

# Selective processing of buildings and faces during working memory: the role of the ventral striatum

Alexa Haeger,<sup>1,2</sup> Hweeling Lee,<sup>2</sup> Juergen Fell<sup>1</sup> and Nikolai Axmacher<sup>2,3</sup>

<sup>1</sup>Department of Epileptology, University of Bonn, Sigmund-Freud-Str. 25, 53127 Bonn, Germany

<sup>2</sup>German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany

<sup>3</sup>Department of Neuropsychology, Institute of Cognitive Neuroscience, Ruhr-University Bochum, Universitätsstrasse 150, 44801 Bochum, Germany

**Keywords:** distraction, fMRI, interference resolution, striatum, working memory

## Abstract

The ventral striatum seems to play an important role during working memory (WM) tasks when irrelevant information needs to be filtered out. However, the concrete neural mechanisms underlying this process are still unknown. In this study, we investigated these mechanisms in detail. Eighteen healthy human participants were presented with multiple items consisting of faces or buildings. They either had to maintain two or four items from one category (low- and high-memory-load condition), or two from one category and suppress (filter out) two items from the other category (distraction condition). Striatal activity was increased in the distraction as compared with the high-load condition. Activity in category-specific regions in the inferior temporal cortex [fusiform face area (FFA) and parahippocampal place area (PPA)] was reduced when items from the other category needed to be selectively maintained. Furthermore, functional connectivity analysis showed significant reduction of striatal–PPA correlations during selective maintenance of faces. However, striatal–FFA connectivity was not reduced during maintenance of buildings vs. faces, possibly because face stimuli are more salient. Taken together, our results suggest that the ventral striatum supports selective WM maintenance by reduced gating of task-irrelevant activity via attenuating functional connectivity without increasing task-relevant activity correspondingly.

## Introduction

Working memory (WM) depends both on regions exerting control functions and on areas supporting the perceptual representation of the information that needs to be maintained (Baddeley *et al.*, 1974). During real-world situations, limited WM capacity requires one to assign transient storage space to relevant pieces of information while filtering out irrelevant ones. The basal ganglia, consisting of the striatum (caudate nucleus and putamen), globus pallidus, nucleus accumbens and subthalamic nucleus, are implicated in such WM processes (Owen *et al.*, 1998; Packard & Knowlton, 2002; Cools, 2005; Frank, 2005; Baier *et al.*, 2010). The striatum in particular is hypothesized to act as a gateway for resolving interfering information by increasing the likelihood of processing relevant information whilst minimizing the influence of irrelevant information (Cools *et al.*, 2006; Dahlin *et al.*, 2008; McNab & Klingberg, 2008; Frank & Fossella, 2011; Badre & Frank, 2012; Scimeca & Badre, 2012). This especially applies for novel items (e.g. Bunzeck & Düzel, 2006; Guitart-Masip *et al.*, 2010). However, the exact mechanisms by which the striatum supports interference resolution during WM maintenance are still unknown.

Here, we investigated the role of the ventral striatum in filtering of task-relevant and task-irrelevant complex representations of faces and buildings during visual WM. Participants performed a modified Sternberg WM task that manipulated target category (faces vs. buildings) and WM load (low, distraction, high) while being scanned. Faces predominantly induce activation in the fusiform gyri [fusiform face area (FFA); Kanwisher *et al.*, 1997, 1999; Maguire *et al.*, 2001], while buildings elicit selective responses in the parahippocampal gyri [parahippocampal place area (PPA); Epstein & Kanwisher, 1998; Maguire *et al.*, 2001]. Thus, we hypothesize that during selective maintenance of one of the two target categories (i.e. during the distraction condition), the striatum acts as a gateway to resolve interfering information by modulating activity in the FFA and PPA.

These hypotheses extend previous work in two aspects. First, we investigated an issue that yielded controversial results in the existing literature, namely whether the striatum facilitates activity in task-relevant regions (Egner & Hirsch, 2005; Gruber *et al.*, 2006), suppresses activity in task-irrelevant regions (Maier *et al.*, 2008), or both (Gazzaley *et al.*, 2005; O'Reilly & Frank, 2006). We addressed this open question by using a novel design. In contrast to previous studies, we chose an experimental task that allowed us to compare maintenance in the presence of distraction with maintenance when only items from a single category were presented, which is important to isolate distraction-related effects. Second, we examined the

Correspondence: Dr N. Axmacher, <sup>3</sup>Department of Neuropsychology, as above.  
E-mail: nikolai.axmacher@ukb.uni-bonn.de

Received 8 August 2014, accepted 19 November 2014

changes in functional interregional connectivity during the different WM conditions. Several studies have investigated functional connectivity between prefrontal cortex (PFC) and category-specific areas (e.g. Fiebach *et al.*, 2006; Gazzaley *et al.*, 2007), and also the modulation of neocortical connectivity by basal ganglia activity has received attention (Den Ouden *et al.*, 2010; Van Schouwenburg *et al.*, 2010). By contrast, no previous study has analysed how interference resolution depends on task-dependent alterations of functional connectivity between the striatum and category-specific areas.

## Materials and methods

### Subjects

Eighteen healthy subjects (13 females; mean age  $\pm$  SD, 24.9  $\pm$  2.1 years, range 20–30 years) gave written informed consent to participate in the functional magnetic resonance imaging (fMRI) study. Exclusion criteria were claustrophobia, any history of neurological or psychiatric disorders, and metallic implantations. Subjects were recruited from the University of Bonn and via the Internet. The study was approved by the local medical ethics committee at the University Hospital in Bonn and performed in conformance with the WMA Declaration of Helsinki.

### Experimental paradigm

Subjects were presented with a modified Sternberg WM task (Fig. 1) that manipulated ‘target category’ (faces, buildings) and ‘WM condition’ (low load, distraction, high load). The stimulus consisted of a  $2 \times 2$  array of pictures that were either:

- (i) low-load condition: two target pictures (two faces or two buildings) and two scrambled pictures (for equal visual input compared with the other conditions);
- (ii) distraction condition: two target pictures (two faces or two buildings) and two distraction pictures (if the target pictures were faces, the distraction pictures would be buildings, and vice versa);
- (iii) high-load condition: four target pictures (four faces or four buildings).

Stimuli consisted of gray-scale images of emotionally neutral faces or buildings from a large database. The stimulus was presented

for 2 s and followed by a visual cue for 1.5 s that signaled whether subjects should remember only faces or buildings. The visual cue appeared in all conditions. Subjects had to maintain the relevant information for 5.2 s, 8 s or 10.8 s. A probe was then presented for 2 s, and subjects had to judge whether the picture was ‘old’ or ‘new’. An ‘old’ response indicated that the probe picture had been presented previously in the  $2 \times 2$  array of pictures. The probability that the probe matched one of the stimuli from the beginning of the trial was 50%. The probe was always consistent to the cue category, for example, if the cue indicated faces, then the probe would be a face. Subjects did not get a feedback about the accuracy of their response. A fixation crosshair was presented for 3.3 s until the next trial. Subjects were given a short practice session outside the scanner before the experiment. The order of the conditions was randomized in all six sessions, and 34 trials were presented in each session (total, 204 trials). A fixation crosshair was presented for 1 min at the end of each session, and the start of the next session was synchronized to the onset of a repetition time (TR). To prevent habituation to the task, the same stimulus type or condition did not occur more than three times in a row. The stimuli were presented through goggles (NordicNeuroLab, Bergen, Norway) using PRESENTATION<sup>®</sup> software (Version 0.70, www.neurobs.com).

### Functional localizer

To create individual masks for the FFA and PPA, a functional localizer experiment was conducted after the end of the main experiment (Berman *et al.*, 2010). Subjects passively viewed blocks consisting of 13 stimuli that were either faces, buildings or scrambled pictures. All stimuli in each block were from the same category. Each picture was shown for 1.5 s. The order of the stimulus blocks was randomized in two sessions, and 15 blocks were presented in each session (total, 30 blocks). A fixation crosshair was presented for 20 s at the end of each session.

### fMRI data acquisition

A Siemens TRIO 3T MRI scanner (Siemens Medical, Erlangen, Germany) was used to acquire both T1 structural volume images [repetition time (TR)/echo time (TE)/inversion time (TI), 1570/3.42/800 ms;

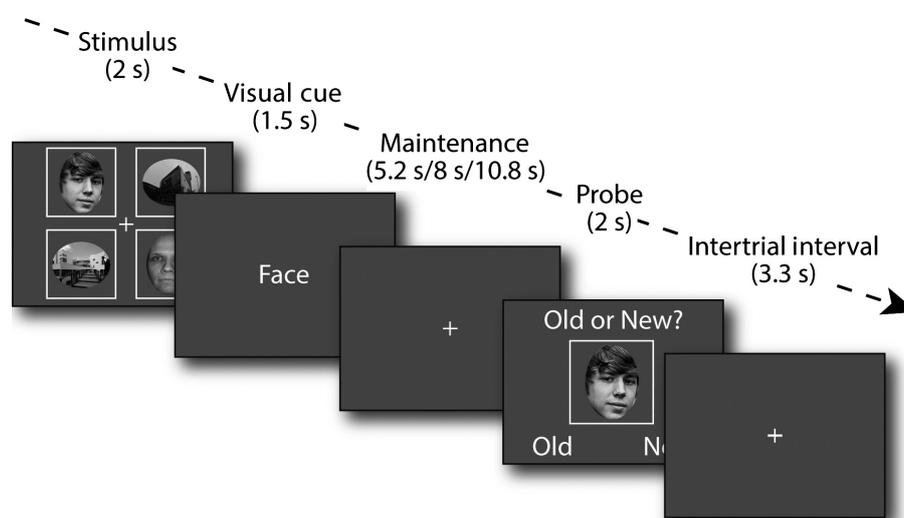


FIG. 1. Experimental paradigm. Experimental paradigm (exemplary trial from the distraction condition with face as target). The stimuli are presented simultaneously and followed by a cue, a maintenance period, and a probe.

160 slices; matrix  $256 \times 256$  mm<sup>2</sup>, spatial resolution  $1 \times 1 \times 1$  mm<sup>3</sup> voxels] and T2\*-weighted axial echo-planar images (EPI) with blood-oxygenation-level-dependent (BOLD) contrast [gradient echo; TR/TE, 2800/35 ms; 40 axial slices parallel to anterior commissure-posterior commissure plane; acquired in ascending direction; matrix  $64 \times 64$  mm<sup>2</sup>, field of view 210 mm, slice thickness 2.5 mm; interslice gap 0.5 mm; spatial resolution  $3.3 \times 3.3 \times 2.5$  mm<sup>3</sup> voxels]. Two functional sessions were acquired, one for the main experiment with a total of 1350 volume images, and one for the functional localizer with a total of 232 volume images. The first three volumes were discarded to achieve steady-state magnetization.

### Behavioral analysis

Subjects' 'old'/'new' responses and reaction times were recorded during the experiment. Accuracy (percentage of correct responses) and response times for the correct trials of each condition were computed for each subject. Repeated-measures ANOVAS on mean accuracy and response times (across subjects' means) with 'target category' (faces, buildings) and 'WM condition' (low, distraction, high load) as within-subjects variables were performed using SPSS (version 21.0). Results were reported after Greenhouse–Geisser correction.

### fMRI data univariate analysis

Functional data were analysed with statistical parametric mapping (SPM8; The Wellcome Center for Neuroimaging, London, UK, <http://www.fil.ion.ucl.ac.uk/spm>). Scans for the 1-min fixation cross-hair between sessions were removed manually, and the data were pre-processed as separate sessions. Scans from each participant were realigned using the first scan as a reference. The EPI images were unwrapped, slice time corrected, spatially normalized into Montreal Neurological Institute (MNI) standard space using parameters from the segmentation of the T1 structural image (Ashburner & Friston, 2005), resampled to  $2 \times 2 \times 2$  mm<sup>3</sup> voxels and spatially smoothed with a Gaussian kernel of 8 mm full-width at half-maximum. The smoothed EPI images were then collapsed across sessions during the 1st level analyses.

### Main experiment

The main experiment was modeled in an event-related fashion with regressors entered into the design matrix after convolving each event-related unit impulse (indexing trial onset) with a canonical hemodynamic response function and its first temporal derivative. The duration of these regressors included the periods during presentation of pictures, visual cue and maintenance phase (i.e. between 8.7 s and 14.3 s, depending on the duration of the maintenance phase). In addition to modeling only the correct trials of the six conditions in our  $2 \times 3$  factorial design, the statistical model included two additional regressors, modeling incorrect trials and the probe picture. Six realignment parameters to account for residual motion artifacts, a linear drift regressor and five session-specific regressors were also included as nuisance covariates. Condition-specific effects for each subject were estimated according to the general linear model and passed to a 2nd level analysis as contrasts. This process involved creating contrast images of the six conditions (depending on WM condition and category) for each subject and entering them into a 2nd level ANOVA. Inferences were made at the 2nd level to allow for a random effects analysis and inferences at the population level (Friston *et al.*, 1994). Unless otherwise stated, we report activations at  $P < 0.05$  family-wise error (FWE) corrected at the cluster level for multiple comparisons of

the whole brain, and using an auxiliary (uncorrected) voxel threshold of  $P < 0.001$  at the whole-brain level and extent threshold of at least 10 voxels before FWE correction for multiple comparisons.

At the random effects level, we identified the neural network involved in interference resolution during WM. We tested for neural activation related to interference resolution by creating a T-contrast of the comparison between the distraction and the high-memory-load condition. In these two conditions, the number of presented items is identical, but only in the distraction condition two of the four presented items can be suppressed during the maintenance period. In addition, we tested for possible effects of the amount of relevant information by contrasting between the high-load and the low-load condition.

Subsequently, we also tested the effect of target category (faces vs. buildings). More specifically, mean parameter estimates of all conditions of each target category for each subject were extracted from the individualized FFA and PPA masks. A repeated-measures ANOVA on mean parameter estimates with 'target category' (faces, buildings) and 'WM condition' (low, distraction, high) as within-subjects variables was performed using SPSS.

### Functional localizer

The functional localizer experiment was modeled in a block-design fashion, with time duration of 19.5 s per block. In addition to modeling the three stimulus types (faces, buildings and scrambled pictures) and their first temporal derivatives, the statistical model included eight additional regressors (one for the 20 s break between the sessions, six realignment parameters to account for residual motion artifacts and a linear drift regressor). Condition-specific effects for each subject were estimated according to the general linear model. Two contrast images were created for each subject: (i) faces > buildings; and (ii) buildings > faces. Individualized masks of FFA and PPA were created from these results (using an uncorrected threshold of  $P < 0.001$ ) and inclusively masked with a fusiform gyrus and a parahippocampal gyrus mask from the wfu-pickatlas toolbox for SPM (version 3.0.4; Maldjian *et al.*, 2003), respectively. For two subjects, the statistical threshold for creating the FFA mask was lowered to  $P = 0.005$  and  $P = 0.01$  and, for one subject, the threshold for creating the PPA mask was lowered to  $P = 0.005$  to have a sufficient number of activated voxels in the subsequent analysis.

### fMRI correlation analysis

To determine the functional connectivity of category-specific regions (i.e. FFA and PPA) with the striatum, correlations between single-trial parameter estimates were computed (Rissman *et al.*, 2004). We made use of this method for connectivity analysis as, in comparison to other techniques like dynamic causal modeling (Friston *et al.*, 2003), construction of a pre-model is not needed and analysis can therefore be performed in a more data-driven manner. It does not allow conclusions about directionality, though (see Discussion). The bilateral striatum (showing activation in the distraction > high-load contrast), FFA and PPA were selected as seed regions, and we averaged the single-trial parameter estimates across all voxels in each of these regions. Both for FFA and PPA, single-trial parameter estimates were extracted in spherical masks with a radius of 8 mm centered at the individual peak coordinates from our functional localizer. For each subject, we modeled 204 covariates of interest (34 trials for each of the six conditions), which were each convolved with a canonical hemodynamic response function and its first temporal derivative, thus resulting in 408 regressors. Six realignment param-

ters to account for residual motion artifacts, a linear drift regressor and five session-specific regressors were also included as covariates of no interest. Parameter estimates for each trial were estimated according to the general linear model. Single trial-based Spearman's rank correlation analyses for each condition were used to determine intra-individual correlations for striatum–FFA connectivity and striatum–PPA connectivity. We did not calculate any correlations between FFA and PPA as we did not have any specific hypotheses on this connection. For statistical conclusion the individual correlation coefficients that have a range between +1 and –1 were Fisher  $z$ -transformed to approach a normal distribution (for details, see Rissman *et al.*, 2004). The  $z$ -transformed values were then entered into a repeated-measures ANOVA with 'WM condition' (low, distraction, high) and 'target category' (faces, buildings) as within-subject variables (Greenhouse–Geisser corrected). Subsequent  $t$ -tests for comparing the different conditions were performed using SPSS.

## Results

### Behavioral results

Figure 2A shows the mean (across subjects' means) accuracy and reaction times for correct trials in the different WM conditions. For accuracy, a repeated-measures ANOVA with 'WM condition' and 'target category' as within-subject variables revealed a main effect of 'WM condition' ( $F_{1,96,33,33} = 20.66$ ,  $P < 0.001$ ), but no effect of 'target category' ( $F_{1,17} = 0.34$ ,  $P = 0.57$ ) and no interaction ( $F_{1,85,31,48} = 0.092$ ,  $P = 0.90$ ). *Post hoc* comparisons showed greater accuracy in the low as compared with both the distraction [low:  $83.7 \pm 9.91\%$  (across subjects' mean  $\pm$  SD) vs. distraction:  $76.9 \pm 9.47\%$ ;  $t_{17} = 3.70$ ,  $P = 0.002$ ] and the high-load condition (high:  $71.1 \pm 7.04\%$ ;  $t_{17} = 6.39$ ,  $P < 0.001$ ), and greater accuracy in the distraction vs. high-load condition ( $t_{17} = 2.80$ ,  $P = 0.012$ ). These results indicate that successful interference resolution is more difficult than maintenance of two items, but less difficult than maintenance of four items, suggesting that participants are indeed capable of filtering out irrelevant items in the distraction condition.

This conclusion is further supported by the reaction time data. Again, we observed a main effect of 'WM condition' ( $F_{1,93,32,81} = 11.77$ ,  $P < 0.001$ ), as well as an effect of 'target category' ( $F_{1,17} = 5.19$ ,  $P = 0.036$ ), but no interaction ( $F_{1,41,23,96} = 0.53$ ,  $P = 0.54$ ). Responses to buildings were generally slower than responses to faces (see Fig. 2B). *Post hoc* comparisons for the different WM conditions (collapsed across both categories) showed that subjects took a shorter time to make a correct response for the low-memory-load ( $1.077 \pm 0.16$ ; low > high:  $t_{17} = -4.72$ ,  $P < 0.001$ ) and distraction ( $1.10 \pm 0.18$ ; distraction > high:  $t_{17} = -2.99$ ,  $P = 0.0083$ ) conditions, as compared with the high-memory-load condition ( $1.16 \pm 0.17$ ). Because reaction times during WM retrieval depend on set size, this suggests that indeed only two items were maintained in the distraction conditions and the other two items were filtered out. Reaction times for distraction and low-memory-load conditions did not differ across subjects ( $t_{17} = 1.54$ ,  $P = 0.11$ ), indicating that subjects were indeed successful in resolving interference.

### fMRI results

#### Univariate analyses (at the whole-brain level)

First, we investigated effects of interference resolution by contrasting activity during the distraction condition with activity during the high-memory-load condition across the two different target

categories. This contrast was chosen because the number of presented items is equal in both conditions, but only in the distraction condition is suppression of the irrelevant category demanded. This contrast revealed significant activation predominantly in the right striatum (caudate nucleus and putamen with its peak coordinates located in the right hemisphere; Fig. 3) as well as in a network of neocortical regions including the inferior parietal lobule and precuneus (a comprehensive list of all significantly activated brain regions is given in Table 1). One may speculate that the predominant right-hemispheric activation is related to a non-verbal strategy employed during maintenance of face and building stimuli. Interestingly, striatal activation was not related to the 'amount' of relevant information, as the striatum did not show enhanced activation in the high- compared with the low-memory-load condition, even when we chose an unusually liberal threshold of  $P < 0.1$ , uncorrected. Furthermore, the absence of any significant interaction between 'target category' and 'WM condition' showed that faces and houses were processed similarly. Figure 3 also shows that on average, there is enhanced striatal activation in the low- as compared with the high-load condition. We presume that this results from the scrambled pictures that were presented together with the relevant items in the low-load condition. The former were included for equalizing visual input but might still induce some interference effect.

We further found in our whole-brain analysis that the PFC was recruited in all WM conditions, but its activity was not modulated by the amount of information (high load vs. low load) or the type of relevant information (faces vs. buildings) to be maintained. In contrast, activity in the parietal cortex was influenced by subjects' selective attention to one of the two categories in the distraction condition (Table 1).

#### Region of interest analyses

Next, we analysed effects of interference resolution in the FFA and PPA (Fig. 4A). Mean parameter estimates (across voxels within each individualized masks of FFA and PPA) were extracted for all WM conditions for each target category. Then, we calculated a repeated-measures ANOVA with 'WM condition' and 'target category' as within-subject variables. For PPA (Fig. 4A), this analysis revealed a main effect of 'target category' ( $F_{1,17} = 72.88$ ,  $P < 0.001$ ) with increased activation during processing of buildings than faces. Furthermore, we observed a significant 'category'  $\times$  'WM condition' interaction ( $F_{1,42,24,06} = 7.24$ ,  $P = 0.007$ ), indicating different category effects in the different WM conditions, but no main effect of 'WM condition' ( $F_{1,96,33,31} = 0.24$ ,  $P = 0.78$ ). In order to test whether selective maintenance of items from one category was rather related to downregulation of irrelevant representations or to upregulation of relevant representations, we analysed category-specific effects in the distraction condition as compared with the low-load and high-load condition. We observed reduced PPA activation during selective maintenance of faces in the distraction condition (i.e. when buildings had to be filtered out) as compared with maintenance of two ( $t_{17} = 8.53$ ,  $P < 0.001$ ) or four buildings ( $t_{17} = 7.42$ ,  $P < 0.001$ ; Fig. 4A). This result suggests that activity within the PPA (i.e. activity related to processing of buildings) is reduced when only faces need to be maintained and buildings need to be filtered out. This effect cannot be explained by the number of buildings presented, because there was no significant difference during maintenance of four as compared with two buildings ( $t_{17} = 0.48$ ,  $P = 0.63$ ). There was also significantly less activation in the distraction target buildings condition, compared with maintenance of two ( $t_{17} = 2.51$ ,  $P = 0.022$ ) or four buildings ( $t_{17} = 2.74$ ,  $P = 0.014$ ),

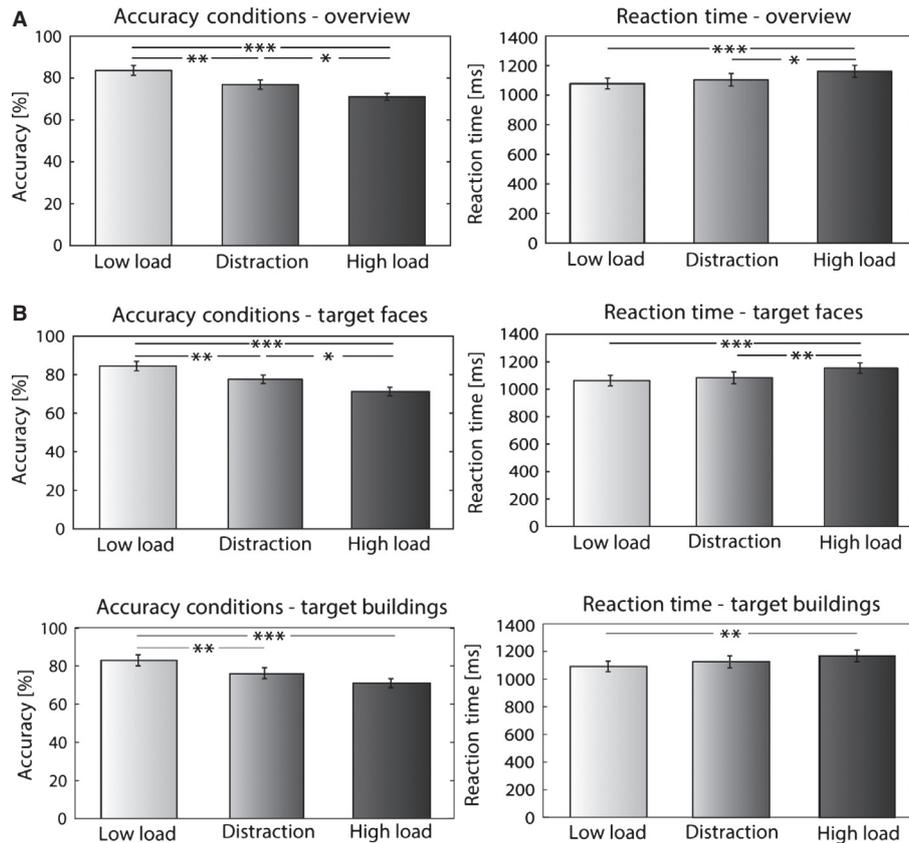


FIG. 2. Behavioral results. (A) Behavioral data: Left, accuracy (% of correct hits). Right, reaction times for correct trials. (B) Behavioral data separated for categories: Left, accuracy (% of correct hits) for target faces (above) and buildings (below). Right, reaction times for correct trials for faces (above) and buildings (below). Error bars indicate standard error of the mean (SEM). \*\*\* $P < 0.001$ , \*\* $P < 0.01$ , \* $P < 0.05$ .

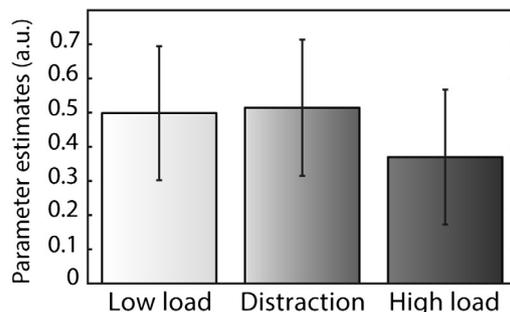
### Striatum:

$y = 4$



Left Right

### Faces:



### Buildings:



FIG. 3. Striatal activation during selective processing of faces and buildings. Effect of interference resolution (distraction > high memory load) in bilateral striatum, displayed on a coronal slice of a normalized structural image (averaged across participants). Height threshold for illustration,  $P < 0.001$  uncorrected. Parameter estimates (mean  $\pm$  SEM) for the different memory load conditions at the peak activation [ $x = 16$ ,  $y = 4$ ,  $z = 16$ ] for faces and buildings.

indicating that activity was not increased during selective maintenance of buildings, but was even reduced.

Results were similar for the FFA (Fig. 4A). As expected, this region was more active during maintenance of faces as compared with buildings (main effect of 'target category':  $F_{1,17} = 73.34$ ,  $P < 0.001$ ). There were no main effects of 'WM condition' ( $F_{1.54,26.22} = 1.94$ ,  $P = 0.17$ ) and no interaction ( $F_{1.73,29.44} = 0.73$ ,  $P = 0.47$ ). Again, we investigated whether selective maintenance of items from one category was rather related to downregulation of

irrelevant representations or to upregulation of relevant representations. Corresponding to our PPA results, we found that FFA activity was reduced during selective maintenance of buildings (i.e. in the distraction condition with 'buildings' as targets) as compared with maintenance of two ( $t_{17} = 8.98$ ,  $P < 0.001$ ) or four faces ( $t_{17} = 4.84$ ,  $P < 0.001$ ). Furthermore, activity during maintenance of two and four faces did not differ ( $t_{17} = 1.36$ ,  $P = 0.19$ ). This shows that activity within the FFA is reduced during selective maintenance of items from the other category (i.e. buildings). Again, there was

TABLE 1. Significant activation in the contrast distraction vs. high memory load

Brain region	Cluster size	MNI coordinates			Z-score (peak)	P-value*
		x	y	z		
Distraction > High load						
Inferior parietal lobule	649	48	-48	30	4.96	0.0019
		50	-52	40	4.17	
		58	-52	22	3.34	
Caudate nucleus	1340	16	20	8	4.77	< 0.001
		16	4	16	4.68	
		14	18	-2	4.49	
Precuneus	382	-10	-68	46	4.01	0.020
		-26	-70	42	3.55	
		-30	-64	56	3.51	

\*P-value FWE-corrected at cluster level for multiple comparisons.

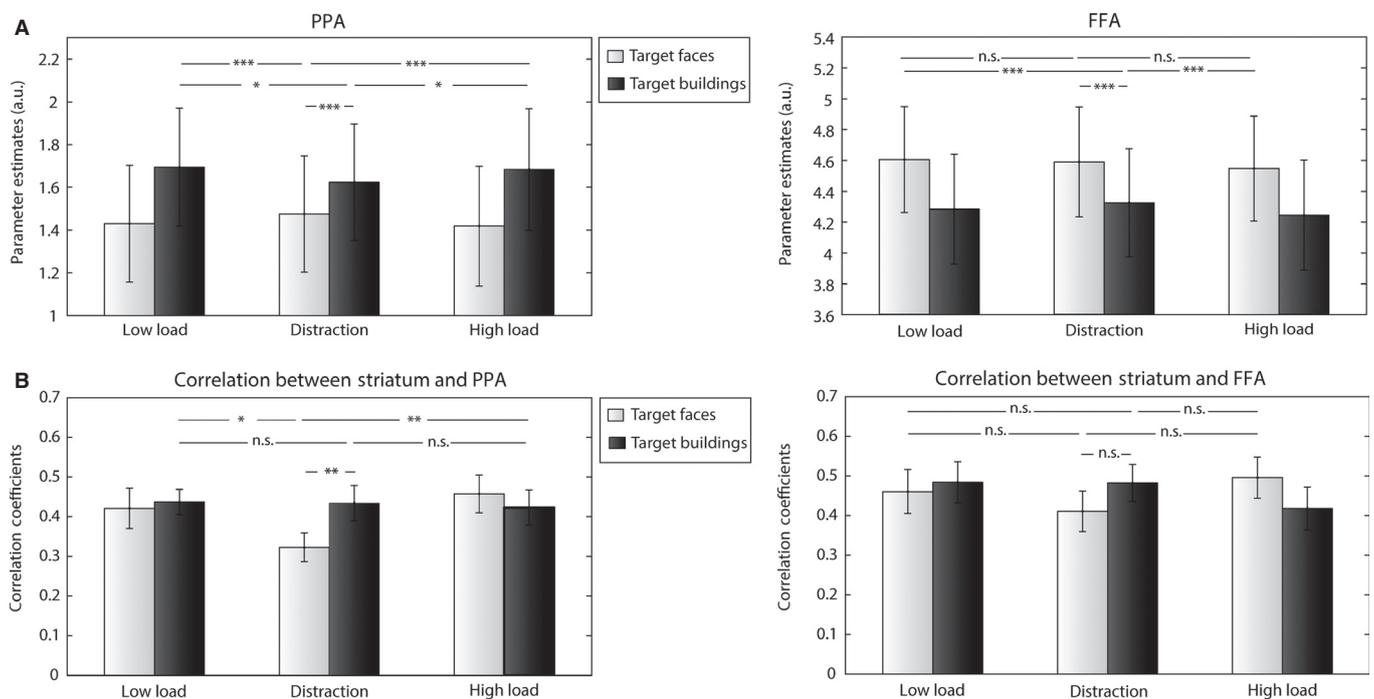


FIG. 4. Activation in PPA and FFA and results from correlation analysis. (A) Parameter estimates (mean  $\pm$  SEM) for the different conditions (Low load, distraction, high load, for target faces and buildings) for PPA (left) and FFA (right). (B) Correlation coefficients (mean  $\pm$  SEM) for connectivity between striatum and PPA (left) and between striatum and FFA (right) for the different conditions (Low load, distraction, high load, for target faces and buildings). \*\*\* $P < 0.001$ , \*\* $P < 0.01$  and \* $P < 0.05$ , 'n.s.' is for 'not significant', resulting from paired  $t$ -tests.

no evidence for upregulation when comparing selective maintenance of faces with maintenance of two ( $t_{17} = 0.46$ ,  $P = 0.65$ ) or four faces ( $t_{17} = 0.81$ ,  $P = 0.43$ ).

#### Functional connectivity analyses

To investigate functional interactions between the striatum and category-specific regions during selective maintenance of faces and buildings (i.e. distraction condition), we assessed functional connectivity between the striatum and FFA on the one hand, and the striatum and PPA on the other hand (Fig. 4B).

For striatum-PPA connectivity, the repeated-measures ANOVA revealed no main effects of 'WM condition' ( $F_{1,95,33,19} = 2.26$ ,  $P = 0.12$ ) or 'target category' ( $F_{1,17} = 1.67$ ,  $P = 0.21$ ), but a

significant interaction ( $F_{1,9,32,46} = 3.70$ ,  $P = 0.037$ ), indicating different category effects in the different WM conditions. In order to elucidate this interaction and as we were particularly interested in results during the distraction condition, we performed paired  $t$ -tests comparing striatum-PPA connectivity during selective maintenance of buildings and faces. We observed higher striatum-PPA connectivity during selective maintenance of buildings as compared with selective maintenance of faces in the distraction condition ( $t_{17} = 3.31$ ,  $P = 0.0042$ ; Fig. 4B). By contrast, no category effects were found in the high- ( $t_{17} = 1.12$ ,  $P = 0.28$ ) and the low-load ( $t_{17} = 0.19$ ,  $P = 0.85$ ) conditions, consistent with the specific recruitment of the striatum in the distraction condition (Fig. 3). Furthermore, we found that striatum-PPA connectivity was reduced during selective maintenance of faces as compared with mainte-

nance of two buildings in the low-load ( $t_{17} = 2.80$ ,  $P = 0.012$ ) or four buildings in the high-load condition ( $t_{17} = 2.97$ ,  $P = 0.0086$ ). This suggests that striatum–PPA connectivity is reduced when buildings need to be filtered out and faces need to be maintained as targets. No increase of striatum–PPA connectivity was observed during selective maintenance of buildings as compared with maintenance of two ( $t_{17} = 0.18$ ,  $P = 0.86$ ) or four buildings ( $t_{17} = 0.29$ ,  $P = 0.77$ ).

For striatum–FFA connectivity, the ANOVA did not show an interaction ( $F_{1,77,30.06} = 2.48$ ,  $P = 0.11$ ). In contrast to the findings for striatum–PPA connectivity, striatum–FFA connectivity did not differ significantly during selective maintenance of buildings and faces [ $t_{17} = 1.43$ ,  $P = 0.17$ ; mean values of correlation coefficients were even higher during selective maintenance of buildings ( $0.48 \pm 0.20$ ) than faces ( $0.41 \pm 0.22$ ); Fig. 3B]. No reduction was observed during selective maintenance of buildings as compared with maintenance of two ( $t_{17} = 0.40$ ,  $P = 0.70$ ) or four faces ( $t_{17} = 0.61$ ,  $P = 0.55$ ), and no increase during selective maintenance of faces as compared with maintenance of two ( $t_{17} = 0.89$ ,  $P = 0.39$ ) or four faces ( $t_{17} = 1.84$ ,  $P = 0.084$ ; in the latter case, connectivity was even in trend reduced as compared with selective maintenance of faces).

These results show that striatum–PPA connectivity is attenuated during selective maintenance of items from the ‘non-preferred’ category (i.e. faces), whereas striatum–FFA connectivity is not.

## Discussion

Here, we investigated the role of the ventral striatum in filtering of task-relevant and task-irrelevant representations during visual WM. Specifically, we examined the neural processes underlying selective WM maintenance of faces or buildings in the presence of interfering stimuli from the opposite category. We observed the following results. (i) The ventral striatum (as well as regions in the parietal lobe) was recruited during interference resolution in a WM task. (ii) Gating of activity in category-specific regions (FFA and PPA) was reduced when the corresponding type of information needs to be filtered out. There was no evidence for upregulation of task-relevant regions. (iii) Functional connectivity between PPA and striatum decreased during selective maintenance of faces, while FFA–striatum connectivity was unaffected during selective maintenance of buildings. Again, we did not find an increase of striatal connectivity with task-relevant regions.

### *Functional role of the striatum for selective maintenance*

Our results are in concordance with computational models of information gating by the basal ganglia and selective WM representations maintained by the PFC and parietal cortex (Frank *et al.*, 2001; Hazy *et al.*, 2006; O’Reilly & Frank, 2006). Crucially, the striatum is hypothesized to act as a gateway for resolving conflicting information by increasing the likelihood of the relevant information whilst minimizing the influence of irrelevant information (Cools *et al.*, 2006; Scimeca & Badre, 2012). The striatum supports this role by acting as a filtering mechanism, i.e. by selectively gating task-relevant information to frontal cortices (Frank, 2011) where this information can be used to generate predictions to guide behavior (Fuster, 1989; Miller & Cohen, 2001). In our study, however, we further show this effect in the presence of complex stimuli like faces and buildings, and how the category-specific regions are influenced by confrontation with distraction.

We further found a significant activation of striatal regions in the low-load condition. This could be due to the presence of scrambled

pictures, which might also lead to moderate degrees of interference. The scrambled pictures were included to equalize visual input and therefore to allow a comparison among the different conditions. Importantly, striatal activation was observed in the low-load condition only when contrasting it against the high-load condition (that did not contain any irrelevant items). By contrast, we did not observe any striatal activation when contrasting activity in the low-load condition against activity during the distraction condition that also required filtering of irrelevant items. However, as we did not include a low-load condition without scrambled pictures, we cannot completely rule out alternative explanations. As mentioned in our Results section, we found recruitment of the PFC in our whole-brain analysis in all WM conditions and activity in the parietal cortex during selective processing. These results are consistent with previous studies on attentional modulation showing that posterior parts of the parietal lobe play a decisive role in the control of spatial attention (Vandenberghe *et al.*, 2001; Simon *et al.*, 2002; Yantis *et al.*, 2002; Leung & Zhang, 2004). In accordance with findings from other studies with a focus on cue-driven shifting of attention (e.g. Lepsien & Nobre, 2007), we also observe in our paradigm a role of posterior parietal regions (i.e. the precuneus) in cue-directed attention to objects during WM. Activation of the intraparietal sulcus predominantly in the left hemisphere is in concordance with studies on attention-deficits due to lesions of the left parietal lobe (Egley *et al.*, 1994).

### *Reduced gating of irrelevant information rather than increased gating of relevant content*

Our results move beyond previous findings by investigating whether selective WM maintenance depends rather on increased gating of relevant information or on reduced gating of irrelevant content. They rather provide support for the latter hypothesis. WM maintenance of items from one category in the presence of interfering items from another category likely requires selective attention to the target category (Gazzaley & Nobre, 2012). We found that selective WM maintenance of faces or buildings was associated with reduced activation in the region supporting processing of distractor items, but not with increased activation in the area where relevant items were maintained. Several previous studies support the idea that the striatum supports selective processing by reduced gating of activity in a region that is not demanded (e.g. Maier *et al.*, 2008). On the other hand, our results appear to contradict previous findings showing both increased processing of target stimuli and reduced processing of distracting items (Gazzaley *et al.*, 2005; Lepsien & Nobre, 2007; Oh & Leung, 2009) or only enhanced task-relevant activity (Egner & Hirsch, 2005). This apparent discrepancy may be explained by baseline differences, i.e. by the fact that we found reduced activity during selective maintenance when compared with interference-free maintenance of information from a single category, which was not investigated in previous studies (e.g. Egner & Hirsch, 2005; Gazzaley *et al.*, 2005; Lepsien & Nobre, 2007; Oh & Leung, 2009).

### *Functional connectivity during selective maintenance*

In addition to the reduced activation of the PPA during selective maintenance of faces, we also observed that striatal–PPA connectivity was decreased when attention was selectively focused on faces. Applying a similar approach, Gazzaley *et al.* (2007) observed increased PPA–prefrontal correlations during selective maintenance of buildings in the presence of interfering faces; again, this study did not investigate maintenance of items from only one category,

which we used as a baseline. Our results suggest that the striatum supports selective WM processing by maintaining functional connectivity to the category-relevant regions, whilst during interference it attenuates its connectivity to the non-relevant region that results in a reduced gating of irrelevant information.

Interestingly, this effect was not symmetrical for the two different categories, but occurred only during selective maintenance of faces; by contrast, striatum–FFA connectivity was unaffected during selective maintenance of buildings. Thus, although FFA activity was reduced during selective maintenance of buildings as compared with maintenance of two or four faces, this effect may not have been mediated by a reduction of FFA–striatal interactions. We can only speculate on the reasons for this discrepancy. It may be that faces are generally more salient to humans, so that face processing cannot be reduced by the striatum alone. Indeed, previous studies have shown that striatal activation depends on stimulus saliency even in the absence of an explicit reward (Zink *et al.*, 2003, 2006).

### Summary and conclusions

To summarize, our data show that the ventral striatum and parietal regions contribute to WM operations involving the resolution of interfering categories (faces vs. buildings). On the one hand, we found that selective maintenance of faces is accompanied by a decrease of distractor-related activity within the PPA and that this reduced gating is probably mediated by a reduction of striatal–PPA connectivity. On the other hand, selective maintenance of buildings is associated with a reduction of distractor-related activity within the FFA. What could be the neural basis of these effects observed in our study? Striatal neurons are predominantly inhibitory and are therefore likely to exert an inhibitory influence on connections with other cortical regions when the striatum is activated. Indeed, findings from recent electroencephalography (EEG; Sauseng *et al.*, 2009) and magnetoencephalography studies (Bonnefond & Jensen, 2012, 2013) suggest that these distractor-related BOLD reductions during selective WM maintenance may correspond to increased (inhibition-related) alpha activity and decreased gamma activity. However, these studies used distractors from the same category as relevant stimuli. In our results, we observe a reduction of functional connectivity from the striatum to the PPA when filtering of buildings is demanded. This suggests that while the striatum exerts a positive influence on the PPA during maintenance of buildings, this facilitating influence is reduced when buildings are irrelevant. In general, the striatum is known to gate (via inhibition of output structures of the basal ganglia, which in turn inhibit the thalamus) processing in neocortical regions, and this is presumably reflected in the positive correlations that we observe between striatum/FFA and striatum/PPA. If one region is not required for the task at hand, this facilitation is reduced, as is the case for striatum/PPA connectivity during selective maintenance of faces in the presence of distracting buildings. By contrast, connectivity between striatum and FFA remains similarly positive in all task conditions. This may reflect a gating, by the striatum, of face information even if this information is not required for the current task. Further studies using electrophysiological recordings could test this interpretation more directly. Therefore, in a follow-up study, our data have to be complemented by electrophysiological and/or combined EEG/fMRI studies addressing resolution of interference between different categories in WM. Future investigations may furthermore answer whether the observed effects also hold for higher WM loads, and whether the suppressed category is still available to some degree at WM retrieval or not.

### Acknowledgements

Alexa Haeger received a BONFOR dissertation stipend of the University of Bonn; Nikolai Axmacher received an Emmy Noether and a Helmholtz grant. The authors would like to thank Nico Kremers, Marcin Leszczynski and Anna Schmidt from their research group for their assistance in data collection.

### Abbreviations

BOLD, blood-oxygenation-level-dependent; EEG, electroencephalography; EPI, echo-planar imaging; FFA, fusiform face area; fMRI, functional magnetic resonance imaging; FWE, family-wise error; PFC, prefrontal cortex; PPA, parahippocampal place area; SPM, statistical parametric mapping; TE, echo time; TI, inversion time; TR, repetition time; WM, working memory.

### References

- Ashburner, J. & Friston, K.J. (2005) Unified segmentation. *NeuroImage*, **26**, 839–851.
- Baddeley, A. & Hitch, G. (1974) Working memory. In Bower, G.H. (Ed.) *The Psychology of Learning and Motivation*, vol 8. Academic, New York, pp. 47–89.
- Badre, D. & Frank, M.J. (2012) Mechanisms of hierarchical reinforcement learning in corticostriatal circuits 2: evidence from fMRI. *Cereb. Cortex*, **22**, 527–536.
- Baier, B., Karnath, H.O., Dieterich, M., Birklein, F., Heinze, C. & Müller, N.G. (2010) Keeping memory clear and stable - the contribution of human basal ganglia and prefrontal cortex to working memory. *J. Neurosci.*, **30**, 9788–9792.
- Berman, M., Park, J., Gonzalez, R., Polk, T., Gehrke, A., Knaffla, S. & Jonides, J. (2010) Evaluating functional localizers: the case of the FFA. *NeuroImage*, **50**, 56–71.
- Bonnefond, M. & Jensen, O. (2012) Alpha oscillations serve to protect working memory maintenance against anticipated distracters. *Curr. Biol.*, **22**, 1969–1974.
- Bonnefond, M. & Jensen, O. (2013) The role of gamma and alpha oscillations for blocking out distraction. *Commun. Integr. Biol.*, **6**, e22702.
- Bunzeck, N. & Düzel, E. (2006) Absolute coding of stimulus novelty in the human substantia nigra/VTA. *Neuron*, **51**, 369–379.
- Cools, R. (2005) Dopaminergic modulation of cognitive function-implications for L-DOPA treatment in Parkinson's disease. *Neurosci. Biobehav. R.*, **30**, 1–23.
- Cools, R., Ivry, R.B. & D'Esposito, M. (2006) The human striatum is necessary for responding to changes in stimulus relevance. *J. Cognitive Neurosci.*, **18**, 1973–1983.
- Dahlin, E., Stigsdotter-Neely, A., Larsson, A., Bäckman, L. & Nyberg, L. (2008) Transfer of learning after updating training mediated by the striatum. *Science*, **320**, 1510–1512.
- Den Ouden, H.E., Daunizeau, J., Roiser, J., Friston, K.J. & Stephan, K.E. (2010) Striatal prediction error modulates cortical coupling. *J. Neurosci.*, **30**, 3210–3219.
- Egley, R., Driver, J. & Rafal, R.D. (1994) Shifting visual attention between objects and locations: evidence from normal and parietal lesion subjects. *J. Exp. Psychol. Gen.*, **123**, 161–177.
- Egner, T. & Hirsch, J. (2005) Cognitive control mechanisms resolve conflict through cortical amplification of task-relevant information. *Nat. Neurosci.*, **8**, 1784–1790.
- Epstein, R. & Kanwisher, N. (1998) A cortical representation of the local visual environment. *Nature*, **392**, 598–601.
- Fiebach, C.J., Rissman, J. & D'Esposito, M. (2006) Modulation of inferotemporal cortex activation during verbal working memory maintenance. *Neuron*, **51**, 251–261.
- Frank, M.J. (2005) Dynamic dopamine modulation in the basal ganglia: a neurocomputational account of cognitive deficits in medicated and non-medicated Parkinsonism. *J. Cognitive Neurosci.*, **17**, 51–72.
- Frank, M.J. (2011) Computational models of motivated action selection in corticostriatal circuits. *Curr. Opin. Neurobiol.*, **21**, 381–386.
- Frank, M.J. & Fossella, J. (2011) Neurogenetics and pharmacology of learning, motivation and cognition. *Neuropsychopharmacology*, **36**, 133–152.
- Frank, M.J., Loughry, B. & O'Reilly, R.C. (2001) Interactions between the frontal cortex and basal ganglia in working memory: a computational model. *Cogn. Affect. Behav. Ne.*, **1**, 137–160.

- Friston, K.J., Holmes, A.P., Worsley, K.J., Poline, J.B., Frith, C.D. & Frackowiak, R.S.J. (1994) Statistical parametric maps in functional imaging: a general linear approach. *Hum. Brain Mapp.*, **2**, 189–210.
- Friston, K.J., Harrison, L. & Penny, W. (2003) Dynamic causal modelling. *NeuroImage*, **19**, 1273–1302.
- Fuster, J.M. (1989) *The Prefrontal Cortex: Anatomy, Physiology, and Neuropsychology of the Frontal Lobe*, 2nd Edn. Raven Press, New York.
- Gazzaley, A. & Nobre, A.C. (2012) Top-down modulation: bridging selective attention and working memory. *Trends Cogn. Sci.*, **16**, 129–135.
- Gazzaley, A., Cooney, J.W., McEvoy, K., Knight, R.T. & D'Esposito, M. (2005) Top-down enhancement and suppression of the magnitude and speed of neural activity. *J. Cognitive Neurosci.*, **17**, 507–517.
- Gazzaley, A., Rissman, J., Cooney, J., Rutman, A., Seibert, T., Clapp, W. & D'Esposito, M. (2007) Functional interactions between prefrontal and visual association cortex contribute to top-down modulation of visual processing. *Cereb. Cortex*, **17**, 125–135.
- Gruber, A.J., Dayan, A., Gutkin, P.S. & Solla, B.S. (2006) Dopamine modulation in the basal ganglia locks the gate to working memory. *J. Comput. Neurosci.*, **20**, 153–166.
- Guitart-Masip, M., Bunzeck, N., Stephan, K.E., Dolan, R.J. & Düzel, E. (2010) Contextual novelty changes reward representations in the striatum. *J. Neurosci.*, **30**, 1721–1726.
- Hazy, T.E., Frank, M.J. & O'Reilly, R.C. (2006) Banishing the homunculus: making working memory work. *Neurosci.*, **139**, 105–118.
- Kanwisher, N., Woods, R.P., Iacoboni, M. & Mazziotta, J.C. (1997) A locus in human extrastriate cortex for visual shape analysis. *J. Cognitive Neurosci.*, **9**, 133–142.
- Kanwisher, N., Stanley, D. & Harris, A. (1999) The fusiform face area is selective for faces not animals. *NeuroReport*, **10**, 183–187.
- Lepsien, J. & Nobre, A.C. (2007) Attentional modulation of object representations in working memory. *Cereb. Cortex*, **17**, 2072–2083.
- Leung, H.C. & Zhang, J.X. (2004) Interference resolution in spatial working memory. *NeuroImage*, **23**, 1013–1019.
- Maguire, E.A., Frith, C.D. & Cipolotti, L. (2001) Distinct neural systems for the encoding and recognition of topography and faces. *NeuroImage*, **13**, 743–750.
- Maier, A., Wilke, M., Aura, C., Zhu, C., Ye, F.Q. & Leopold, D.A. (2008) Divergence of fMRI and neural signals in V1 during perceptual suppression in the awake monkey. *Nat. Neurosci.*, **11**, 1193–1200.
- Maldjian, J.A., Laurienti, P.J., Kraft, R.A. & Burdette, J.H. (2003) An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *NeuroImage*, **19**, 1233–1239.
- McNab, F. & Klingberg, T. (2008) Prefrontal cortex and basal ganglia control access to working memory. *Nat. Neurosci.*, **11**, 103–107.
- Miller, E.K. & Cohen, J.D. (2001) An integrative theory of prefrontal cortex function. *Annu. Rev. Neurosci.*, **24**, 167–202.
- Oh, H. & Leung, H.C. (2009) Specific and nonspecific neural activity during selective processing of visual representations in working memory. *J. Cognitive Neurosci.*, **22**, 292–306.
- O'Reilly, R.C. & Frank, M.J. (2006) Making working memory work: a computational model of learning in the prefrontal cortex and basal ganglia. *Neural Comput.*, **18**, 283–328.
- Owen, A.M., Doyon, J., Dagher, A., Sadikot, A. & Evans, A.C. (1998) Abnormal basal ganglia outflow in Parkinson's disease identified with PET. Implications for higher cortical functions. *Brain*, **121**, 949–965.
- Packard, M.G. & Knowlton, B.J. (2002) Learning and memory functions of the basal ganglia. *Annu. Rev. Neurosci.*, **25**, 563–593.
- Rissman, J., Gazzaley, A. & D'Esposito, M. (2004) Measuring functional connectivity during distinct stages of a cognitive task. *NeuroImage*, **23**, 752–763.
- Sauseng, P., Klimesch, W., Heise, K.F., Gruber, W.R., Holz, E., Karim, A.A., Glennon, M., Gerloff, C., Birbaumer, N. & Hummel, F.C. (2009) Brain oscillatory substrates of visual short-term memory capacity. *Curr. Biol.*, **19**, 1846–1852.
- Scimeca, J.M. & Badre, D. (2012) Striatal contributions to declarative memory retrieval. *Neuron*, **75**, 380–392.
- Simon, O., Mangin, J.F., Cohen, L., Le Bihan, D. & Dehaene, S. (2002) Topographical layout of hand, eye, calculation, and language-related areas in the human parietal lobe. *Neuron*, **33**, 475–487.
- Van Schouwenburg, M.R., den Ouden, H.E. & Cools, R. (2010) The human basal ganglia modulate frontal-posterior connectivity during attention shifting. *J. Neurosci.*, **30**, 9910–9918.
- Vandenberghe, R., Gitelman, D.R., Parrish, T.B. & Mesulam, M.M. (2001) Functional specificity of superior parietal mediation of spatial shifting. *NeuroImage*, **14**, 661–673.
- Yantis, S., Schwarzbach, J., Serences, J.T., Carlson, R.L., Steinmetz, M.A., Pekar, J.J. & Courtney, S.M. (2002) Transient neural activity in human parietal cortex during spatial attention shifts. *Nat. Neurosci.*, **5**, 995–1002.
- Zink, C.F., Pagnoni, G., Martin, M.E., Dhamala, M. & Berns, G.S. (2003) Human striatal response to salient nonrewarding stimuli. *J. Neurosci.*, **23**, 8092–8097.
- Zink, C.F., Pagnoni, G., Chappelow, J., Martin-Skurski, M. & Berns, G.S. (2006) Human striatal activation reflects degree of stimulus saliency. *NeuroImage*, **29**, 977–983.