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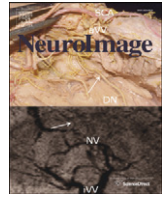
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Human anterior prefrontal cortex encodes the ‘what’ and ‘when’ of future intentions

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ABSTRACT

On a daily basis we form numerous intentions to perform specific actions. However, we often have to delay the execution of intended actions while engaging in other demanding activities. Previous research has shown that patterns of activity in human prefrontal cortex (PFC) can reveal our current intentions. However, two fundamental questions have remained unresolved: (a) how does the PFC encode information about future tasks while we are busy engaging in other activities, and (b) how does the PFC enable us to commence a stored task at the intended time? Here we investigate how the brain stores and retrieves future intentions during occupied delays, i.e. while a person is busy performing a different task. For this purpose, we conducted a neuroimaging study with a time-based prospective memory paradigm. Using multivariate pattern classification and fMRI we show that during an occupied delay, activity patterns in the anterior PFC encode the content of ‘what’ subjects intend to do next, and ‘when’ they intend to do it. Importantly, distinct anterior PFC regions store the ‘what’ and ‘when’ components of future intentions during occupied maintenance and self-initiated retrieval. These results show a role for anterior PFC activity patterns in storing future action plans and ensuring their timely retrieval.

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Introduction

Every day we form and maintain intentions for actions we want to perform later. A fundamental challenge is to endogenously track our plans and future intentions while we actively engage in current tasks. For instance, imagine you are cooking pasta while reading this paper. You need to stop reading in about 8 min and drain the pasta. While you are busy following your current intention to read, regions of your brain maintain ‘what’ prospective task is lined up next (drain pasta) and ‘when’ it has to be reactivated (in 8 min). In the absence of definite external cues (e.g. alarms or clocks), you need to rely on endogenous processes (time-keeping) to self-regulate the maintenance and retrieval of your future intention (e.g. preparing pasta for dinner). This capacity to maintain delayed intentions and execute them after a long time delay, during which we often perform other demanding tasks, is often referred to as prospective memory (Brandimonte et al., 1996; Burgess et al., 2011; Ellis, 1996).

Previous research suggests that processing delayed intentions and the temporal organization of planned actions involve the anterior prefrontal cortex (aPFC) (Haynes et al., 2007; Koechlin, 2011; Koechlin et al., 1999; Ramnani and Owen, 2004; Sakai and

Passingham, 2002; Soon et al., 2008). The PFC has been proposed as the locus of long-term planning and intentional behavior. This is in part because PFC neurons have the capacity to maintain representations over long durations, inhibit responses and task sets, and fire over extended temporal periods and across events (Aron et al., 2004; Fuster, 2000; Fuster and Alexander, 1971). Furthermore, research in monkey and human prefrontal function suggests that an anterior to posterior gradient within the PFC supports the control of temporally pending to immediate action (Badre, 2008; Koechlin and Hyafil, 2007). Theories of prefrontal cortex function suggest that more anterior PFC regions may be involved in tasks that are planned for execution at a later stage in a sequence or a hierarchical structure, as well as tasks that require branching or multitasking, and tasks with a higher level of representational abstraction (Badre and D’Esposito, 2007, 2009; Botvinick, 2007, 2008; Christoff et al., 2009; Fuster, 1997, 2000; Goldman-Rakic, 1987; Koechlin et al., 2003; Ramnani and Owen, 2004). Moreover, previous neuroimaging studies on prospective memory have suggested that univariate activity in the anterior prefrontal cortex is correlated with event-based (Burgess et al., 2007; Gilbert, 2011; Gilbert et al., 2005, 2006; Okuda et al., 2007; Simons et al., 2006) as well as time-based prospective memory (McFarland and Glisky, 2009; Okuda et al., 2007; see Burgess et al., 2011 for a review). But do these regions also encode information regarding the future task and conditions of its execution, i.e. the ‘what’ and ‘when’ of a prospective intention?

Previous multi-voxel pattern classification studies on delayed intentions suggest that the medial and lateral anterior PFC encode the

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content of a future intention during a delay of 2.5–12 s while subjects merely concentrate on the upcoming task (Haynes et al., 2007; Soon et al., 2008). Moreover, a recent event-based prospective memory study (Gilbert, 2011) could decode the anticipated retrieval-cue from the medial anterior PFC. On the other hand, lesion studies show that lateral aPFC damage can lead to impaired prospective memory (Burgess et al., 2000); and it has been suggested that the lateral aPFC is involved in higher levels of hierarchically organized action (Badre and D'Esposito, 2009; Christoff et al., 2009; Koechlin et al., 2003) and cognitive branching (Koechlin et al., 1999). However, the computational role of the lateral anterior PFC in prospective memory remains unclear. Multivariate or content-specific analysis of functional imaging of prospective memory can help reveal the information processing role of the lateral anterior PFC in the storage of future intentions.

Interestingly, while many univariate studies stress the role of the lateral aPFC in prospective memory (Burgess et al., 2003, 2011; Reynolds et al., 2009), more recent univariate studies (Benoit et al., 2011) and a series of multivariate studies (Gilbert, 2011; Haynes et al., 2007; Soon et al., 2008) on delayed intentions indicate that the medial anterior PFC may also play a role in the maintenance of future task information during an intention delay. Finally, so far it has remained unclear whether and where the PFC encodes the content of specific future intention components ('what' and 'when') while subjects perform other tasks. On the basis of this body of literature, we hypothesized that the medial and lateral anterior PFC may store information about an upcoming task during filled delays, such as the occupied delay of a time-based prospective memory paradigm.

We investigated the representation of future intentions across a long retention period while subjects were busy with another task. We designed a time-based prospective memory paradigm (Burgess et al., 2011; Ellis, 1996) in which participants had to encode an intention and could only execute it after a self-estimated delay duration of 15–25 s. During the delay participants were occupied with a demanding ongoing task (color judgment) and therefore were not actively rehearsing the prospective intention (either parity or magnitude judgment). Throughout the experiment, all stimuli afforded the performance of both the ongoing and the delayed tasks; that is, the implementation of the delayed intention had to be self-initiated. Moreover, participants did not receive any feedback regarding their performance.

Employing long delay durations (15–25 s) allowed us to dissociate the representation of intentions in two distinct temporal phases: 1) while being maintained (maintenance phase), and 2) while being retrieved and prepared for execution (retrieval phase). Importantly, subjects needed to rely on internal time-keeping processes to determine when to switch to the delayed task. Therefore, an internally generated go-signal was required to terminate the delay period, and initiate the switch to the prospective task. We hypothesized that information regarding future intentions would be retained in activity patterns of the aPFC (Badre, 2008; Koechlin and Hyafil, 2007). To test this, we used searchlight pattern classification (Haynes and Rees, 2006; Kriegeskorte and Bandettini, 2007; Kriegeskorte et al., 2006) to decode both the prospective task ('what') and the intended delay duration ('when') during maintenance and retrieval of prospective intentions.

We found that the anterior PFC encoded both 'what' and 'when' components of a future intention during temporally distinct phases of an intention delay. During the delay in which the intention is maintained, the dorsomedial aPFC encoded the 'what' of future intention, while dorsomedial and bilateral aPFC regions encoded the 'when' or the intended time-delay (see Supplementary Table 2). Interestingly, the dorsomedial aPFC regions in the 'when' analysis were found to lie ventral to the dorsomedial aPFC regions that stored 'what' information (see Supplementary Tables 1 and 2). During retrieval, the ventrolateral aPFC encoded the prospective 'what', while the dorsomedial aPFC encoded the prospective 'when' information.

Materials and methods

Participants

Twenty healthy adult subjects took part in the study and gave written informed consent to the experiment. Subjects were scanned while performing 5 sessions with 12 blocks of 50 s length each. The experiment was approved by the local ethics committee and was conducted according to the Declaration of Helsinki. All subjects reported to be right-handed and had normal or corrected to normal vision. Eight subjects were excluded due to poor task performance defined as below 80% successful blocks (see Results). The final sample consisted of 12 subjects (6 female, mean age = 26, range 23 to 28 years).

Experimental paradigm

We designed a time-based prospective memory paradigm with two delayed task ('what') conditions and three delay duration ('when') conditions (2×3 design). On every block, subjects first received a visual instruction consisting of a number and a task (Fig. 1A). These cues instructed them to perform a task (parity or magnitude judgment) after the specified delay duration (15, 20, or 25 s). Subjects had to self-estimate the delay duration while performing an ongoing task, and switch to the future task as soon as they endogenously detected the end of the delay.

The instruction was followed by a series of 18 trials (2 s each) with numbers that were green or red (Fig. 1C). All number stimuli allowed performing three different tasks (Fig. 1B): Color judgment ('is the number red or green?'), parity judgment ('is the number odd or even?') or magnitude judgment ('is the number bigger or smaller than 5?'). Participants were instructed to always perform the color judgment task during the delay while remembering which future task (parity or magnitude) to perform after the delay. Since the stimuli afforded performing all tasks, participants had to decide when the self-estimated delay was over and self-initiate a switch to the prospective task (parity or magnitude).

Stimuli and responses

All stimuli were designed using MATLAB 7.0 (The MathWorks) and Cogent Graphics toolbox developed by John Romaya at the LON at the Wellcome Department of Imaging Neuroscience. The stimuli consisted of a number, surrounded by 6 response symbols (Fig. 1C). For every number, 3 tasks and 6 potential responses were possible (red/green, odd/even, and bigger/smaller than 5, Fig. 1B). On every trial, the six response symbols were pseudo-randomly located on 6 fixed spatial positions around fixation (Fig. 1C). On each trial, subjects pressed one of 6 buttons, each corresponding to a position on the screen, to indicate their response choice. The responses were collected using 6 buttons (2×3) distributed on two manual button boxes, one for each hand (see Supplementary methods). Prior to scanning, subjects completed two training sessions to learn the symbols, familiarize themselves with the button boxes, and practice the delayed intention task. Please note that the pseudorandom spatial arrangement of response symbols on every trial ensured that there was no contamination between task responses and button presses or locations on the screen.

During the delay, subjects were to remember the future task (parity or magnitude judgment) while performing the ongoing task (color judgment) until the end of the self-estimated delay. Meanwhile, they endogenously estimated the passage of time and self-initiated a switch to the prospective task as soon as they decided that the intended duration had passed. The stream of visual input was present throughout the experiment, independent of the task the subject was currently performing. Subjects' responses indicated which task they were currently performing (for criteria of successful blocks see Results). Importantly, in order to ensure that endogenous processes

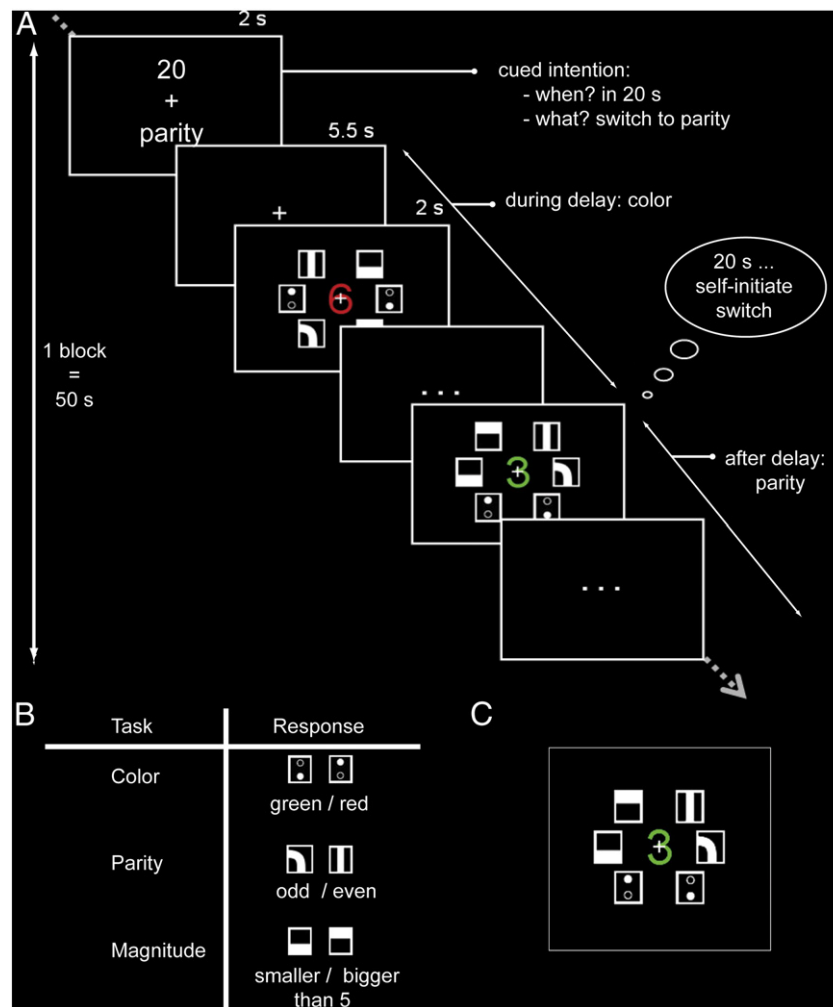


Fig. 1. Prospective intention paradigm. We designed a time-based prospective memory paradigm as follows. (A) At the beginning of each block, subjects received a visual instruction cueing them which task to store (parity or magnitude) and after which time delay to start performing it (15, 20, or 25 s). Then subjects saw a stream of trials each showing a central number that could either be green or red. During the delay subjects performed an ongoing task, which consisted of judging the color of the central numbers. As soon as subjects believed the delay to have elapsed they switched and began to perform the stored prospective task (parity/magnitude) on the central numbers. (B) Each of the 6 response symbols represents a possible response to one of the 3 tasks; color (green, red), parity (odd, even) and magnitude (smaller than 5, bigger than 5). (C) Symbols' location randomly changed on every trial. To indicate a response, subjects indicated the location of the corresponding symbol on that trial via manual button press. To do this, they pressed one of 6 buttons corresponding to the 6 symbol position on the screen. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

regulated the delay duration we did not provide our subjects with any explicit time-measurement cues. Therefore, subjects' internal time-keeping determined the end of the delay, and triggered the go-signal to *self-initiate* a switch to the prospective task (parity or magnitude).

fMRI acquisition

A Bruker 3 T Medspec 30/100 scanner was used to acquire T2*-weighted functional images using an echo planar imaging (EPI) sequence (TR = 2500 ms; TE = 30 ms; FOV 192 × 192 × 110). For each run 244 functional MR EPI volumes were acquired per subject (37 ascending axial slices per volume, slice thickness 2 mm, in-plane resolution 3 mm × 3 mm, 1 mm interslice gap resulting into an isotropic resolution of 3 × 3 × 3 mm). For every subject 5 runs (12 blocks each) of functional MRI were acquired.

Preprocessing of fMRI data

Data were preprocessed using SPM2 (<http://www.fil.ion.ucl.ac.uk/spm>). The functional images were temporally corrected for slice

timing and spatially realigned to account for between-scan movement. The images were then transformed into standard MNI space by first coregistering them with the mean functional image, followed by spatial normalization to the MNI EPI template.

GLM analysis (finite impulse response regressors)

As a precursor to the multivariate decoding analysis we first applied two separate general linear models (GLM) (Friston et al., 1994) to the data of each run. One GLM was designed for 'what' and one for 'when' aspects of the prospective intentions (Fig. 2A). In order to preserve maximum temporal resolution, the models had to be estimated for each scan in their respective trials. To do this, we used finite-impulse-response (FIR) regressors (Henson, 2004). For every condition, parameters were estimated using a general linear model (GLM) with a finite impulse response (FIR) basis function. FIR sets average the BOLD response for each bin of a number of successive time bins (or 'mini boxcars') separately (Henson et al., 2001). Here, each time bin represents one full-brain scanned volume of 2.5 s length. These time bins are time locked to the onset of an event to which the model corresponds. We estimated separate

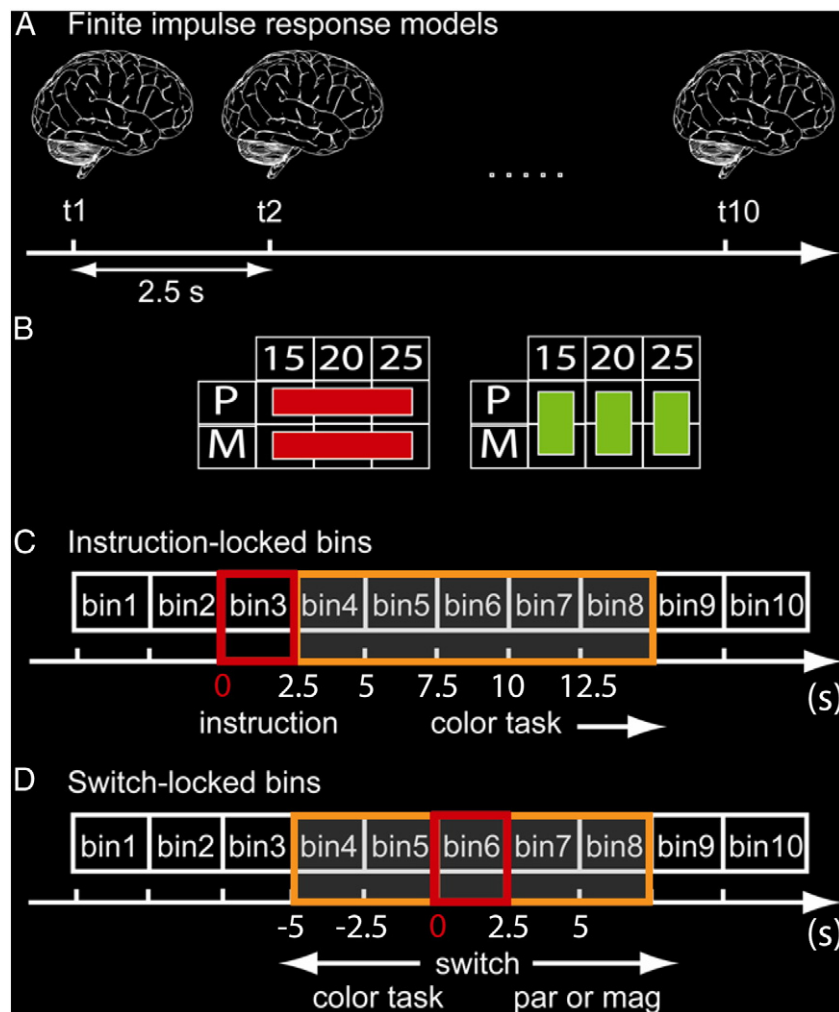


Fig. 2. Finite impulse response GLM for time-resolved decoding. (A) Two separate general linear models (GLM) were estimated for 'what' and 'when' conditions. The task or 'what' model (red) consisted of 2 task conditions (parity versus magnitude) collapsed across time-delays. The time-delay or 'when' model (green) consisted of 3 conditions (15, 0, or 25 s) collapsed across tasks. (B) For each run, finite impulse response (FIR) models were fitted to the data for task and time conditions separately. Here each time bin represents one full-brain scanned volume of 2.5 s length. FIR regressors were estimated time-locked to two major events of a block as follows. (C) In instruction-locked models 10 regressors were time-locked to the onset of instruction. (D) In switch-locked models, 10 regressors were time-locked around the behavioral onset of the switch to the prospective task. The instruction and switch events are marked in red. The areas framed in orange mark the time-bins for which group statistics were later calculated (see [Materials and methods](#)). Time bins are indexed relative to the beginning of the window of analysis. The onsets are shifted by two volumes (scans) to account for the hemodynamic delay. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

general linear models (using FIR) for 'what' (parity vs. magnitude) and 'when' (15, 20, or 25 s) conditions. For each condition we separately estimated models that were time-locked to the instruction or the switch (Fig. 2). These models were later used for time-resolved decoding (Supplementary Fig. 1).

The GLM for task-decoding ('what' condition) consisted of four sets of 10 FIR regressors (Fig. 2B). Two sets (one per future task) were time-locked to the instruction (ranging 10 volumes after, and including, the behavioral onset of instruction, Fig. 2C). They modeled the maintenance of the two prospective tasks (parity/magnitude). The remaining two sets comprised of 10 time bins time-locked to (centered around) the switch to the prospective task. Please note that the switch-locked regressors were locked to the actual time of switch (not the instructed time), i.e. to the first time-bin in which the participants started to perform the prospective task. For instance, say the instruction was to switch after 15 s but a participant actually switched 17.5 s after the instruction. Then the actual time of switch is the scan measured not 15 s, but 17.5 s after the instruction. Accordingly, the switch-locked regressor would be locked to the later time-bin (17.5 s after instruction). The analysis window of the switch-locked model covered 25 s (10 bins) starting 7.5 s (3 bins)

before the behavioral onset of the switch (see Fig. 2, please note that the corresponding scanned onsets are shifted by 2 bins or 5 s). Importantly, previous studies using time-resolved decoding suggest a 5 s hemodynamic delay between the behavioral onset and the corresponding peak BOLD response (Bode and Haynes, 2009; Soon et al., 2008). Taking into account the 2 bins volume-shift, the model covered 5 bins before to 3 bins after the volume corresponding to the switch event (Fig. 2D). These regressors modeled the retrieval of the two prospective tasks (Fig. 2A). In total, two instruction-locked and two switch-locked regressors modeled the maintenance and retrieval of parity and magnitude as future intentions during the delay period.

Similarly, the GLM for time decoding ('when', Fig. 2A) consisted of instruction-locked and switch-locked sets of 10 finite-impulse-response (FIR) regressors. Three sets (one per instructed duration) were time-locked to the instruction and modeled the maintenance of the three prospective duration conditions (15, 20, or 25 s). The three remaining sets were time-locked to the switch to the prospective task and modeled the retrieval of the prospective intention. Please note that we have shifted all onsets and resulting parameter estimates by 5 s (2 bins) to account for the hemodynamic delay (Figs. 2C and D).

Searchlight pattern classification

In order to identify which brain regions encode information about the 'what' and 'when' components of prospective intentions, we analyzed the subjects' fMRI signals using multi-voxel pattern classification (Haynes and Rees, 2006; Kriegeskorte and Bandettini, 2007; Kriegeskorte et al., 2006). We performed four time-resolved multivariate decoding analyses (Bode and Haynes, 2009; Soon et al., 2008; Supplementary Fig. 1). The aim was to assess from which brain regions and which time-points a classifier could learn to decode the 'what' and 'when' components during two separate phases: (1) during the *maintenance* phase where a subject is busy with the ongoing task; (2) during the *retrieval* phase where the subject switches from the ongoing to the prospective task. These analyses were separately conducted for the 'what' aspect (parity or magnitude) and the 'when' aspect (15, 20, or 25 s) of the prospective intention. We applied a moving searchlight approach (Haynes and Rees, 2006; Kriegeskorte and Bandettini, 2007; Kriegeskorte et al., 2006) to search for information in local response patterns in a spatially unbiased fashion. The results were maps of local pattern information, which were obtained as follows.

First, we investigated information concerning the *prospective task* during the *maintenance* phase. For each subject *S* and each center voxel *V* in their brain, we defined a spherical cluster with a radius of 4 voxels (Haynes and Rees, 2006). For all *N* voxels in this cluster, each run *R*, each timepoint *T* and each condition *C* (parity/magnitude) we extracted the unsmoothed parameter estimates of the instruction-locked GLM model. Then we performed a separate decoding analysis for each timepoint *T*. Data from 4 out of 5 runs were used as training vector, to train a linear support vector classifier (LIBSVM, <http://www.csie.ntu.edu.tw/~cjlin/libsvm>, Haynes and Rees, 2006) with a fixed regularization parameter $C = 1$. The classifier was given the *N*-dimensional pattern vectors for each of the two task conditions for each of the 4 training vectors. Then, we assessed how well this classifier could assign the labels for the remaining independent 5th run, or the test vector. This procedure was repeated 5 times, each time leaving out a different run as test data. This 5-fold cross validation using independent training and test data avoids problems of 'double dipping' and circular analysis (Kriegeskorte et al., 2009; Vul and Kanwisher, 2010; Vul et al., 2009). The classification accuracy was averaged across the 5 runs and was taken as an index of the local task-related information at position *V* of subject *S* at timepoint *T*. The process was repeated for every subject *S*, every time-point *T* and every voxel *V* throughout the whole brain. The results were 10 instruction-locked whole-brain maps of prediction accuracies (one per time-bin) for each subject, reflecting how well the prospective task can be decoded (Supplementary Fig. 1).

Accuracy maps for each subject and timepoint were smoothed with a 6 mm FWHM Gaussian kernel and entered into a one-way ANOVA with the factor time as within subject independent variable. We performed a T-contrast against chance level (50%) on time-bins 4 to 8 (see shaded areas in Fig. 2C and Fig. 4) to identify regions with significant task-related information during the maintenance phase (Fig. 3B). For this we applied a whole brain family wise error (FWE) correction at $p < .05$ at voxel level (Supplementary Table 1, regions indicated with a *). In order to avoid missing significant regions due to this conservative threshold, we further relaxed the extend threshold to $p < 0.001$ cluster level FWE correction using a height threshold of $p < 0.0001$ and extent threshold $k > 0$ voxels (Supplementary Table 1, regions identified in italics). Please note that a test of any earlier phases immediately following the instruction would be ambiguous because it could be contaminated by information related to visual aspects of the instruction. A similar procedure was applied to switch-locked parameter estimates for the retrieval phase, using time bins 4 to 8 which covered two time-bins before and two after the switch event (see area framed in orange in Fig. 2D, Results, Fig. 3C, and Fig. 4). Given the two prospective task conditions, chance level for the two 'what' analyses was at 50%.

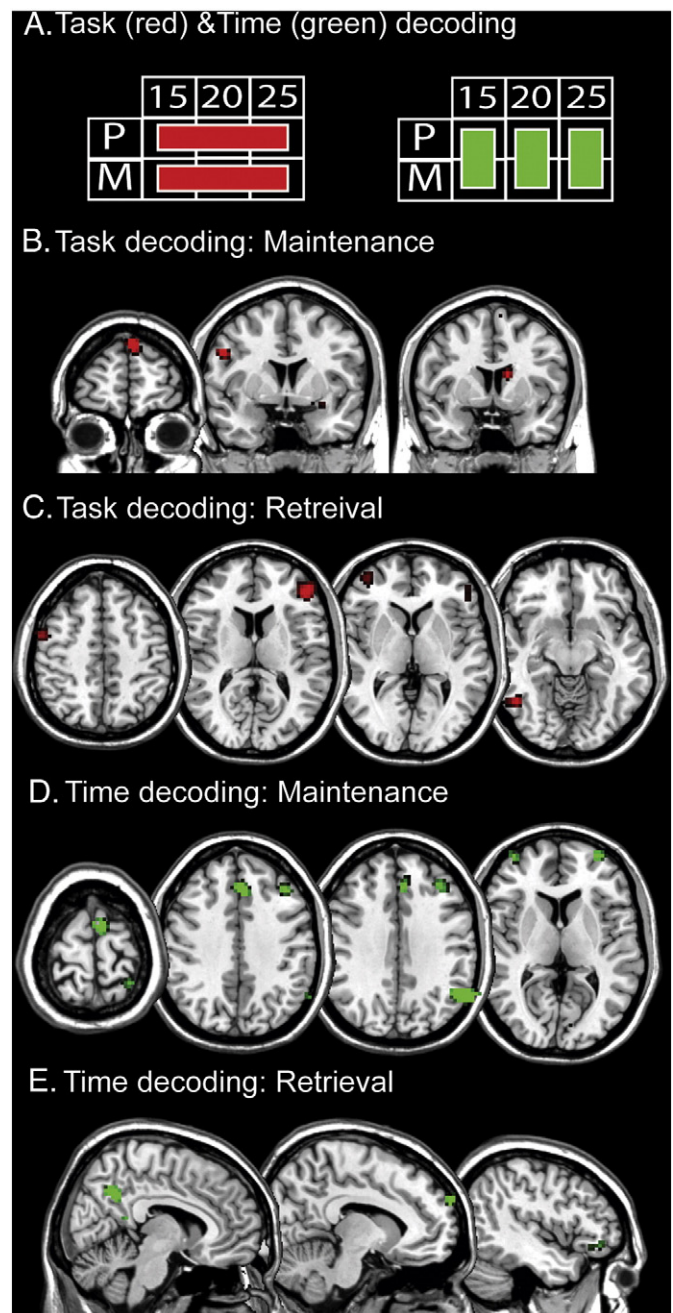


Fig. 3. Brain regions encoding the 'what' and 'when' of prospective intentions during maintenance and retrieval. Searchlight pattern classification (Haynes and Rees, 2006) was used to identify regions which encoded the prospective task and time-delay. (A) In order to identify brain regions encoding the prospective task (parity or magnitude) trials were collapsed across the different timing conditions (red). In order to identify brain regions encoding the delay (15, 20, or 25 s) we collapsed trials across the different tasks (green). (B) Brain regions encoding the future task during maintenance included the dorsomedial anterior PFC, and the left SMA (see Supplementary Table 1). (C) Brain regions encoding task during retrieval included right DLPFC, left inferior temporal lobe, left anterior PFC, and left BA 6 (see Supplementary Table 1). (D) Brain regions encoding the delay duration during maintenance include bilateral anterior PFC, the right dorsolateral PFC, the ACC, the SMA, the cerebellum, and right posterior parietal lobe (see Supplementary Table 2). (E) Brain regions with time information at retrieval: the dorsomedial aPFC, DLPFC, and the precuneus (see Supplementary Table 2). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Similar analyses were applied for time-decoding. First, we decoded the 3 delay conditions during all instruction time and switch-locked time-bins. The outcomes were 10 instruction-locked and 10 switch-locked accuracy maps of 'when' information per

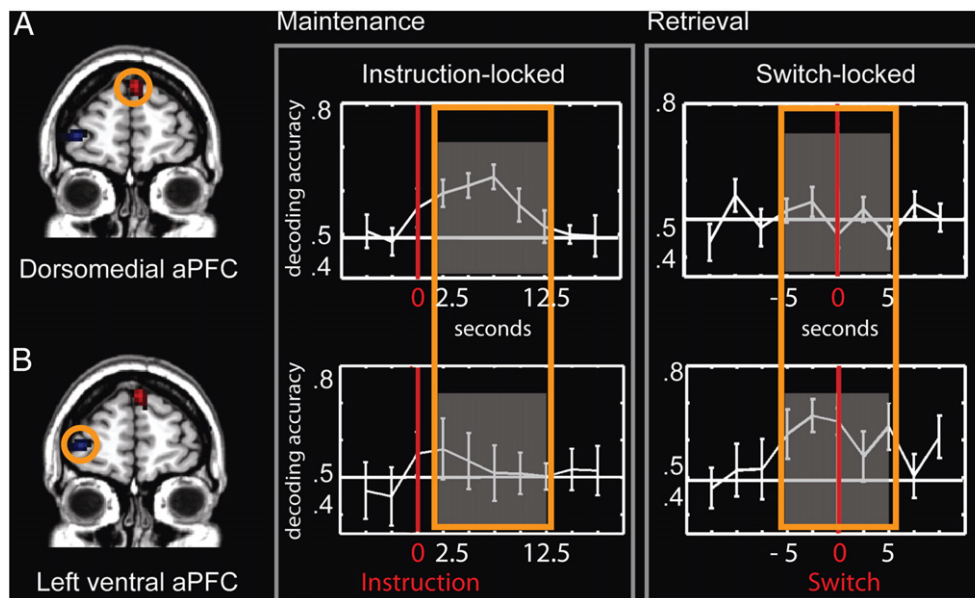


Fig. 4. The role of aPFC in the maintenance vs. retrieval of 'what' information. Group statistics were applied to identify regions encoding the prospective task ('what') across all subjects during maintenance (instruction-locked time-bins) and retrieval (switch-locked time-bins). T-contrasts (averaged over the periods of time specified in orange frames) were applied to prediction accuracy maps of all subjects (Fisher's Z-transformed correlation coefficients). (A) During maintenance, a region in the dorsomedial anterior PFC encoded prospective task information most significantly (upper left plot). This region did not reveal significant task information at retrieval (upper right plot). (B) During retrieval, left ventrolateral aPFC encoded prospective 'what' information most significantly (lower right plot). This region did not encode significant task information during the maintenance phase (lower left plot). Error bars and accuracy values are plotted for illustrative purposes only. Red lines mark the instruction in maintenance plots, and mark the endogenous task-switch in retrieval plots. Orange frames indicate time bins included in T-contrasts in the second level analysis for maintenance (instruction-locked, left) and retrieval (switch-locked, right) phases respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

subject. We then subjected time-bins 4 to 8 of the maintenance or instruction-locked phase to second level analysis using T-contrasts on ANOVAs (see Fig. 3D, Supplementary Table 2). Secondly, we applied a second level T-contrast on the 5 time-bins leading up to the switch event in switch-locked 'what' analysis (see Fig. 3D, Supplementary Table 2). Given the three 'when' conditions, chance level for the time-decoding analysis was at 33.3%.

Results

Behavioral results

Subjects underwent two training sessions prior to scanning. They were first trained on each task separately. This ensured that their responses to all three tasks were correct on average on 96% of trials ($SD = 1.8\%$). The second training consisted of full experimental blocks. A block was considered successful if all of the following criteria were true: 1) the subject did not forget to switch; 2) the subject correctly switched to the instructed task; 3) there were at least three color trials prior to the switch (i.e. minimum delay duration was 12.5 s) and at least three trials after (minimum task performance 7.5 s); and 4) the subject did not change the task they performed after the switch until the end of the trial. Importantly, participants were instructed to favor task accuracy over timing accuracy. They were explicitly instructed not to lose track of switching to the correct task and not to sacrifice accuracy of color judgments by paying too much attention to keeping track of the time. Participants were especially instructed to ensure to switch to the instructed task. Task accuracy was explained as a) accuracy of performance on the color task, b) accuracy of switch to the prospective task, and c) accuracy of performance on the prospective task. On the basis of behavioral performance in the scanner, only the neuroimaging data from 12 subjects (6 female) who successfully completed more than 80% of blocks were further analyzed.

Subjects produced delay durations that were on average 4.3 s longer than the instructed durations cued (means = 18.3, 24.9, and 29.1 s with

S.D.s = 3.3, 4.5, and 5.1 s for instructed duration of 15, 20, and 25 s respectively). We compared the effect of task (color, magnitude, and parity conditions) on reaction times using a one-way repeated measures ANOVA. We did not find significant differences among the accuracies of responses to the three tasks ($F(2, 11) = 0.8$, $p = 0.47$). Moreover, using two paired-sample *T*-tests we compared both reaction times and accuracy of responses to the color task while subjects maintained parity versus magnitude as future intention. We did not find a significant difference in accuracies ($t(11) = -0.29$, $p = 0.77$) or reaction times ($t(11) = 0.075$, $p = 0.94$) to the ongoing task between the two prospective intention conditions.

We further analyzed the behavioral data in order to investigate whether there were effects of the delay condition (15, 20, or 25 s) on the behavioral performance during the delay. Non-significant outcomes would make it highly unlikely that differences in neural activity during the delay period are due to differences in color-task performance rather than the 'when' intention component. We applied four two-factor repeated measures ANOVAs where the first factor was delay condition and the second factor was defined by bin number in either instruction-locked time-bins (first 4 time bins, or 10 seconds) or switch-locked time-bins (3 time-bins prior to the switch). The dependent variable was defined either by reaction times or accuracy of responses to the color task. Where determined necessary by Mauchly's test the degrees of freedom were corrected for sphericity using the Greenhouse–Geisser estimates. We found no significant main effect of delay condition on reaction times during instruction-locked ($F(2, 22) = 1.819$, $p = 0.186$) or switch-locked ($F(2, 22) = 0.930$, $p = 0.409$) time bins. Neither was there a significant main effect of the delay conditions on the accuracy of responses during the four instruction-locked ($F(1.141, 12.552) = 0.832$, $p = 0.394$, $\epsilon = 0.571$) or the three switch-locked ($F(1.345, 14.796) = 1.170$, $p = 0.316$, $\epsilon = 0.673$) time bins of the delay period. Finally, although there was a main effect of bin number on the color task performance, as is expected in task-switching paradigms, there was no significant interaction between the delay condition and bin number in instruction-locked reaction times ($F(6, 66) =$

1.357, $p=0.110$), switch-locked reaction times ($F(1.731, 19.039)=0.708$, $p=0.486$, $\epsilon=0.433$), instruction-locked accuracies ($F(1.427, 15.700)=1.357$, $p=0.110$, $\epsilon=0.238$), or switch-locked accuracies ($F(4, 44)=0.361$, $p=0.835$). Therefore, it is highly unlikely that behavioral differences during the delay period may drive the 'when' decoding results in instruction-locked and switch-locked conditions.

Neuroimaging results

All results are family-wise-error (FWE) corrected for multiple comparisons at voxel level ($p<0.05$), or at cluster level (Friston et al., 1996) with a height threshold of $p<0.0001$ and extent threshold $k>0$ voxels (see Supplementary Tables 1 and 2, voxels that survived whole brain voxel level correction with $p<0.05$ are indicated with a *). The first analysis assessed any task-related ('what') information during the *maintenance phase* of prospective intentions. Patterns of neural activity in the dorsal medial aPFC (at the border of Brodmann areas 9 and 10, Fig. 3B) contained significant information about the prospective task (this region also survived more conservative threshold: FWE corrected at voxel level, $p<0.05$, Supplementary Table 1). Other regions included the right caudate, the left Brodmann area 6, and medial PFC regions including the BA 9 and the pre-supplementary motor area (pre-SMA, border of BA 8 and BA 32, see Supplementary Table 1). Please note the sustained above-chance decoding accuracies over a period of 10 s, starting from time bin 4 (that is 2.5 s or 1 time bin after the shifted onset of instruction, see time course of decoding in Fig. 4). This long time-course of maintenance shows that information during the instruction-locked phase cannot be merely attributed to residual information from the instruction event.

The second analysis assessed any task-related ('what') information during the retrieval phase of prospective intentions. Similar to all four contrasts applied here, we employed a T-contrast on a period of 5 time bins. Here we analyzed time bins that were locked to task switch to identify regions with information about the prospective task during retrieval. Since the 'what' information was relevant after the switch, we placed the 5-bin T-contrast 2 bins before and 2 after the switch point. We found that immediately before subjects switched to the stored task, 'task' information was encoded in the left anterior prefrontal cortex (BA 10 and BA 46) and the right inferior frontal triangle (mostly BA 45 and partly BA 46) (Fig. 3C). The spatial patterns in the left PFC were more ventral and anterior than those within the right PFC. Other regions with significant task decoding prior to the switch included left inferior temporal cortex and left frontal Brodmann area 6. Importantly, the ventrolateral aPFC regions, which contained task information during retrieval, did not contain significant information during maintenance. Conversely, the dorsomedial aPFC regions that were task-informative during maintenance did not reveal task information during retrieval (FWE corrected at voxel level $p<0.05$, or at cluster level, $k>0$, height threshold $p<0.0001$, Fig. 4, see Supplementary Table 1).

The third analysis assessed information about the intended *delay duration* ('when') during the maintenance phase. This information is required for the timely and endogenous retrieval of future intentions. We analyzed time bins that were time-locked to the instruction in order to identify regions that encoded the delay-duration a subject intended to wait for (15, 20, or 25 s). A group T-test revealed the ACC and the PPC, as well as the bilateral anterior PFC, the right DLPFC, the SMA, and the cerebellum (FWE corrected at voxel level, $p<0.05$, Supplementary Table 2).

The final analysis assessed time-delay ('when') information during retrieval. A T-test was applied to the 5 time-bins prior to the switch. Please note that this analysis differs from the T-contrast applied in 'what' decoding at retrieval (second analysis above). This is because the 'what' information could still be present after the switch,

while information regarding 'when' to switch was no longer relevant after the switch event. Therefore, we investigated 'when' information during the time-bins that led up to the switch. We hypothesized that different regions may encode the 'when' information differently during this retrieval period. In order to avoid strong hypotheses regarding the time-course of 'when' decoding prior to the switch, we employed a T-contrast that allowed us to identify regions with significant mean decoding accuracy over the time period leading up to the switch. With a relaxed hypothesis regarding the time-course of information, we could detect regions which encoded the retrieval criteria, or duration information, in an assumption-free fashion. Regions with 'when' information prior to the switch included the dorsomedial aPFC (BA10), the precuneus, the right ventrolateral PFC including the orbitofrontal cortex (BA 47) and the inferior frontal triangle (BA 45, Fig. 3D, Supplementary Table 2). These regions also survived more conservative thresholds (FWE corrected at voxel level, $p<0.05$, Supplementary Table 2).

Discussion

Here we investigated how the brain stores and retrieves future intentions while we are actively engaging in another task. To our knowledge, this is the first study to investigate the computational role of the prefrontal cortex in representing the content of *time-based* prospective memory (as opposed to *event-based* prospective memory, see Gilbert, 2011). Our results show for the first time, that the anterior prefrontal cortex (aPFC) may play a computational role in the maintenance and retrieval of intention components during time-based prospective memory. We have demonstrated that the anterior prefrontal cortex retains information about 'what' subjects intend to do next and 'when' they intend to do it although they are occupied with another task. Importantly, during the maintenance and endogenous retrieval of intentions the 'what' and 'when' components of prospective intentions were encoded in distinct aPFC regions.

Previous monkey and human studies suggest that prefrontal and anterior PFC regions encode future goals and their value (Genovesio et al., 2006b; Isoda and Hikosaka, 2007; Miller and Cohen, 2001; Sylvain and Koechlin, 2010). Other studies suggest that the aPFC also plays a role in prospective memory, prospective time estimation, and task-set preparation (Burgess et al., 2003; Genovesio et al., 2006a; McFarland and Glisky, 2009; Okuda et al., 1998; Okuda et al., 2007; Sakai, 2008). However, it has remained unclear whether aPFC activity merely correlates with maintenance processes, or encodes the *content* of specific intention components over long occupied delays. Our results support the latter, and extend previous findings in four important ways. We found prospective 'what' information in a) the dorsomedial aPFC during maintenance; and b) the ventrolateral aPFC and lateral PFC during retrieval. We decoded prospective 'when' information from c) bilateral and medial aPFC during maintenance; and d) the dorsomedial aPFC and lateral PFC during retrieval. A discussion of these major findings follows.

Decoding the 'what' component of future intentions

On the basis of the literature on prospective memory (Burgess et al., 2011; Gilbert et al., 2009; Simons et al., 2006), intentions and task-sets (Haynes et al., 2007; Sakai and Passingham, 2002; Soon et al., 2008), and prefrontal cortex function (Badre, 2008; Koechlin et al., 2003) we hypothesized that the aPFC would encode the content of future intention. In confirmation of this hypothesis, we found that during the maintenance phase the dorsomedial aPFC encoded the 'what' component of prospective intentions. This is in line with the what-when-whether model of intentional action (Brass and Haggard, 2007; Haggard and Brass, 2008), which suggests that 1) the medial PFC activity plays a role in the selection of the 'what'

component of intentional action, and 2) the dorsomedial PFC (BA 9) activation increases when subjects decide ‘whether’ to execute an intention or to voluntarily withhold immediate execution. Moreover, the medial PFC (including the pre-SMA and the ACC) has been shown to mediate the control and regulation of subsequent behavior in task switching and conflict monitoring in both human and monkey (Isoda and Hikosaka, 2007; Monsell, 2003; Nachev et al., 2005; Rushworth et al., 2004; Sakai, 2008). We suggest that the dorsomedial aPFC and mPFC (see Supplementary Table 1) encode the prospective ‘what’ component and inhibit prospective task operation until the go-signal arrives, i.e. the ‘whether’ component is positively determined. This is also in line with findings that the mPFC mediates strategy adjustment (Isoda and Hikosaka, 2007; Mueller et al., 2007; Nachev et al., 2005).

During retrieval, prospective ‘what’ information was decoded from lateral aPFC and the right inferior frontal cortex (IFC). Previous studies have suggested that the lateral aPFC activity changes during self-initiated and stimulus-independent thought (Gilbert et al., 2005, 2006, 2009; Koechlin and Hyafil, 2007; Koechlin et al., 1999). Other studies suggest that the ventral gradient of the PFC is involved in retrieval and initiation of action sequences (Badre and D’Esposito, 2007). Moreover, lesion studies stress the role of the right IFC in inhibiting competing responses (Aron et al., 2004; Demakis, 2003). However, previous studies have not shown whether the lateral aPFC encodes the *content* of self-generated thought. Here these regions encoded the ‘what’ content at the end of the delay period while subjects retrieved prospective intentions endogenously, and prepared and inhibited the future task operation until the switch.

The computational role of anterior PFC regions in PM maintenance

Whereas the dorsomedial aPFC encoded the prospective task during maintenance briefly after a stimulus-based intention formation, the ventrolateral aPFC contained task information during the stimulus-independent retrieval. Our findings are consistent with the suggested medial versus lateral functional dissociation within the aPFC (Burgess et al., 2011; see Fig. 4). One possible explanation for this dissociation is that the medial aPFC efficiently stores the prospective task (‘what’), while withholding its execution until the ‘whether’ component is positively determined (Brass and Haggard, 2007; Haggard and Brass, 2008). This is in line with the hypothesis that anterior PFC regions select action representations that are pending for future execution, while more posterior PFC regions represent temporally proximal actions (Badre, 2008; Koechlin and Hyafil, 2007).

We suggest that the computational role of the aPFC in the representation of future intentions may rely on the level of abstraction of the future intention (e.g. due to complexity of task-rules, Badre and D’Esposito, 2007) or the ongoing task load (Koechlin and Hyafil, 2007). Consistently, a recent event-based prospective memory study (Gilbert, 2011) applied decoding analysis to decode anticipated visual cues and prepared motor responses. The study could not decode the motor intentions from the anterior PFC, but the anticipated retrieval cues could be decoded from the ventral medial aPFC. Importantly, while the lateral aPFC enhanced cue-detection and retrieval, it did not encode the content of anticipated cues or motor responses. In comparison, the present study employs more abstract tasks with complex task-rules, a self-regulated delay and self-initiated retrieval. This implies a higher task-load during a long delay period. Moreover, in this paradigm there are no task-dependent changes in the visual stimuli; therefore our results cannot be interpreted as visual cue anticipation. In conclusion, the aPFC may play a content-specific computational role in the maintenance and retrieval of abstract intentions (as the present study), but a content-free role in the representation of simpler motor intentions (Gilbert, 2011).

Moreover, higher task-load during the delay period in the present paradigm may result in more anterior representations of future

intentions due to the engagement of posterior regions with the ongoing task. Consistently, Haynes et al. (2007) had decoded the content of future intentions under task-free delays in more posterior and ventral aPFC regions compared to the present findings. Our results show that the aPFC retains information regarding delayed intentions that are not in the focus of attention. This is consistent with the hypothesis that more anterior PFC regions serve the control and ‘efficient protection’ of temporally distant plans and pending actions (Badre, 2008; Koechlin and Hyafil, 2007; Koechlin et al., 1999).

To our knowledge this is the first multivariate study to suggest a computational role for the lateral aPFC in prospective memory. Moreover, the dorsomedial aPFC region here is more dorsal to regions with prospective task information in previous studies decoding delayed intentions (Gilbert, 2011; Haynes et al., 2007). One hypothesis is that this reflects differences in intention maintenance due to systematic differences in the paradigms. First, in Haynes et al. (2007) subjects had no other task during the delay but to focus on the upcoming activity. In short, their maintenance was ‘task-free’. However, in the present prospective memory paradigm participants were busily occupied with another task during the maintenance delay, i.e. their maintenance delay was ‘occupied’. Secondly, while the task was freely selected at formation in the previous study, in the present study the intention was formed on the basis of an instruction. Finally, whereas the previous paradigm employed an externally triggered retrieval, the present paradigm required an endogenous self-retrieval in the absence of any external cues. Taken together the two studies suggest a role for the dorsomedial prefrontal cortex in the representation of future intentions. This is consistent with the suggestion that the dorsomedial aPFC may be involved in maintenance processes in prospective memory (Benoit et al., 2011). Further specification of the computational role of the dorsal–ventral aPFC gradient requires further systematic experimentation.

Decoding the ‘when’ component of future intentions

Previous neuroimaging and lesion studies have shown that the aPFC plays a role in prospective memory retrieval in general (Burgess, 2000; Burgess et al., 2011; Gilbert et al., 2009; Simons et al., 2006), and especially in time-based prospective memory (PM) (McFarland and Glisky, 2009; Okuda et al., 1998; Okuda et al., 2007). Therefore, we hypothesized to decode ‘when’ information in (especially lateral) aPFC regions. Confirmingly, during the maintenance phase dorsomedial and bilateral aPFC regions together with regions previously suggested to be involved in time-estimation (see below) contained information about the ‘when’ component. During retrieval, ‘when’ information was encoded in the aPFC, the VLPFC, and the precuneus. The aPFC and the precuneus are highly connected regions previously shown to encode the timing of free action (Soon et al., 2008). A potential role for the information in these regions is to determine ‘whether’ to switch. Moreover, our findings are also in line with the suggested role of the PFC in perceiving elapsed time (Genovesio et al., 2006a; Lucchetti et al., 2005). Alternatively, these results could indicate the computational role of the aPFC in the representation of retrieval conditions (Burgess et al., 2011).

The posterior regions with ‘when’ information during maintenance have been previously indicated in time estimation studies. For instance, monkey studies have suggested that time-estimation is mediated by the posterior parietal cortex, premotor and dorso-lateral PFC, the anterior cingulate, and the cerebellum. Lesions or transcranial magnetic stimulation of these regions can cause deficits in time estimation (Buetti and Walsh, 2009; Genovesio et al., 2006a; Ivry and Spencer, 2004; Janssen and Shadlen, 2005; Koch et al., 2002; Lewis and Miall, 2003; Lucchetti et al., 2005). The present study extends these results by showing that the aPFC and these time-estimation regions may encode the *intended* prospective durations.

A computational role for aPFC in PM retrieval

An alternative explanation of the ‘when’ decoding results could be that patterns of activity in anterior PFC regions more generally reflect retrieval criteria, i.e. conditions under which the intention has to be carried out. Under this interpretation, in time-based prospective intentions this pattern would indicate the intended target time of retrieval or maintenance duration, while in event-based prospective memory this pattern may reflect the retrieval cue or event (Benoit et al., 2011; Burgess et al., 2011; Gilbert, 2011). Therefore, the computational role of the aPFC regions with ‘when’ information in our study may not be specific to timing processes. These results may reflect a more general computational role for the aPFC in prospective memory retrieval.

Taken together, we hypothesize that 1) during maintenance regions with information about the retrieval criteria or ‘when’ information (bilateral aPFC and above-mentioned timing regions) would be required to determine a match of elapsed-time to target time and regulate the delay duration. Once this match was achieved, 2) during retrieval regions with ‘when’ information (dorsomedial PFC and precuneus) would determine ‘whether’ to initiate the future action. With this information, an endogenous go-signal would initiate the retrieval of the delayed intention. As the end of the delay approached, the competing response would be prepared and inhibited (via VLPFC) until the moment of task-switching.

A crucial question is, which other cognitive processes could underlie the decoded ‘when’ results? One alternative possibility is that the cue-locked ‘when’ information reflected the fact that subjects thought more about the future task on shorter delays. For several reasons we believe such an account to be unlikely. First, as mentioned above, most regions found to contain ‘when’ information have been previously reported in studies of duration estimation in both monkeys and humans. Second, we did not find any effect of the different delay durations on the ongoing color task as would be expected if subjects’ attention was shifting to the prospective intention. Moreover, if the ‘when’-information is instead related to attention to the prospective intention, this could predict large overlaps between regions with ‘what’ and ‘when’ information. In contrast, ‘when’-informative regions rarely overlapped with regions containing ‘what’ information (Supplementary Tables 1 and 2).

Finally, the switch-locked ‘when’ information could equivalently represent *retrospective* duration (elapsed time) or *prospective* duration. Moreover, subjects could equivalently track *when to stop* performing the present task or *when to start* performing the future task. However, the present design need not distinguish them because either strategy could sufficiently determine the ‘when’ component of the future intention (Brass and Haggard, 2007). Future studies are required to 1) dissociate the neural representation of prospective versus elapsed durations, and 2) decompose the neural representations of inhibition versus initiation strategies.

Concluding remarks

To summarize, our results have demonstrated for the first time that both lateral and medial anterior prefrontal cortex may play a computational role in the maintenance and retrieval of prospective memory. Using a time-based prospective memory paradigm, we have shown that the aPFC can reveal ‘what’ subjects intend to do next and ‘when’ they intend to do it, even while they are currently busy with another task. We could decode ‘what’ subjects intended to do next from the activity patterns of a) the dorsomedial aPFC during intention maintenance; and b) the ventrolateral aPFC during endogenous retrieval. Moreover, we could decode ‘when’ they intended to implement their intentions c) from bilateral and medial aPFC during the maintenance delay; and d) from the medial aPFC and the precuneus during the endogenous retrieval. Importantly,

here for the first time we were able to identify the computational role of the lateral aPFC in prospective memory retrieval as predicted by theories of PFC function (Badre, 2008; Koechlin et al., 2003). The medial–lateral and dorsal–ventral aPFC findings may suggest a systematic role for aPFC in prospective memory tasks with different intention components, i.e. the ‘what’ and ‘when’ components, or different task and retrieval criteria. This computational or content-representational role confirms and goes beyond the hypothesis that univariate activation in lateral aPFC may be involved in PM retrieval (see Burgess et al., 2011 for a review). Interestingly, activation in the dorsomedial aPFC was previously thought to merely decrease under ongoing plus PM versus ongoing task alone conditions. Our multivariate analysis of patterns of activation in this region reveals that it may carry task information under PM conditions, i.e. in the maintenance phase of delayed intentions. A more systematic explanation of the functional roles of the dorsal versus ventral mPFC in intention maintenance requires further systematic experimentation.

Extensions of the current paradigm can help clarify the architecture of intention storage in the human brain. Furthermore, methodological extensions of the current findings, e.g. with optical imaging, may unfold new possibilities for the development of noninvasive and prefrontal-specific Brain Computer Interface (BCI) devices. Such devices may enhance tracking of long-term intentions in locked-in patients suffering from executive deficits (e.g. in Alzheimer’s) or the locked-in syndrome.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at [doi:10.1016/j.neuroimage.2012.02.079](https://doi.org/10.1016/j.neuroimage.2012.02.079).

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