920 × 1080 pixels and a refresh rate of 144 Hz. The experiment consisted of 9 experimental blocks with 48 trials each. The experiment setup is shown in Figure 1.

Between the blocks, participants could decide via button press when to continue. Each trial consisted of a central fixation cross presented for 500 ms. After that, the "cloud" of 30 rectangular moving dots was presented for 1000 ms spanning a viewing angle of 4.72°. The 30 random dots changed positions at a speed of 9 pixels per frame, which created the illusion of motion. The coherence of motion with dots moving either towards the left or right direction was manipulated by varying the percentage of dots moving in the same direction. Specifically, we included 3 levels of coherence, with 5%, 15%, or 35% of all presented dots moved in the same direction. This coherence manipulation varied the SNR of the incoming visual information, which is known to affect the efficiency of sensory evidence accumulation (Ratcliff et al., 2009). The moving directions of the remaining dots were random. Each coherence condition occurred equally frequent in each of the 9 experimental blocks (i.e., 16 times in each experimental block). The response interval was 1000 ms. Participants were instructed to report a "left" motion with the Y key and a coherent "right" motion with the M key on a standard German PC keyboard.

Estimating Parameters of Drift Diffusion Model

The drift diffusion model captures perceptual decision making as a process of continuous sampling of noisy sensory evidence until a decision boundary in favor of one of the choice options is reached (rightward or leftward motion in our case). According to the model, the distributions of choice accuracy and reaction times (RTs) across trials depend on a number of parameters, 3 of which are central in most perceptual decision processes. As mentioned in the introduction, the drift rate (v) models the efficiency with which decision evidence could be integrated across trials to approach the decision boundaries: high drift rates reflect more efficient evidence integration. The boundary separation parameter (a) indicates the amount of evidence needed until a decision threshold is reached: wider decision boundaries would reflect more cautious but slower decisions. The non-decision time parameter (Ter) captures the time taken by sensory encoding and motor processes. To estimate the values of these 3 parameters for each participant, we applied the EZ-diffusion model

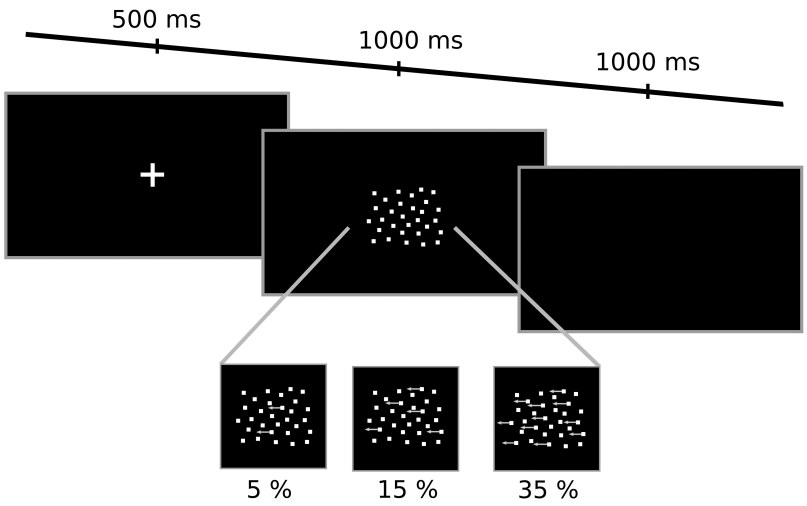

Figure 1. Illustration of the experimental setup and the moving dot stimuli. The fixation cross was presented for 500 ms, the moving dots for 1000 ms. In the "cloud" of moving dots, the extent of motion coherence was varied in 3 steps by manipulating the percentages (i.e., 5%, 15%, or 35%) of dots moving in the same direction, that is, either towards left or right. The rest of the dots move randomly.

(Wagenmakers et al., 2007) to our data to further characterize potential effects of dopamine pharmacology on different aspects of the perceptual decision process. The EZ model was used, because the parameter fitting procedure is more straight-forward than in the classical Ratcliff diffusion model. Moreover, the EZ model is optimized for experiments having a more limited number of trials. The Ratcliff model requires the entire RT distribution (i.e., including error trials). Error trials will therefore have to occur in a reasonable frequency (Wagenmakers et al., 2007). We applied the EZ model to individual participant's data from each of the 3 coherence conditions separately to estimate the 3 drift diffusion parameters described above. The parameters are estimated based on the individual's choice accuracy as well as the mean and variance of RTs of the correct responses. In the context of the moving dot task, these 3 parameters presumably reflect the efficiency of integrating sensory information for perceived motion (v), stringency of the decision criterion (a), and sensorimotor processing time (Ter). Before applying the model to the data, RT distributions associated with choices made in each of the 3 states were inspected separately for the coherence condition. All distributions can be characterized as ex-Gaussian, which is expected for RT distributions. We fit the data from all 3 coherence conditions separately. The starting point Z was not modelled. This is because there is reason to assume that there is a bias with the subjects to prefer 1 of the 2 possible response options. Also, the experimental procedure did not induce such a bias.

Statistical Analysis

The data were analyzed using mixed effects ANOVAs. The factor "motion coherence" (i.e., 5%, 15%, and 35%) was included as a 3-level, within-subject factor, and the factor "placebo/drug" was included as a 2-level within subject factor. The factor "dosage" (25 or 50 mg/kg bodyweight) was included at a 2-level between-subject factor. Greenhouse-Geisser correction was applied for all analyses and posthoc tests were Bonferroni-corrected. Separate ANOVAs were calculated for the different DDM parameters (i.e., v, a, and Ter) as well as for the basic RT and accuracy data. For descriptive statistics, the mean and SEM are given. For nonsignificant results including the factors "dosage" and "placebo/drug," we also ran Bayesian analyses to examine the probability of the null hypothesis being true, given the obtained data ($P(H_0|D)$) (Wagenmakers, 2007; Masson, 2011); that is, we evaluated the relative strength of evidence for the null hypothesis. The Bayesian analysis was performed base on the sum of squares of the error term and the effect term provided by the ANOVAs (Wagenmakers, 2007; Masson, 2011). For the descriptive statistics, the mean and SEM are given.

Results

For the mean RTs, the mixed effects ANOVA revealed a main effect of "motion coherence" ($F(2,96)=231.56$; $P<.001$; $\eta_p^2=.83$). As expected, RTs became shorter with increasing coherency levels (5% = 738 ms ± 0.019; 15% = 665 ms ± 0.015; 35% = 567 ms ± 0.012). All other main or interaction effects were not significant (all $F<2.35$; $P>.101$). Concerning the accuracy, similar to the results of RTs there was only a main effect "motion coherence" ($F(2,96)=911.22$; $P<.001$; $\eta_p^2=.95$). It is shown that the accuracy increased with increasing coherency levels (5% = 59.0% ± 0.7; 15% = 77.6% ± 1.0; 35% = 88.6% ± 0.8). No other main or interaction effect was significant (all $F<1.32$; $P>.255$).

For the drift rate (v), the mixed effects ANOVA revealed a main effect of "motion coherence" ($F(2,96)=677.75$; $P<.001$; $\eta_p^2=.93$) showing that the drift rate was largest in the 35% (0.24 ± 0.008) compared to 15% (0.14 ± 0.005) and 5% motion condition (0.04 ± 0.005). Importantly, there was an interaction dose x motion coherence x drug/placebo ($F(2,96)=3.49$; $P=.034$; $\eta_p^2=.07$), which is shown in Figure 2. All other main or interaction effects were not significant (all $F<0.44$; $P>.643$).

Further analyses of the interaction dose x motion coherence x drug/placebo showed that there was an interaction motion coherence x drug/placebo in the group receiving 0.25 mg/kg MPH ($F(2,48)=5.40$; $P=.008$; $\eta_p^2=.18$), but not in the group receiving 0.50 mg/kg MPH ($F(2,48)=0.53$; $P=.589$; $\eta_p^2=.02$). In the group receiving 0.25 mg/kg MPH, posthoc tests show that there was no difference between MPH and placebo in 5% and the 15% motion conditions (all $t<-1.61$; $P>.120$). However, the drift rate was larger under MPH administration than placebo in the 35% motion condition ($t(24)=-2.24$; $P=.017$), suggesting that the efficiency of sensory evidence accumulation became higher.

Concerning the boundary separation parameter (a), the mixed effects ANOVA revealed only a main effect of "motion coherence" ($F(2,48)=3.58$; $P=.032$; $\eta_p^2=.07$), and it is shown that parameter a was larger in the condition with 15% coherency compared with the other coherency condition (5% = 0.095 ± 0.002; 35% = 0.095 ± 0.003). All other main or interaction effects were not

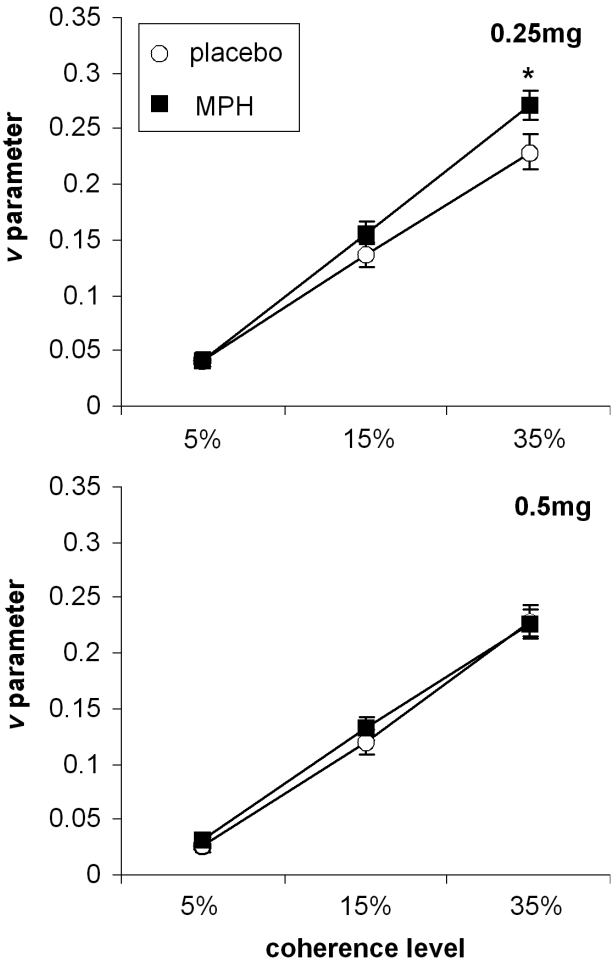

Figure 2. The interaction MPH dosage x motion coherence x drug/placebo is shown for the drift rate parameter (v) of the DDM. The top panel shows results of MPH dosage level at 0.25 mg/kg, whereas the bottom panel shows results at the dosage level of 0.5 mg/kg group are shown. Dosage was manipulated between groups (the mean and SEM are given).

significant (all $F<0.26$; $P>.771$). The Bayesian analysis of the data revealed that $P(H_0|D)=0.97$. Thus, the Bayesian analysis provides very strong evidence for the null hypothesis, that is, that there is no differential effect of MPH/placebo, motion coherency, and drug dosage on the boundary separation parameter (*a*).

Concerning the duration of nondecisional processes (*Ter*) there was, again, only a main effect of "motion coherence" ($F(2,48)=136.42$; $P<.001$; $\eta_p^2=.74$). *Ter* was largest in the 5% motion condition (0.51 ± 0.01) and decreased in the 15% (0.45 ± 0.1) and 35% motion condition (0.4 ± 0.007). All conditions differed from each other ($P<.001$). No other main or interaction effects were significant (all $F<0.41$; $P>.665$). In the Bayesian analysis it is shown that $P(H_0|D)=0.95$. Thus, the Bayesian analysis provides very strong evidence for the null hypothesis, that is, that there is no differential effect of MPH/placebo, motion coherency, and drug dosage on the duration of non-decisional processes (*Ter*).

Even though the sessions in which MPH or placebo was administered were counterbalanced across subjects, we also examined whether test order affected the results. Additional control analyses showed that including this variable in the above analyses did not change the pattern of results, that is, there was no main or interaction effect including the factor test order (all $F<0.31$; $P>.711$).

Discussion

In the current study, we examined the effects of dopamine modulation of subprocesses of visual perceptual decision making by modeling the behavioral data using DDM. This was done in a double-blind, randomized, placebo-controlled study in healthy young adults. The results show that only the drift rate (*v*), but not the boundary/threshold separation (*a*) or the duration of non-decisional processes (*Ter*) is modulated. The lack of modulatory effects for the parameters *a* and *Ter* were supported by a Bayesian analysis of the data, which provided very strong evidence for the null hypotheses. This underlines that the modulatory effects of MPH on the dopaminergic system are targeting specific subprocesses during perceptual decision making.

The current findings show that the modulation of the efficiency of sensory evidence accumulation (indexed by the drift rate *v*) by MPH depends on 2 factors: the degree to which the dopaminergic system is modulated using MPH (i.e., MPH dosage) and the SNR of the incoming visual information. Significantly higher drift rates in MPH compared with placebo administration were only observed using a dosage of 0.25 mg/kg bodyweight, and this effect was restricted to the condition where the coherence of stimulus motion was sufficiently high (i.e., with at least 35% of dots coherently moving in the same direction). No drug/placebo modulations in any of the coherence levels were observed using an MPH dosage of 0.5 mg/kg bodyweight. MPH acts as a mixed dopamine/norepinephrine transporter blocker, thus increasing dopamine (norepinephrine) levels in fronto-striatal structures (Volkow et al., 1999; Skirrow et al., 2015). The results therefore show that increased dopaminergic concentrations in these circuits foster the efficiency of sensory evidence accumulation. This is in line with theoretical conceptions suggesting that the dopaminergic system regulates the SNR of neural information processing (Servan-Schreiber et al., 1990; Li et al., 2001; Yousif et al., 2016; Ziegler et al., 2016). Enhancing SNR of sensory inputs by dopamine modulation may enhance the distinctiveness of sensory-perceptual representations, leading to more efficient accumulation of information (Li and Rieckmann, 2014; Yousif et al., 2016). Notably, this seems to be the case only once the SNR of incoming sensory information is above a sufficient level of signal strength. This is evidenced by the lack of modulatory effects in the 2 experimental conditions with lower coherence of the moving dots stimuli. This finding cannot be attributed to the degree to which the dopaminergic system was modulated, as when the MPH concentration was doubled (i.e., 0.5 mg/kg MPH was administered), no modulations of the drift rate compared with placebo were observed in the conditions with lower sensory SNR either. Importantly, this finding also suggests that there is an optimal level of dopaminergic activity in which the efficiency of sensory evidence accumulation is maximally amplified. This likely reflects an effect of the generally inverted-U function relating DA signaling and cognition (Cools and D'Esposito, 2011). It is possible that the MPH dosage of 0.5 mg/kg has shifted the dopamine system beyond the optimal level and thus not yielding treatment benefit on performance, while the 0.25 mg/kg dosage shifted the dopamine system to the optimal level and that is why the efficiency of information accumulation was increased.

From the current data, we can only speculate which functional neuroanatomical structures are associated with the observed effects. In principle, functions of the prefrontal cortex as well as striatal areas may be associated with these effects. Yet, MPH acts as a mixed dopamine/norepinephrine transporter blocker (Volkow et al., 1999; Skirrow et al., 2015) and DAT regulates dopamine turnover at the striatal level (Ciliax et al., 1999), but not at a neocortical level where enzymes regulate dopaminergic turnover (Goldberg and Weinberger, 2004). It is therefore possible that the effects observed are related to striatal processes. In line with that interpretation, DDM-like processes have been shown to be associated with the basal ganglia (Forstmann et al., 2008, 2010). Moreover, it has been shown that the basal ganglia receive signals from primary sensory cortices (Hikosaka et al., 1989; Redgrave and Gurney, 2006; Znamenskiy and Zador, 2013; Reig and Silberberg, 2014) and that there is evidence from animal research that striatal dopamine modulates interactions between perceptual processes (Ward and Brown, 1996; Bao et al., 2001; Brown et al., 2010). All these aspects make it likely that striatal processes play an important role in the observed modulatory effects. However, this needs to be further validated in future studies.

Whereas the role of dopamine modulation of the efficacy of sensory evidence accumulation (the *v* parameter) during visual perceptual decision making is clearly based on the data reported here and previous evidence, the role of dopamine in affecting decision boundary is still equivocal. Whereas our observation of the boundary separation parameter being not affected by MPH administration corroborates other findings also showing no modulations of the boundary separation parameter by a pharmacological modulation of the dopamine system (Winkel et al., 2012), it has recently also been shown that the effects of dopamine agonist, pergolide, counteracted the impairing effect of inhibitory transcranial magnetic stimulation on multiple aspects of perceptual decision making, including drift rate, boundary separation, and sensory noise (Yousif et al., 2016). The empirical inconsistencies regarding dopamine's role in affecting decision threshold may in part arise from the specifics of dopamine pharmacology applied and experimental conditions. Nonetheless, our finding that the boundary separation parameter remained stable using a drug that modulates striatal dopamine concentrations by affecting DAT suggests that striatal dopaminergic levels are not important to be considered as a factor modulating the amount of information needed for a decision. Specifically, this does not in general undermine theoretical considerations suggesting that the strength of the cortico-striatal

synapse modulates the decision threshold (Lo and Wang, 2006), which is assumed to be generally important for perceptual decision-making processes (Beste et al., 2008; Tomkins et al., 2013; Beste et al., 2014, 2017); instead, it suggests that the criterion setting process may rather be modulated by top-down cortical dopamine modulation. However, this conjecture awaits further empirical validations. At this point, it should be noted that drugs modulating DAT in monkeys have been to modulate novelty-seeking behavior but not the rate at which monkeys learned what cues are predictive for rewards (Costa et al., 2014). Future studies may therefore be conducted to examined with computational, model-driven aspects showing differential modulatory profiles of striatal dopamine-related functions. These may also more precisely examine the role of norepinephrine in perceptual decision making.

In summary, the study suggests that dopamine modulates specific perceptual decision-making subprocesses, that is, the efficacy of evidence accumulation during perceptual decision making. This modulation depends on 2 factors: the level of pharmacological upregulation of dopamine neurotransmission and the SNR of the incoming visual information. Dopamine affects perceptual decision-making subprocesses only when dopamine concentration is not shifted beyond an optimal level and the incoming information is not too noisy.

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Statement of Interest

None.

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