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ORIGINAL ARTICLE

A computational analysis of flanker interference in depression

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Background. Depression is characterized by poor executive function, but – counterintuitively – in some studies, it has been associated with highly accurate performance on certain cognitively demanding tasks. The psychological mechanisms responsible for this paradoxical finding are unclear. To address this issue, we applied a drift diffusion model (DDM) to flanker task data from depressed and healthy adults participating in the multi-site Establishing Moderators and Biosignatures of Antidepressant Response for Clinical Care for Depression (EMBARC) study.

Method. One hundred unmedicated, depressed adults and 40 healthy controls completed a flanker task. We investigated the effect of flanker interference on accuracy and response time, and used the DDM to examine group differences in three cognitive processes: prepotent response bias (tendency to respond to the distracting flankers), response inhibition (necessary to resist prepotency), and executive control (required for execution of correct response on incongruent trials).

Results. Consistent with prior reports, depressed participants responded more slowly and accurately than controls on incongruent trials. The DDM indicated that although executive control was sluggish in depressed participants, this was more than offset by decreased prepotent response bias. Among the depressed participants, anhedonia was negatively correlated with a parameter indexing the speed of executive control ($r = -0.28$, $p = 0.007$).

Conclusions. Executive control was delayed in depression but this was counterbalanced by reduced prepotent response bias, demonstrating how participants with executive function deficits can nevertheless perform accurately in a cognitive control task. Drawing on data from neural network simulations, we speculate that these results may reflect tonically reduced striatal dopamine in depression.

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Introduction

How does depression affect higher-order cognition? Given its association with maladaptive rumination (Nolen-Hoeksema, 1991) and abnormal frontal lobe function (Wagner *et al.* 2006), one might expect depression to weaken executive function, which encompasses the exertion of cognitive control to achieve goals despite obstacles. Indeed, a meta-analysis of 113 studies found broadly negative effects of major depressive disorder (MDD) on executive function (Snyder, 2013), linking MDD to impaired performance on tasks tapping inhibition, set-shifting, and working memory updating. Thus, the negative relationship between depression and executive function is well-established.

However, a close reading of the literature reveals a puzzle: several studies report positive effects of depression and sad mood on tasks that would seem to depend on executive function. For instance, Snyder *et al.* (2014) reported that, although anxiety impaired selection from amongst competing response options in three language tasks, increased depression facilitated selection (after accounting for variance associated with anxiety). Along similar lines, Au *et al.* (2013)

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assessed the effects of sad, positive, and neutral moods on decision-making during financial trading. Across two experiments, sad mood was associated with accurate decisions and conservative allocation strategies, leading to financial gains. By contrast, positive mood was linked to inaccurate decisions coupled with aggressive allocations, leading to poor outcomes: while participants in sad moods profited, those in positive moods incurred net losses. Although sad mood and depression are not equivalent, the fact that excessive sadness is a cardinal symptom of depression (APA, 2013) makes these results surprising: one might have expected a negative effect of sad mood on complex financial decisions, which surely involve executive function.

Research with the Eriksen flanker task (Eriksen & Eriksen, 1974) has also yielded counterintuitive findings. Several versions of the flanker task exist, but they share a common structure: participants must report the identity of a centrally presented stimulus that is surrounded by flankers, which call for either the same response as the central stimulus (congruent condition) or the opposite response (incongruent condition). In the arrow flanker task, participants report the direction (left or right) of a central arrow that is flanked by arrows pointing in the same direction (congruent: <<<<< or >>>>) or the opposite direction (incongruent: <<><< or >><>>). Typically, response time (RT) is slower and accuracy is lower in the incongruent condition due to interference introduced by the misleading flankers. Resisting this interference suggests intact executive function.

Against this backdrop, results from two flanker studies are striking (Dubal *et al.* 2000; Dubal & Jouvent, 2004). In these studies, undergraduates with severe anhedonia responded more slowly but also more accurately on incongruent trials than did healthy participants, suggesting that executive function was delayed but intact. Because anhedonia is the second cardinal symptom of MDD (APA, 2013), these data accentuate the paradox: MDD is associated with executive dysfunction, but its defining symptoms – anhedonia and sadness – are sometimes associated with high accuracy on cognitive control tasks. Finally, there is evidence that this result extends to clinical samples, as several studies that have administered the flanker and Stroop tasks to adults with MDD and healthy controls have found slower but more accurate responses in depressed participants, although the accuracy effect is typically non-significant in small samples (e.g. Siegle *et al.* 2004; Chiu & Deldin, 2007; Holmes & Pizzagalli, 2010).

If depression involves diminished executive function, what explains this pattern? To date, answers to this question have appealed to cognitive styles. Depressed individuals adopt a deliberative, analytical stance towards information processing (Andrews *et al.* 2007; Andrews & Thomson, 2009). When a task calls for rapid, intuitive decisions, this is counterproductive and accuracy suffers (e.g. Ambady & Gray, 2002). But when fast responses are likely to produce errors, the careful approach associated with depression can support high accuracy.

This naturally raises a second question: why is depression associated with a systematic information processing style? One possibility is that depressed individuals are especially motivated to avoid the negative emotions triggered by errors (e.g. Robinson *et al.* 2007). Alternatively, depression rumination may be an evolved response that serves to limit distraction and focus cognitive resources in order to identify the causes of low mood (Andrews & Thomson, 2009). These explanations are intriguing, but it may prove useful to study depression in the context of computational models of response inhibition, which provide quantitative estimates of specific cognitive processes that may be sensitive to MDD. We take this approach by applying a modified drift diffusion model (DDM; Ratcliff & McKoon, 2008; Noorani & Carpenter, 2013) to flanker data from healthy controls and a large depressed sample.

Briefly, the model decomposes performance in the flanker task into separate parameters that reflect prepotent response bias, response inhibition, and executive function, providing an opportunity to determine which (if any) of these parameters is affected by depression (Hübner *et al.* 2010; White *et al.* 2011; Pe *et al.* 2013). Furthermore, because the DDM has been fit to data from neural network simulations of cortico-striatal-thalamic circuits (Ratcliff & Frank, 2012; see also Wiecki & Frank, 2013), results from the DDM may suggest hypotheses about brain function in depression. Response inhibition depends on fronto-striatal circuits that receive dopaminergic projections from the midbrain (Wiecki & Frank, 2013), and that are dysfunctional in anhedonic depression (Epstein *et al.* 2006; Pizzagalli *et al.* 2009; Treadway & Zald, 2011; Dillon *et al.* 2014). Consequently, slow but accurate performance in tasks that probe response inhibition – such as the flanker task – may reflect dysfunction in fronto-striatal circuitry, and results from the DDM could suggest which aspects of this circuitry are most strongly affected by depression (Montague *et al.* 2012; Wiecki *et al.* in press).

Method

The data described here were collected in a multi-site study entitled 'Establishing Moderators and Biosignatures of Antidepressant Response for Clinical Care for Depression' (EMBARC) (http://clinicaltrials.gov/show/NCT01407094). Recruiting sites are Columbia University Medical Center in New York City,

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Massachusetts General Hospital in Boston, the University of Texas Southwestern Medical Center in Dallas, and the University of Michigan in Ann Arbor. Participants with unipolar depression completed several behavioral, self-report, and physiological assessments prior to enrolling in a double-blind, placebo-controlled clinical trial designed to identify biomarkers of response to sertraline and bupropion. Data collection is ongoing and the blind is unbroken, thus we are unable to consider treatment outcomes. We present an analysis of flanker task data from the first 100 depressed participants enrolled in the study and 40 healthy controls. McLean Hospital was responsible for analysis of flanker data.

Participant recruitment, eligibility criteria, and reimbursement

Participants were recruited using flyers and posters, and by research coordinators who visited local clinics. Participants provided informed consent following procedures approved by site IRBs. Adults aged 18–65 years of all races and ethnicities were invited to participate. Eligible depressed participants met DSM-IV criteria for non-psychotic MDD, as assessed via the SCID-I/P (First *et al.* 2002), and scored ⩾14 on the self-report version of the 16-item Quick Inventory of Depression Symptomatology (QIDS-SR_{16}; Rush *et al.* 2003); this cut-off corresponds to moderate depression. Exclusion criteria included: lifetime psychotic depressive, schizophrenic, bipolar, schizoaffective, or other Axis I psychotic disorder; current primary diagnosis of obsessive compulsive disorder; substance dependence in the past 6 months (excluding nicotine) or substance abuse in the past 2 months; active suicidality; or unstable medical conditions that would likely require hospitalization during the study. Critically, no depressed participant was being treated with antidepressant or other psychotropic medication for at least 3 weeks when the data described here were collected.

Data from two depressed individuals were excluded due to difficulty following instructions and technical problems, leaving a sample of 98 depressed participants and 40 healthy controls. Controls did not meet criteria for any current or lifetime history of mood, anxiety, eating, dementing, or psychotic disorder, did not meet any of the other exclusion criteria in place for the depressed group, and had a QIDS-SR score of <8. Participants were paid $50 for the session, which included additional testing not described here.

Questionnaires

Participants in the EMBARC study complete an extensive clinical evaluation battery, including clinician- and participant-rated instruments probing various domains, including lifetime diagnosis, personality traits, and social functioning. Because flanker performance is sensitive to anhedonia (Dubal *et al.* 2000; Dubal & Jouvent, 2004) and may be influenced by depressive severity (Chiu & Deldin, 2007), we concentrate on data from the QIDS-SR_{16} and the Snaith Hamilton Pleasure Scale (SHAPS; Snaith *et al.* 1995). The QIDS-SR_{16} is a self-report instrument that assesses core DSM-IV diagnostic criteria for MDD. It has acceptable psychometric properties and demonstrates convergent validity with other measures of depression (Rush *et al.* 2003). The SHAPS was used to assess hedonic capacity and was scored dimensionally, with higher scores indicating greater anhedonia (Franken *et al.* 2007). Finally, we also tested the hypothesis that flanker performance would be negatively associated with the number of depressive episodes reported (we thank an anonymous reviewer for this suggestion). The distribution of number of depressive episodes was positively skewed, thus we binned these data into six categories (number of episodes: 1, $n = 10$; 2–3, $n = 17$; 4–5, $n = 13$; 6–10, $n = 27$; 11–30, $n = 16$; >30, $n = 7$; unrecorded, $n = 2$).

Flanker task

Participants completed a 30-trial practice session that included 15 congruent and 15 incongruent trials. The flanking arrows were presented alone (duration: 100 ms) and were then joined by the central arrow (50 ms); the total stimulus duration was thus 150 ms. Participants were asked to indicate whether the center arrow pointed left or right by pressing a button, and accuracy and RT were recorded.

Participants then completed five blocks of 70 trials (46 congruent, 24 incongruent), for a total of 350 trials (230 congruent, 120 incongruent). To ensure adequate difficulty, a response deadline corresponding to the 85th percentile of the RT distribution on incongruent trials in the preceding block was established; for the first block, the practice RT distribution was used (Holmes *et al.* 2010). Stimulus presentation was followed by a fixation cross (1400 ms). If the participant did not respond by the response deadline, a screen reading 'TOO SLOW!' was presented (300 ms). Participants were told that if they saw this screen, they should speed up. If a response was made before the deadline, the 'TOO SLOW!' screen was omitted and the fixation cross remained on screen for the 300 ms interval. Finally, each trial ended with presentation of the fixation cross for an additional 200–400 ms. Thus, trial duration varied between 2050–2250 ms. The sequence of congruent and incongruent trials was created using optseq2 (http://surfer.nmr.mgh.harvard.edu/optseq/) and was identical across participants.

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While data collection was ongoing, block-by-block feedback was added to the paradigm to maintain performance at desired levels. If participants made fewer than three incongruent errors in a block, the following instructions were presented after the block: 'Remember to respond as QUICKLY as possible while still being accurate'. If ⩾6 incongruent errors were made, the screen read, 'Remember to respond as ACCURATELY as possible while still being fast'. Otherwise, the screen read, 'Please respond as quickly and accurately as possible'. Block-by-block feedback was presented to 7/40 controls and 42/98 depressed participants.

Quality control

Quality control checks were used to exclude datasets characterized by unusually poor performance. First, for each participant outlier trials were defined as those in which the raw RT was <150 ms or the log-transformed RT exceeded the participant's mean ± 3S.D., computed separately for congruent and incongruent stimuli. Second, we excluded datasets with: ⩾35 RT outliers (>10% of trials), <200 outlier-free congruent trials, <90 outlier-free incongruent trials, or <50% correct for congruent or incongruent trials. Data from 92 depressed and 37 healthy participants passed these checks and constitute the final sample. Trials characterized by RT outliers were excluded from all analyses.

Analysis of flanker interference effects on accuracy and RT

We computed linear mixed models on trial-level RT and accuracy data using the lme4 package (version 1.1.7) in the R software environment (R Core Team, 2013). In the first model, RT was the dependent variable. We expected depressed adults to respond more slowly than controls, particularly in response to incongruent stimuli (Snyder, 2013), thus we included Group and Stimulus as independent variables. Furthermore, errors are typically faster than correct responses on incongruent but not congruent trials in the flanker task (Wiecki & Frank, 2013), and there is evidence of hypersensitivity to errors in MDD (Chiu & Deldin, 2007; Holmes & Pizzagalli, 2008), thus Accuracy was added as another independent variable. Site was included as covariate. In the second model, accuracy was the dependent variable and the independent variables were Group and Stimulus, with Site as a covariate. Because accuracy was scored as 0 or 1, logistic regression was used for this model. Participant was entered as a random effect in both models. Follow-up tests for significant interactions were conducted using the lsmeans (version 2.11) package in R. Additional analyses focused on congruency sequence effects (Gratton *et al.* 1992) and post-error behavioral adjustments (Rabbitt, 1966; Laming, 1979) did not reveal any group differences; they are presented in the Supplementary online Appendix.

Computational modeling

Our computational model uses a modified version of the Linear Approach to Threshold with Ergodic Rate (LATER; Noorani & Carpenter, 2013); the key modification is that noise in the accumulation process is explicitly modeled. This should not yield qualitatively different interpretations as these models are closely related (Bogacz *et al.* 2006; Donkin *et al.* 2011). Behavior reflects the output of three mechanisms: (i) a prepotent, reflexive mechanism biased to respond according to the distracting flankers; (ii) inhibitory control, which can suppress the prepotent response tendency; and (iii) executive control, needed to initiate the correct response on incongruent trials. As shown in Fig. 1, each mechanism is modeled as a drift process that progresses towards a shared threshold (i.e. one model parameter – denoted 'a' – controls the threshold setting for all three mechanisms). The drift processes reflect the accumulation of evidence from the stimulus presented on each trial, and they are noisy to simulate noise in the environment and sensory systems. The response executed by the model depends on which drift process crosses its threshold first. See online Appendix for details regarding the algorithm used to simulate trial-level data.

On congruent trials, responses are committed when the prepotent accumulator reaches threshold; because all arrows point in one direction on congruent trials, the inhibitory and executive control mechanisms are inactive. By contrast, the less frequent incongruent trials involve a race between the prepotent accumulator, which responds in agreement with the flanking arrows (Fig. 1, top), and the executive control unit, which responds according to the central arrow (Fig. 1, bottom). Onset of the executive control accumulator is delayed by a constant (Fig. 1, bottom left) that simulates time needed to retrieve and apply rules on incongruent trials (i.e. respond to the central arrow, not the flankers; Wiecki & Frank, 2013). If the prepotent accumulator crosses its threshold first, the model commits an error (Fig. 1, top right). By contrast, if the executive control accumulator wins the race, the model makes the correct response (Fig. 1, bottom right). Finally, the inhibitory control accumulator acts as a brake, stopping the prepotent accumulator when its threshold is reached (Fig. 1, middle). Thus, the model has the following parameters: a shared threshold setting for all accumulators; drift rates for the prepotent, inhibitory, and executive control accumulators; a delay to onset for the executive control accumulator;

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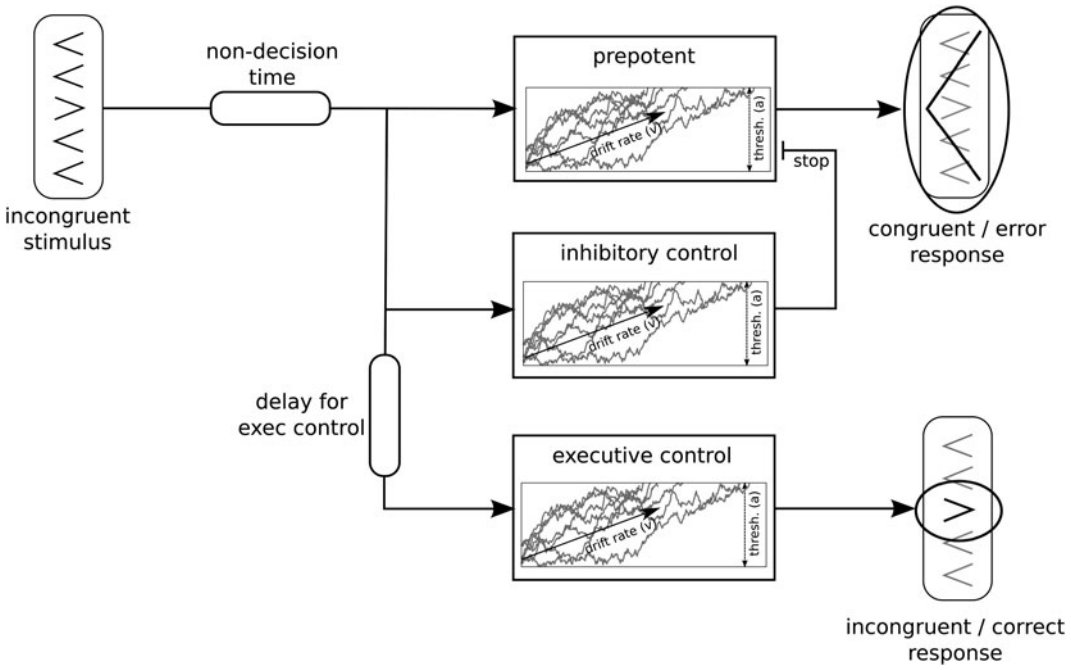

Fig. 1. Computational model, adapted from the LATER model (Noorani & Carpenter, 2013) for application to the flanker task.

and a constant, non-decision time capturing motor execution (Fig. 1, top left). RT corresponds to the passage time of the winning accumulator.

We fit the DDM to each participant's full distribution of RT data from congruent and incongruent trials simultaneously, and used Powell optimization (Powell, 1964) with basin hopping (Wales & Doye, 1997) to find the best-fitting model parameters while avoiding local maxima. Threshold settings and prepotent drift rate were shared across congruent and incongruent trials, while the inhibitory and executive control parameters were only fit to data from incongruent trials. Model fit was evaluated by probability density approximation (PDA; Turner & Sederberg, 2014), which uses kernel density estimation of samples generated by the model (see online Appendix for details) and does not require a closed-form solution of the likelihood function. Optimal model fits were found by maximizing the summed log-likelihood (evaluated using PDA) of the RT and choice data from each subject. Weakly informative priors were placed on model parameters to constrain extreme model fits. Finally, we compared best-fitting DDM parameters across the groups.

Results

Demographics and clinical measures

There were no group differences (ts < 1.1, ps > 0.27) in age (controls: 36.22 ± 14.32; depressed: 39.16 ± 12.99) or years of education (controls: 15.77 ± 4.52; depressed: 15.06 ± 2.43). QIDS-SR_{16} scores were higher in depressed participants (18.48 ± 2.87) *versus* controls (1.46 ± 1.30), reflecting eligibility criteria. The mean QIDS-SR_{16} score in the depressed group indicates moderate depression (Rush *et al.* 2003). SHAPS scores were higher in depressed participants (33.83 ± 5.99) *versus* controls (21.05 ± 5.37) ($t_{127} = 11.27$, $p < 0.001$).

Flanker interference effects

RT

Controls (Fig. 2*a*) and depressed participants (Fig. 2*b*) responded more quickly on correct congruent trials *versus* correct incongruent trials, consistent with flanker interference. Both groups showed the opposite pattern when making errors, generating faster RTs on incorrect incongruent trials *versus* incorrect congruent trials. This pattern led to a Stimulus × Accuracy interaction ($Z = 22.82$, $p < 0.001$).

The model also returned a Group × Accuracy interaction ($Z = 3.28$, $p = 0.001$), and a Group × Stimulus interaction ($Z = 2.05$, $p = 0.040$). Follow-up contrasts linked the Group × Accuracy interaction to a difference on correct trials: depressed participants were slower than controls ($Z = -2.49$, $p = 0.013$). There was no difference on error trials ($p = 0.424$). The Group × Stimulus interaction reflected a difference on incongruent trials, with depressed participants responding more slowly than

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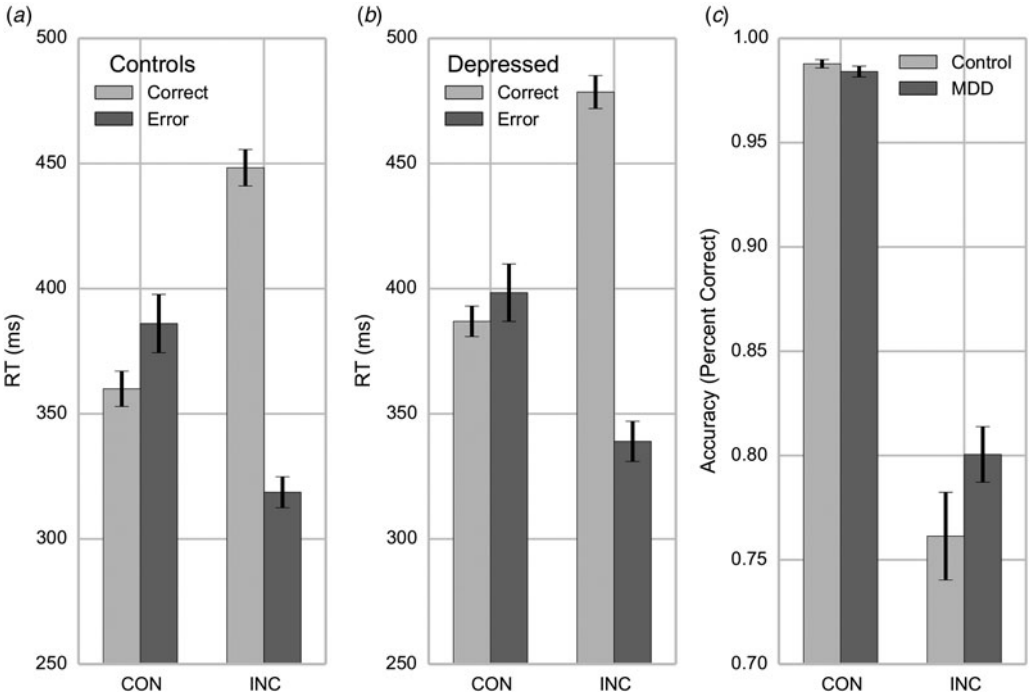

Fig. 2. Flanker interference effects on (*a*) response time (RT) in controls, (*b*) RT in depressed participants, and (*c*) accuracy in both groups. Error bars indicate standard error of the mean. CON, Congruent; INC, incongruent.

controls ($Z = -2.09$, $p = 0.037$). Depressed participants were also slower on congruent trials, but this difference was not significant ($p = 0.242$). Thus, depressed participants responded more slowly than controls, with significant differences for correct responses and responses to incongruent stimuli. Slow responses on incongruent trials are common in depressed samples, consistent with executive function deficits (Snyder, 2013).

Accuracy

As shown in Fig. 2*c*, both groups were more accurate when responding to congruent *versus* incongruent stimuli, consistent with flanker interference. However, depressed participants were more accurate than controls on incongruent trials, leading to a Group × Stimulus interaction ($Z = 3.90$, $p < 0.001$). Follow-up linear contrasts confirmed a (marginal) Group effect on incongruent trials ($Z = -1.94$, $p = 0.053$) that was absent on congruent trials ($Z = 0.68$, $p = 0.495$). This result echoes reports of better accuracy on incongruent trials in sad and anhedonic samples (Dubal *et al.* 2000; Au *et al.* 2013).

Block-by-block feedback

Two analyses investigated whether including block-by-block feedback for some participants influenced the RT and accuracy results. First, the linear models were re-computed with Version (feedback, no feedback) as an additional covariate. Version was not significant in either model, and all interactions reported above remained significant. Second, we re-computed the original models including only participants who did not receive feedback (33 controls, 42 MDD). Again, all reported interactions remained significant. Thus, including block-by-block feedback for some participants did not strongly influence the findings.

Computational modeling

Table 1 shows best-fitting parameter values from the model. The executive control drift rate on incongruent trials was lower in depressed versus healthy participants ($t_{127} = -2.05$, $p = 0.043$), consistent with slower executive function. However, the prepotent drift rate was also lower in depressed participants ($t_{127} = -2.40$, $p = 0.018$). This is intriguing because weak prepotent bias might offset the executive control deficit (see online Appendix for distributions of both parameters).

To test this hypothesis, we conducted simulations in which the model was used to generate artificial RT and accuracy data. In the first simulation, all model parameters were set to the best-fitting values for controls with the exception of the executive control drift rate, which was matched to the best-fitting value for the depressed participants. As shown in Fig. 3, this resulted in prolonged incongruent RT but no group difference in accuracy. In the second simulation, we returned the executive control drift rate to the controls' value

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Table 1. *Mean (±S.D.) best fitting parameter values from the drift diffusion model*

Model parameter	Healthy controls	Depressed participants
Non-decision time (ms)	212 ± 34	207 ± 59
Prepotent drift rate*	7.00 ± 1.45	6.37 ± 1.28
Inhibitory drift rate	9.76 ± 1.95	9.67 ± 2.18
Executive control: drift rate*	10.38 ± 2.61	9.28 ± 2.80
Executive control: delay to onset (ms)	131.23 ± 25.27	138.97 ± 34.99
Threshold	1.05 ± 0.33	1.14 ± 0.44

* Depressed < Controls, $p < 0.05$.

but set the prepotent drift rate to the best-fitting value for depressed participants. As can be seen in Fig. 3, this modulation accounted for the increase in accuracy but failed to capture the slow RTs seen on correct incongruent trials in depressed participants. The fact that there is no variability in accuracy when allowing executive control drift rate to change nor variability in RT when allowing prepotent drift rate to change is expected because these two parameters affect incongruent RT and accuracy independently in this parameter setting. In the third simulation, we set both the executive control and prepotent drift rates to best-fitting values for the depressed group, leaving all other parameters set to optimal values for controls. This yielded the pattern most similar to data from depressed participants (Fig. 3): responding on correct incongruent trials was slower, and the incongruent error rate was reduced. We corroborated this finding by performing model comparison using the Bayesian Information Criterion (BIC): lower scores indicate better model fit. The best-fitting model was the one that allowed for group differences in executive control and prepotent drift rate (BIC = 115.13); manipulating only executive drift rate (BIC = 124.33) or prepotent drift rate (BIC = 179.03) produced worse fits. Thus, accurate performance can emerge if executive control is sluggish, provided prepotent response bias is also decreased. The combination is critical: neither factor alone could account for the data.

Correlations

As shown in Fig. 4, we found a significant Pearson correlation between anhedonia, as assessed by the SHAPS total score, and executive control in the MDD group ($r = -0.28$, $p = 0.007$). The correlation with prepotent drift rate was not significant ($r = -0.09$, $p = 0.40$), and neither drift rate was correlated with QIDS-SR_{16} scores in the MDD group. Number of depressive episodes was positively correlated with congruent accuracy ($r = 0.23$, $p = 0.03$) and median correct RT on incongruent trials ($r = 0.22$, $p = 0.04$).

Discussion

This study yielded three main results. First, responding on incongruent trials was slower but (marginally) more accurate in depressed *versus* healthy participants. Second, the DDM uncovered slow executive control and reduced prepotent response bias in the MDD group, with simulations indicating that the combination of these two factors best accounted for the observed group differences in accuracy and RT. Third, executive control was negatively correlated with anhedonia in depressed participants. These findings extend recent DDM research in depression and point to a candidate neural mechanism: tonically reduced striatal dopamine.

Using the DDM to probe depression

This study extends recent work by Vallesi *et al.* (2015) that used the standard DDM to analyze data from a color perception task. Relative to controls, depressed participants in that study showed a lower drift rate that was negatively correlated with Hamilton Depression Rating Scale (HAMD) scores (Hamilton, 1960). The current findings extend this study in two ways. First, the modified DDM afforded increased precision: we also found a negative effect of depression on drift rate, but it was specific to executive control and prepotency. Second, because the HAMD is sensitive to several facets of depression (Bagby *et al.* 2004), it is difficult to know which ones are related to reduced drift rate. We found a negative relationship between executive control drift rate and anhedonia, linking this particular aspect of depression to deficits in executive function. Assessing the reliability and specificity of this relationship is a key goal for future work.

Additional points of convergence with the report by Vallesi *et al.* (2015) merit consideration. First, neither study found a group difference in non-decision time, which captures processes such as response execution. This suggests that the observed group differences do not reflect psychomotor slowing. Second, neither study found an effect of depression on decision threshold. Consequently, the results do not simply reflect a speed-accuracy trade-off in depressed participants, because such a trade-off should yield a threshold difference (Dutilh *et al.* 2012).

Reduced striatal dopamine in depression

We speculate that reduced executive and prepotent drift rates in depression reflects dysfunction in circuits

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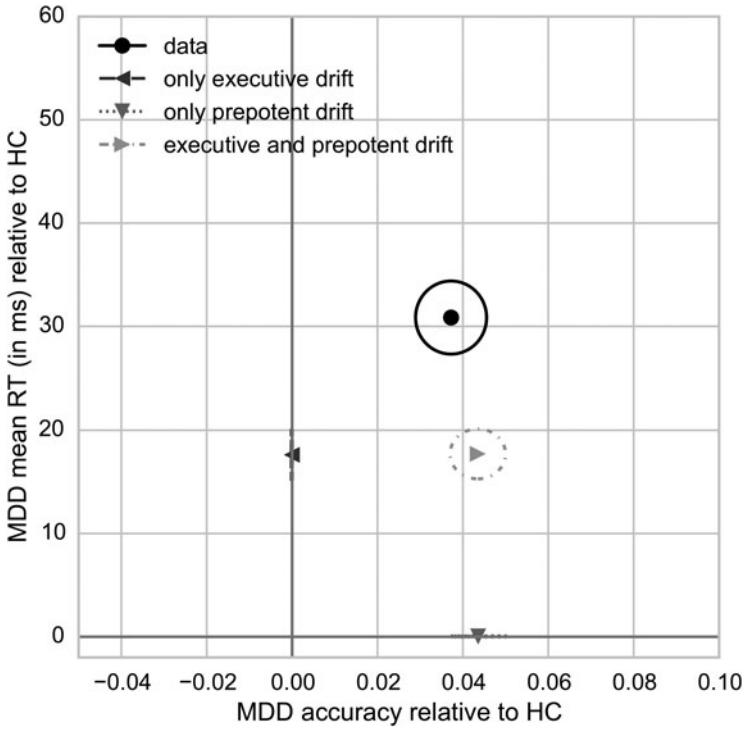

Fig. 3. Response time (RT) simulations isolate the effects of particular cognitive processes on behavior. Points indicate accuracy on incongruent trials (x axis) and mean RT on correct incongruent trials (y axis) for major depressive disorder (MDD) subjects relative to healthy controls (HC). Ellipses indicate standard error of the mean. The collected data revealed that depressed participants were slower and more accurate than controls on incongruent trials ('data', circle). Simulated data show that manipulation of only the executive control drift rate ('only executive drift', left-facing arrowhead) captured slowing in the MDD group but not the group difference in accuracy (difference relative to model with all parameters set to HC values). Conversely, manipulation of only the prepotent drift rate ('only prepotent drift'; down-facing arrowhead) captured increased accuracy in the MDD group but not the increased RT (difference relative to model with all parameters set to HC values). Simultaneous adjustment of the executive control and prepotent drift rates ('executive and prepotent drift'; right-facing arrowhead) yielded results that most closely match the combination of increased accuracy and prolonged incongruent RT in depressed participants. Note that the overall model fit displayed here is sub-optimal because, in order to isolate the effect of manipulating the prepotent and executive drift rates, all other parameters were set to best-fitting values from controls; overall model fit is improved when all parameters are set to optimal values for the MDD group.

that connect the basal ganglia to the frontal cortex, and that receive dopaminergic innervation from the midbrain. Selective activation of basal ganglia neurons in the Go and NoGo pathways acts to facilitate or suppress action plans stored in frontal cortex, making their execution more or less likely (Chevalier & Deniau, 1990; Mink, 1996). The balance between facilitation and suppression is modulated by dopamine, which excites Go neurons and inhibits NoGo neurons (Frank, 2005). Low concentrations of striatal dopamine disinhibit NoGo neurons and weakly activate Go neurons, leading to response slowing (Wiecki *et al.* 2009; Wiecki & Frank, 2010). This is true for habitual actions (parameterized by the prepotent drift rate) and volitional actions (parameterized by the executive control drift rate) (Wiecki & Frank, 2013). Thus, low striatal dopamine could account for reduced prepotent and executive control drift rates in depressed participants, consistent with independent evidence of abnormal striatal dopamine concentration and function (Treadway & Zald, 2011; Dillon *et al.* 2014). To resolve the paradox introduced earlier, tonically reduced striatal dopamine may help explain the coexistence of executive function deficits and accurate performance in depressed samples. Moreover, the positive correlation between number of depressive episodes and correct RT on incongruent trials indicates that mechanisms supporting action selection may be sensitive to cumulative effects of depression. Neuroimaging techniques sensitive to dopamine are needed to test these conjunctures.

Our data are intriguing in light of work on predictors of antidepressant treatment response. Specifically, psychomotor slowing predicts a poor response to selective serotonin reuptake inhibitors (SSRIs; Taylor *et al.* 2006; Bruder *et al.* 2014) but a good response to bupropion (Herrera-Guzmán *et al.* 2008; Bruder *et al.* 2014), which

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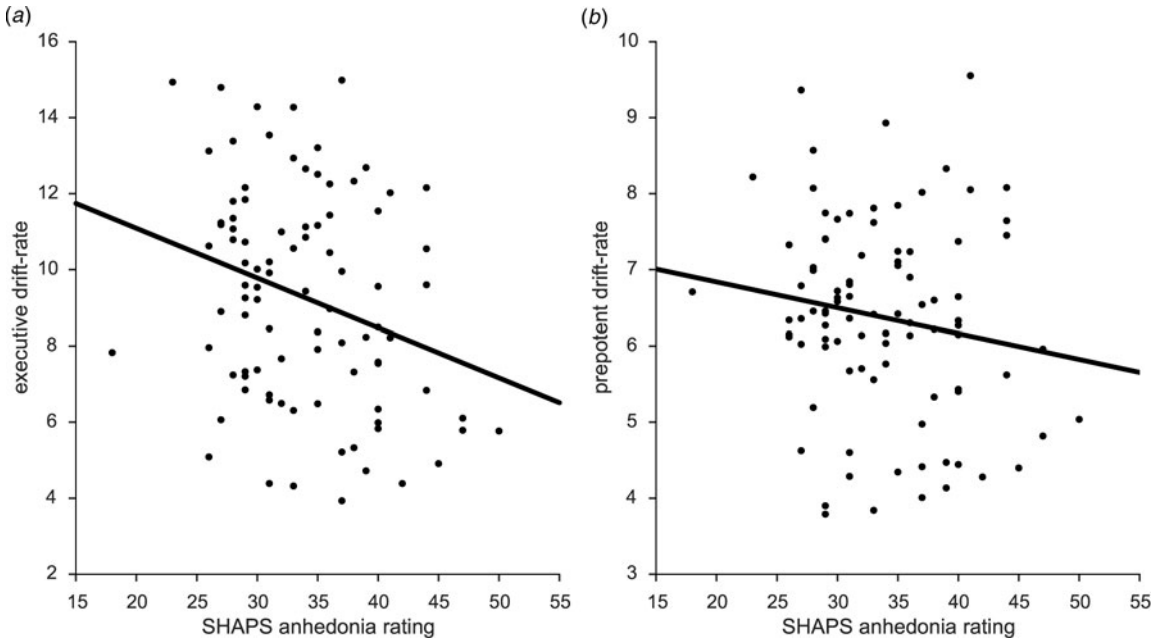

Fig. 4. Self-reported anhedonia was negatively correlated with executive control drift rate (*a*) but not prepotent drift rate (*b*) in the depressed group. SHAPS, Snaith Hamilton Pleasure Scale.

is a dopamine/noradrenaline reuptake inhibitor. The current results raise the possibility that slow but accurate performance on the flanker task, although not directly attributable to psychomotor slowing, may predict a better response to bupropion *versus* SSRIs. When treatment outcome data from the EMBARC study are available, we will be able to test this hypothesis.

Limitations

Two important limitations deserve mention. First, negative effects of depression are typically strongest in unconstrained tasks (Hertel, 1997). The flanker task features clear instructions and few response options, thus it may be less sensitive to depression and depressive rumination than more open-ended tasks. Second, while the computational model used here has been validated on the related antisaccade task (Noorani & Carpenter, 2013), other models have been successfully applied to the flanker task (Hübner *et al.* 2010; White *et al.* 2011). The relationship between these models is not well-established, and they might suggest negative effects of depression on different parameters.

Conclusions

Depressed participants responded more slowly and accurately than controls in the flanker task, consistent with prior findings. Because depression impairs executive function, highly accurate performance has been difficult to explain. We used computational modeling to show that reduced prepotent response bias offset slow executive control in MDD, and we speculate that these abnormalities may reflect reduced striatal dopamine.

Supplementary material

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0033291715000276.

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Declaration of of Interest

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