

Two networks involved in producing and realizing plans

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ABSTRACT

Planning is essential for normal daily activities. Although the dorsolateral prefrontal cortex (DLPFC) is thought to be crucially involved in planning, it remains to be understood whether this contribution is attributable to working memory requirements of the tasks and when it occurs, whether during initial planning or during subsequent plan execution. Here, we compared patterns of activation observed when participants planned and executed their plans to solve Tower of Hanoi problems to when they had to memorize and reproduce externally presented sequences of moves. The DLPFC was preferentially active during initial planning relative to both plan execution and initial memorization of sequences of moves. By contrast, plan execution relied on posterior temporal areas, inferior frontal regions and the dorsolateral premotor cortex. We attribute activation in DLPFC to generation and evaluation of abstract sequences of responses, and activation in the regions underlying plan execution to rehearsal of planned sequences of moves.

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1. Introduction

The ability to develop and execute plans is crucial for tackling a wide range of daily situations effectively. Human planning, however, entails a complex set of cognitive processes. To generate a goal-directed behavioral sequence may well involve creating and ordering subgoals, developing hypotheses how each may be tackled and checking that achieving one does not destructively affect the achievement of another and if it does revising the overall procedure. Once apparently successful, the structure of the necessary steps must then be encoded in memory. Plan execution can then follow, involving the retrieval and executing of the individual steps, checking throughout that the plan is proceeding appropriately (Shallice, 1982; Unterrainer & Owen, 2006).

The planning processes described above appear necessary for adequate performance on the so-called “Tower” tasks such as the Tower of Hanoi (TOH; Simon, 1975) or Tower of London (TOL; Shallice, 1982). These tasks require the transfer of objects (disks and balls, respectively) on pegs from an initial start state into a goal end-state in the minimum number of moves. There is considerable neuropsychological evidence that successful performance

on these tests depends on the integrity of the frontal lobes (e.g. Goel & Grafman, 1995; Morris, Miotto, Feigenbaum, Bullock, & Polkey, 1997; Owen, Downes, Sahakian, Polkey, & Robbins, 1990; Shallice, 1982). Consistent with this, contemporary human brain imaging techniques have shown that mid-dorsolateral prefrontal cortex (mid-DLPFC) and/or more anterior regions like frontopolar cortex (FPC) are critically engaged by these kinds of test (e.g. Baker et al., 1996; Fincham, Carter, van Veen, Stenger, & Anderson, 2002; Kaller, Rahm, Spreer, Weiller, & Unterrainer, 2011; Rowe, Owen, Johnsrude, & Passingham, 2001).

Several studies have, however, emphasized the working memory component of planning in order to explain impaired performance on Tower tasks observed in various clinical conditions, such as frontal lesions (e.g. Goel & Grafman, 1995), Parkinson's disease (e.g. Altgassen, Phillips, Kopp, & Kliegel, 2007), intellectual disability (Numminen, Lehto, & Ruoppila, 2001) and schizophrenia (Badcock, Michiel, & Rock, 2005). It has been suggested that problems in maintaining a coordinated sequence of moves in mind during planning can give rise to slowed and less efficient plan execution in patients with frontal lesions (e.g. Carlin et al., 2000; Owen et al., 1990). Moreover computational models have also stressed the crucial role of working memory for TOH problem solving (Goel, Pullara, & Grafman, 2001; see also Altmann & Trafton, 2002; Fincham et al., 2002). For instance, in the first of these models, it was shown that the effects of frontal lobe lesions can be simulated by reducing the working memory resources available for problem solving; and this was held to support the working memory hypothesis of frontal lobe functions, more specifically of the mid-DLPFC (Goel et al., 2001).

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In line with this position, activation in mid-DLPFC was attributed to the working memory components of the task in past functional imaging studies of TOL (e.g. Baker et al., 1996; Owen, Doyon, Petrides, & Evans, 1996; van den Heuvel et al., 2003; Wagner, Koch, Reichenbach, Sauer, & Schlösser, 2006; but see Kaller et al., 2011), with activity in the more anterior FPC region being instead associated with planning specific processes such as, for instance, the selection and evaluation of sequences of moves (Baker et al., 1996) or integration of goal-subgoal sequences (van den Heuvel et al., 2003). Thus, in the PET study of Owen et al., TOL problem solving was directly contrasted with a spatial working memory condition in which participants had to memorize and then reproduce sequences of moves initially executed by the computer. The mid-DLPFC was found to contribute equally to the two tasks. However, in neither of the two tasks, was an “Initial phase” (i.e. planning ahead and sequence memorization in the Planning and Memory tasks, respectively) distinguished from an “Execution phase” (i.e. plan execution and sequence reproduction in the two tasks, respectively) and this left unresolved the issue whether DLPFC contributed equally to the two phases within each task. For instance, a potential critical role of DLPFC in planning could have been hidden by pooling across initial and execution phases, if the relation between the patterns of activation between the two phases in this region differed between planning and memory. Moreover in metaanalyses of patients with lesions restricted to lateral prefrontal cortex, the storage aspects of working memory function appear to be unaffected by the lesion (D’Esposito & Postle, 1999; see also Postle, Berger, & D’Esposito, 1999, for related arguments). Span is not impaired.

Unfortunately, functional imaging studies which investigate initial planning and plan execution separately are rare. Two notable exceptions are the studies of Unterrainer et al. (2004) and of Newman, Greco, and Lee (2009). In the first of these studies, although the two phases were not directly compared against each other, the authors were able to show that the right PFC contributed to both initial planning and plan execution. Plan execution and initial planning were directly compared more recently by Newman et al. (2009), who showed that a left prefrontal cortex (PFC) region contributed more to initial planning than plan execution while the opposite pattern held true for a right PFC one. Of importance, as a relatively short planning phase (i.e. 5 s) was used in this study, planning was also likely to take place during the execution of the complex plans required by 6-move TOL problems.

The present study employs event-related functional magnetic resonance imaging (fMRI) MRI as a method to investigate further the relationship between producing and realizing plans and working memory maintenance. It follows the PET study of Owen, Doyon, et al. (1996) in being concerned with whether an externally ordered working memory task, requiring short-term retention and reproduction of sequences of spatial moves and matched to the Tower task, activates similar brain regions to those activated by a planning task, represented here by a set of TOH problems. However, as discussed above, unlike this earlier PET study, the current experiment was designed to distinguish between an initial phase and an execution phase in both the two tasks. Thus the design allows a comparison to be made between the patterns of activation in the two tasks, separately for the two phases. In particular, we assessed whether the mid-DLPFC contributes to planning over and above the effects of working memory and plan execution. Moreover, we followed Badre and D’Esposito’s (2007) argument that a parametric variation in task complexity can show different effects on the level of activation of task-related regions. Thus, in line with previous TOL/TOH studies (see Unterrainer & Owen, 2006), we employed TOH problems and working memory sequences of graded complexity.

2. Material and methods

2.1. Participants

Eighteen right-handed healthy volunteers (9 females, 26.16 ± 5.67 years) participated in the study. No participant had an existing neurological or psychiatric illness. All gave written informed consent and were reimbursed for their time (25 Euros). The study was approved by the independent Ethics Committee of the “Santa Maria della Misericordia” Udine Hospital.

2.2. Stimuli and design

There were two main experimental conditions in this study. We refer to the first experimental condition as the *Planning* task as this was based on the TOH planning test (e.g. Simon, 1975). In the Planning task, participants were asked to solve a number of TOH problems. The problems varied in the number of moves required to reach a solution. In an *easy problem* a solution could be reached in 2 or 3 moves while in a *difficult problem*, a solution could be only reached in 4 or 5 moves. The second experimental condition was a mnemonic analog of the planning task and we refer to this as the *Memory* task. This task required participants to memorize and reproduce sequences of single moves made by the computer on the same visual array as the TOH test. In a similar fashion to the Planning task, sequences of moves in the Memory task varied in their length. There were short sequences consisting of 2 or 3 moves (*easy memory condition*) and long sequences of 4 or 5 moves (*difficult memory condition*).

In both experimental tasks, the participants were presented in the scanner with two sets of three “disks” (i.e. rectangles) of variable width (large, medium, and small: 4.6, 3.3, 2 cm respectively; 1.9 cm height), one in the bottom half of the screen and the other in the top half of the screen. The three disks were positioned in three pegs of equal height (9.8 cm). Each peg could hold one, two or three disks.

On each trial of the Planning task, the three disks were distributed in predetermined positions across the pegs shown in both the upper and lower displays. Participants were instructed that the disks in the top half of the screen formed the goal configuration and that such configuration had to be reproduced in the bottom half of the screen, by appropriately moving the corresponding disks (start configuration; Fig. 1A). To move disks between pegs, participants were required to use, with their right hand, a three-button response-key where each button corresponded to one peg. The index, middle and ring fingers corresponded to the leftmost, middle and rightmost peg in the screen, respectively. Volunteers had to use two button presses to indicate a move. The first press indicated the source peg (its topmost disk), and the second press indicated the destination peg. Participants were informed that two types of moves were not allowed: (i) initiating a move when another was not yet completed; (ii) placing a larger disk on top of a smaller disk. When such moves were attempted, the computer recorded the attempts but did not respond. At any time, a participant could place a disk back into its original position, by performing a sequence of button presses opposite to the one just executed.

On each trial of the Planning task, participants were first asked to plan the most appropriate (i.e. the shortest) sequence of moves to solve the specific problem and second to start executing the sequence. In other words, they were told to refrain from making a first move until they were confident that they could run off a well planned sequence of moves. To pass to the next trial, participants had to press a button placed under their left index finger. Two separate phases were distinguished in the Planning task (Fig. 1A) (see later in Section 2 and the last of Section 3 for a minor modification used in both the Planning and the Memory tasks). The *Initial* phase went from the presentation of a planning trial to the first button press and specified the time spent by participants planning the correct sequence of moves. The *Execution* phase went from the first button press to the end of sequence execution (i.e. left button press) and indicated the time spent by participants executing the planned sequence of moves.

On each trial of the Memory task, the arrangement of disks was the same in the start (bottom half of the screen) and goal (top half of the screen) configurations (Fig. 1B). This was done to prevent unintentional planning in this task. Participants were instructed to watch while the computer made a series of single moves (by convention of the smallest disk only, again to prevent unintentional planning) in the top half of the screen, and then had to attempt to repeat exactly the same sequence of moves (in the start configuration). At the end of each sequence made by the computer, the smallest disk always finished back in its original position. The pace of each move was fixed at 1.5 s; a value derived from a pilot study which had shown that this led to a similar level of performance in the two tasks (see also Fig. 2A). Participants knew they had to start reproducing a sequence when they saw a vertical movement in the start configuration of the smallest disk up onto the corresponding peg. Response buttons for sequence reproduction were the same as those used in the Planning task, as was the method of responding (i.e. two button presses for each move). As in the Planning task, participants had to press the button placed under their left index finger to move to the next trial.

In a similar fashion to the Planning task, the Memory task also consisted of two phases (Fig. 1B) (see also the last of Section 3). The *Initial* phase went from the onset of the memory trial (i.e. beginning of the sequence of moves shown by the computer) to the first button press, which indicated that the sequence was complete and the participant was ready to reproduce it. The *Initial* phase specified the time spent by

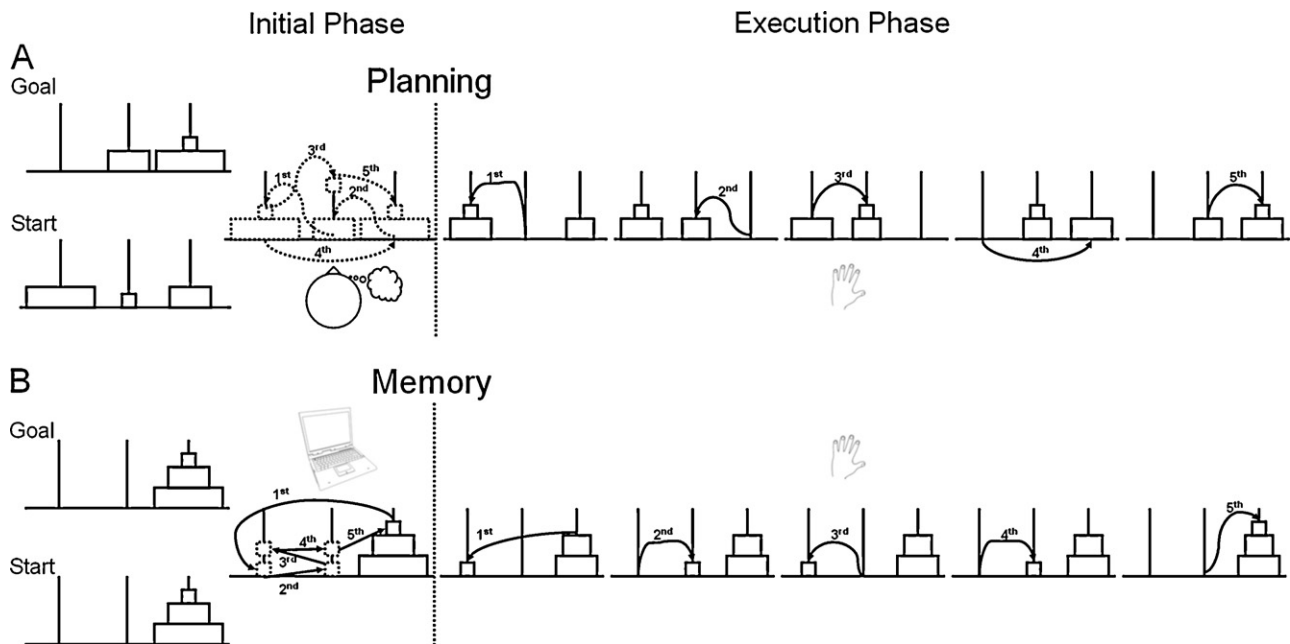


Fig. 1. Experimental paradigm. There were two experimental tasks in the study. In both Planning and Memory tasks, participants were presented with two sets of three rectangles arranged in three pegs, one in the bottom half of the screen (start configuration) and the other in the top half of the screen (goal configuration). (A) Planning task. A 5-move problem is presented. In the Initial phase, participants have to plan the minimum sequence of moves necessary to reproduce the goal configuration by mentally moving rectangles in the start configuration. In the Execution phase, participants are required to execute the planned moves. (B) Memory task. A 5-move sequence is presented. In the Initial phase, participants have to memorize a sequence of single moves made by the computer. In the Execution phase, participants are required to execute the memorized sequence.

participants memorizing the moves. The *Execution* phase went from the first button press to the end of the sequence reproduction (i.e. left button press) and indicated the time spent by participants reproducing the memorized sequence of moves.

Overall, the Planning and Memory tasks had similar perceptual and motor components, so their corresponding patterns of activation can be directly compared. In the main analysis we therefore investigated which regions contribute more to Planning than Memory, and vice versa. Nevertheless, the key aspect of the present study concerned the possibility of comparing the two tasks during the Initial phase and the Execution phase, separately, as well as comparing the two phases within each task.

2.3. Procedures

The experimental procedure involved 216 trials in total for the Planning and the Memory tasks. Each trial involved a unique TOH problem or memory sequence. The trials were organized into 3 fMRI runs of 72 trials each. In 38 of these 72 trials, participants were required to solve TOH problems (i.e. Planning trials) while in the remaining 34 trials they had to maintain sequences of moves in working memory and reproduce them later (i.e. Memory trials). The slightly different number of trials in the two tasks, based on RT data of a pilot study, enabled a similar number of scans to be acquired per participant for each of the two tasks (the mean number of EPI volumes for each run (correct trials only) were 157 and 170, respectively for Planning and Memory; the difference not being significant). In a similar way, the distribution frequency of event types was also fixed in order to acquire a roughly similar number of scans for each type of event (the mean number of EPI volumes for each run and for all the four main types of event (correct trials only) were 75, 82, 92, and 78, respectively for easy planning, difficult planning, easy memory, and difficult memory). In more detail, the total 114 TOH problems consisted of: (i) 42 2-move problems; (ii) 32 3-move problems; (iii) 22 4-move problems; and (iv) 18 5-move problems. The total 102 memory trials consisted of: (i) 36 2-move sequences; (ii) 27 3-move sequences; (iii) 21 4-move sequences; and (iv) 18 5-move sequences. The eight event types were distributed approximately equally across the three runs.

As explained in the previous section, the design was self-paced; so each run had a different duration. On average the first run lasted for 20.10 min (± 3.27 ; range: 15.56–26.63 min), the second for 16.26 min (± 1.93 ; range: 13.63–19.86 min) and the third for 14.92 min (± 1.56 ; range: 13.20–18.56 min), thus denoting a considerable degree of learning taking place during the experiment. The total time of fMRI scanning was on average of 51.6 min (± 6.3 ; range: 43.26–64.10 min).

In each run, Planning and Memory trials were grouped in small blocks typically of six trials each. Five 6-trial blocks of each of the two tasks alternated one after the other beginning with a block of Planning trials. For reasons given above, the last two blocks of each run consisted respectively of eight Planning trials and four Memory trials. Within each block of a specific task, there was at least one repetition

of each corresponding event type (e.g. one 5-move TOH problem was present in each block of Planning trials). The order of event types within each block was randomly selected. Before each block of trials, an instruction appeared on the screen for 1500 ms warning the participants about the upcoming task: “Plan the moves” (“Pianifica le mosse” in Italian), or “Remember the moves” (“Memorizza le mosse” in Italian). As explained in the previous section, participants were asked to press a button when ready to pass to the next trial; the latter was presented after a jitter of 1.5–2.5 s. Moreover, fixation blocks of 15 s each were added at the beginning, at the middle (i.e. before the 37th trials) and at the end of each run. A fixation cross appeared in the middle of the screen during these blocks. During fMRI, each participant's button press was recorded using a response pad. The responses were analysed both in terms of RT and accuracy. Accuracy (% correct) was defined in terms of numbers of TOH problems and sequences of moves respectively solved and reproduced in the minimum number of moves, predefined for each trial. All the reported behavioral and fMRI analyses refer to correct trials only.

Before fMRI scanning, participants practiced the tasks for approximately 5 min. Participants were first explained the test and then presented with two mini-blocks of three trials each. The first block consisted of three planning trials (2-, 3-, and 5-move problems) while the second was formed by three memory trials (2-, 3-, and 5-move sequences). The same procedure was used in the practice phase as during fMRI scanning. However, the problems used during practice were different from those used during fMRI. Finally, once in the scanner but before fMRI took place, participants were allowed to familiarize themselves with the response-key setup. A single configuration given by three-disks arranged in three pegs was shown in the middle of the screen and participants were required to perform 10 meaningless, but allowed, moves (i.e. not planning-related). The configuration automatically disappeared from the screen when participants made 20 key presses.

2.4. fMRI methods: acquisition and analyses

Images were acquired using a 3-T MRI scanner (Achieva 3.0T Philips Medical Systems, Netherlands) equipped with a standard quadrature head coil and for echo-planar imaging (EPI). Head movement was minimized by mild restraint and cushioning. Thirty-four slices of functional MR images were acquired using blood oxygenation level-dependent imaging (3.59 mm $\times$ 3.59 mm, 4 mm thick, repetition time = 2 s, time echo = 35 ms; flip angle: 90; field of view, FOV: 23 cm, acquisition matrix: 64 $\times$ 64; SENSE factors: 2 in anterior-posterior direction), covering the entire cortex. At the beginning of the scanning session, anatomical scans were also acquired for each participant, using a T1-weighted MP-RAGE (magnetization-prepared, rapid acquisition gradient echo).

The experimental stimuli were controlled using the Presentation software (Neurobehavioral Systems, Inc.) and delivered within the scanner by means of MR-compatible goggles mounted on the coil. SPM8 (Wellcome Department of Cognitive

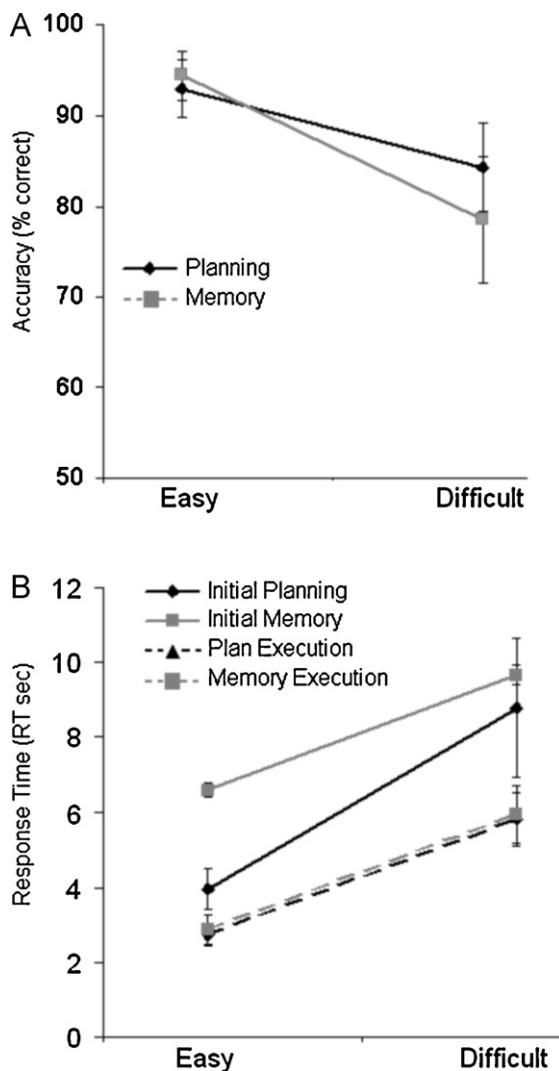


Fig. 2. Behavioral results during fMRI. (A) Mean percentage of TOH problems (Planning task) and memory sequences (Memory task), respectively solved and reproduced within the minimum number of moves, for both Easy (2- and 3-move trials) and Difficult (4- and 5-move trials) conditions. (B) Mean RT data in the Initial and Execution phases of both tasks (Planning and Memory), for both Easy and Difficult conditions. Bars indicate standard deviation.

Neurology; www.fil.ion.ucl.ac.uk/spm/software/spm8/) was used for data preprocessing and statistical analyses. For all participants 1549 volumes were acquired on average (516 volumes on average for each fMRI-run; the last participant was excluded from this estimate since, due to a technical problem, only 141 volumes were acquired during his third run); the first 5 volumes were discarded for each run to allow the magnetization reach steady state. All images were corrected for head movement; slice-acquisition delays were corrected using the middle slice as reference. All images were then normalized to the standard SPM EPI template and spatially smoothed using an 8 mm FWHM Gaussian filter. The high-pass filter was set to the cutoff value of 128 s (the analyses were also carried out using a cutoff value of 256 s which did not affect the results).

All subsequent analyses of the functional images were performed using the general linear model implemented in SPM8. First, for each participant, the data were fitted at every voxel using a combination of effects of interest. For the Initial phase of correct trials, we modeled the onset of each Planning and Memory trial separately for the Easy (i.e. 2-move and 3-move) and Difficult (i.e. 4-move and 5-move) conditions, and convolved with the hemodynamic response function (HRF). Each of the four event types (i.e. Planning/Memory and Easy/Difficult) was modeled using a boxcar with a variable duration, so that the resulting beta values represented an estimate of the neural response per unit time spent (i) planning or (ii) memorising a sequence of moves (i.e. Planning and Memory task, respectively). The duration of each boxcar function corresponded to the latency of the first button press generated by the participant in the corresponding event type. Four other regressors of interest modeled the Execution phase of the corresponding event types in both the Planning and Memory tasks. Thus, for both the Easy and Difficult conditions of the two tasks,

we modeled separately the onset of each first button press and convolved it with the HRF. As for the Initial phase, each event type was modeled using a boxcar with a variable duration, so that the resulting beta values represented an estimate of the neural response per unit time spent (i) executing a planned sequence of moves or (ii) reproducing a memorized sequence of moves (i.e. Planning and Memory task, respectively). The duration of each boxcar function corresponded to the latency of the left index button press. In general, the block-duration of the 8 regressors described above corresponded to the latencies reported in Fig. 2B.

In addition, the model comprised the onset of each instruction period (block-duration = 1.5 s) and also, as two separated regressors, the Initial phase and the Execution phase of each incorrect trial, convolved with the HRF. These three regressors were excluded from subsequent group-level analyses. Finally, the first-level analyses also included the parameters of the realignment (motion correction) as covariates of no interest.

Next, we obtained eight contrast images per participant, corresponding to the eight conditions of interest (the Initial phase and the Execution phase of the Easy and Difficult conditions of the two tasks) and pooling across the three runs. These eight contrasts were then submitted to a full factorial ANOVA for group-level random effects statistical inference. In this ANOVA we tested for (i) the main effects of Planning vs. Memory, (ii) the simple main effects of Planning vs. Memory separately for the Initial phase and the Execution phase, (iii) the simple main effects of Initial phase vs. Execution phase separately for the Planning task and the Memory task, and (iv) the two-factor interactions between Task (Planning, Memory) and Phase (Initial, Execution). An inclusive masking procedure was applied to the within-task contrasts (e.g. Planning: Initial phase minus Execution phase). Accordingly, the main effects of Planning minus baseline and Memory minus baseline were used as masking contrasts respectively in the Planning and the Memory tasks. The use of an inclusive masking procedure allows one to look at phase-related within-task differences in regions which are globally positively activated in the task but not in regions negatively activated in the task, the activation of which may reflect default-mode network (DMN) activity (e.g. Raichle, 2010). Finally, the simple main effects of Difficult minus Easy conditions were also tested in the two tasks.

Correction for non-sphericity (Friston et al., 2002) was used in the ANOVA to account for possible differences in error variance across conditions and any non-independent error terms for the repeated measures. Statistical threshold was set to $p\text{-corr.} = 0.05$ corrected for multiple comparisons at the cluster level using FWE (cluster size estimated at $p\text{-unc.} = 0.0001$), considering the whole brain as the volume of interest. Furthermore, the SPMs constituting the inclusive masks were thresholded at the default $p < 0.05$ and the contrasts to be masked (e.g. Planning: Initial phase minus Execution phase) were thresholded at $p < 0.0001$ and then corrected for multiple comparisons at the cluster level ($p\text{-corr.} = 0.05$ using FWE).

Moreover, it is important to consider design efficiency. The Initial and Execution phases occurred consecutively in our experiment. One possibility is that this could cause overlap of task-related cognitive processes and activations between the first and the second phase. However, if this is not compensated for by the inherent variability of response times over problems one could expect there to be strong correlations between regressors in the design matrix; this would reduce the opportunity to distinguish the observed effects in the brain relating to the two phases (e.g. Andrade, Paradis, Rouquette, & Poline, 1999). In fact, the orthogonality matrix calculated for our experiment shows that collinearity among regressors is not a confound in our study. A low degree of collinearity was obtained for all pairs of regressors in the matrix [range: 0.001–0.540; with most values < 0.2 and 1 meaning that two regressors are colinear (i.e. not orthogonal)].

Finally, in a supplementary analysis we divided the Initial phase of each task into two subphases: Initial* and Pre-execution. In the Memory task, the Initial* phase went from the onset of the memory trial to the completion of the computer moves while the Pre-execution phase went from the completion of the computer moves to the first button press which indicated the individual beginning of the sequence reproduction. The Pre-execution phase should involve motor preparation but also any rehearsal or planning of the subsequent moves. The Initial* phase would then be restricted more specifically to the time spent by participants memorizing the moves even more clearly than in the basic analysis. The duration of the Pre-execution phase was on average 1.38 and 1.39 s respectively for the Easy and Difficult conditions.

For completeness of the design, two corresponding subphases were also identified in the initial planning phase. In this task, the Initial* phase went from the presentation of a planning trial to 1.38 s and 1.39 s (respectively for the Easy and Difficult conditions) before the first button press. The Pre-execution phase consisted of the two time periods (i.e. 1.38 and 1.39 s respectively for the two conditions) which preceded the first button press. In the planning task, while the Initial* phase clearly reflects the time spent by participants planning the correct sequence of moves, the Pre-execution phase should relate to any potential rehearsal and preparation processes taking place immediately before the Execution phase.

In the supplementary ANOVA, we tested for the effects of Planning vs. Memory for both the Initial* and Pre-execution phases and for the simple main effects of Initial* phase vs. Pre-execution phase separately for the Planning task and the Memory task. This was done by specifying a model similar to that described above with the only exception being that this additional model included the Initial* and Pre-execution phases, separately for both tasks. The same statistical threshold to that used in the basic analysis was used in this additional ANOVA.

3. Results

3.1. Behavioral data

The percentage of TOH problems and memory sequences, respectively solved and reproduced within the minimum number of moves, is shown in Fig. 2A for both Easy and Difficult conditions. In general, participants performed both tasks adequately solving 84.2% of the difficult TOH problems perfectly and reproducing 78.5% of the difficult memory sequences perfectly. A 2×2 repeated measure ANOVA with the factors of Task (Planning/Memory) and Condition (Easy/Difficult) showed that the two tasks were performed equally well [$F(1, 17) = 2.18, p = 0.16$] showing that the matching of task difficulty had been carried out successfully as a result of the pilot behavioral study; the analysis also showed that the Easy condition was globally performed better than the Difficult condition [$F(1, 17) = 54.02, p < 0.001$]. There was a significant two-factor interaction [$F(1, 17) = 5.85, p < 0.05$] which arose because, although there was no difference between the tasks in the Easy condition [$F(1, 17) = 1.83, p = 0.19$], the Memory task was slightly more difficult than the Planning task in the Difficult condition [$F(1, 17) = 4.47, p = 0.05$].

The RT data of correct trials are shown in Fig. 2B. In both tasks, the Initial phase was longer in the Difficult condition than in the Easy condition [$t(17) = 53.83, p < 0.001$ and $t(17) = 7.33, p < 0.001$, respectively for the Memory and the Planning tasks]. In the Initial phase, timing in the Memory task reflected the fixed pace of the computer-generated moves derived from the pilot behavioral study. This duration was not different from the initial planning time in the Difficult condition [$t(17) = 1.09, p = 0.29$] but was longer than the initial planning time in the Easy condition [$t(17) = 11.67, p < 0.001$].

As far as the Execution phases of the tasks are concerned, a 2×2 repeated measure ANOVA with the factors of Task (Planning/Memory) and Condition (Easy/Difficult) showed that execution time did not differ between the two tasks [$F(1, 17) = 0.92, p = 0.35$] but that difficult TOH problems or memory sequences naturally took longer than easy problems or sequences [$F(1, 17) = 249.26, p < 0.001$]. Finally the two-factor interaction was not significant [$F(1, 17) = 0.03, p = 0.85$]. Overall, the findings on the Planning task are consistent with previous results on both the TOH and TOL puzzles (e.g. Morris et al., 1997; Newman, Carpenter, Varma, & Just, 2003; Owen, Doyon, et al., 1996).

3.2. Neuroimaging data

The main aim of the fMRI analyses was to investigate whether Planning and Memory relied on similar brain activations and to what extent such activations are modulated by the Initial phases of the tasks as contrasted with the Execution phases. Accordingly, we first report the findings for the main effects of Planning vs. Memory. Next, we will turn to patterns of activation related to the same contrasts carried out separately for the Initial and Execution phases of the tasks (e.g. Initial phase: Planning minus Memory). Third, we focus on the simple main effects of Initial phase vs. Execution phase carried out separately for the Planning and the Memory tasks. Moreover, we corroborate these sets of findings by testing for the two-factor interactions between Task (Planning, Memory) and Phase (Initial, Execution). Finally, in a supplementary ANOVA, we also investigate whether Planning and Memory led to different brain activation patterns during the Initial* and Pre-execution phases.

3.2.1. Main effects of Planning vs. Memory

First, we compared overall activation during Planning with that during Memory. This contrast revealed activation in two clusters

(Table 1, first contrast). The largest cluster was located in posterior brain regions bilaterally, its peak of activation being in the left cuneus with activation extended to the cerebellum bilaterally. A second region in the right middle frontal gyrus corresponded to the location of the frontal eye fields (FEF; e.g. Kaller et al., 2011). The opposite contrast (i.e. Memory minus Planning) led to activation in the middle and superior temporal areas bilaterally, in the left supramarginal gyrus, and in both the mid/posterior and ventral/anterior portions of the left inferior frontal gyrus (ventrolateral PFC – VLPFC, see Table 1, second contrast). Of importance, Planning and Memory did not differ in terms of mid-DLPFC activation. This finding and more generally those reported above are in line with the PET results of Owen, Doyon, et al. (1996). However, unlike this study, we found that the FPC was not more active during Memory than Planning.

3.2.2. Initial phase: Planning vs. Memory

Next, we focused on the Initial phase of the tasks. We compared activation during planning of a sequence of moves with that observed during sequence memorization (i.e. Initial phase: Planning minus Memory; Table 2, first contrast). As in the corresponding main effect of Planning minus Memory, this contrast revealed activation in posterior brain regions and in the FEF regions (e.g. Table 1, first contrast). However, unlike the overall main effect, activation was also found in bilateral fronto-parietal regions including the inferior and superior parietal lobe and the mid-DLPFC. Activation in the left hemisphere also includes a marginal effect in the left dorsal anterior premotor cortex area (pre-PMd; see Badre & D'Esposito, 2007; Badre, Kayser, & D'Esposito, 2010), a region very close to what was termed the inferior frontal junction area by Brass and colleagues (IFJ; e.g. Brass, Derrfuss, Forstmann, & von Cramon, 2005).

In the Initial phase, we also tested for areas more active during sequence memorization than sequence planning (i.e. Initial phase: Memory minus Planning; Table 2, second contrast). In a similar fashion to the corresponding main effect in the overall comparison of Memory with Planning, this contrast produced bilateral activation in posterior temporal regions, in the supramarginal gyrus and in the left inferior frontal gyrus (IFG) (see also Table 1, second contrast). Nevertheless, unlike for the overall main effect, when the initial phase was considered alone, activation was also found in the precentral gyrus bilaterally. Activation in this latter region was reasonably close to the dorsal premotor cortex region (PMd) of Badre and D'Esposito (2007) and Badre et al. (2010). Fig. 3 illustrates the areas that, in the Initial phase, showed an effect of Planning > Memory (in red) and Memory > Planning (in green), plus the signal plots for the left and right mid-DLPFC, left and right parietal cortex, left pre-PMd/IFJ region, left and right PMd regions, and the left IFG including all the eight event types obtained by crossing the following factors (Task: Planning/Memory; Phase: Initial/Execution; Condition: Easy/Difficult).

Of interest, in the frontal cortex, the plots relating to the left and right mid-DLPFC show an effect of task difficulty in these regions in the Initial phases of the tasks (IPd–IPe and IMd–Ime in the plots). This appears different from the plots related to the left pre-PMd/IFJ and the PMd regions which show relatively constant contribution of these areas to initial planning (vs. initial memory) and initial memory (vs. initial planning). Consistent with this, when we tested for the effect of Difficult condition > Easy condition separately for the Initial phases of the two tasks, we found significant effects in the mid-DLPFC bilaterally but not in the left pre-PMd/IFJ or PMd regions. Of importance, in both tasks, this contrast also revealed activation in the FPC bilaterally, while activation in the IFG was only found when the contrast was performed for the memory task (cf. Supplementary Fig. 1). Overall, bilateral activation in frontoparietal regions with increasing complexity in planning processes is

Table 1
Planning vs. Memory.

Anatomical localization	~BA	MNI coordinates x y z			p-corr.	Z value	Voxels per cluster
Regions more active during Planning than Memory							
L cuneus	17	−14	−92	0	<0.001	7.54	18,750
R superior occipital gyrus	19	32	−88	20		6.93	
L cuneus	19	−30	−92	24		6.67	
R cuneus	17	14	−94	0		6.68	
R superior parietal lobe	7	10	−64	56		6.61	
L cerebellum	−	−32	−78	−20		6.50	
L middle occipital gyrus	18	−34	−76	−8		6.52	
L precuneus	7	−22	−80	52		5.43	
R middle occipital gyrus	18	28	−82	−4		6.09	
L fusiform gyrus	37	−46	−64	−12		5.75	
R cerebellum	−	32	−64	−12	5.72	<0.002	238
R middle frontal gyrus	6	26	0	54	4.76		
Regions more active during Memory than Planning							
L middle temporal gyrus	21	−64	−56	0	<0.001	6.31	1534
L supramarginal gyrus	40	−60	−50	24		5.27	
L superior temporal gyrus	22	−66	−32	6	<0.001	4.34	430
R middle temporal gyrus	21	64	−22	−16		5.32	
R superior temporal gyrus	22	68	−38	−6		4.49	
L inferior frontal gyrus	44	−52	14	14	<0.004	4.92	179
L inferior frontal gyrus	47	−42	38	−8	<0.02	4.84	110

Stereotactic MNI coordinates for significant clusters (random effects, cluster-level $p < 0.05$ corrected, estimated at $p < 0.0001$ uncorrected) given in millimeter with effect sizes (z scores) and cluster extent. In the voxels per cluster column, cluster extent is reported in correspondence of the main peak. Subpeaks were selected dividing each cluster into Brodmann areas (BA) and then selecting peaks within each area.

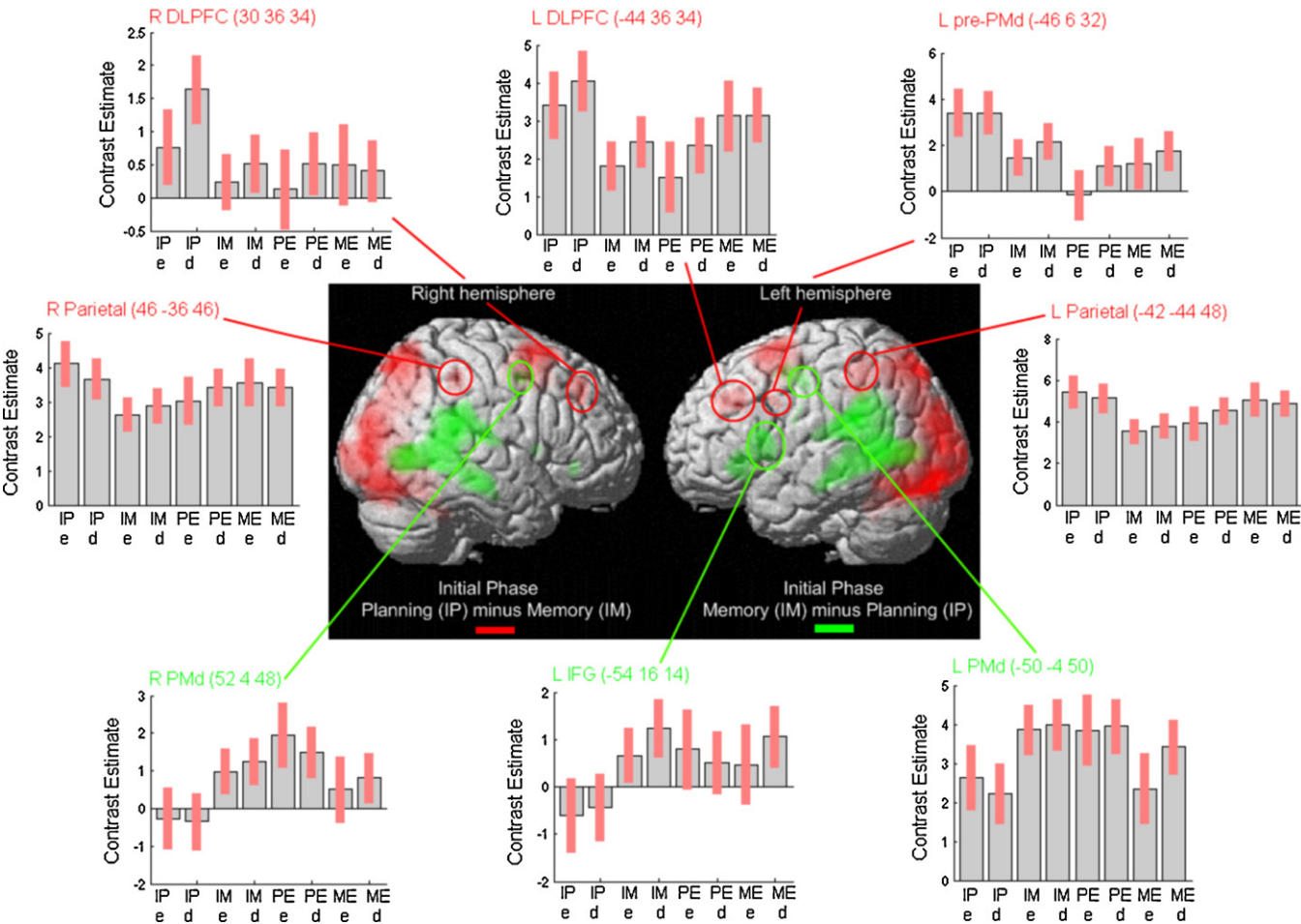


Fig. 3. Initial phase: effect of Planning minus Memory (in red) and Memory minus Planning (in green). Brain activation in both hemispheres is reported along with signal plots for all the eight event types for the right and left dorsolateral prefrontal cortex (DLPFC), right and left dorsolateral prefrontal cortex (pre-PMd), right and left dorsal premotor cortex (PMd), and left inferior frontal gyrus (IFG). All signal plots depict activity in experimental conditions (event types) relative to baseline (in arbitrary units [a.u.], $\pm 90\%$ confidence interval); plots report the pattern of activity at activation's peaks (i.e. single voxels) selected from the whole-brain contrast SPM maps. The eight event types are obtained by crossing the following factors: Task (Planning/Memory; P/M in the plots), Phase (Initial/Execution; I/E in the plots), and Condition (Easy/Difficult; e/d in the plots). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

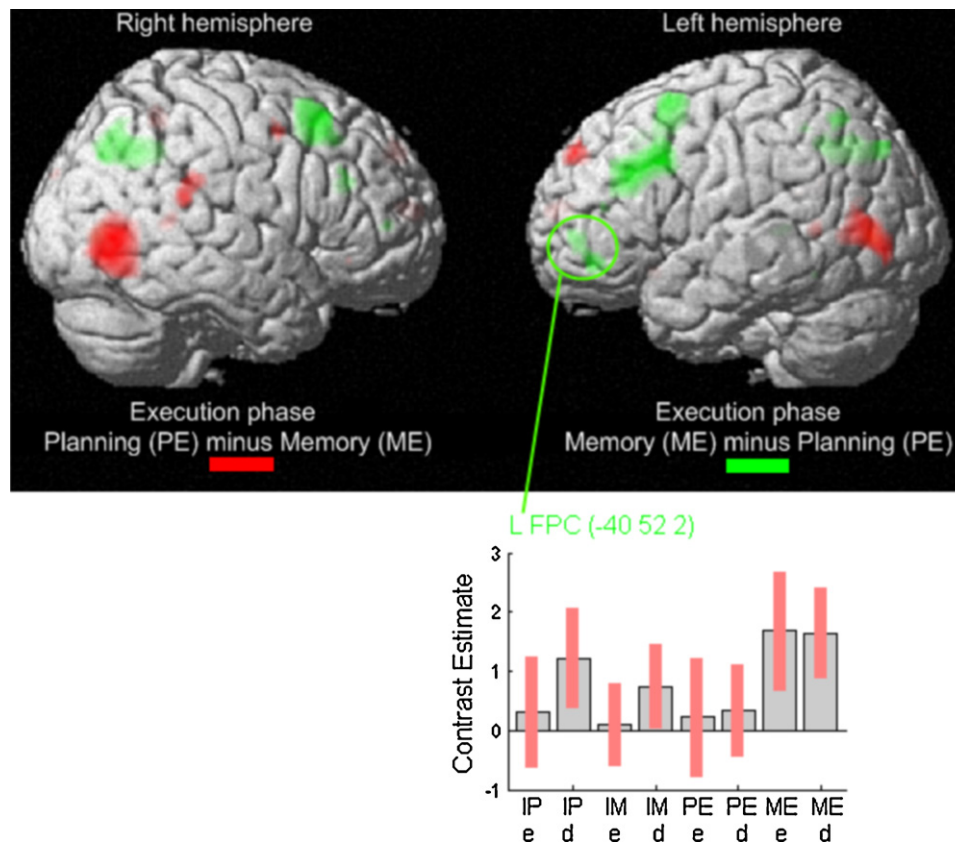


Fig. 4. Execution phase: effect of Planning minus Memory (in red) and Memory minus Planning (in green). Brain activation in both hemispheres is reported along with the signal plot for all the 8 event types for the left frontopolar cortex (FPC). See legend of Fig. 3 for more details on signal plots. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

consistent with previous results on both the TOH and TOL puzzles (e.g. Fincham et al., 2002; van den Heuvel et al., 2003).

Finally, it should be noted that patterns of activation similar to those described above for the two simple main effects (i.e. Initial phase: Planning minus Memory and reversed) were found when Easy and Difficult conditions were considered separately. However there was an exception; when we tested for the contrast “Initial phase: Planning minus Memory” and considered only the Easy conditions, no significant effect was found for the right mid-DLPFC.

Supplementary material related to this article found, in the online version, at doi:10.1016/j.neuropsychologia.2012.03.005.

3.2.3. Execution phase: Planning vs. Memory

The Planning and Memory tasks were also compared during the Execution phase. The first contrast compared activation during the execution of a pre-planned sequence of moves with the execution of a memorized sequence of moves (Execution phase: Planning minus Memory; Table 3, first contrast). In this contrast, we found bilateral activation in regions of the posterior temporal lobe similar to those showing an effect of Memory minus Planning during the Initial task phase (Table 2, second contrast). The right supramarginal gyrus and the left superior and medial frontal gyri were also activated in this contrast. Although the plots reported in Fig. 3 concerning the PMd cortex suggest that this region is bilaterally more active for Planning than Memory during task execution (PE–ME in the plots), the effects in this area did not survive the specific cluster-level correction criterion.

Second, we compared patterns of activation occurring during the execution of a memorized sequence of moves with those arising during the execution of a planned sequence of moves (Execution phase: Memory minus Planning; Table 3, second contrast).

This contrast led to bilateral fronto-parietal activations involving the mid-DLPFC, the inferior/superior parietal lobe, the left pre-PMd/IFJ region, and the left FPC. However, activation in the right mid-DLPFC was only significant when cluster size was estimated at $p\text{-unc.} < 0.0005$ ($x y z = 38\ 30\ 24$, $z = 4.35$; and $52\ 30\ 30$, $z = 3.84$; cluster size = 175 voxels, $p\text{-corr.} = 0.044$). Fig. 4 illustrates the areas that showed an effect of Planning > Memory (in red) and Memory > Planning (in green) in the Execution phase, plus the signal plot for the left FPC including all the eight event types.

As was done for the Initial phase, the effect of Difficult condition > Easy condition was also tested separately for the two tasks during the Execution phase. The contrast did not lead to any significant activation when tested in the Memory task. However, a region in the middle frontal gyrus corresponding to the FEF, the precuneus, and the middle occipital gyrus were found to be more active bilaterally during the execution of complex plans than easy plans (cf. Supplementary Fig. 2).

Supplementary material related to this article found, in the online version, at doi:10.1016/j.neuropsychologia.2012.03.005.

3.2.4. Within-task contrasts

The activation patterns related to the Initial and Execution phases were compared in the two tasks separately. To this end, we used the main effects of Planning minus baseline (in the Planning task) and Memory minus baseline (in the Memory task) as masking contrasts. We first examined for the Planning task whether there were regions preferentially active during the Initial phase than the Execution phase. Activation was found in this contrast in posterior brain regions such as the precuneus bilaterally, in regions corresponding to the FEF, and, in the left hemisphere, in both the mid-DLPFC and the pre-PMd/IFJ region (Table 4, first contrast and

Table 2
Initial Phase: Planning vs. Memory.

Anatomical localization	~BA	MNI coordinates x y z			p-corr.	Z value	Voxels per cluster		
Regions more active during Planning than Memory (initial phase)									
L lingual gyrus	18	−2	−76	2	<0.001	>8	21,668		
R lingual gyrus	18	2	−76	2		>8			
L cerebellum	−	−34	−78	−20		7.44			
L cuneus	17	−12	−92	0		7.78			
L superior parietal lobe	7	−24	−68	46		7.15			
R fusiform gyrus	19	22	−62	−10		6.97			
R precuneus	7	10	−64	56		7.18			
R cuneus	17	16	−86	0		7.74			
L inferior parietal lobe	40	−42	−44	48		5.95			
R cerebellum	−	6	−78	−28		5.50			
L fusiform gyrus	37	−52	−52	−16		4.63			
R middle frontal gyrus	6	26	6	54		<0.001		7.50	1238
L middle frontal gyrus	6	−22	6	56		<0.001		6.93	1135
L middle frontal gyrus	9	−44	36	34		<0.002		5.27	212
R inferior parietal lobe	40	46	−36	46	<0.004	5.00	181		
L middle frontal gyrus	9	−46	6	32	0.06	4.56	62		
L cingulate gyrus	8/32	−4	20	46	<0.007	4.49	148		
R cingulate gyrus	8/32	8	20	44		4.48			
R middle frontal gyrus	8	36	36	44	<0.009	4.35	139		
R middle frontal gyrus	9	30	36	34		4.30			
Regions more active during Memory than Planning (initial phase)									
L middle temporal gyrus	21	−64	−56	2	<0.001	>8	3750		
L supramarginal gyrus	40	−60	−50	24		7.65			
L middle temporal gyrus	37	−56	−72	4		6.34			
L transverse temporal gyrus	41/42	−64	−22	16		4.69			
R middle temporal gyrus	37	54	−66	0	<0.001	7.82	4276		
R superior temporal gyrus	22	62	−38	18		7.54			
R inferior temporal gyrus	20	50	−24	−14		7.74			
R supramarginal gyrus	40	60	−34	24		7.37			
R transverse temporal gyrus	41/42	56	−18	14		5.27			
L inferior frontal gyrus	44	−54	16	14	<0.001	5.37	732		
L inferior frontal gyrus	45	−48	30	−4		5.32			
L precentral gyrus	6	−50	−4	50	<0.004	5.13	184		
R precentral gyrus	6	52	4	48	= 0.13	5.06	39		
					= 0.007 FWE				

Stereotactic MNI coordinates for significant clusters (random effects, cluster-level $p < 0.05$ corrected, estimated at $p < 0.0001$ uncorrected) given in millimeter with effect sizes (z scores) and cluster extent. In the voxels per cluster column, cluster extent is reported in correspondence of the main peak. Subpeaks were selected dividing each cluster into Brodmann areas (BA) and then selecting peaks within each area.

red areas in the top part of Fig. 5). Overall, all these regions were similar to those showing an effect of Planning minus Memory in the Initial phase of the tasks. Given the effects of difficulty found in the initial task analyses (cf. Supplementary Figs. 1 and 2), the Initial phase minus Execution phase contrast (Planning task) was carried out considering the Difficult condition only. Activation was then

found also in the right mid-DLPFC ($x y z = 30 \ 34 \ 34$; $z = 4.14$; cluster size estimated at p -unc. < 0.001).

The Execution phase minus Initial phase contrast carried out for the Planning task led to activation of several clusters (Table 4, second contrast and green areas in the top part of Fig. 5). The largest one was a swathe of cortex that involved the motor cortex bilaterally

Table 3
Execution Phase: Planning vs. Memory.

Anatomical localization	~BA	MNI coordinates x y z			p-corr.	Z value	Voxels per cluster
Regions more active during Planning than Memory (execution phase)							
R middle temporal gyrus	37	50	−66	0	<0.001	7.06	867
L middle temporal gyrus	37	−50	−74	2	<0.001	5.44	407
R superior temporal gyrus	22	58	−38	18	<0.01	4.58	131
R supramarginal gyrus	40	60	−34	26		4.60	
L superior frontal gyrus	9	−14	54	40	<0.02	5.20	107
Medial frontal gyrus	10	0	58	14	<0.05	4.34	75
Regions more active during Memory than Planning (execution phase)							
R middle frontal gyrus	6/8	32	16	50	<0.001	5.45	489
L middle frontal gyrus	6/8	−26	14	52	<0.001	5.10	372
R inferior parietal lobe	40	42	−58	38	<0.001	5.58	437
L middle frontal gyrus	9/46	−40	30	26	<0.001	4.95	656
L middle frontal gyrus	6/9	−48	10	34		4.22	
L lingual gyrus	18	−4	−74	2	<0.04	4.42	78
L precuneus	7	−32	−68	38	<0.001	4.97	343
L superior parietal lobe	7/40	−46	−60	54		4.42	
R medial frontal gyrus	8	10	24	46	<0.009	4.68	139
L cingulate gyrus	8/32	−6	22	46		4.11	
L inferior frontal gyrus	10	−40	52	2	<0.008	4.43	142

Stereotactic MNI coordinates for significant clusters (random effects, cluster-level $p < 0.05$ corrected, estimated at $p < 0.0001$ uncorrected) given in millimeter with effect sizes (z scores) and cluster extent. In the voxels per cluster column, cluster extent is reported in correspondence of the main peak. Subpeaks were selected dividing each cluster into Brodmann areas (BA) and then selecting peaks within each area.

Table 4

Within-task contrasts.

Anatomical localization	~BA	MNI coordinates x y z			p-corr.	Z value	Voxels per cluster
Planning: Initial phase minus Execution phase							
R middle frontal gyrus	6	28	8	54	<0.001	7.75	792
L middle frontal gyrus	6	−22	6	56	<0.001	6.98	665
L precuneus	7/19	−28	−76	36	<0.001	5.86	846
L superior parietal lobe	7	−24	−68	42		5.16	
L middle occipital gyrus	19	−34	−94	16		4.69	
L cingulate gyrus	8/32	−6	20	48	<0.006	5.38	158
R cingulate gyrus	8/32	8	22	46		4.42	
L middle frontal gyrus	9	−46	8	32	<0.008	4.78	141
L middle frontal gyrus	9	−42	28	28	<0.009	4.62	137
R precuneus	7	10	−60	52	<0.05	4.42	76
R superior parietal lobe	7/19	32	−70	38	<0.04	4.02	79
Planning: Execution phase minus Initial phase							
L postcentral gyrus	40	−48	−34	20	<0.001	>8	11,467
R transverse temporal gyrus	41/42	48	−22	16		>8	
L postcentral gyrus	1/2	−54	−20	48		>8	
L transverse temporal gyrus	41/42	−60	−16	12		>8	
R precentral gyrus	4	34	−26	48		>8	
L precentral gyrus	4/6	−26	−18	74		>8	
R supramarginal gyrus	40	60	−32	26		>8	
R cingulate gyrus	24	8	−2	44		7.23	
L cingulate gyrus	31	−10	−26	44		6.68	
L inferior frontal gyrus	38/44	−54	12	−12		6.01	
R precentral gyrus	6	50	0	52		4.30	
L precentral gyrus	6	−52	−6	50		3.88	
R insula	13	40	0	10	<0.001	>8	1265
R putamen	−	34	−16	0		6.61	
R superior temporal gyrus	22	58	6	4		5.34	
R middle temporal gyrus	37	56	−66	0	<0.001	6.67	583
R middle temporal gyrus	21/22	44	−48	4		5.12	
L middle temporal gyrus	21	−56	−58	2	<0.001	6.09	383
L middle temporal gyrus	37	−54	−68	6		5.28	
L cerebellum	−	−30	−44	−36	<0.001	6.78	3716
R cerebellum	−	30	−40	−34		4.50	
R inferior frontal gyrus	47	46	30	−6	0.05	5.82	70
Memory: Initial phase minus Execution phase							
No suprathreshold voxels							
Memory: Execution phase minus Initial phase							
L postcentral gyrus	2	−48	−28	50	<0.001	>8	15,715
L precentral gyrus	6	−26	−18	74		>8	
L transverse temporal gyrus	41	−50	−18	14		>8	
R postcentral gyrus	2/3	42	−24	46		>8	
L insula	13	−34	−2	8		>8	
L cingulate gyrus	24	−2	−8	48		7.26	
R precentral gyrus	6	40	−20	66		7.62	
R transverse temporal gyrus	13/41	46	−22	16		>8	
R cingulate gyrus	24	10	−2	44		7.18	
R superior frontal gyrus	6	22	−10	72		5.94	
L inferior parietal lobe	40	−46	−54	40		5.58	
R inferior parietal lobe	40	44	−58	40		4.11	
L lingual gyrus	18	−4	−74	0	<0.001	>8	11,037
R lingual gyrus	19	6	−68	−10		>8	
L cerebellum	−	−30	−48	−32		7.81	
R cerebellum	−	30	−48	−32		7.55	
L cuneus	18	−10	−86	10		4.45	
R cuneus	18	14	−82	10		4.27	
R insula	13	40	0	8	<0.001	>8	1908
R putamen	−	36	−18	0		>8	
R superior temporal gyrus	38	60	8	−10		4.91	
R thalamus	−	20	−12	12		5.23	
R superior temporal gyrus	41	38	−36	6		4.66	
L middle frontal gyrus	9	−36	38	34	0.05	4.57	68

Stereotactic MNI coordinates for significant clusters (random effects, cluster-level $p < 0.05$ corrected, estimated at $p < 0.0001$ uncorrected) given in millimeter with effect sizes (z scores) and cluster extent. In the voxels per cluster column, cluster extent is reported in correspondence of the main peak. Subpeaks were selected dividing each cluster into Brodmann areas (BA) and then selecting peaks within each area.

and extended to the bilateral PMd region. Moreover, in a similar way to the contrast: Planning minus Memory (Execution phase), activity was also found bilaterally in the middle temporal gyrus and in the supramarginal gyrus. Finally, the cerebellum, insula, putamen, and the inferior frontal gyrus were also more active during plan execution than initial planning.

With regard to the Memory task, we first tested whether there were regions more active during the Initial phase than during the Execution phase. This contrast only showed a statistical trend in a region of the left PMd cortex (BA 6: $xyz = -46\ 0\ 48$, $z = 4.42$, $p = 0.10$ at FWE voxel-level correction) close to that found more active for initial memory than initial planning (i.e. $xyz = -50\ -4\ 50$)

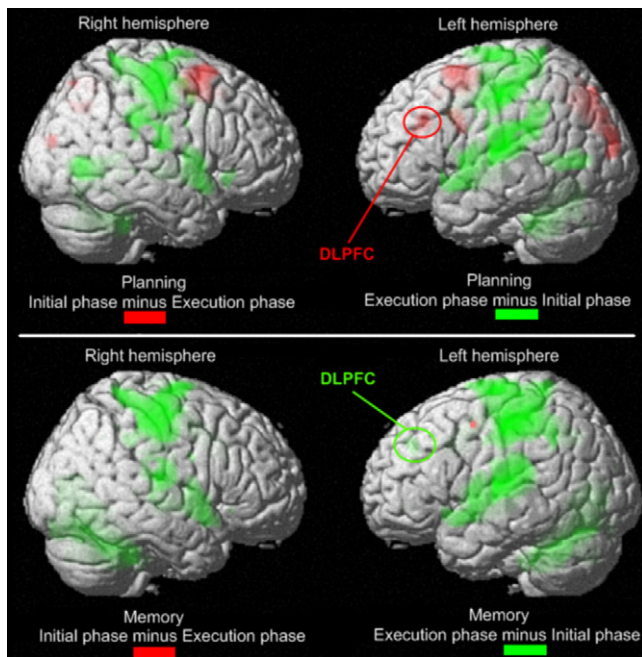


Fig. 5. Within-task contrasts. Brain activation in both hemispheres is reported for: top part of the figure: Planning: Initial phase minus Execution phase (in red) and Execution phase minus Initial phase (in green); bottom part of the figure: Memory: Initial phase minus Execution phase (in red) and Execution phase minus Initial phase (in green). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

and more active for plan execution than initial planning (i.e. $x,y,z = -52 -650$).

Finally, in the Memory task we compared the Execution phase with the Initial phase. This contrast revealed activation in four clusters (Table 4, fourth contrast and green areas in the bottom part of Fig. 5). The largest one involved the motor cortex bilaterally; activation in this cluster did not extend anteriorly to the PMd cortex as much as during plan execution. A second large cluster involved posterior brain regions while a third centred in the right insula and extended to the putamen, the superior temporal gyrus and the thalamus. Of importance, the left mid-DLPFC also activated in this contrast thus confirming the contribution of this region to sequence reproduction (cf. simple main effect of Execution phase: Memory minus Planning).

3.2.5. Task (Planning, Memory) $\times$ Phase (Initial, Execution) interactions

In order to corroborate the previous set of findings, we tested for the two interactions between Task and Phase. The interaction testing for areas more active during Planning compared with Memory, namely Initial phase vs. Execution phase [Initial phase (Planning minus Memory) minus Execution phase (Planning minus Memory)] showed activation in posterior visual brain regions and, more importantly, in frontal and parietal regions bilaterally. In the frontal cortex, the mid-DLPFC bilaterally and the left pre-PMd/IFJ region were active (Table 5, first contrast).

Testing for the opposite interaction (i.e. [Initial phase (Memory minus Planning) minus Execution phase (Memory minus Planning)]), revealed activation in the posterior middle and superior temporal areas bilaterally, the supramarginal gyrus, the ventral/anterior part of the IFG, and the PMd region bilaterally (Table 5, second contrast). Of interest, neither of the interactions was significant in the FPC.

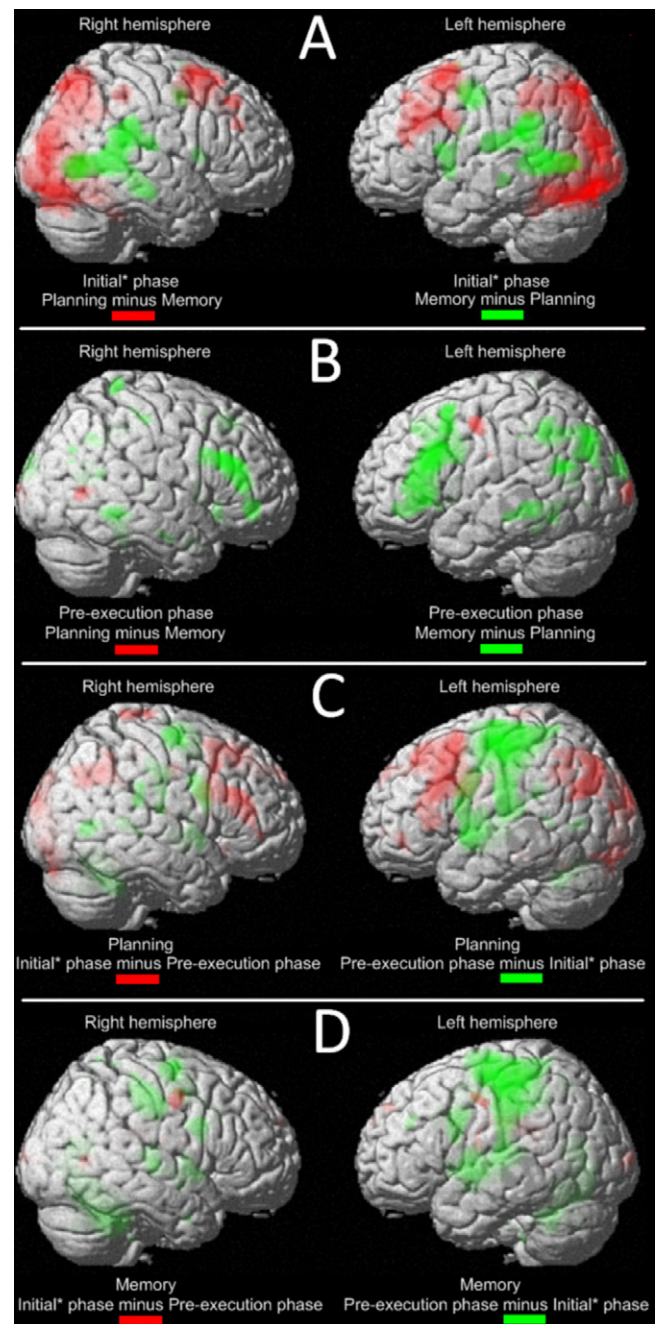


Fig. 6. Brain activation in both hemispheres is reported for: (A) Initial* phase: effect of Planning minus Memory (in red) and Memory minus Planning (in green); (B) Pre-execution phase: effect of Planning minus Memory (in red) and Memory minus Planning (in green); (C) Planning: Initial* phase minus Pre-execution phase (in red) and Pre-execution phase minus Initial* phase (in green); (D) Memory: Initial* phase minus Pre-execution phase (in red) and Pre-execution phase minus Initial* phase (in green). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

3.2.6. Initial* and Pre-execution phases

First, the Planning and Memory tasks were compared during the Initial* phase. The corresponding contrast executed for Planning minus Memory revealed a pattern of activation very similar to that found when the Initial phase was considered in the main analysis (cf. red areas in Fig. 3). Thus, we found bilateral activation in posterior brain regions, in the FEF regions, and in fronto-parietal regions including the mid-DLPFC and the left pre-PMd/IFJ area (red areas in Fig. 6A). The opposite contrast, namely Initial* phase: Memory

Table 5
Interactions.

Anatomical localization	~BA	MNI coordinates xyz			p-corr.	Z value	Voxels per cluster
Initial phase (Planning minus Memory) minus Execution phase (Planning minus Memory)							
L lingual gyrus	18	−2	−76	2	<0.001	>8	5848
R fusiform gyrus	19	22	−60	−10		5.39	
L fusiform gyrus	19	−26	−60	−10		5.09	
L cuneus	17	−8	−100	2		4.35	
L cerebellum	−	−34	−78	−20		4.90	
R middle frontal gyrus	6	28	10	54	<0.001	7.15	1237
R middle frontal gyrus	8/9	40	26	46		3.90	
L middle frontal gyrus	6	−24	10	58	<0.001	7.19	1641
L cingulate gyrus	8/32	−6	20	46		5.40	
R cingulate gyrus	8/32	8	22	44		5.53	
L precuneus	7	−28	−72	36	<0.001	6.90	2620
L inferior parietal lobe	40	−44	−44	48		5.96	
R precuneus	7	10	−62	54		4.42	
L middle occipital gyrus	19	−24	−88	18		4.49	
L middle frontal gyrus	9	−44	36	34	<0.001	5.96	831
L middle frontal gyrus	6/9	−46	10	34		5.38	
R precuneus	7/19	34	−64	36	<0.001	5.54	980
R inferior parietal lobe	40	50	−38	48		4.57	
R middle occipital gyrus	19	36	−84	20		4.16	
R middle frontal gyrus	9	44	34	28	0.06	4.11	60
Initial phase (Memory minus Planning) minus Execution phase (Memory minus Planning)							
R middle temporal gyrus	37	52	−66	0	<0.001	>8	3614
R superior temporal gyrus	22	62	−38	18		7.58	
R supramarginal gyrus	40	60	−34	24		7.49	
R transverse temporal gyrus	41/42	56	−18	14		4.64	
R inferior temporal gyrus	20	50	−24	−14		7.24	
L middle temporal gyrus	21/22	−52	−52	4	<0.001	7.54	2681
L supramarginal gyrus	40	−54	−38	24		7.21	
L middle temporal gyrus	37	−52	−72	4		6.97	
L inferior temporal gyrus	20	−54	−24	−12		4.45	
L transverse temporal gyrus	41/42	−62	−22	18		4.12	
R precentral gyrus	6	52	2	48	<0.03	5.90	93
L precentral gyrus	6	−50	−4	50	<0.005	5.60	162
R inferior frontal gyrus	47	46	32	−8	<0.03	5.03	102
L inferior frontal gyrus	45/47	−48	30	−2	<0.04	4.44	85
L superior frontal gyrus	9	−14	54	38	<0.05	4.87	75
L cingulate gyrus	31	−8	−24	40	<0.004	4.67	176
L cingulate gyrus	31	8	−22	42		4.29	
L cingulate gyrus	31	−8	−52	26	<0.04	4.25	83

Stereotactic MNI coordinates for significant clusters (random effects, cluster-level $p < 0.05$ corrected, estimated at $p < 0.0001$ uncorrected) given in millimeter with effect sizes (z scores) and cluster extent. In the voxels per cluster column, cluster extent is reported in correspondence of the main peak. Subpeaks were selected dividing each cluster into Brodmann areas (BA) and then selecting peaks within each area.

minus Planning also led to a pattern very similar to that obtained in the main analysis (cf. green areas in Fig. 3). Thus, activation was found bilaterally in posterior temporal regions, in the supramarginal gyrus, in the PMd region, and in the left IFG (green areas in Fig. 6A).

The Planning and Memory tasks were also compared during the Pre-execution phase. The first contrast compared activation during the pre-execution of a planned sequence of moves with the pre-execution of a memorized sequence of moves (Pre-execution phase: Planning minus Memory; red areas in Fig. 6B). In this contrast, we found activation in the right posterior middle temporal gyrus and in the left PMd cortex (xyz –48 –4 48, $Z = 5.56$, p -corr. = 0.012, cluster size = 112 voxels), a region very close to that showing a task $\times$ phase interaction (Table 5, second contrast), being preferentially active during Initial memory and during plan execution. The opposite contrast (Pre-execution phase: Memory minus Planning; green areas in Fig. 6B) led to activation in parietal and frontal regions including the mid-DLPFC in both hemispheres, similar to the corresponding contrast carried out for the Execution phase (cf. green areas in Fig. 4).

In addition, the activation patterns related to the Initial* and Pre-execution phases were directly compared in the two tasks separately. For the Planning task, regions preferentially active during the Initial* phase than the Pre-execution phase (red areas in Fig. 6C)

involved posterior brain regions and frontoparietal regions bilaterally (i.e. mid-DLPFC, pre-PMd/IFG, IFG, FPC, and inferior/superior parietal cortex). The opposite contrast, namely Pre-execution phase minus Initial* phase in the Planning task (green areas in Fig. 6C) gave rise to bilateral activation in regions of the motor, PMd, and temporal cortices, which already showed an effect of Planning: Execution phase minus Initial phase in the main analysis (cf. green areas in the top part of Fig. 5).

Finally, for the Memory task, the contrast Initial* phase minus Pre-execution phase led to bilateral activation in the PMd region (xyz –46 –10 42, $Z = 4.87$, p -corr. = 0.039, cluster size = 73 voxels; xyz 50 –4 42, $Z = 5.10$, p -corr. = 0.028, cluster size = 84 voxels) (red areas in Fig. 6D). The opposite contrast, namely Pre-execution phase minus Initial* phase (green areas in Fig. 6D) returned activation in bilateral motor and temporal regions as well as a marginal effect in the left mid-DLPFC (xyz –42 38 30, $Z = 4.20$, p -corr. = 0.07, cluster size = 55 voxels). This was the region showing a task $\times$ phase interaction (Table 5, first contrast), being preferentially active during sequence reproduction and during initial planning.

4. Discussion

In the present study we investigated the functional neuroanatomy of creating and executing plans and the extent to which

the underlying brain systems reduce to those required by any working memory task. To this end a planning task based on the Tower of Hanoi was contrasted with a task controlling for working memory maintenance using the same sort of material. To equate the overall accuracy of the two types of task a constant speed of presentation was used with the working memory task with the speed determined by a pilot experiment. It turns out that to achieve equivalent overall levels of accuracy, the time required to plan for easy problems is less than that required for memory encoding but for difficult problems the times do not differ significantly. The time required to retrieve a plan and a memory is identical.

In the main analysis, we analyzed the patterns of activation during two distinct phases, Initial and Execution, in the performance of both tasks. We found that a network involving frontoparietal regions (i.e. mid-DLPFC bilaterally, left pre-PMd/IFJ, inferior/superior parietal cortex) contributed more to initial planning than sequence memorization (i.e. Initial phase: Planning minus Memory) and to sequence reproduction than plan execution (Execution phase: Memory minus Planning). Direct comparisons of the two phases within each task, confirmed the contribution of the mid-DLPFC, especially in the left hemisphere, to initial planning and sequence reproduction. Thus this region was more active for initial planning than plan execution and during sequence reproduction than sequence memorization (see also supplementary material for analyses concerning TOH problems with unambiguous and ambiguous goal hierarchy). In our study we also found activation in a second brain network which involved the posterior temporal areas, inferior parietal regions (e.g. supramarginal gyrus), the inferior frontal gyrus and the PMd region bilaterally. This network contributed more to sequence memorization than initial planning and to plan execution than both initial planning and, to a less extent, sequence reproduction.

Moreover, in a supplementary analysis we divided the Initial phase of each task into two subphases. The aim was that the time the participants spent in motor programming of the sequence of moves would be represented in the Pre-execution phase. This would leave the Initial* phase as a pure measure of any cognitive planning of moves (in the Planning task) or memorizing the moves (in the memory task). The similarity of the activations for Pre-execution phase minus Initial* phase for the two tasks (cf. green areas in Fig. 6C and D) (e.g., the motor cortex) strongly suggested that the assumptions of the more refined analysis were justified.

Of importance, the findings of the supplementary analysis clearly supported those of the basic analysis. Thus, the results strengthened the idea that a network involving frontoparietal regions is crucially involved in initial planning (cf. red areas in Fig. 6A and C) and that, within this network, the mid-DLPFC especially in the left hemisphere, also contributes to the later stages of the memory task, namely immediately before and during sequence reproduction (cf. green areas in Fig. 6B and D). With regards to the second network, the findings have confirmed that regions such as, for instance, the PMd cortex are preferentially involved during initial memorization (cf. green areas in Fig. 6A and red areas in Fig. 6D) but also immediately before and during plan execution (cf. red areas in Fig. 6B and green areas in Fig. 6C).

Finally, in the present study we scanned the same number of male and female participants in order to investigate whether there were any gender differences in planning, as shown in some previous studies (Boghi et al., 2006; Cazzato, Basso, Cutini, & Bisiacchi, 2010; Rönnlund, Lövdén, & Nilsson, 2001) but not in other ones on the topic (Schuepbach et al., 2002). The results of the analyses related to gender differences are reported in the supplementary material.

Supplementary material related to this article found, in the online version, at doi:10.1016/j.neuropsychologia.2012.03.005.

In the next sections of the Discussion we focus on the patterns of activation related to these two networks, emphasizing the pattern shown by the mid-DLPFC. We then conclude by discussing the relevance of the present findings on Planning and Spatial working memory for the more general issue regarding the different axes of organization of the PFC (e.g. Badre et al., 2010).

Activation of a network of frontoparietal regions in the present study is consistent with results of previous PET and fMRI studies on planning (e.g. see Owen, Doyon, et al., 1996; Unterrainer & Owen, 2006) and on spatial working memory (D'Esposito et al., 1998; Smith & Jonides, 1997) as well as with the general idea that this network activates in novel situations whenever the need for supervisory control increases (e.g. Hampshire, Thompson, Duncan, & Owen, 2008).

As far as this network is concerned, the pattern of activation found for the mid-DLPFC suggests a contribution of this region to cognitive planning over and above that of setting up a working memory representation. In fact, in the main analysis, when the patterns of activation occurring in the initial memory phase were subtracted from the initial planning phase, activation in the mid-DLPFC was observed. This held generally true for the left mid-DLPFC and it was also the case for the right mid-DLPFC particularly when the Difficult condition alone was considered in the analysis. Also if activation in mid-DLPFC during initial planning did merely reflect encoding of intermediate steps in memory, then, during task execution, one would not expect to find a difference in activation in this region between the two tasks. In fact, we found increased activation in mid-DLPFC during sequence reproduction (and immediately before it) compared with plan execution.

Considering the memory aspects of the study, on the current account, the initial phase of Planning creates an organized structure which provides more effective retrieval cues for later recall than the simple memorization presumably induced by rote rehearsal in the initial phase of the Memory task. Behaviorally this is clear. Despite initial planning being actually insignificantly quicker than initial memory for difficult sequences, retrieval is significantly better in the Planning condition. Indeed in a PET study of encoding of randomly ordered categorized lists, with and without a demanding distractor task (Fletcher, Shallice, & Dolan, 1998) the area held to be responsible for creating the subjective organization of the list when it could be effectively achieved was the left mid-dorsolateral region, an area showing greater activation for Initial Planning compared to Initial Memory in the current study. By contrast in our Initial Memory condition, Broca's area is significantly more active which would fit with a combination of verbalization, maintenance rehearsal and reconversion to visual form being the strategy used in the Memory condition (see also below). That the left mid-DLPFC is highly active during sequence reproduction (and immediately before it) in the Memory task, compared with plan execution is not surprising on this view as list recall is much impaired in patients with posterior left dorsolateral lesions (Alexander, Stuss, & Fansabedian, 2003) as is manipulation of verbal working memory (Postle et al., 1999).

Turning to the key issue planning, it requires a variety of operations beyond that of maintaining a representation of intermediate problem-states on-line. For instance, it requires the generation of a set of appropriate moves and the evaluation of structured sequences of moves. We argue that in our study the role played by mid-DLPFC during initial planning, at least by the left mid-DLPFC, is one of generation of a structured sequence of moves to solve each problem; this is a complex operation required in easy as well as difficult problems but involving very few working memory demands in the easy conditions.

Our interpretation of mid-DLPFC's function in planning receives support from findings in the domain of inductive reasoning. By using the Brixton Spatial Anticipation test (Burgess & Shallice, 1996) on a brain-damaged population and, in a related fMRI study,

on healthy adults, we have recently advocated a role for the mid-DLPFC, especially in the left hemisphere, of hypothesis generation independently of working memory (Crescentini et al., 2011; Reverberi, D'Agostini, Skrap, & Shallice, 2005). Moreover, it should be noted that the pattern of activation found in the present experiment for the left and right mid-DLPFC is in line with the results reported by Newman et al. (2003). These authors found a consistent activation of the left mid-DLPFC across different levels of planning complexity together with a more specific involvement of right mid-DLPFC at high levels of complexity. It could be argued that while generation of moves is required throughout planning of problem solutions, evaluation of the appropriateness of a sequence of moves is needed especially when the required sequence gets more complex. Of interest, such a function was attributed to the right mid-DLPFC in a very recent fMRI study of planning (Kaller et al., 2011) and it is more generally consistent with a role of this region in monitoring and checking (Shallice, Stuss, Alexander, Picton, & Derksen, 2008; Stuss & Alexander, 2007; Vallesi & Crescentini, 2011; Vallesi, McIntosh, Shallice, & Stuss, 2009).

Although we mentioned that, in line with recent arguments (Kaller et al., 2011; Newman et al., 2003, 2009), left and right mid-DLPFC may be involved in somewhat different aspects of planning, we should note that some of the effects found in our study produced bilateral activation in this region. More generally, the present findings appear consistent with the idea that the prolonged plan execution time, which is sometimes observed in frontal patients (e.g. Carlin et al., 2000; Owen et al., 1990), could be due to their inability to generate a solution in the Initial task phase efficiently, namely before making the first move.

The planning-specific role which we attributed to mid-DLPFC was based on an experimental design which allows one to distinguish an Initial and an Execution phase (and an Initial* and a Pre-execution phase). We showed that when the two main phases were combined for the analysis, in line with past evidence (Owen, Doyon, et al., 1996), mid-DLPFC contributed equally to Planning and Spatial working memory (Table 1, first contrast). Thus, we need to consider whether it is appropriate to assume that the attributed activation in mid-DLPFC to the working memory component of tasks, for instance in some past neuroimaging studies on planning (e.g. Baker et al., 1996; van den Heuvel et al., 2003; Wagner et al., 2006), is due to the use of designs which do not distinguish an Initial and an Execution phase. Typically in these studies, participants are not required to execute their plans but have to hold in mind a dynamic count of the number of moves and then report the number as a measure of performance. This procedure confounds the Initial and Execution phases of the task and could well increase the working memory and monitoring demands as well.

The last issue pertaining to the frontoparietal network concerns the left pre-PMd/IFJ region. In the Planning task, this region was found to be consistently activated in all contrasts which led to activation in the left mid-DLPFC; this suggests that the two regions work in concert during planning. Nevertheless, unlike the left mid-DLPFC, the degree of activation in the left pre-PMd/IFJ region did not vary with planning complexity (cf. signal plots in Fig. 3 and supplementary Fig. 1). One possibility for the relatively constant contribution of this area to planning is that it globally operates to represent task-rules (see Brass et al., 2005, for related arguments) or solution schemas – acquired procedures – that must be continually active during solution attempts (Shallice & Cooper, 2011).

We now briefly turn to the second of the two networks, namely that involving the temporal lobes, inferior frontal and parietal regions and the PMd area. We argue that activation of these regions reflects the effects of the specific strategies adopted by participants during sequence memorization (vs. initial planning) and during plan execution (vs. initial planning and also sequence reproduction). In a different fashion from initial planning, during sequence

memorization participants were simply required to watch a spatial sequence and hold it in short-term memory until it could be reproduced. Mental rehearsal could be an efficient organizational strategy to encode the sequences shown by the computer. Both verbal and visuospatial rehearsal could mediate the encoding. For instance, verbal mediation would occur when verbal labels are assigned to the three pegs during memorization (e.g. left-most peg then right-most peg then again left-most peg, for a 3-move sequence) while visuospatial rehearsal could occur if participants try to mentally visualize the movements of the disk on the pegs. Past research had shown that rehearsing information in verbal and spatial working memory activates left- and right-hemisphere regions respectively (e.g. Smith, Jonides, & Koeppel, 1996; see also Awh & Jonides, 2001). Thus, the bilateral activation in the network found in our study suggests mediation of both verbal and spatial memory processes in the encoding of memory sequences.

Mental rehearsal could have also played a role during plan execution. In our task, participants had no time pressure to start executing a plan; the linear increase in RT data obtained in the Execution phase of the Planning task as a function of task difficulty (2-, 3-, 4-, and 5-move problems; data not shown in Fig. 2B), suggests that participants efficiently used the initial planning time to construct an appropriate sequence of moves in all conditions of the task. From this perspective, the sequences of moves generated during the Initial phase could simply be retrieved/rehearsed during the Pre-execution and Execution phases.

In line with a mental rehearsal type of strategy, previous studies attributed to the IFG and the lateral PMd region of the left hemisphere a role in subvocal repetition of individual items in verbal short-term memory while short-term storage was associated with the left inferior parietal cortex (supramarginal gyrus) or the left superior temporal regions (see Leff et al., 2009; Shallice & Cooper, 2011; Warrington, Logue, & Pratt, 1971). Of importance, rehearsal in spatial working memory has been associated with roughly similar regions (Awh, Smith, & Jonides, 1995; De Renzi & Nichelli, 1975; see also Awh & Jonides, 2001). Moreover, visuospatial rehearsal, and to a less extent verbal rehearsal as well, have been proposed to be involved in the TOL/TOH tasks (Morris, Ahmed, Syed, & Toone, 1993; Phillips, Wynn, Gilhooly, Della Sala, & Logie, 1999; Welsh, Cicerello, Cuneo, & Brennan, 1995). More generally, the present findings are consistent with previous evidence suggesting that the IFG and the PMd region are active in tasks that, while requiring the organization and the execution of a sequence of spatial moves retained in short-term memory, limit the requests of manipulation of the stored sequence (Owen, Evans, & Petrides, 1996).

Finally we conclude by briefly discussing the relevance of the present findings with respects to recent conceptualizations on the organization of control processes in lateral PFC. Our results appear consistent with recent researches suggesting that PFC may be functionally organized to support a hierarchical organization of control along a rostro-caudal axis involving respectively the PMd, prePMd, mid-DLPFC, and FPC regions (Badre & D'Esposito, 2007; Badre et al., 2010). Thus, in our study, the lateral PMd area could be involved in basic mnemonic processes such as mental rehearsal as well as in movement preparation. By contrast, more anterior regions like pre-PMd/IFJ and mid-DLPFC may be engaged in more complex planning processes. At the apex of the hierarchical organization of cognitive control there would be the FPC. Consistent with this, we found bilateral activation in this region only in specific situations such as in the Difficult condition during the Initial phase of both tasks and, in the left hemisphere, during sequence reproduction. In our view, these conditions generally require one to assess different move alternatives or disk configurations together with their consequences while maintaining the current intermediate-state in mind. The operation of integrating the outcome of multiple cognitive operations relates to the concepts of intention formation, cognitive branching and

subgoal often attributed to FPC, particularly in the left hemisphere (e.g. Bunge, Helskog, & Wendelken, 2009; Burgess, Quayle, & Frith, 2001; Koechlin & Hyafil, 2007; Ramnani & Owen, 2004). Admittedly, it remains possible that FPC activation in the present study may reflect, at least in part, increasing task difficulty or working memory demands.

Our findings are also generally consistent with a two-stage model concerning the function of the PFC in memory processes proposed by Petrides (1994; see also Petrides, 2000) and tested by Owen and colleagues (Owen, Evans, et al., 1996; Owen, Doyon, et al., 1996; see also Postle et al., 1999). In agreement with the original proposal, we showed that ventral portions of the IFG (i.e. BA 45/47) may be involved in the organization of sequences of responses based on information initially received from posterior association areas. Second, we provide evidence that the mid-DLPFC (BA 9/46) would be engaged when active monitoring and manipulation of information within working memory is required. Finally, as already mentioned, although there was some interhemispheric difference in some of the regions involved in the study (e.g. pre-PMd/IFG, mid-DLPFC), most of the activations in the present experiment were bilateral. This emphasizes the need of further studying the organizational criteria of processing in the left-right axis of the brain.

5. Conclusions

The present study provides evidence that planning and spatial working memory rely on similar brain networks although at very different stages of the task. Critically, within these networks, the mid-DLPFC appeared to contribute to initial planning over and above the effects of working memory maintenance. We have argued that mid-DLPFC is critically involved in the generation and evaluation of abstract sequences of responses. By contrast, plan execution, in a similar way to initial sequence memorization, relied on a network involving posterior temporal areas, inferior parietal and frontal regions and the dorsolateral premotor cortex. Activation of this network was held to be linked to rehearsal of planned sequences of moves.

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