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Selective Attentional Enhancement and Inhibition of Fronto-Posterior Connectivity by the Basal Ganglia During Attention Switching

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The prefrontal cortex and the basal ganglia interact to selectively gate a desired action. Recent studies have shown that this selective gating mechanism of the basal ganglia extends to the domain of attention. Here, we investigate the nature of this action-like gating mechanism for attention using a spatial attention-switching paradigm in combination with functional neuroimaging and dynamic causal modeling. We show that the basal ganglia guide attention by focally releasing inhibition of task-relevant representations, while simultaneously inhibiting task-irrelevant representations by selectively modulating prefrontal top–down connections. These results strengthen and specify the role of the basal ganglia in attention. Moreover, our findings have implications for psychological theorizing by suggesting that inhibition of unattended sensory regions is not only a consequence of mutual suppression, but is an active process, subserved by the basal ganglia.

Keywords: DCM, fMRI, human, prefrontal cortex, striatum

Introduction

The limited processing capacity of our brain requires us to select relevant information for further processing and filter out irrelevant information from our complex environment. Over the years, influential studies provided evidence for a model in which this selection is achieved by attentional gain of sensory information. One key region in this model is the prefrontal cortex, which enhances processing of task-relevant representations by exerting top–down control over sensory areas (Miller and Cohen 2001). However, it is unclear how the prefrontal cortex knows which stimuli are task-relevant. Recent models suggest that the prefrontal cortex might interact with the subcortical basal ganglia to control attention (Hazy et al. 2007). The basal ganglia receive information from virtually the entire brain (including limbic structures) and, consequently, they receive all information necessary to assign behavioral relevance to external stimuli, given the current state of the body and environment. Anatomically, the prefrontal cortex and basal ganglia are connected via a set of functionally segregated circuits, allowing transmission of cortical signals to the basal ganglia, and via the thalamus, back to the cortex (Alexander et al. 1986). Most research on these cortico-basal ganglia circuits has focused on the motor circuit, connecting the motor cortex and the putamen, and this has led to a variety of models of basal ganglia function: Inhibitory connections between the basal ganglia and thalamus have provided the basis for classic models, emphasizing their role in the inhibition of task-irrelevant actions (Hikosaka and Wurtz 1989; Alexander and Crutcher 1990; Nambu et al. 2002; Aron 2007). Conversely, other models have highlighted their importance for the selection of task-relevant actions, for example, by lowering response thresholds (Lo and Wang 2006; Forstmann et al. 2008). A third group of models suggests that desired actions are selectively gated by a combination of these mechanisms: a focal release mechanism for selecting task-relevant actions and an inhibitory mechanism for inhibiting task-irrelevant actions (Mink 1996; Cui et al. 2013; Surmeier 2013).

Computational models suggest that, to control attention, the prefrontal cortex and basal ganglia interact via similar selective gating mechanisms. Specifically, they suggest that the basal ganglia select which of multiple prefrontal representations guides behavior (Frank 2005, 2011; Hazy et al. 2007). However, the inhibitory versus facilitatory nature of this attentional gating mechanism remains unclear. For example, there is controversy about whether attentional inhibition is an active top–down process (Gazzaley et al. 2005; Chadick and Gazzaley 2011) or a passive consequence of biased competition via mutual inhibition in the posterior cortex (Desimone and Duncan 1995).

In a recent neuroimaging study, we found evidence for an attentional gating mechanism by the basal ganglia. Using dynamic causal modeling (DCM) of fMRI data, we showed that the basal ganglia increased connectivity between the prefrontal cortex and visual cortex during attention switching (van Schouwenburg et al. 2010). Here, we aim to extend these findings by investigating the mechanisms underlying such selective gating by the basal ganglia.

We adopt a network approach to 1) extend models of basal ganglia function from the motor to the cognitive domain and 2) dissociate cognitive models of active versus passive attentional inhibition. Specifically, we ask whether the basal ganglia select task-relevant representations for attention by focally releasing inhibition of task-relevant representations and/or by inhibiting task-irrelevant representations. A spatial attention-switching paradigm was used, enabling comparison of blood oxygen level–dependent (BOLD) signals in the task-relevant and task-irrelevant visual hemifields by assessing spatially selective BOLD signals. DCM was used to assess whether these effects are controlled by the basal ganglia through selective attentional gating of prefrontal top–down connections with the relevant and/or irrelevant visual cortex. More specifically, DCM allowed us to assess whether the basal ganglia increase fronto-posterior connectivity with the newly attended visual hemifield and/or decrease fronto-posterior connectivity with the now irrelevant visual hemifield (Fig. 1).

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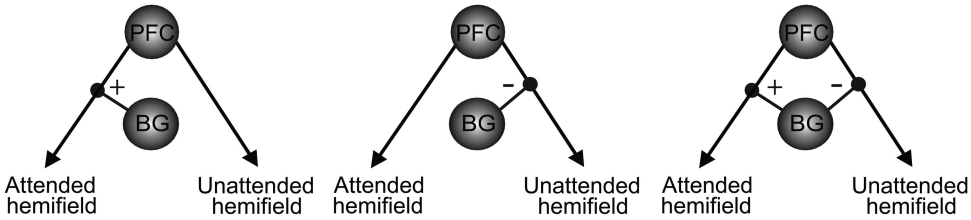

Figure 1. Tested models of basal ganglia function in top–down attention. Three alternative models of basal ganglia (BG) function were tested. BG activity could 1) increase connectivity between the prefrontal cortex (PFC) and the attended hemifield, 2) decrease connectivity between the prefrontal cortex and the unattended hemifield, or 3) selectively gate prefrontal top–down signals through a combination of these mechanisms.

Materials and Methods

Subjects

Data are reported from 17 subjects (4 males, mean age 20.5, range 18–25). Thirty-two subjects were prescreened behaviorally during an intake session. Only subjects who performed well on the task (for reasons described below) (accuracy>50% on repeat trials; 5 excluded), and who were able to maintain fixation during the task as assessed by visual inspection of eye tracking data (6 excluded) were invited for the fMRI session. Of the 21 subjects who were scanned, 2 were excluded due to excessive head movement in the scanner (>2× voxel size), 2 were excluded as they completed <25% of the task. One subject who completed 90% of the experiment was included in all analyses.

Exclusion criteria were claustrophobia, neurological, cardiovascular diseases or psychiatric disorder, regular medication (more than 3 times per week for at least a 1-month period; excluding contraceptive medication or vitamin supplements) or recreational drugs use (more than 2 times per month), heavy smoking (at least 1 cigarette every day or more than 5 cigarettes on any day), excessive alcohol consumption (more than 10 drinks per week) or metal parts in the body. All subjects had normal or corrected-to-normal vision and were right-handed. They all gave written informed consent and were compensated for participation. The study was approved by the local ethics committee.

Paradigm

Following our prior work (van Schouwenburg et al. 2010), we used a spatial attention-switching paradigm in which subjects were instructed to switch attention when they detected a change in a stimulus at an unattended location. Subjects had to fixate on a centrally presented fixation cross and to covertly attend to a stimulus either on the left or right side of the fixation cross. Stimuli consisted of a pattern of moving dots that could move in 1 of 4 directions (left, right, up, down). On each trial, as soon as they detected a change, subjects had to indicate the direction of the moving dots on the attended side by pressing 1 of 4 buttons with the index and middle fingers of their left and right hands (leftward movement: right index finger, rightward movement: right middle finger, upward movement: left middle finger, downward movement: right index finger). The direction of motion on each trial was random and, as a consequence, the response hand (left vs. right) was not confounded by the attended hemifield (left vs. right). Note that stimuli were presented in a continuous stream and were not separated by an intertrial interval. No feedback was presented to the subjects. The start of a new repeat trial was defined as a change in the direction of motion at the attended side. On repeat trials, random noise was presented at the unattended side. After a variable number of correct responses, a switch trial was presented on which a change in the direction of motion at the attended side was accompanied by an initiation of motion at the unattended side (Fig. 2). Switch trials required subjects to switch their attention (covertly) to the other side and make a button press that corresponded with the direction at the newly attended side. On switch trials, the direction of motion at the attended side was always incongruent with that at the unattended side enabling us to identify the attended stimulus. Only trials on which subject switched successfully (identified based on their response) were included for further analyses. After a successful switch, motion at the newly unattended side changed to random noise. No change in direction occurred at the newly attended side and hence no response was required; these events were not analyzed.

The stimuli consisted of 600 dots that were replotted at each time frame, at a 60-Hz refresh rate. A subset of the dots moved coherently in one direction while the other dots were replotted randomly on each time frame. Coherence of the dots varied between 30% and 75% with steps of 5%. The time between the onset of subsequent repeat trials (trial duration) varied between 1.3 and 6.7 s (mean 3.3 s standard deviation [SD] 0.02 s) and was randomized across trials. To decrease predictability of trial onset, shorter trial durations were more frequent than longer ones (according to a Poisson distribution), and the same trial duration was not repeated more than twice in a row. In addition, the coherence level on repeat trials was not repeated more than twice in a row. Responses were collected for the whole trial duration. A switch trial was presented after 3–8 consecutive correct responses on repeat trials (randomized according to a Poisson distribution). As a consequence, subjects with few correct responses progressed very slowly on the task. To keep scanning time to a minimum, we excluded subjects that had an accuracy below 50% on the prescreening. The required number of correct responses was not repeated more than twice consecutively. A total of 100 switch trials were presented, 10 of each coherence level. The same coherence was not presented on 2 consecutive switch trials. Because subjects responded more slowly on switch trials compared with repeat trials the trial duration for switch trials was increased (between 2.6 and 6.7 s, average trial duration 3.5 ± SD 0.10 s) to prevent subjects from missing too many switch trials. The experiment was divided in 5 blocks with breaks in-between. Subjects were presented with an average of 651 repeat trials (± SD 86 trials). The paradigm was programed using PsychToolbox in Matlab.

Behavioral Analysis

We focused behavioral analysis on reaction times and accuracy. The difference between reaction times on switch trials and repeat trials was assessed using a paired sample *t*-test and we report effects at $P < 0.05$ (two-tailed). We report mean reaction times ± SEM across subjects.

fMRI Data Acquisition

Whole-brain imaging was performed on a 3-Tesla MR scanner (Magnetrom Trio Tim, Siemens Medical Systems, Erlangen, Germany). Functional data were obtained using a multiecho gradient T_2*-weighted echo-planar scanning sequence (Poser et al. 2006) with BOLD contrast (38 axial-oblique slices, repetition time, 2.32 s; echo-times, 9.0, 19.3, 30, and 40 ms; in plane resolution, 3.3 × 3.3 mm; slice thickness, 2.5 mm; distance factor, 0.17; field of view, 211 mm; flip angle, 90°). Visual stimuli were projected on a screen and were viewed through a mirror attached to the head coil. In addition, a high-resolution T_1-weighted magnetization-prepared rapid-acquisition gradient echo anatomical scan was obtained from each subject (192 sagittal slices; repetition time, 2.3 s; echo time, 3.03 ms; voxel size, 1.0 × 1.0 × 1.0 mm; field of view, 256 mm).

fMRI Data Analysis

Data analysis was performed using SPM8 software (Statistical Parametric Mapping; Wellcome Trust Centre for Cognitive Neuroimaging, London, UK). Anatomical images were spatially coregistered to the mean of the functional images and normalized using a unified

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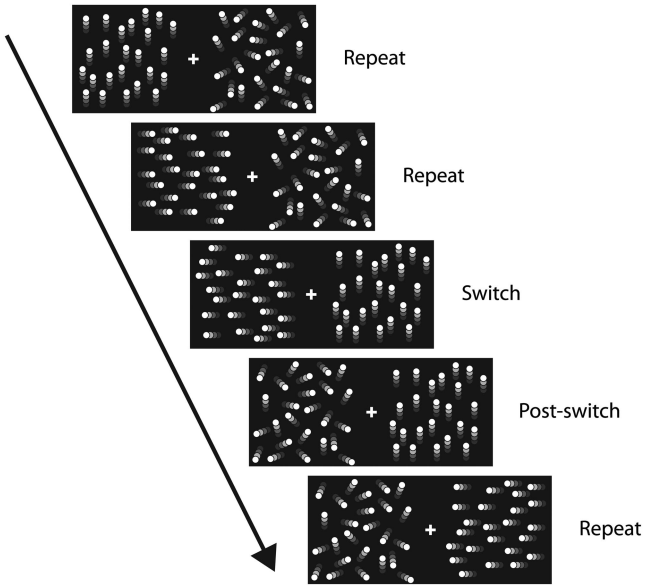

Figure 2. Attention-switching paradigm. Subjects were instructed to covertly attend to the left or right visual hemifield. On each trial (repeat trials), they had to discriminate the direction of a moving dot pattern at the attended side, while ignoring the unattended side (random noise). On switch trials, a moving dot pattern at the unattended side triggered a switch in attention. Subjects then continued performing the task at the opposite visual hemifield. Postswitch events (on which no response was required) were excluded from the analyses.

segmentation approach. For the functional data, realignment parameters were estimated for the images acquired at the first echo time and subsequently applied to images resulting from the 3 other echoes. The echo images were combined by applying a PAID-weight algorithm assessing the signal-to-noise ratio as described by Poser et al. (2006). Thirty volumes, acquired before each session, were used as input for this algorithm. Further preprocessing procedures of functional images consisted of slice-timing correction, spatial normalization using the same transformation matrix as estimated from the anatomical images and spatial smoothing using a Gaussian kernel of 6-mm full width at half-maximum. These preprocessed images were used for all analyses.

In a general linear model, we included 4 regressors of interest according to the 2×2 factorial design: 1) switch attention to left, 2) switch attention to right, 3) repeat attention left, 4) repeat attention right. In addition, we modeled all error trials, missed trials, trials after an error or missed trial, and the first trial after a switch trials (on which no response was required) in a (single) regressor of no interest. In addition, the 6 realignment parameters were modeled as regressors of no interest. All paradigm-related regressors were modeled as delta functions at the onset of the trial and were convolved with a canonical hemodynamic response function including time derivatives. Time series were high-pass filtered (128 s).

Parameter estimates for the regressors of interest, derived from the mean least-squares fit of the model to the data, were estimated at the (subject-specific) first level and were used in a second-level random-effects analysis to assess consistent effects across subjects.

Regions of Interest

In line with our previous study (van Schouwenburg et al. 2010) and our hypotheses outlined in the Introduction, we focused on 4 regions of interest (ROI). ROIs of the basal ganglia and prefrontal cortex were defined using the automated anatomical labeling interface (Tzourio-Mazoyer et al. 2002). Following our prior work (van Schouwenburg et al. 2010), the ROI of the basal ganglia included the caudate nucleus, the putamen, and the pallidum, ROI analyses of the prefrontal cortex focused on the inferior frontal gyrus (IFG) pars opercularis. ROIs of the visual cortex were defined separately for the left and right hemisphere and included V1, V2, V3, V4, and V5 according to the Jülich probabilistic atlas (Eickhoff et al. 2007). Moving dot stimuli are known to activate the motion-sensitive V5/MT region (Zeki et al. 1991; Rees et al. 2000). The main contrast switch versus repeat activated large portions of the visual cortex including peak voxels near coordinates that have previously been reported to coincide with human V5/MT (Kayser et al. 2010) (left [−42 −74 8], $t = 12.59$; right [46 −66 4], $t = 12.42$) (Fig. 4). Overlap with human V5/MT was less clear for the contrasts comparing switch directions (switch-to-left vs. switch-to-right trials and vice versa); clusters were more medial and more inferior than previously reported (Fig. 4, Table 1). Because the primary goal of this study was to elucidate the mechanism underlying spatially selective effects in posterior visual cortex, we focused analyses on visual regions that showed these spatially selective effects. We used MarsBaR (Brett et al. 2002) for definition of ROIs and ROI data extraction.

Inferences were drawn at the voxel level, corrected for multiple comparisons in our small search volumes (ROIs) ($P_{svc} < 0.05$). The height threshold at the voxel level was set at $P < 0.001$ uncorrected for multiple comparisons.

Dynamic Causal Modeling

We used nonlinear DCM (Stephan et al. 2008) to test our hypothesis that top–down influences from the IFG to the visual cortex were modulated by the basal ganglia in a selective manner. More specifically, we aimed to assess whether the basal ganglia increased connectivity between the IFG and the visual cortex that processes the newly attended visual hemifield, and/or decreased connectivity between the IFG and the visual cortex that processes the now irrelevant visual hemifield.

Nonlinear DCM models the hidden neural dynamics of a system of interacting brain regions. Using a nonlinear state equation, neural state changes in the tested DCMs were governed by 3 sets of parameters: 1) driving inputs: parameters that model how brain regions respond to external stimuli, 2) fixed effective connectivity parameters: reflect the coupling between modeled regions driven by the direct inputs, 3) modulation of fixed connections by the neural activity in one of the modeled regions. This model of neural dynamics is combined with a hemodynamic model that describes the transformation of neural activity into a BOLD response. More detail on DCM can be found elsewhere (Friston et al. 2003; Stephan et al. 2008). The posterior probabilities of the parameters from the neural as well as the hemodynamic model are estimated from the measured BOLD data using a Bayesian inversion scheme, implemented in DCM10.

DCM Specification

We constructed a nonlinear DCM, which was based on the model in our previous study, including the basal ganglia, the IFG, and the left and right visual cortex (Fig. 3) (van Schouwenburg et al. 2010). The models included top–down connections from the IFG to the visual cortex nodes. These 2 top–down connections were modulated by basal ganglia activity. Attention to the left and the right visual hemifield were modeled as input to the right and left visual cortex, respectively, and attention switching was modeled as input to the IFG.

In the current implementation of DCM, it is not possible for a modulatory connection to be modulated itself by an external input. Therefore, it is not possible to assess the modulatory influence of basal ganglia activity on fronto-posterior connections during attention switching from left to right versus switching from right to left. In order to test spatially selective gating by the basal ganglia, we created 2 time series for the same basal ganglia voxels: one time series in which we excluded all task-related variance of left-lateralized events (i.e., repeat and switch trials on which subjects were attending/switched to the left hemifield), and one time series in which we excluded all task-related variance of right-lateralized events (i.e., repeat and switch trials on which subjects were attending/switched to the right hemifield). Thus, in each basal ganglia node, only the variance related to trials in which attention was directed to one particular visual hemifield was present. Switch to right was modeled as input to the node containing variance related to right-lateralized events and switch to left was modeled as input to the node containing variance related to left-lateralized events. This model allows us to test the modulatory influence of basal ganglia

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activity on fronto-posterior connections selectively during attention switching and separately for the 2 switch directions.

To assess selective gating by the basal ganglia 3 sets of models were constructed (Fig. 3). The first model set assessed (excitatory) modulation by the basal ganglia of frontal connections to task-relevant visual cortex (i.e., processing the newly attended visual hemifield). The second model set assessed (inhibitory) modulation by the basal ganglia of frontal connections to the task-irrelevant, now unattended, visual hemisphere. In the third model, we included both task-relevant and task-irrelevant modulatory influences of the basal ganglia.

An additional mechanism that can lead to differences in processing of task-relevant and task-irrelevant representations is mutual lateral inhibition of visual areas. Enhanced processing of the task-relevant visual hemifield would lead to enhanced suppression of the task-irrelevant visual hemifield. To assess such effects, the above-described models were constructed with and without reciprocal connections between the left and right visual cortex. Thus, the final model space included 6 models.

Time Series Extraction

For each node, regional time series were summarized by computing the first eigenvector across all voxels within 3 mm of the peak voxel(s) at the group level. For the basal ganglia and the IFG, peak voxels were selected based on the switch versus repeat contrast. We selected the peak voxel within the right IFG [52 12 24] ROI. Our decision to select voxels from the right hemisphere was based on our previous study (van Schouwenburg et al. 2010), the fact that switch-related signals were strongest in the right hemisphere and previous results indicating that the right IFG plays an important role in the deliberate and selective focusing of attention on current relevant information (Gazzaley et al. 2004; Hampshire et al. 2007; Petrides and Pandya 2009). For the basal ganglia, we extracted the (average) time series from peaks in the left [−16 6 −2] and right [18 4 4] basal ganglia. For the left and right visual cortex, peak voxels were selected based on the switch-to-left versus switch-to-right contrast within the right visual cortex ROI [22 −80 −10] and the switch-to-right versus switch-to-left contrast within the left visual cortex ROI [−30 −76 −12]). All time series were mean-centered and variance explained by motion regressors and other regressors of no interest (i.e., error trials) was removed. Additionally, as described above, for the basal ganglia nodes, variance explained by task regressors associated with either "attention left" (both repeat and switch trials) or "attention right" was removed. This resulted in 2 basal ganglia time series with lateralized task-related variance. Importantly, data for both basal ganglia nodes were extracted only once (averaged over the left and right basal ganglia); we did not intend to assess lateralized effects of basal ganglia function.

Table 1
Main effects of task

Region	Cluster size	Local maximum			Statistics
		x	*y*	*z*	*t*-Value
Switch–repeat					
BG	314	30	18	0	10.35
	88	12	−6	16	8.97
	760	−16	6	−2	7.28
	135	18	4	4	6.71
IFG	1135	52	12	24	11.70
	298	−44	4	28	7.62
Visual cortex	6926	−24	−68	−8	14.83
	67	18	−66	28	7.75
Switch to left–switch to right					
Right visual cortex	846	22	−80	−10	10.36
Switch to right–switch to left					
Left visual cortex	973	−30	−76	−12	7.05

Peak voxels (and their corresponding cluster size) are reported that are significant at the voxel level, corrected for multiple comparisons across small volumes of interest.

Bayesian Model Selection

We used the negative free energy approximation to the log model evidence (Friston and Stephan 2007; Stephan et al. 2007) to compare models at the group level, using random-effects Bayesian model selection (BMS) (Penny et al. 2004). The approximated log model evidence balances model fit and model complexity, thereby allowing for comparison of models with different degrees of complexity. One can then derive the exceedance probability XP_k, that is, the probability that a particular model k is more likely than any other model considered, given the group data. To assess evidence for the presence or absence of reciprocal visual cortex connections, we separated the model space into families of models that in- or excluded these reciprocal connections. To assess evidence of excitatory and/or inhibitory modulation by the basal ganglia, we separated the model space into 3 families grouped by the presence/absence of each of these connections (Fig. 3).

Bayesian Model Averaging and Parameter Inference

We then looked at the parameters of the models in the winning family. When it was not possible to distinguish between families based on the model evidence, we used Bayesian model averaging (Penny et al. 2010) to calculate an average parameter estimate for each connection and subject across a set of models, weighted by the posterior

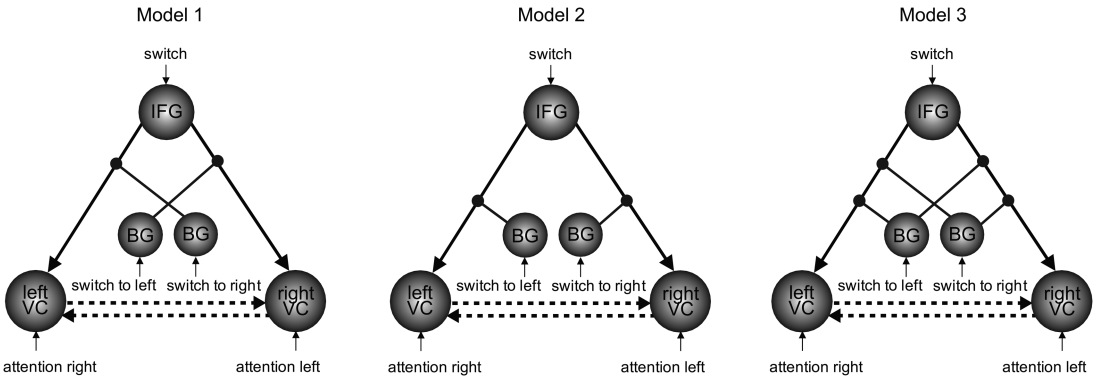

Figure 3. Tested dynamic causal models of BG function in top–down attention. All models included the right IFG, left and right visual cortex nodes (VC) and BG. Note that the BG node was divided into 2 time series that included variance related to left-attended versus right-attended trials, respectively. Hence, the models do not test for left versus right BG function. Top–down connections from the IFG were modulated by BG activity during switch-to-left and switch-to-right trials. We tested 3 alternative models of BG function. BG activity could modulate fronto-posterior connectivity on the visual cortex contralateral (model 1) or ipsilateral (model 2) to the side attention was being switched to, or both (model 3). Model 1 assesses excitatory modulation of fronto-posterior connections to the visual hemisphere that processes the newly attended visual hemifield. Model 2 assesses inhibitory modulation of fronto-posterior connections to the visual hemisphere that processes the now unattended visual hemifield. Model 3 embodies both these effects. These 3 models of BG function were constructed with and without reciprocal connections between the left and right visual cortex (dashed lines). Thus, the final model space included 6 models.

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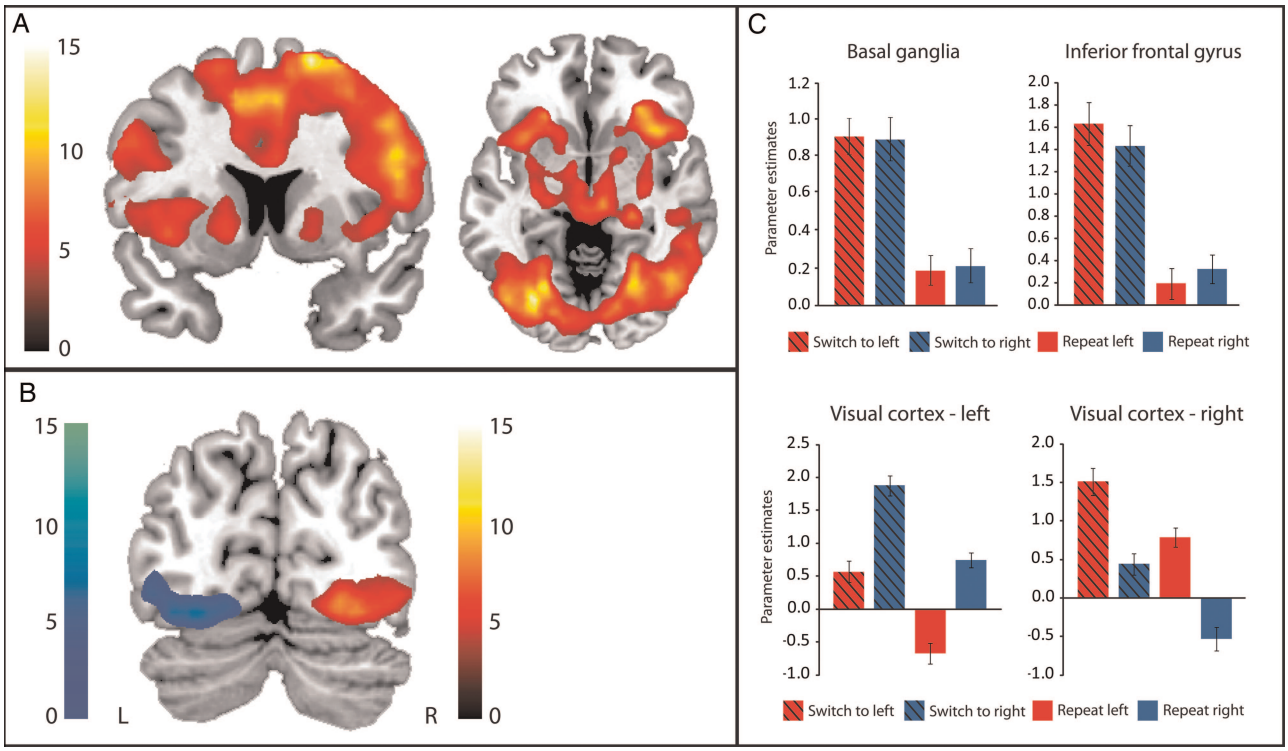

Figure 4. Univariate fMRI results (*A*) Main effect on BOLD signal for the attention-switching contrast (switch trials vs. repeat trials). (*B*) Switching to the left visual hemifield compared with switching to the right visual hemifield increased BOLD signal in the right visual cortex (red). The opposite contrast showed increased BOLD signal in the left visual cortex (blue). Bars indicate *t*-values, and maps are thresholded for a *t*-value of 3.68, corresponding to a *P*-value of 0.001 uncorrected for multiple comparisons. Maps were superimposed on a skull-stripped template in MNI space and displayed using MRIcroN (Rorden et al. 2007). (*C*) Graphs show the pattern of activation for the 4 different trial types in the BG, IFG, and the left and right visual cortex. Plotted data were extracted from the peak voxels from the contrast of interest, as described in the subsection "time series extraction" in the Materials and Methods section.

probability of each model. This procedure enables inference about model parameters while accounting for differences in model evidence. Our hypothesis was that selective gating by the basal ganglia can explain spatially selective effects in visual cortex. To test this hypothesis, we assessed the significance of parameter estimates of the modulatory influence of basal ganglia response on fronto-posterior connections in a 2 × 2 repeated-measures ANOVA with the factors "switch direction" (switch-to-left vs. switch-to-right trials) and "hemisphere" (left visual cortex vs. right visual cortex). Post hoc *t*-tests were performed to determine the direction of the interaction.

Results

Behavioral Results

On average participants responded correctly on 88% of the repeat trials (range 61–99%), which was well above chance level of 25%. On switch trials, participants had an average accuracy of 97% (range 91–100%). Reaction time analyses of correct trials revealed that subjects responded significantly more slowly on switch trials (1329.7 ± 37 ms) compared with repeat trials (940.6 ± 28.5 ms)($t_{16} = 18.7$, $P < 0.0005$). This evidences that subjects engaged in the task and is in line with previous findings (van Schouwenburg et al. 2010). Additional analyses showed that participants were significantly faster and more accurate on trials with a high coherence level compared with low coherent trials (see Supplementary material).

fMRI Results

Whole-brain analysis of the attention-switching contrast revealed the expected fronto-subcortico-parietal network (cluster-level corrected for multiple comparisons) (Fig. 4*A*). As predicted, the basal ganglia showed a significantly increased response when subjects covertly switched their attention between visual hemifields (Fig. 4, Table 1). This effect was found bilaterally in the ventral pallidum (MNI coordinates [−16 6 −2], $t = 7.28$, $P_{svc} < 0.0005$ and [18 4 4], $t = 6.71$, $P_{svc} = 0.001$) very close to clusters in our previous studies which involved attention switching between different dimensions of the same stimulus, rather than spatial attention switching (van Schouwenburg et al. 2010, 2013). In line with our previous study, we also found significant clusters in the IFG and visual cortex (Fig. 4, Table 1).

To assess whether the visual cortex responded in a spatially selective manner, we compared trials on which subjects switched attention from the left to the right visual hemifield (switch to right) with trials on which subjects switched attention from the right to the left visual hemifield (switch to left). The right visual cortex showed increased BOLD signal for switch to left compared with switch to right ([22 −80 −10], $t = 10.36$, $P_{svc} < 0.0005$), while the opposite contrast showed an increase in the left visual cortex ([−30 −76 −12], $t = 7.05$, $P_{svc} < 0.0005$) (Fig. 4, Table 1). Thus, consistent with our predictions, processing was increased for the newly attended visual hemifield (in the contralateral visual hemisphere) compared with the now irrelevant visual hemifield (in the ipsilateral visual hemisphere).

DCM Results

Next, we asked whether these spatially selective effects in the visual cortex were accompanied by selective modulation of

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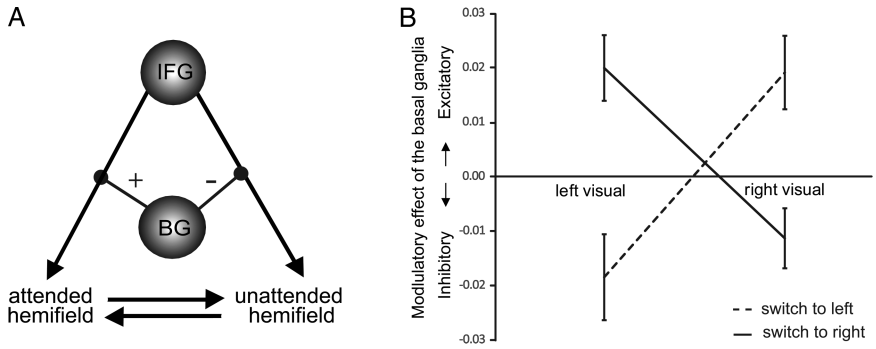

Figure 5. Results from Bayesian model averaging. (*A*) The average model showed that the BG both suppress previously attended visual information and enhance the newly attended visual information, via modulation of frontal top–down connections. (*B*) In line with this model, the BG inhibited connection strength with the left visual cortex when subjects switched attention to the left visual hemifield, but enhanced connection strength with the left visual cortex when subjects switched attention to the right visual hemifield. The opposite pattern was observed in the right visual cortex.

fronto-posterior connectivity by the signal in the ventral pallidum. We constructed 6 alternative models, in a 2 × 3 factorial design, with 1) present or absent reciprocal connections between left and right visual cortex and 2) modulation by the ventral pallidal signal of frontal-posterior connections to task-relevant and/or task-irrelevant visual cortex (Figs 1 and 3). Family-wise model comparison showed that the models with the reciprocal visual cortex connections outperformed the models without these connections (XP = [0.99; 0.01]). Family-wise model comparison did not confirm one model of ventral pallidal gating to outperform the other models (XP = [0.33; 0.34; 0.33]). Therefore, all models that included the reciprocal connections were included in the Bayesian model average to draw inferences about the ventral pallidum modulatory influence.

In the averaged model, the modulatory influence of the ventral pallidum on fronto-posterior connections showed a significant interaction between switch direction (switch-to-left trials vs. switch-to-right trials) and hemisphere (left visual cortex vs. right visual cortex) ($F_{1,16} = 11.2$, $P = 0.004$)(Fig. 5). Post hoc *t*-tests revealed that the ventral pallidum increased connectivity between the IFG and the visual cortex that processed the newly attended hemifield (right visual cortex on switch-to-left trials: $t_{16} = 2.8$, $P = 0.012$, left visual cortex on switch-to-right trials: $t_{16} = 3.3$, $P = 0.004$). Conversely, the ventral pallidum decreased connectivity between the IFG and visual cortex that processed the now unattended hemifield (left visual cortex on switch-to-left trials: $t_{16} = -2.3$, $P = 0.033$, right visual cortex on switch-to-right trials: $t_{16} = -2.0$, $P = 0.058$). Importantly, 11 of 17 subjects showed this full interaction on the individual level (Supplementary Fig. 1). A post hoc analysis revealed a significant correlation between the individual interaction effects and the degree to which the combined model had greater evidence over the other 2 models (Supplementary Fig. 2). The correlation was positive such that subjects with a larger interaction effect showed greater model evidence for the combined model compared with the other 2 models.

The parameters reflecting top–down effects of prefrontal cortex on left and right visual cortex were positive. This suggests that, during a switch in attention, the prefrontal cortex increases activity in visual cortex. It is exactly this top–down effect of the prefrontal cortex that is modulated by ventral pallidal activity as a function of switch direction.

In conclusion, ventral pallidal activity enhanced prefrontal influence on the newly task-relevant visual cortex while it suppressed prefrontal influence on the task-irrelevant visual cortex during attention switching.

Discussion

Classical models of attention highlight the role of the prefrontal cortex. Although it is clear that the basal ganglia also contribute to attentional control, the unique contribution of the basal ganglia to attention has remained unclear. It has been suggested that the basal ganglia act as a selective gate that selects which among multiple maintained prefrontal cortex goal representations guides current behavior (Hazy et al. 2007; Frank and Badre 2012).

In this study, we aimed to assess the inhibitory versus facilitatory nature of the proposed selective gating mechanisms of the basal ganglia during attention switching. We found that switch-related basal ganglia signal enhanced fronto-posterior connectivity with parts of the visual cortex that process the newly attended visual information, while decreasing fronto-posterior connectivity with parts of the visual cortex that process visual information that is no longer relevant. This suggests that basal ganglia function can be described by a model in which selective gating is achieved by a combination of enhanced task-relevant processing and suppressed task-irrelevant processing. This is in line with current anatomical and computational models of the basal ganglia that assert that the anatomy of the basal ganglia is perfectly suited to simultaneously perform these seemingly contradicting operations (Mink 1996; Frank 2011).

The model including both inhibitory and excitatory connections did not outperform the other 2 models in a direct model comparison. One explanation for this might be that BMS penalizes models for the number of parameters in the model. In other words, the increase in model fit for the model including both inhibitory and excitatory connections might have been counterbalanced by the higher number of parameters in this model. Given that we could not use model selection to answer our question on the excitatory versus inhibitory modulation, we used Bayesian model averaging to integrate out the uncertainty over model space, and analyzed the averaged model parameters to assess evidence for excitation versus inhibition. Bayesian model averaging showed the expected crossover

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effect, which provides strong evidence for both excitation and inhibition. Closer inspection of the parameters showed that 65% of the subjects showed this crossover effect on the individual level. Our finding of a correlation between the individual crossover effects and individual differences in model evidences supports the idea that the combined model might have been penalized for the additional parameters and further justifies our use of Bayesian model averaging (Supplementary material).

Consistent with our previous study, we observed switch-related effects in the pallidum, which is one of the primary output nuclei of the basal ganglia and sends continuous inhibitory output to the cortex, via the thalamus. Information that is processed by the input nuclei of the basal ganglia (caudate nucleus and putamen) is transmitted via inhibitory connections either directly, or via the external segment of the globus pallidus (GPe) to the output nuclei. Depending on the direct or indirect route, activation of the striatum will lead to disinhibition of the cortex (via the direct or "Go" pathway), or further inhibition of the cortex (via the GPe, the indirect or "NoGo" pathway). Thus, one mechanism by which the basal ganglia might alter prefrontal top–down function is by gating (inhibiting and enhancing) the input to the prefrontal cortex, and determining which of multiple currently active prefrontal representations can bias competition between posterior regions (Mink 1996; Hazy et al. 2007). It might be noted that, according to this hypothesis, there does not have to be a net effect on the BOLD response in the prefrontal cortex due to simultaneous increases in signal related to task-relevant representations and decreases in signal related to task-irrelevant representations. In future work, this input gating hypothesis can be tested using multivariate pattern classification analyses. Alternatively, the basal ganglia might modulate prefrontal output to the visual cortex (via the thalamus). Indeed, there is anatomical evidence for direct projections from the basal ganglia to (albeit higher order parts of) the visual cortex (Middleton and Strick 2000). DCM enables modeling of functional interactions between regions and hence our results cannot disentangle these alternative anatomical models of basal ganglia gating. The fact that the pallidum, rather than the striatum showed strong switch-related signal is perhaps more consistent with the first model, given that the pallidum is the main output nucleus of the basal ganglia to the cortex.

In our previous work, we had already provided evidence for attentional gating of top–down projections by the basal ganglia (van Schouwenburg et al. 2010). However, this study did not enable us to disentangle the 3 potential mechanisms underlying this selective gating, that is, inhibition of irrelevant information, enhancement of relevant information or a combination of both. The current study supports the third hypothesis, that is, that the basal ganglia ensure attentional gating of prefrontal representations by both enhancing cortical processing of task-relevant representations, and inhibiting task-irrelevant representations.

Several previous studies have reported modulation of functional signals in task-relevant and task-irrelevant regions as a function of attention (Gazzaley et al. 2005; Polk et al. 2008; King et al. 2010). These have shown that signals are decreased in unattended sensory regions, but increased in attended sensory regions. This attentional gain has generally been thought to originate from the prefrontal cortex, which increases processing in attended sensory regions and by virtue of mutual suppression inhibits unattended sensory regions (Desimone and Duncan 1995). Our findings also have implications for psychological accounts of attentional inhibition, suggesting that inhibition of task-irrelevant processing is not simply a side effect or corollary of biased competition through mutual suppression, but also involves an active top–down process. Indeed, the indirect pathway of the basal ganglia provides an anatomically plausible mechanism for instantiating such active suppression.

Our findings are consistent with task-switching studies that have found a correlation between activity in task-irrelevant regions and switch-cost, suggesting that the failure to suppress the previously relevant information causes the response slowing that is associated with task switching (Yeung et al. 2006). Here, we provide evidence that switching indeed involves inhibition of previously attended sensory information as well as enhancement of newly attended sensory information.

We instructed subjects to focus attention on the relevant hemifield on repeat trials and to switch attention in a bottom-up manner. However, we cannot exclude the possibility that subjects divided their attention across both hemifield to some extent to detect the change and switch accordingly. Nevertheless, the attentional modulation found in visual cortex suggests that participants at least focused relatively more on the attended side than the unattended side.

Our finding of a switch-related increase in BOLD signal in the prefrontal cortex and basal ganglia is in line with previous studies of spatial attention switching (Gitelman et al. 1999; Perry and Zeki 2000). The aim of the current study was to assess selective gating by the basal ganglia. To this end, we focused univariate and DCM analyses on the basal ganglia and the prefrontal cortex, which are known to interact via fronto-striatal loops. Future studies might aim to assess how other brain regions that have been associated with spatial attention switching, notably the parietal cortex and frontal eye fields (Corbetta and Shulman 2002; Serences and Yantis 2007), may extend the current model.

In summary, we used a spatial attention-switching paradigm, in combination with fMRI and DCM, to test the role of the basal ganglia in attentional control. Our data suggest that the basal ganglia interact with the prefrontal cortex to direct attention both toward behaviorally relevant information as well as away from irrelevant information. This extends current models of basal ganglia function from the motor to the cognitive domain.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.

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Notes

Conflict of Interest: R.C. is consultant for Abbott Laboratories, but is not an employee or stock shareholder.

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Supplementary Material

Individual DCM parameters

We showed using Bayesian model averaging that the modulatory influence of the ventral pallidum on fronto-posterior connections showed a significant interaction between 'switch direction' (switch to left trials versus switch to right trials) and 'hemisphere' (left visual cortex versus right visual cortex)($F_{1,16} = 11.2$, $p = 0.004$)(**Figure 5**). Here we present the DCM parameters for each subject separately.

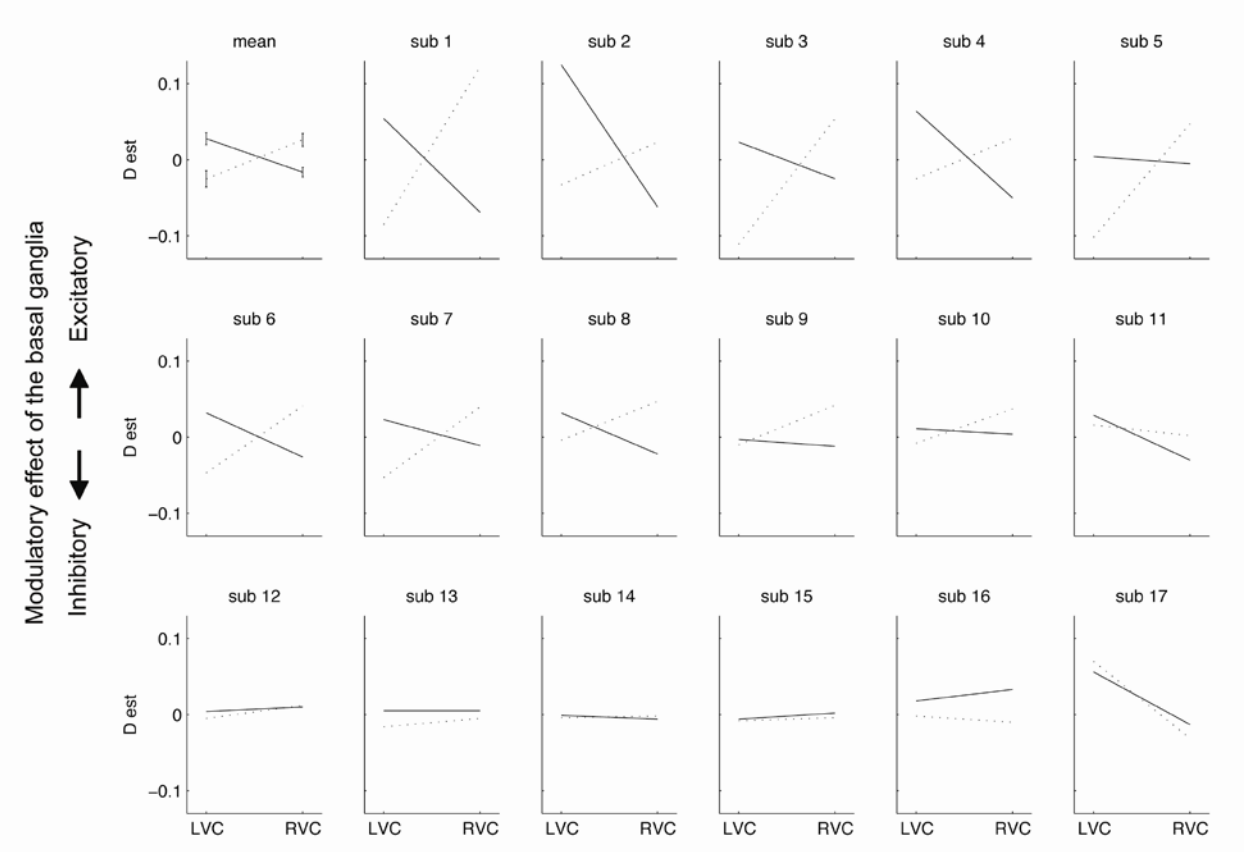

Figure S1 – Individual DCM parameters reflecting modulatory effect of ventral pallidum on fronto-posterior connections to the left and right visual cortex (LVC = left visual cortex, RVC = right visual cortex) for 'switch to left' trials (dotted lines) and 'switch to right' trials (solid lines). The upper left graph shows the mean across subjects (as in Figure 5).

In addition, we assessed whether there was an association between the individual DCM parameters and differences in model evidence between the tested models. To this end we calculated the magnitude of the interaction between ‘switch direction’ and ‘hemisphere’ (left visual cortex versus right visual cortex) for each participant. Next, we subtracted the average model evidence for the inhibitory and excitatory model from the model evidence for the combined model and correlated this with the individual interaction effects. The correlation was strongly significant ($r = 0.765$, $p = 0.0003$) which is in line with the idea that the combined model might have been penalized for the extra parameters. The figure below clarifies why the additional parameters are sufficient to account for some of the subjects’ data when the interaction is larger, but just not quite in others when it is smaller, and further justifies the motivation for using Bayesian model averaging in our paper.

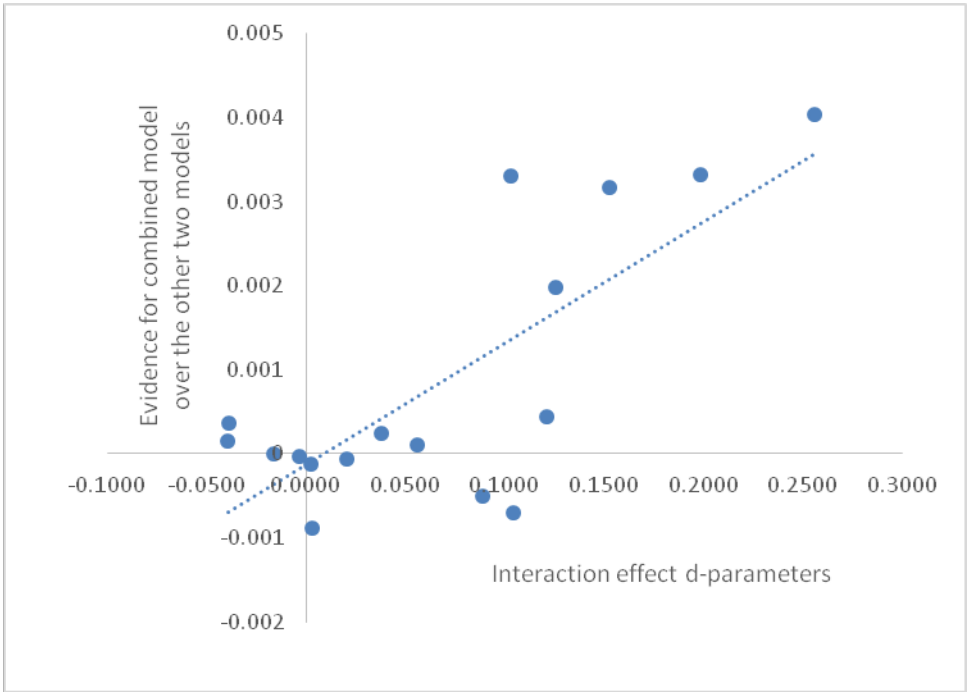

Figure S2 – Correlation between individual interaction effects of the d-parameters (extracted from Bayesian model averaging results) and evidence for the combined model minus the average evidence of the inhibitory and excitatory models.

Behaviour as a function of coherence

Our stimuli consisted of dots which moved coherently in one direction in the presence of noise (i.e. dots that were replotted randomly on each time frame). Coherence of the dots varied between 30% and 75% with steps of 5%. Here we present the speed and accuracy of responses across the ten coherence levels (correct trials only). Repeated measures analyses (10 levels) showed that participants were significantly faster and more accurate on trials with a high coherence level compared with trials with low coherence for both repeat trials (RT: $F = 22.8$, $p < 0.0005$; accuracy: $F = 4.2$, $p < 0.0005$) and switch trials (RT: $F = 10.8$, $p < 0.0005$; accuracy: $F = 6.9$, $p < 0.0005$)(table S3).

Table S3 –Reaction times (RT)(mean ± SEM in ms) and accuracy (Acc)(mean ± SEM in % correct) on repeat and switch trials for the different coherence levels (% of coherently moving dots).

		Coherence (%)									
		30	35	40	45	50	55	60	65	70	75
Repeat	RT(ms)	1060±40	1010±38	961±30	948±33	913±26	909±27	913±28	911±30	890±24	904±26
	Acc(%)	87±3	88±2	90±2	92±2	92±2	93±2	91±2	92±2	92±2	92±2
Switch	RT(ms)	1637±58	1420±46	1372±53	1356±62	1278±39	1295±51	1267±49	1278±61	1244±43	1227±54
	Acc(%)	83±4	94±2	94±2	98±1	98±1	99±1	98±1	95±1	98±1	97±2