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NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage xx (2006) xxx – xxx

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2 Parallel memory systems for talking about location and age in 3 precuneus, caudate and Broca's region

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10 Received 24 January 2006; revised 3 May 2006; accepted 3 May 2006

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13 **Language comprehension relies on processing of context. Working**
 14 **memory (WM) evoked by linguistic cues for spatial and nonspatial**
 15 **aspects of a visual scene was investigated by correlating fMRI BOLD**
 16 **signal (or 'activation') with reaction times (RTs). Subjects were asked**
 17 **to indicate either the relative positions or ages of people or objects**
 18 **(referenced by the personal pronouns "he/she/it") in a previously**
 19 **shown image. Good performers of a particular task showed shorter**
 20 **RTs than poor performers. Task-specific activation that is greater in**
 21 **good performers than poor ones is taken to indicate involvement of a**
 22 **given region in performance of the task. Our results indicate that**
 23 **dorsoposterior precuneus supports spatial WM during linguistic**
 24 **processing while a network of areas including the caudate support**
 25 **nonspatial WM in categorization of age. We argue that within-subjects**
 26 **variation of RTs across trials reflects effort. Good performers have**
 27 **higher activity in precuneus as a function of effort compared to poor**
 28 **performers during the spatial task, whereas the opposite is found for**
 29 **the nonspatial task, providing further evidence for specifically spatial**
 30 **WM in dorsoposterior precuneus. Task-independent performance-**
 31 **related modulations of activity were found in Broca's area and**
 32 **amygdala. Broca's area activity increased with effort in both tasks,**
 33 **with a greater increase in good performers than in poor performers,**
 34 **consistent with the region's general role in verbal WM. By contrast,**
 35 **activation in amygdala decreased with effort, with a greater decrease in**
 36 **good performers. We take this deactivation to reflect performance-**
 37 **mediating emotional control. These findings indicate that multiple**
 38 **parallel memory systems are available during language processing,**
 39 **appropriate for different tasks, with performance reflecting which**
 40 **system is selected trial-by-trial and subject-by-subject.**

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Introduction

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44 Language comprehension relies on context. Consider a semi-
 45 realistic cocktail party question like: "The man who was standing
 46 in front of you a moment ago, was he older than you?" We
 47 usually comprehend and answer such questions quite easily, but
 48 when examining the process in detail, we find that it requires a
 49 complex set of cognitive functions. First, it requires perceptual
 50 experiences of persons occupying changing positions in the
 51 environment relative to each other and relative to the observer.
 52 Next, it requires retention of this experience in memory, then
 53 audition to perceive the question, and a working memory system,
 54 accessing both stored semantic, episodic and pragmatic knowl-
 55 edge, must extract the appropriate experience from memory and
 56 map sentence elements onto the correct elements of this represen-
 57 tation. In order to answer the question, a further evaluation of the
 58 representation is required, building either on specific knowledge
 59 about the age of the relevant person relative to the listeners own age,
 60 or on a comparison based on the subject's acquired general
 61 knowledge of visual age characteristics.

62 The power of language lies in its ability to convey such
 63 complex representations by simple means (i.e., strings of sounds),
 64 and the only way for this to be possible is by making use of highly
 65 specific inferences from the context of the utterance. A basic level
 66 noun (Rosch, 1978) like "man" or personal pronouns like "he/she/
 67 it" strongly underspecify their meaning, since the number of
 68 possible references they can have is innumerable. This means that
 69 words like "he/she/it", that are among the 30 most frequently used
 70 words in English (Leech et al., 2001), only become comprehen-
 71 sible within the context of discourse. And, as exemplified above,
 72 contextual monitoring relies on memory, over both short and long
 73 durations, of what was said, perceived and learned before the
 74 sentence was uttered.

75 Very little research, however, has been done to investigate the
 76 neural underpinnings of contextual specification taking place
 77 during linguistic processing. A small number of neuroimaging

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Available online on ScienceDirect (www.sciencedirect.com).

78 studies have been investigating discourse, but results have been
79 inconclusive (e.g., Caplan and Dapretto, 2001; Ferstl and von
80 Cramon, 2002; Xu et al., 2005). An apparent assumption would be
81 that contextual specification relies on memory systems involved in
82 nonlinguistic processing (e.g., O’Keefe and Nadel, 1978; Talmy,
83 2000). However, apart from a few PET studies investigating spatial
84 imagery related to verbal instructions (Mellet et al., 1996, 2002),
85 this has not been tested.

86 Studies in humans and other animals suggest the presence of
87 multiple complementary memory systems working in the brain,
88 e.g., ‘declarative’ and ‘procedural’ memory (Squire and Zola-
89 Morgan, 1991) or, in the spatial domain ‘place’ and ‘habit’ systems
90 (McDonald and White, 1993; White and McDonald, 2002). These
91 systems each have a different “style” of processing and interact by
92 simultaneous parallel influence on behavioral output and by
93 directly influencing each other. Such interactions can be cooper-
94 ative (leading to similar behaviors) or competitive (leading to
95 different behaviors). In addition, a distinction has been drawn
96 between short-term or ‘working’ memory and long-term memory
97 (LTM) systems (e.g., Atkinson and Shiffrin, 1971; Baddeley and
98 Hitch, 1974) in terms of the timescales over which they operate.

99 Processing of spatial knowledge occurs in the parietal and
100 hippocampal regions (e.g., Burgess et al., 1999, 2002). Damage to
101 parietal cortex can lead to deficits such as neglect (Mesulam,
102 1981), simultagnosia (Coslett and Saffran, 1991) or optical apraxia
103 (Perenin and Vighetto, 1988). Parietal regions are part of the dorsal
104 visual stream (Ungerleider and Mishkin, 1982) for spatiodynamic
105 processes and have also been shown to play an important role in
106 spatial memory processing (Ungerleider et al., 1998), as in imagery
107 (Fletcher et al., 1995; Mellet et al., 1996, 2002; Kosslyn et al.,
108 1997) with damage leading to possible neglect in “representational
109 space” (Bisach and Luzzatti, 1978). Parietal regions are thought to
110 be especially involved in short-term storage of spatial information
111 (Smith and Jonides, 1998), a function consistent with the
112 visuospatial component of working memory (Baddeley and Hitch,
113 1974).

114 Human working memory for verbal, as compared to visuospa-
115 tial, information is thought to involve separable subsystems
116 (Baddeley and Hitch, 1974; Baddeley, 1986), with short-term
117 storage occurring in posterior (e.g., parietal) neocortical areas, and
118 manipulation and rehearsal depending on prefrontal areas (such as
119 Broca’s area for maintaining verbal stimuli and language compre-
120 hension, see, e.g., Shallice, 1988; Paulesu et al., 1993; Smith and
121 Jonides, 1998; Logie et al., 2003; Fiebach et al., 2005). Evidence
122 for the idea that the spatial working memory system is also
123 selectively involved in the processing of spatial meaning in
124 language (Mellet et al., 1996, 2002; Wallentin et al., 2005) comes
125 from patients suffering from Williams syndrome (Williams et al.,
126 1961) who exhibit impoverished spatial processing but relatively
127 spared language skills, with the exception of language with spatial
128 meaning (Bellugi et al., 1999; Phillips et al., 2004). The
129 impairment is consistent with dysfunctional ‘dorsal stream’
130 (Goodale and Milner, 1992) processing (Atkinson et al., 1997;
131 Paul et al., 2002) and may be related to abnormalities in parietal
132 cortex (Meyer-Lindenberg et al., 2004).

133 In contrast to parietal systems, the hippocampal system is
134 thought to be structured around the formation of a “cognitive map”
135 (O’Keefe and Nadel, 1978; Burgess et al., 2002; White and
136 McDonald, 2002) that identifies the spatial relationship between
137 different large-scale landmarks (O’Keefe and Burgess, 1996).
138 Hippocampal activation has been shown to be involved in

mediating performance during real-time navigation in a virtual
reality setting (Maguire et al., 1998; Hartley et al., 2003; Iaria et al.,
2003).

A complementary type of memory to these ‘explicit’ or
‘declarative’ systems exists in the dorsal striatum (e.g., caudate
nucleus) and supports the learning of slowly modulated “skills” or
“habits” in both humans (Gabrieli, 1998) and other animals
(Squire and Zola-Morgan, 1991; White and McDonald, 2002).
This is a system for learning associations between stimuli that
generalize over events, such as the relationship between a cue and a
reward (Packard and McGaugh, 1996). In the spatial domain,
navigation performance through virtual reality space is mediated
by parietal and hippocampal activity (Maguire et al., 1998; Hartley
et al., 2003), while performance during following a known route
(Hartley et al., 2003) or in using nonspatial navigation strategies
(Iaria et al., 2003) is correlated with activation in caudate. This
“nondeclarative” system may in fact also have a role in language
processing, as caudate stimulation has been found to induce
language disturbances (Van Buren, 1963; Gil Robles et al., 2005).

In addition, a third memory system is proposed to reside in the
amygdala (White and McDonald, 2002) where it modulates direct
links between individual stimuli and reinforcers. Motivational
aspects of complex social behavior involve amygdala (see Adolphs,
2003, for a review). This might also apply to communicative
situations.

To investigate the involvement of these different memory
systems during language comprehension in a realistic way, we
designed a paradigm that contrasted listening to sentences cueing
knowledge about spatial and nonspatial aspects of the same visual
scene. During fMRI scanning, subjects were shown images with
two persons (a man and a woman) and a chair (Fig. 1).
Subsequently, subjects were asked to recall spatial and nonspatial
aspects of the same image elements, accessed using referential
personal pronouns (“he/him”, “she/her”, “it/it”, “you/you”)
embedded in whole sentence questions.

We further investigated whether differences in processing
efficiency across and within subjects was correlated with specific
patterns of brain activity. Response time was used as a continuous

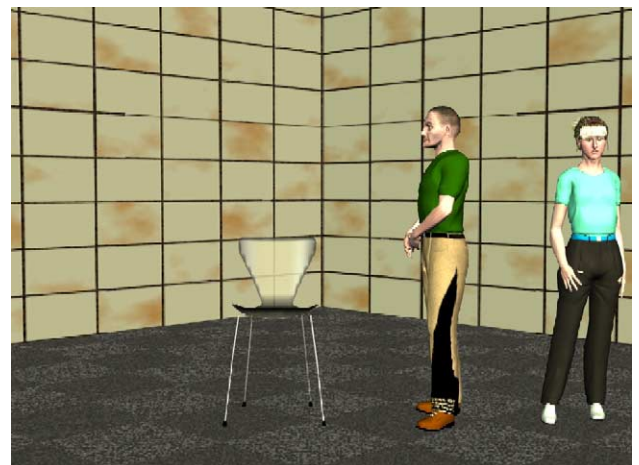


Fig. 1. Example stimuli. 40 images like this were shown for 3000 ms. Each contained a man, a woman and a chair. Subsequently subjects were asked to recall the relationship between these objects along a spatial axis, e.g.: “Was he/she/it in front of him/her/it/you?” and along a nonspatial, e.g., “Was he/she/it older than him/her/it/you?”

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177 measure of performance. This was done to distinguish task related
178 activity from activity often found in, e.g., parietal regions that
179 covary with attention demand without necessarily mediating
180 performance on specific tasks (Shulman, 1997; Gusnard et al.,
181 2001; Mazoyer et al., 2002; McKiernan et al., 2003; Fox et al.,
182 2005; Fransson, 2005).

183 The literature on nonlinguistic memory implies that perfor-
184 mance differences during verbally cued recall of spatial and
185 nonspatial content should lead to predictable differences in
186 activation in the abovementioned memory systems (e.g., *Ventre-*
187 *Dominey et al., 2005*). In answering questions about the spatial
188 features of a previous experience, differential activation should be
189 seen in parietal cortex and/or hippocampus between subjects as a
190 function of individual subjects' general level of performance. In
191 addition, we should also expect to see differences within each
192 subject as a function of variations in performance or effort across
193 individual trials. Answering questions about nonspatial aspects of
194 the same experience (regarding the slowly-learned classifications
195 of age) should involve the dorsal striatum. Performance effects in
196 dorsal striatal activation should again be seen according to sub-
197 jects' general abilities to solve the task, while variations in per-
198 formance from trial to trial should correlate with activity in non-
199 spatial working memory systems.

200 We thus predicted that we would find task-specific spatial
201 modulations of the hippocampal/parietal system, both within and
202 between subjects, and that we would find task-specific nonspatial
203 modulations of caudate, but only between subjects. Furthermore,
204 we predicted to see context independent performance modula-
205 tions of verbal working memory in regions such as Broca's
206 region.

207 **Methods**

208 *Stimuli*

209 *Images*

210 40 images like Fig. 1 were constructed using Poser 5 software
211 (Curious Labs, Santa Cruz, USA), each containing a man ("he/
212 him"), a woman ("she/her"), and a chair ("it/it"). The individual
213 characters and objects in the image were designed to differ only
214 slightly in age. This was done in order to match task difficulty
215 between spatial and nonspatial tasks.

216 *Sentences*

217 Four question sentence types each asked subjects to recall
218 specific information about the image:

219
220 Spatial allocentric information: "Was he/she/it in front of him/
221 her/it?"

222 Spatial egocentric information: "Was he/she/it in front of you?"

223 Nonspatial allocentric information: "Was he/she/it older than
224 him/her/it?"

225 Nonspatial egocentric information: "Was he/she/it older than
226 you?"

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228 Spatial questions always asked: "Was X in front of Y?"

229 Nonspatial questions always asked: "Was X older than Y?"

230 Therefore, all sentences contained the same number of syllables
231 and had exactly the same duration (2000 ms). Question sentences
232 were delivered verbally to avoid primary perceptual overlap with

the image stimuli. Sentences were recorded in a neutral female 233
voice and played through the standard pneumatic headphones of 234
the scanner. 235

In this article, only results related to the space–non-space 236
dichotomy are covered. Data from the allocentric and egocentric 237
conditions are collapsed in group analyses. 238

Experimental design

40 event sequences (each 30 s) made up the experiment. These 240
sequences included the display of a visual image, four subsequent- 241
ly verbally presented questions about the contents of the image. 242

Images were shown for 3000 ms after which a white fixation- 243
cross appeared in the middle of the screen. After a short 244
semirandom delay (1000–3000 ms, mean 2000 ms), the four 245
2000 ms questions were played with 4000–8000 ms semirandom- 246
ized intervals (mean interstimulus interval 6000 ms). The order of 247
the four types of questions in the sequence was counterbalanced 248
across events. 249

Subjects were asked to look at the image and to try to remember 250
the content. Due to the relatively small projection screen, subjects 251
were asked to consider objects in the middle of the image as in 252
front of themselves and objects in the periphery as not. They were 253
told not to rehearse possible questions during encoding. For each 254
sentence, they were asked to respond "yes/no" by button press as 255
quickly and accurately as possible with either right index finger or 256
right middle finger. 257

Since one aim of the experiment was to use response time as a 258
performance measure, balancing task difficulty along this dimen- 259
sion was very important. Accomplishing this came at the cost of 260
not having a strong handle on whether nonspatial responses were 261
correct or not (age judgements provide an ethologically valid but 262
somewhat subjective task). 263

Because of the small differences in age between the different 264
characters in the images and the difficulty of determining and 265
exact age of the chairs, there were no strictly correct or incorrect 266
answers to the nonspatial questions. Subjects were informed of 267
this prior to testing, and objective error rates were only calculated 268
for the spatial question types. To get a tentative evaluation of 269
responses during the nonspatial task, subjects were shown the 270
images from the experiment after scanning and asked to judge the 271
age of the characters and objects. The answers were compared to 272
the individual subject's responses during scanning. But due to the 273
large possible variability of this response measure, it was only 274
used to investigate the relationship to other performance measures 275
(see behavioral results section) and not taken into account during 276
the analysis of scanning data. 277

In order to secure a full understanding of the paradigm, subjects 278
were submitted to a prerun of two event cycles (two times an image + 279
four questions) like those in the experiment prior to scanning. 280

Subjects

21 healthy volunteers (9 female, 12 male), mean age 22.2 ± 1 282
(SEM) years participated in the experiment. All subjects were right 283
handed and reported having English as their primary language. All 284
participants gave informed written consent in accordance with 285
requirements of the local medical ethics committee. Subjects were 286
paid 15 £ for their participation. One subject was subsequently 287
excluded from the study due to performance not exceeding chance 288
level on the spatial task. 289

290 *Scanning parameters*

291 Functional images were acquired on a 3-T MR system with a
 292 standard head coil (Siemens Allegra, Erlangen, Germany). 470
 293 contiguous multislice T2*-weighted images were obtained using
 294 an echo planar imaging sequence with the following parameters:
 295 repetition time (TR): 2600 ms, echo time (TE): 30 ms, flip angle:
 296 90°. 40 sequential, descending 2-mm axial slices (with 1-mm gap
 297 between slices) were obtained per volume with an inplane
 298 resolution of 3 × 3 mm. The first 5 images from each session
 299 were discarded from the analysis due to burn in T1 effects.

300 *Data analysis*

301 Raw data were reconstructed and converted into Analyze
 302 format, spatially realigned (Friston et al., 1995a), unwarped
 303 according to all six motion parameters (Andersson et al., 2001),
 304 slice time corrected, and normalized (Ashburner and Friston, 1999)
 305 to the MNI template using SPM2 (Statistical Parametric Mapping,
 306 Wellcome Department of Imaging Neuroscience, University
 307 College London, London, UK; <http://www.fil.ion.ucl.ac.uk>) exe-
 308 cuted in MATLAB (Mathworks Inc., Sherborn, Massachusetts,
 309 USA). After normalization, the images were smoothed with a
 310 10-mm full-width at half-maximum Gaussian filter.

311 A design matrix was made, including a regressor with onsets
 312 for all images (duration 3000 ms) and separate regressors for each
 313 sentence type (duration 2000 ms), a parametric modulation
 314 regressor was included for each sentence type, using response
 315 time measurements as modulation parameters. Lastly, a “Button
 316 Press” regressor, including all button press measurements, was
 317 included to model activation related to motor output. All events
 318 were modeled using the standard hemodynamic response function
 319 of SPM2.

320 The model fit to the data was estimated for each participant
 321 using a general linear model (Friston et al., 1995b) with a 128-s
 322 high-pass filter, global scaling and AR(1) modeling of serial
 323 correlation.

324 Individual T-contrasts related to the different task effects and
 325 response time modulations were created from the estimated β
 326 weights, and these were used in a second level random effects
 327 analysis (a one-tailed T test for each first level contrast type) in
 328 order to facilitate inferences about population effects (Friston et
 329 al., 1999). Significance threshold for task main effects was set
 330 to $P < 0.05$, family wise error (FWE) corrected for multiple
 331 comparisons.

332 For the performance analyses, response time was considered to
 333 be the most valid performance parameter, since it is a continuous
 334 variable, both within and between subjects (see behavioral results
 335 section for an evaluation of response time as performance
 336 measure). Both task-independent and task-specific performance-
 337 related effects were estimated in three ways:

- 338
 339 – *Within-subjects* response time modulations, both across
 340 sentences and task specific, were found using the estimated
 341 β weights from the parametric modulation regressors. These
 342 were then subjected to a second level random effects analysis
 343 (a one-tailed T test for each first level contrast type).
 344 – *Between-subjects* performance effects were found by using
 345 each subject’s mean response time to spatial questions in a
 346 second level regression with effects of the All sentences >
 347 Baseline and the Space > Nonspace contrasts.

- *Within and Between subjects* were found by combining the
 two above analyses. Mean response time was used in a second
 level regression analysis on the parametric modulation
 estimates.

Significance threshold for the performance-related analyses was
 set to $P < 0.001$ (uncorrected for multiple comparisons—given our
 interest in prespecified regions, i.e., precuneus, hippocampus,
 caudate, amygdala and Broca’s region), $k > 40$ voxels.

Putative anatomical regions were located using WFU (Wake
 Forest University School of Medicine) Pickatlas (Maldjian et al.,
 2003, 2004) referencing the aal atlas (Tzourio-Mazoyer et al.,
 2002).

Results*Behavioral data*

Mean response time from the sentence onset for the spatial task
 was 3010 ms (SEM 72 ms) and 3020 ms (SEM 68 ms) for the
 nonspatial task. A two-sample t test showed no difference between
 the two tasks ($t = -0.09$, $P = 0.92$). Subjects responded correctly
 on average 82% of the spatial trials (range: 69–95%). A significant
 correlation between response time and percent correct responses on
 the spatial task ($r = -0.58$, $P < 0.008$). This shows that subjects
 who responded most correctly also had the shortest mean response
 time.

Percent correct responses for the nonspatial task were only
 estimated compared to the responses of the other subjects and
 using a comparison of subject responses and their age judgements
 during a post-scan reviewing of the experimental images (see
 Methods section).

For each nonspatial question, on average 74% of the subjects
 produce the same response (on average 79% produce the same for
 every spatial question). This indicates a significant consensus on
 what the “correct” answers to these questions should be. Thus,
 responses are not given at random. Further, if we compare
 individual subject’s percentage correct responses, when measured
 according to the consensus response, with percentage correct
 responses according to subject’s own post-experimental judge-
 ments of image elements (age of persons and chairs) then again
 we see a significant correlation ($r = 0.62$, $P < 0.007$). Subjects
 thus not only agree with each other on what is the correct
 response, their responses are also in agreement with their own
 post-scan age judgements. According to the post-scan judgements
 subjects answer correctly on 59% of the questions (range 46–
 74%). This is significantly above chance level ($P < 0.0001$).
 Since age judgement was deliberately made quite difficult to
 match the difficulty of the spatial questions, it is not surprising
 that subjects’ responses are not in total agreement with their own
 post-scan judgements. We can therefore safely conclude that
 responses are not given randomly during the nonspatial task, and
 the assumption that subjects with the shortest average response
 time had most correct responses is strengthened by the fact that
 this crude between-subjects measure of percentage correct
 responses correlates negatively with response time ($r = -0.46$,
 $P < 0.05$).

Within subjects, there was a significant response time difference
 ($t = 5.2$, $P = 0.000008$) between space trials where the subject
 responded correctly (mean RT = 2830 ms, SEM = 47 ms) and trials

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405 where the subject responded incorrectly (mean RT = 3212 ms,
406 SEM = 57 ms), compared with a two sample *t* test. This indicates
407 that questions that take longer to answer are more difficult, i.e.,
408 they require more effort, hence the longer response time.

409 Response times across the spatial and nonspatial conditions
410 were also found to be highly correlated ($r = 0.93$, $P < 0.000001$),
411 suggesting that subjects who performed well on spatial tasks also
412 performed well on nonspatial tasks.

413 Together, these results clearly show that response time is a good
414 performance measure, both within and between subjects. Between-
415 subjects shorter average response time indicates better perfor-
416 mance. Within-subjects longer response time indicates increased
417 effort.

418 Scanning data

419 Main effects

420 *Space > Nonspace.* A network of regions involved in secondary
421 spatiodynamic perceptual processing was seen more active in
422 spatial questions than in nonspatial questions, including most
423 prominently the dorsal precuneus, but also temporal occipital
424 parietal (TOP) junction and inferior parietal lobule, both bilaterally,
425 and left posterior middle temporal (LPMT) gyrus (Table 1, Fig. 2).

426 *Nonspace > Space.* Compared to spatial questions, the nonspa-
427 tial questions gave rise to a higher activation primarily in

428 ventrofrontal (BA 9/10/11/47) and ventroanterior temporal (BA 428
429 20/21) areas, but also posterior cingulate (BA 31) and bilateral
430 angular gyri/inferior parietal lobule (BA 40) were more active in
431 the nonspatial recall conditions (Table 1, Fig. 2).

432 (To further validate these findings, we performed an analysis on
433 a model including correct and incorrect trials from each condition
434 in separate regressors. The comparison between the spatial and
435 nonspatial task, when limited to the correct trials, yielded
436 practically identical results to those reported here. A figure
437 showing these effects is obtainable as supplementary material.)

438 Within-subjects effects

439 Results from the within-subjects analysis indicate common
440 strategies used for task solving during the experiment. However,
441 these results must be read cautiously, since they mix good and poor
442 performers and thus may also mix good and bad task solving
443 strategies.

444 *Task independent.* We see a positive within-subject response
445 time modulation in bilateral inferior frontal gyrus (BA 44/45/47),
446 anterior cingulate/SMA, and precuneus, regardless of task,
447 indicating that these are regions that are activated when attention
448 demand is increased, regardless of the individual subject's overall
449 performance. The opposite pattern is seen in auditory cortex and
450 amygdala, bilaterally, suggesting that short response time is also
451 a result of attention paid to the auditory stimulus and the emotional
452 state of the subject (Table 2).

t1.1 Table 1

t1.2 Experimental main effects

| t1.3 fMRI contrast | Putative anatomical regions—Brodmann | x | y | z | Z Score |
|----------------------------------|--|-----|-----|-----|---------|
| t1.4 <i>Space > Nonspace</i> | R. Sup. Front. gyrus—BA 6 | 24 | 10 | 66 | 4.97 |
| t1.5 | L. Post. Mid. Temp. gyrus—BA 37 | -56 | -66 | 0 | 5.63 |
| t1.6 | L. Post. Mid. Temp. gyrus—BA 39 | -42 | -64 | 18 | 5.29 |
| t1.7 | R. Post. Inf./Mid. Temp. gyrus—BA 37 | 62 | -58 | -8 | 5.55 |
| t1.8 | L. cuneus/precuneus—BA 31 | -16 | -64 | 22 | 5.00 |
| t1.9 | R. cuneus/precuneus—BA 31 | 20 | -64 | 22 | 5.12 |
| t1.10 | L. TOP junction—BA 19/39 | -36 | -82 | 32 | 5.09 |
| t1.11 | R. TOP junction—BA 19/39 | 40 | -84 | 32 | 5.80 |
| t1.12 | L. Inf. Par. lobule—BA 40 | -38 | -40 | 52 | 5.36 |
| t1.13 | R. Inf. Par. lobule—BA 40 | 46 | -40 | 60 | 5.05 |
| t1.14 | R. Sup. Occ. gyrus—BA 19/31 | 26 | -68 | 28 | 4.84 |
| t1.15 | R. Sup. Par. lobule—BA 7 | 22 | -74 | 58 | 5.91 |
| t1.16 | L. precuneus—BA 7 | -12 | -68 | 62 | 5.87 |
| t1.17 | L. precuneus—BA 7 | -12 | -60 | 50 | 5.67 |
| t1.18 | R. precuneus—BA 7 | 10 | -58 | 64 | 6.43 |
| t1.19 | R. precuneus—BA 7 | 6 | -74 | 56 | 5.67 |
| t1.20 | | | | | |
| t1.21 <i>Nonspace > Space</i> | L/R. rectal gyrus—BA 11 | 2 | 36 | -24 | 6.84 |
| t1.22 | L. Sup. Med. Front. gyrus—BA 9/10 | -6 | 56 | 38 | 6.24 |
| t1.23 | R. Sup. Med. Front. gyrus—BA 9/10 | 4 | 60 | 28 | 5.66 |
| t1.24 | L. Inf. Orb. Front. gyrus—BA 47 | -36 | 30 | -18 | 5.83 |
| t1.25 | L. Sup. Med. Front. gyrus—BA 8 | -6 | 32 | 56 | 5.17 |
| t1.26 | L. Inf. Temp. gyrus/Temp. pole—BA 21/38 | -58 | -6 | -34 | 4.99 |
| t1.27 | L. Inf. Temp. gyrus—BA 20 | -56 | -12 | -26 | 4.87 |
| t1.28 | R. Inf. Temp. gyrus—BA 20 | 62 | -16 | -28 | 5.58 |
| t1.29 | L. Inf. Temp. gyrus—BA 21 | -46 | 6 | -40 | 5.59 |
| t1.30 | R. Post. cingulate gyrus—BA 31 | 8 | -46 | 30 | 5.14 |
| t1.31 | R. angular gyrus/Inf. Par. lobule—BA 40x | 54 | -62 | 36 | 5.28 |
| t1.32 | Cerebellum x | -32 | -36 | -28 | 5.23 |

t1.33 Peak activation MNI coordinates for SPM contrasts of verbally cued recall of spatial image content (“in front of”) versus nonspatial image content (“older than”). Significance threshold: $P < 0.05$, FWE-corrected for multiple comparisons.

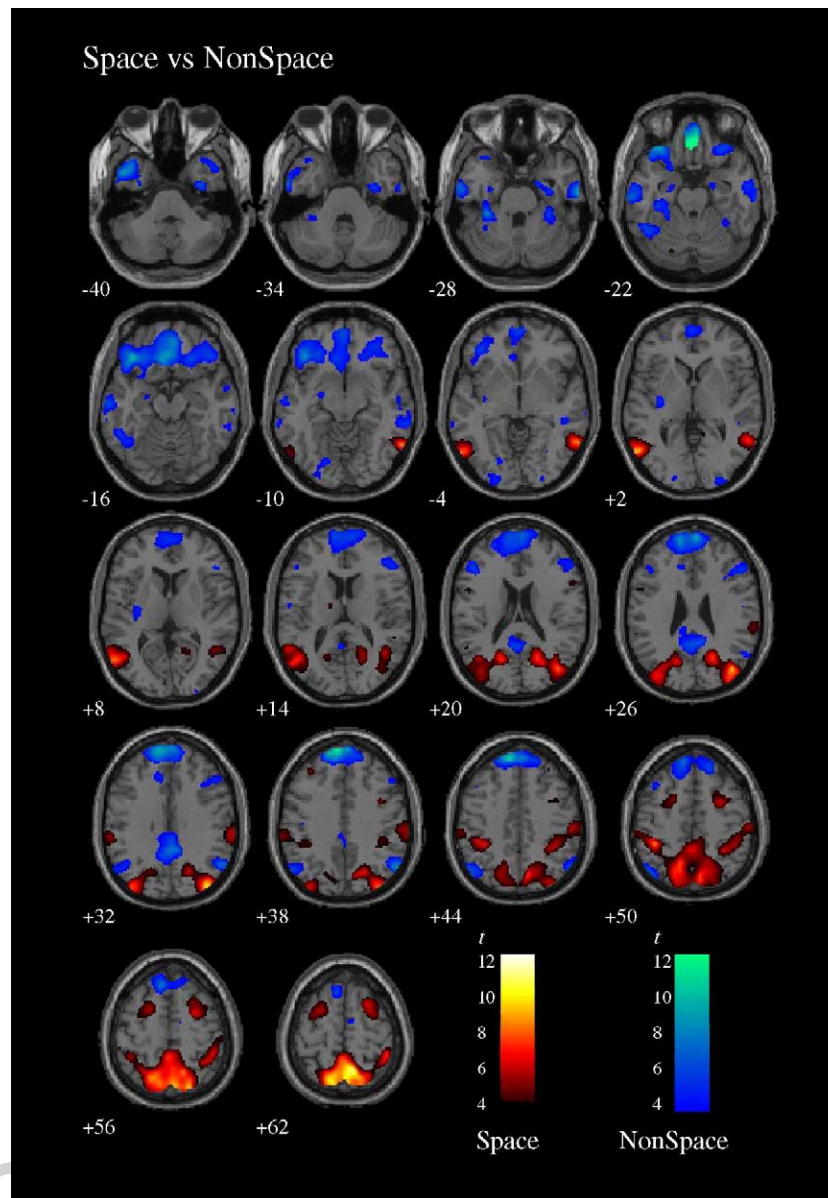


Fig. 2. Space versus NonSpace: Verbally cued recall of spatial image content (“in front of”) versus nonspatial image content (“older than”) overlaid on a representative single subject brain, thresholded at $P = 0.001$, uncorrected for multiple comparisons.

453 *Task specific.* Bilateral regions of the temporal–occipital–
 454 parietal junction are modulated more by space than by nonspatial
 455 tasks. SMA and left temporal pole are modulated mostly by the
 456 nonspatial task (Table 2).

457 *Between-subjects effects of performance*

458 Results from a between-subjects analysis indicate areas
 459 where activation correlates with subject performance. Regions
 460 where activity is higher in good performers than in poor per-
 461 formers are taken to be involved in efficient solving of a given
 462 task.

463 *Task independent.* Good performers have a higher insula,
 464 temporal, and SMA activation compared to poor performers,
 465 regardless of task. Poor performers show a higher activation in
 466 amygdala during the experiment, regardless of task (Table 3).

467 *Task specific.* Adept subjects have a higher activation in
 468 precuneus during the spatial task, compared to the nonspatial task
 469 (Table 3, Figs. 3 and 6B), and a higher activation in caudate and
 470 other regions during the nonspatial task relative to the spatial task
 471 (Table 3, Fig. 3). The correlation with task-specific spatial
 472 activation versus baseline produces a better fit in precuneus
 473 ($r = -0.47$, $P = 0.03$), compared to the nonspatial estimates
 474 ($r = -0.16$, $P = 0.48$). The opposite is true for caudate (Space:
 475 $r = -0.33$, $P = 0.14$; NonSpace: $r = -0.52$, $P = 0.016$). This
 476 suggests that the performance correlation in precuneus with the
 477 space > nonSpace contrast, primarily is driven by the spatial
 478 conditions, whereas the correlation with response time seen in
 479 caudate with the nonSpace > space contrast primarily is driven by
 480 the nonspatial condition. Among the regions apparently correlated
 481 with nonspatial performance, we also find a peak in right
 482 hippocampus. When looking at task-specific performance correla-

t2.1 Table 2

t2.2 Within-subjects effects

| t2.3 | Contrast | Putative anatomical regions—Brodmann areas | x | y | z | Z Score |
|-------|---|--|-----|-----|-----|---------|
| t2.4 | <i>Within subjects (task independent)</i> | | | | | |
| t2.5 | Up with effort | L. Sup. Front. gyrus—BA 10 | −32 | 58 | 20 | 5.27 |
| t2.6 | (positive RT modulation) | R. Sup. Front. gyrus—BA 10 | 32 | 52 | 28 | 3.75 |
| t2.7 | | L. Mid. Front. gyrus—BA 9 | −36 | 38 | 36 | 3.85 |
| t2.8 | | L. Inf. Front. operculum—BA 44/45 | −46 | 14 | 22 | 5.46 |
| t2.9 | | L. Inf. Front. gyrus—BA 47 | −42 | 18 | −4 | 3.78 |
| t2.10 | | R. Inf. Front. gyrus—BA 47 | 42 | 20 | −6 | 4.60 |
| t2.11 | | R. Precent. gyrus—BA 8 | 46 | 8 | 46 | 4.33 |
| t2.12 | | Cingulate—BA 32 | 0 | 36 | 36 | 5.03 |
| t2.13 | | SMA/Cingulate—BA 6/32 | −4 | 18 | 46 | 5.81 |
| t2.14 | | SMA—BA 6 | 0 | 16 | 66 | 5.33 |
| t2.15 | | L. insula—BA 13 | −34 | 26 | 0 | 3.94 |
| t2.16 | | L. Temp. pole—BA 38 | −50 | 18 | −14 | 3.86 |
| t2.17 | | L. Mid. Front. gyrus—BA 6 | −28 | 0 | 50 | 4.63 |
| t2.18 | | R. precuneus—BA 7/31 | 18 | −64 | 22 | 4.74 |
| t2.19 | | R. Ling. gyrus/Post. cingulate BA 17/30 | 6 | −66 | 10 | 4.55 |
| t2.20 | | L. TOP junction—BA 19/39 | −34 | −78 | 26 | 3.83 |
| t2.21 | | R. TOP junction—BA 19/39 | 42 | −76 | 22 | 4.16 |
| t2.22 | | L. precuneus—BA 7 | −8 | −78 | 44 | 3.66 |
| t2.23 | | R. precuneus—BA 7 | 2 | −50 | 56 | 3.69 |
| t2.24 | | L. Calc. sulcus—BA 17 | −2 | −86 | 4 | 4.45 |
| t2.25 | Down with effort | R. Orb. front.—BA 10 | 8 | 54 | −8 | 3.77 |
| t2.26 | (negative RT modulation) | L. Ventr. Med. Front. region—BA 11/32 | −18 | 32 | −8 | 3.61 |
| t2.27 | | R. Ventr. Med. Front. region—BA 11/32 | 18 | 38 | −8 | 4.42 |
| t2.28 | | R. Precent. gyrus—BA 6 | 52 | −12 | 36 | 3.41 |
| t2.29 | | R. Precent. gyrus—BA 6 | 30 | −22 | 70 | 4.59 |
| t2.30 | | R. Mid. Temp. gyrus—BA 21 | 62 | −12 | −8 | 6.21 |
| t2.31 | | L. Sup. Temp. gyrus—BA 41/42 | −56 | −16 | 6 | 5.08 |
| t2.32 | | R. Sup. Temp. gyrus—BA 41/42 | 66 | −22 | 6 | 5.05 |
| t2.33 | | R. Sup. Temp. gyrus—BA 41/42 | −44 | −32 | 16 | 5.36 |
| t2.34 | | L. postcentral gyrus—BA 2/3 | −14 | −46 | 74 | 4.47 |
| t2.35 | | R. postcentral gyrus BA 2/3 | 18 | −38 | 74 | 4.33 |
| t2.36 | | L. amygdala | −28 | 0 | −16 | 4.22 |
| t2.37 | | L. putamen | −28 | −12 | 8 | 4.53 |
| t2.38 | | R. putamen | 28 | −8 | 2 | 3.96 |
| t2.39 | | | | | | |
| t2.40 | <i>Within subjects (task specific)</i> | | | | | |
| t2.41 | Space more up with effort than | L. TOP junction—BA 19/39 | −20 | −60 | 16 | 3.86 |
| t2.42 | nonspace (RT modulation space > RT | L. TOP junction—BA 19/39 | −26 | −74 | 20 | 3.60 |
| t2.43 | modulation nonspace) | R. TOP junction—BA 19/39 | 30 | −88 | 28 | 3.47 |
| t2.44 | Nonspace more up with effort than | L. Temp. pole—BA 38 | −26 | 10 | −26 | 3.93 |
| | space (RT modulation nonspace > RT | | | | | |
| | modulation space) | | | | | |

t2.45 Peak activation MNI coordinates for SPM contrast showing task independent and task-specific parametric modulation of response time. Significance threshold: $P < 0.001$, uncorrected for multiple comparisons.

483 tions in the peak voxel against baseline we see a much stronger
 484 correlation to the spatial task ($r = 0.37$) than the nonspatial ($r =$
 485 -0.09). This suggests that what we are seeing is in fact a
 486 performance-related deactivation of the hippocampus during the
 487 spatial task, rather than a nonspatial activation.

488 *Combined within and between-subjects effects of performance*

489 The combined analysis shows regions where activation within-
 490 subjects increases in relation to increased effort as a function of
 491 subjects' overall performance level. This analysis therefore
 492 distinguishes between good and bad task solving strategies during
 493 the experiment.

494 *Task-independent effects.* Task-independent correlation between
 495 effort related variations within-subjects and between-subjects

496 general performance levels are seen in Broca's region (Fig. 4, 496
 497 right panel), orbitofrontal cortex and precuneus regions. These are 497
 498 regions that adept subjects activate more during attention 498
 499 demanding trials (but see Discussion section for an explanation 499
 500 of why this is not true for precuneus). In contrast, less adept 500
 501 subjects have higher modulation of amygdala (Fig. 4, middle 501
 502 panel), temporal pole, inferior temporal regions, SMA, and 502
 503 midbrain than adept (Table 4). 503

504 *Task-specific effects.* The most dorsal part of the precuneus (Fig. 504
 505 4—left panel, and Fig. 6C) shows a task-specific performance- 505
 506 related difference of within-subject modulations. This difference is 506
 507 also present in superior parts of the posterior frontal cortex, 507
 508 whereas the opposite pattern is observed in cingulate, temporal 508
 509 pole, insula, and deep midbrain regions (Table 4). The precuneus 509

t3.1 Table 3

t3.2 Between-subjects effects

| t3.3 | Contrast | Putative anatomical regions—Brodman area | x | y | z | Z Score |
|-------|---|--|-----|-----|-----|---------|
| t3.4 | <i>Between subjects—task independent</i> | | | | | |
| t3.5 | Good performers high | R. insula—BA 13 | 28 | 20 | −10 | 4.03 |
| t3.6 | Negative correlation: mean RT and [all sentences > baseline] | L. insula—BA 13 | −40 | 0 | 2 | 3.94 |
| t3.7 | | L. STG—Heschl's gyrus—BA 41 | −36 | −30 | 8 | 3.91 |
| t3.8 | | L. Sup. Temp. gyrus—BA 42 | −64 | −12 | 4 | 3.81 |
| t3.9 | | R. Mid. Temp. gyrus—BA 21 | 52 | 0 | −18 | 3.69 |
| t3.10 | | SMA—BA 6 | −6 | −2 | 52 | 3.62 |
| t3.11 | Poor performers high | L. Temp. pole—BA 38 x | −40 | 20 | −24 | 4.13 |
| t3.12 | Positive correlation: mean RT and [all sentences > baseline] | R. amygdala x | 20 | 8 | −28 | 4.23 |
| t3.13 | | R. amygdala x | 32 | 0 | −22 | 3.92 |
| t3.14 | | L. amygdala x | −22 | −10 | −24 | 3.93 |
| t3.15 | | R. cuneus—BA 19 x | 10 | −88 | 26 | 3.78 |
| t3.16 | | L. cuneus—BA 19 x | −12 | −84 | 32 | 3.69 |
| t3.17 | <i>Between subjects—task specific</i> | | | | | |
| t3.18 | <i>Good performers space higher</i> | | | | | |
| t3.19 | than nonspace | R. Sup. Temp. gyrus—BA 22 | 70 | −22 | 2 | 3.89 |
| t3.20 | Negative correlation: mean RT and [Space > NonSpace] | R. precuneus—BA 7 | 18 | −48 | 48 | 3.68 |
| t3.21 | <i>Good performers nonspace higher</i> | | | | | |
| t3.22 | than space | R. SMA—BA 6 | 4 | 16 | 56 | 4.23 |
| t3.23 | Negative correlation: mean RT and [Nonspace > Space] | R. Inf. Front. gyrus—BA 47 | 56 | 26 | −6 | 3.48 |
| t3.24 | | R. Inf. Front. gyrus—BA 44 | 54 | 2 | 16 | 3.74 |
| t3.25 | | R. Temp. pole—BA 21/38 | 46 | 8 | −34 | 4.45 |
| t3.26 | | R. hippocampus | 40 | −16 | −16 | 4.37 |
| t3.27 | | R. fusiform gyrus—BA 20 | 38 | −32 | −22 | 3.71 |
| t3.28 | | L. parahippocampal gyrus—BA 27 | −20 | −32 | −10 | 3.79 |
| t3.29 | | R. caudate | 8 | 12 | 6 | 3.62 |
| t3.29 | | C. midbrain—pontine nuclei | 0 | −24 | −30 | 3.61 |

t3.30 Peak activation MNI coordinates of SPM correlation analysis between-subject mean response time and task independent and task-specific experimental main effects. Significance threshold: $P < 0.001$, uncorrected for multiple comparisons.

510 region found here lies in the same region that showed the most
511 significant difference in the main effect contrast (Figs. 6A, C, D),
512 showing that activity in this region is highly task specific. When
513 looking at a peristimulus time histogram for the peak voxel found
514 in this analysis, we see that this region is not just active during
515 recall of spatial relations, but also during encoding, suggesting that
516 the effect is related to the processing of spatial relations in general
517 (Fig. 5).

518 Discussion

519 Precuneus

520 In this study, our main effects analysis of linguistically cuing
521 spatial aspects versus nonspatial aspects of a scene shows that the
522 dorsal part of the precuneus is strongly activated when recalling
523 spatial information (Figs. 2, 6A), underlining that this region is part
524 of the secondary perceptual system for spatiodynamic processing
525 (Ungerleider and Mishkin, 1982), and that this region also plays an
526 important, task specific, role in short-term memory processes
527 related to spatial relations (Baddeley and Hitch, 1974; Casey et al.,
528 1998; Ungerleider et al., 1998; Burgess et al., 2001b), imagery
529 (Mellet et al., 1996, 2002; Kosslyn et al., 1997) and in the
530 processing of sentences with a concrete spatial meaning (Wallentin
531 et al., 2005).

532 Further, we show here for the first time how an analysis of
533 performance-related activation differences between subjects (Fig.

6B) and changes within subjects as a function of increased effort
(Fig. 6C) yields strong support to this conclusion. Together (Fig.
6D), this clearly suggests that dorsoposterior precuneus activation
mediates spatial performance in a highly task-specific manner.

Two of our results seem to contradict this conclusion at face
value, but not on further inspection. First, within subjects (Table 2),
we observe an apparent task-independent upregulation of precu-
neus as a function of increased effort. The reason we see this is that
the within-subjects analysis does not distinguish between good and
poor performers. Since good performers upregulate precuneus
activity with effort during the spatial task and poor performers
upregulate precuneus activity with effort during the nonspatial task
(Fig. 4, top), together, this may show up as an apparent task-
independent upregulation with effort in an analysis that does not
take performance into account. When poor performers upregulate
activity in posterior precuneus as a function of effort, but in the
wrong task (i.e., the nonspatial task), this may be a strategy that
contributes to making them poor performers in the first place.
Second, we observe a nearby precuneus region that shows
performance-related task-independent upregulation with effort
(MNI coordinates [4, −66, 52], see Table 4).

Precuneus is a large region, and it may not be devoted to spatial
imagery throughout. However, in this case, when looking at the
effects of effort in the spatial and nonspatial tasks separately in this
peak voxel, we find that the seemingly task-independent upregu-
lation actually consists of a highly significant correlation with
spatial performance ($r = -0.76$, $P = 0.00007$) and a nonsignificant
correlation with nonspatial performance ($r = -0.14$, $P = 0.55$).

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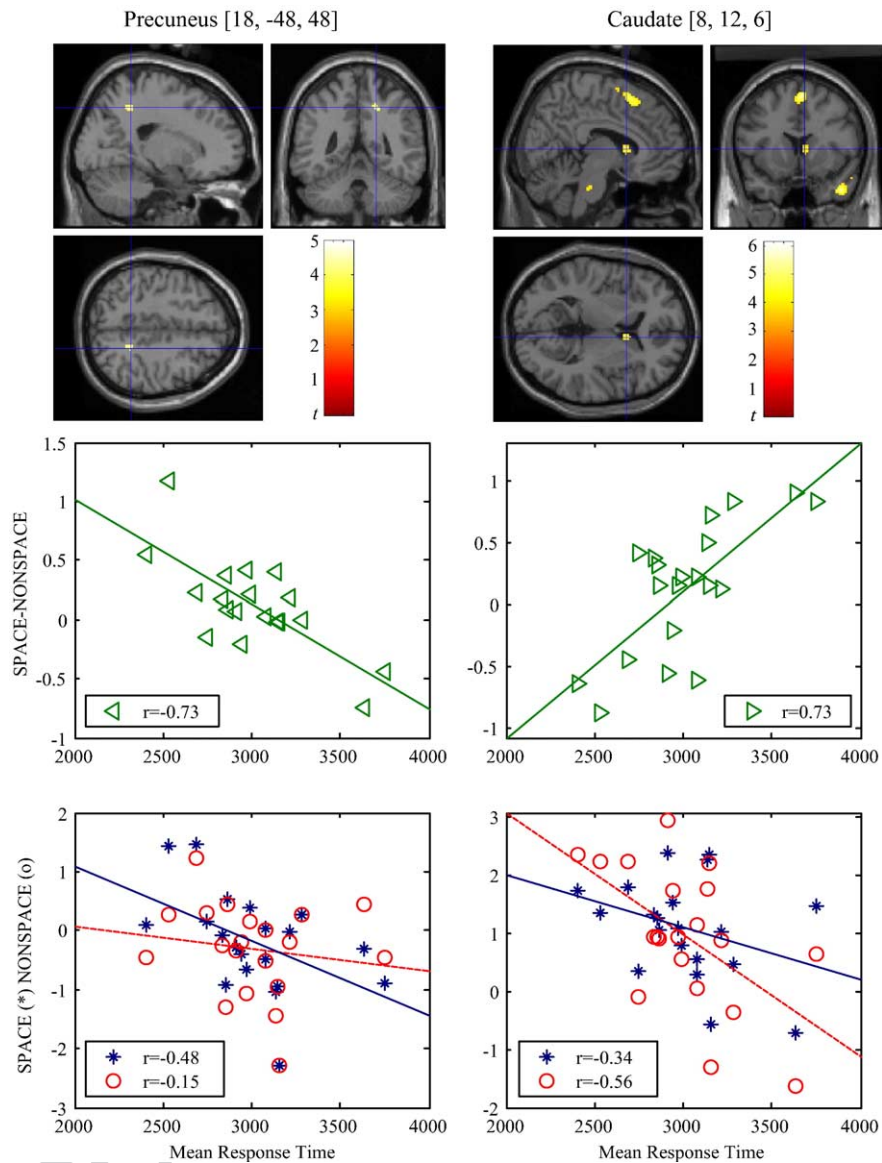


Fig. 3. Effects of the subject's performance level on precuneus and caudate activation. Top: brain regions where performance level (measured as mean response time: lower is better) correlates with condition contrasts ($P < 0.001$, uncorrected). In (left panel) precuneus [MNI: 18, -48, 48] good performers have a greater activation during the spatial task than during the nonspatial task, whereas this is less so in poor performers. In (right panel) caudate head [MNI: 8, 12, 6] good performers have greater activation during the nonspatial task than during the spatial task. Middle: scatterplots with least square linear fits showing these between-subjects performance correlation effects (mean RT for the space condition against the space–nonspace contrast) in the peak voxel in precuneus ($r = -0.73$, $P = 0.0002$) and caudate head ($r = 0.73$, $P = 0.0003$). Bottom: scatterplots with least square fits showing performance against single condition effects relative to baseline in the same voxels in precuneus: Space-Baseline (asterisk, $r = -0.48$, $P = 0.03$), Nonspace-Baseline (circle, $r = -0.15$, $P = 0.51$), and in caudate: Space-Baseline (asterisk, $r = -0.34$, $P = 0.14$); Nonspace-Baseline (circle, $r = -0.56$, $P = 0.01$). Note that the spatial contrast estimates (solid line) produces a better correlation in precuneus, compared to the nonspatial (dashed line) estimates. The opposite is true for caudate. This suggests that the negative correlation in the precuneus from the space–nonspace contrast is primarily driven by the spatial condition, and that the positive correlation in caudate is primarily driven by the nonspatial condition.

562 This finding can be explained by the fact that the task-independent
 563 analysis, as performed in SPM2 using a global null hypothesis, not
 564 in a strict sense is a test of conjoined effects (Nichols et al., 2005).
 565 A very strong effect in a single task can drive the contrast towards
 566 significance, in the absence of an effect in the other task. This is
 567 clearly what we are seeing in this instance, and thus, rather than
 568 contradicting task specificity, this result actually supports it.

569 Nonlinguistic studies have directly compared visuospatial
 570 working memory with nonspatial working memory, most often

571 memory for letters. Some found no difference between tasks in the
 572 parietal lobe (Smith et al., 1996; D'Esposito et al., 1998; Nystrom
 573 et al., 2000; Zurowski et al., 2002), whereas others have found a
 574 clear effect (Gruber and von Cramon, 2003; Ventre-Dominey et al.,
 575 2005). The studies that did not find a task-specific effect in this
 576 region all found a task-independent effect. We argue that these
 577 inconsistencies may reflect the fact that analyses that do not
 578 distinguish between good and bad performers run the risk of not
 579 distinguishing between good and bad task solving strategies.

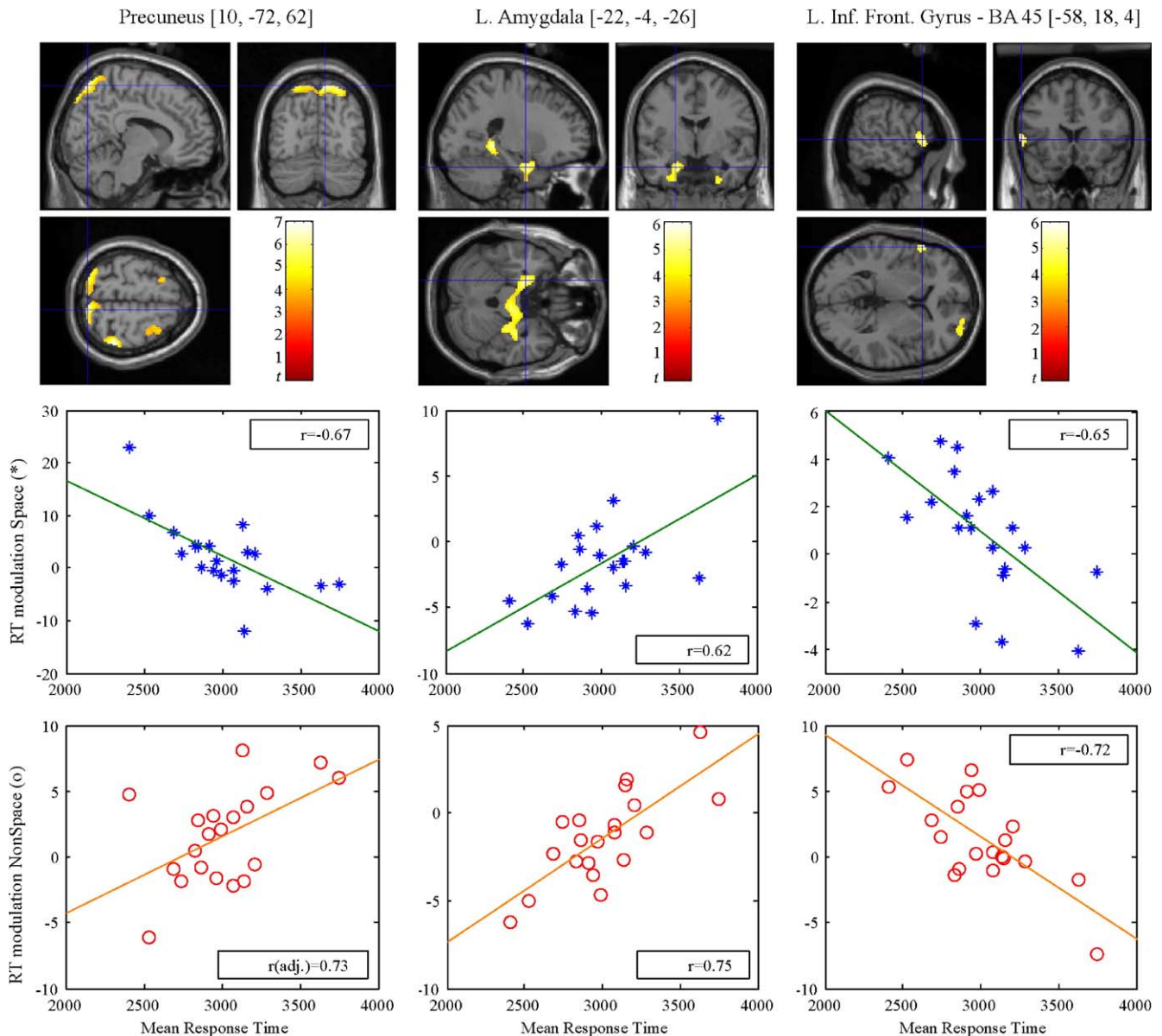


Fig. 4. Interactions between effects of effort per trial on activation and the subject's performance level. Activation can be modulated by the effort of responding to each individual trial (measured as response time per trial: higher = more effort). Top: brain regions where modulation of activation by effort correlates with performance level across subjects (mean response time: lower is better) at $P < 0.001$, uncorrected. In (left panel) precuneus [MNI: 10, -72, 62], we see a task-specific correlation for the space condition, such that better performers show more activation on more effortful spatial trials, i.e., a negative correlation between mean RT and the [RT modulation Space - RT modulation Nonspace] contrast. In (middle panel) amygdala [MNI: -22, -4, -26] and (right panel) Broca's region [MNI: -58, 18, 4], we see task-independent correlations. Good performers deactivate amygdala as a function of increased effort in both types of trial, i.e., a positive correlation between mean RT and the [RT modulation Space + RT modulation Nonspace] contrast, whereas they activate Broca's region as a function of effort in both types of trial, i.e., a negative correlation between mean RT and the [RT modulation Space + RT modulation nonspace]. Middle and bottom: scatterplots showing correlations between performance level and modulation by effort for each of the two conditions in precuneus, amygdala and Broca's region. In (left) precuneus [MNI: 10, -72, 6-2] RT modulation in the space condition correlates negatively ($r = -0.67$, $P = 0.001$) with mean RT, whereas robust regression for the Nonspace condition shows a strong positive correlation ($r(\text{adj.}) = 0.73$, $P < 0.001$). Thus, adept subjects upregulate precuneus with effort during the spatial task and downregulate it with effort during the nonspatial tasks: indicating a specific role in successfully performing the spatial task. In (middle) amygdala [MNI: -22, -4, -26] mean response time correlates positively with RT modulations for both space ($r = 0.62$, $P < 0.004$) and nonspace conditions ($r = 0.75$, $P = 0.0001$). Thus, adept subjects downregulate amygdala with effort more than inept subjects, regardless of task. In (right) Broca's region—BA 45 [MNI: -58, 18, 4] mean response time correlates negatively with RT modulations for both spatial ($r = -0.65$, $P < 0.002$) and nonspatial ($r = -0.72$, $P < 0.0004$) tasks. Thus, adept subjects upregulate Broca's region with effort more than inept subjects, regardless of task.

580 Subjects may seek to solve nonspatial memory tasks using a spatial
 581 strategy and vice versa. Our study clearly shows that involving the
 582 dorsoposterior parietal region in a spatial task is a good task
 583 solving strategy on a trial-by-trial basis, whereas it is less efficient

for the nonspatial task, even though the two tasks share the same
 concrete context.

Concreteness is considered an important parameter in imagery
 studies (Paivio, 1995). Again, however, some studies have shown

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t4.1 Table 4
t4.2 Within and between-subjects effects

| t4.3 Contrast | Putative anatomical regions—Brodmann areas | x | y | z | Z Score |
|--|--|-----|-----|-----|---------|
| t4.4 <i>Between and within subjects—task independent</i> | | | | | |
| t4.5 Good performers up with effort | R. Sup. Orb. Front. gyrus—BA 10 | 24 | 62 | -2 | 4.37 |
| t4.6 Negative correlation: mean RT and | L. Inf. Front. gyrus—BA 45 | -58 | 18 | 4 | 4.32 |
| t4.7 [all within-subject RT modulations] | Precuneus—BA 7* | 4 | -66 | 52 | 3.62 |
| t4.8 | R. angular gyrus—BA 40 | 44 | -60 | 54 | 3.50 |
| t4.9 Poor performers up with effort | L. Mid. Orb. Front. gyrus—BA 10 | -14 | 50 | -2 | 4.09 |
| t4.10 Positive correlation: mean RT and | R. Sup. Front. gyrus—BA 6 | 22 | -12 | 66 | 3.66 |
| t4.11 [all within-subject RT modulations] | L. SMA—BA 6 | -6 | -18 | 58 | 3.60 |
| t4.12 | R. SMA—BA 6 | 6 | 8 | 66 | 3.48 |
| t4.13 | L. Pre-/postcentral gyrus—BA 3/4/6 | -56 | -8 | 42 | 3.59 |
| t4.14 | R. Pre-/postcentral gyrus—BA 3/4/6 | 58 | 0 | 36 | 3.37 |
| t4.15 | R. Temp. pole—BA 38 | 42 | 10 | -34 | 4.41 |
| t4.16 | L. amygdala | -22 | -4 | -26 | 4.28 |
| t4.17 | R. fusiform gyrus—BA 20 | 26 | -4 | -42 | 3.65 |
| t4.18 | R. parahippocampal gyrus—BA 35 | 26 | -22 | -24 | 3.97 |
| t4.19 | L. supramarginal gyrus—BA 40 | -66 | -24 | 34 | 3.82 |
| t4.20 | L. lingual gyrus—BA 19 | -22 | -42 | -2 | 4.21 |
| t4.21 | R. midbrain—substantia nigra | 8 | -20 | -24 | 4.09 |
| t4.22 | | | | | |
| t4.23 <i>Between and within subjects—task specific</i> | | | | | |
| t4.24 Good performers up more with space effort | L. Mid. Front. gyrus—BA 6 | -22 | 12 | 60 | 3.85 |
| t4.25 Negative correlation: mean RT and | R. Sup. Front. gyrus—BA 6 | 28 | 4 | 60 | 3.63 |
| t4.26 [within-subject RT space–nonspace] | R. Post. Inf. Front. gyrus | 62 | -56 | -10 | 4.27 |
| t4.27 | R. Sup. Par. lobule—BA 7 | 46 | -42 | 62 | 4.78 |
| t4.28 | R. Sup. Par. lobule—BA 7 | 24 | -76 | 56 | 4.62 |
| t4.29 | R. precuneus—BA 7 | 10 | -72 | 62 | 4.80 |
| t4.30 Good performers up more with nonspace effort | Midbrain—pontine nuclei | 4 | -20 | -30 | 4.73 |
| t4.31 Negative correlation: mean RT and | R. Temp. pole—BA 38 | 44 | 6 | -36 | 3.98 |
| t4.32 [within-subject RT nonspace–space] | L. insula—BA 13 | -38 | 4 | -2 | 3.93 |
| t4.33 | R. Mid. cingulate—BA 32 | 16 | 14 | 36 | 3.94 |

t4.34 Peak activation MNI coordinates of SPM correlation analysis between-subject mean response time and task independent and task-specific within-subjects
t4.35 parametric response time effects. Significance threshold: $P < 0.001$, uncorrected for multiple comparisons.

* This precuneus correlation is only seemingly task independent. See discussion section for details.

588 an effect of concreteness in the parietal region (Just et al., 2004;
589 Sabsevitz et al., 2005; Wallentin et al., 2005) whereas others did
590 not find this (Mellet et al., 1998; Tyler et al., 2001; Noppeney and

Price, 2004). We repeat that in our study, there is no difference in
concreteness, since questions refer to the same image. Based on
our findings, we therefore suggest that studies seeing concreteness
effects in parietal cortex may be those that somehow include
differences in spatial information in the stimuli rather than it being
an effect of concreteness in itself (see also Cabeza and Nyberg,
2000).

Together, our findings are consistent with the large literature
implicating dorsoposterior parietal regions in spatial working
memory processing. They extend this literature by showing how
this system can also be accessed through language and by
incorporating performance measures in the analysis to rule out
nuisance effects commonly found in this region (Shulman, 1997;
Gusnard et al., 2001; Mazoyer et al., 2002; McKiernan et al., 2003;
Fox et al., 2005; Fransson, 2005). We thus provide strong evidence
for the notion that dorsoposterior precuneus is involved not only in
nonlinguistic spatial processes but also in efficient task-specific
processing of language with a spatial reference.

Hippocampus

While the hippocampus is involved in remembering/processing
locations in an environmental framework, specifically relative to
large/stable boundaries and landmarks (Burgess et al., 2002), we
did not find any evidence that it is necessarily involved in all
processing of locations (i.e., relative to other people or small

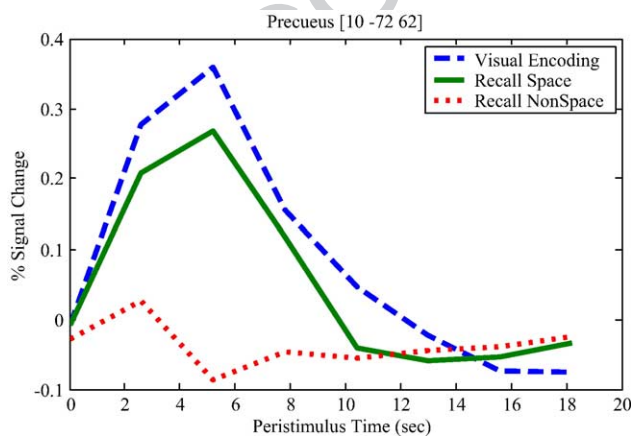


Fig. 5. PSTH. peristimulus time histogram for right precuneus [10, -72, 62]. Adjusted average BOLD signal change for visual encoding and for verbally cued spatial and nonspatial recall across subjects in the peak activation voxel for the combined between and within-subjects performance modulation. We see that even without accounting for performance differences, activity in this region is clearly spatial and thus involved both in nonverbal encoding and verbally cued recall.

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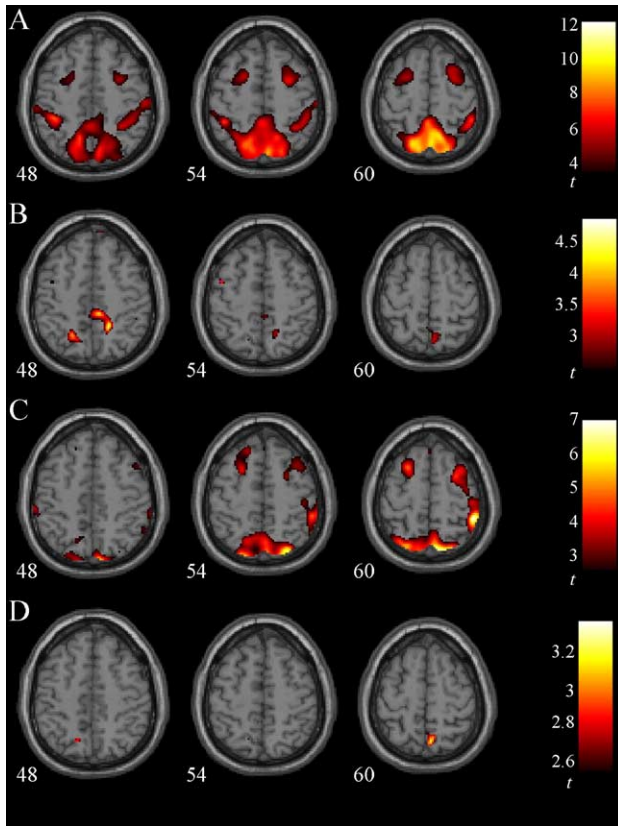


Fig. 6. Parietal main effects and performance effects of spatial recall. Main effect: Space > Nonspace ($P < 0.001$, uncorrected). (B) Between-subjects performance correlation: Space > Nonspace ($P < 0.01$). (C) Between- and within-subjects performance correlation: Space > Nonspace ($P < 0.01$, uncorrected, for illustration). (D) Regions of overlap between panels A–C ($P < 0.01$, uncorrected, against conjunction null hypothesis).

objects). This negative finding is consistent with place cell results in rats where place cell firing has been shown to be controlled by large-scale geometric determinants (O'Keefe and Burgess, 1996), but not smaller “landmarks” placed inside the experimental arena (Cressant et al., 1997). Rather, processing this kind of short-term object centered spatial relations depend on parietal or prefrontal areas (Ungerleider et al., 1998; Burgess et al., 1999) that cooperate with the medial temporal lobe only insofar as the spatial relations concerned become encoded into long-term memory (Burgess et al., 2001a). We further speculate that due to attentional limitations access to the hippocampal “place” system, and the parietal “space” system might be a competitive process, leading to one system deactivating when the other activates. This hypothesis would be in concordance with resting state studies finding anticorrelations of activity between medial temporal and posterior parietal regions (Fox et al., 2005). It would also explain why the only observed performance-related between-subjects hippocampal activation differences is a down-regulation of the hippocampus in the spatial condition (see Results section for details).

635 Caudate

Whether or not caudate damage leads to language deficits remains controversial (Van Buren, 1963; Olsen et al., 1986; Hillis

et al., 2004; Gil Robles et al., 2005). Interestingly, patients suffering from Huntington's disease, a neurodegenerative disorder predominantly affecting the head of caudate, show language deficits strikingly similar to those of patients with stroke-related nonthalamic subcortical lesions, especially on complex lexico-semantic tasks, suggesting that specific language deficits may be coupled to nonthalamic subcortical dysfunction (Chenery et al., 2002). Our nonspatial task was a verbally mediated classification task where subjects, based on their knowledge of age traits in humans and in objects, were told to judge whether one was older than the other. Slowly learned complex classification tasks have been shown to modulate caudate during learning (Poldrack et al., 1999, 2001). But in our study, no learning was possible, since every image presented new pairs of people and no response feedback was given. We therefore predicted that we would only see a between-subjects performance effect in caudate, reflecting individual subjects' preexperimental age judgement skills. This is exactly what we find, yielding further support to theories stating that this region, known to be involved in associative memory processing in rats (White and McDonald, 2002), has an analogous function in humans. As seen in this study, this function is also important for aspects of efficient language processing, and focusing on these aspects might help explain the mixed results obtained in clinical studies. It must be stated, however, that since we have no strong measure of whether subjects answer correct or not to the nonspatial questions (but see the behavioral results section), this result must be interpreted with a certain amount of caution.

Amygdala

Amygdala is known to modulate direct links between individual stimuli and reinforcers in rats (White and McDonald, 2002). In this study, which had no explicit reinforcement components, we see strong, bilateral task-independent deactivations of amygdala, both within subjects as a function of increased effort and between subjects as a function of performance. Good performers are those that manage to downregulate amygdala most. This is in concordance with findings showing that amygdala activation can be manipulated through conscious emotional self-regulation (Schaefer et al., 2002). More generally, the region is known to play a role in value assignment (Paton et al., 2006), as in conditioned fear responses and in the processing of aversive stimuli (Davis, 1992), in the processing of incentive or “wanting” (Berridge, 1996; Berridge and Robinson, 2003), and also in social behavior (as reviewed by Adolphs, 2003). Higher levels of amygdala activity in this experiment might reflect task-irrelevant emotional processing of the stimuli or experimental set up (e.g., the hostile scanner environment). Alternatively, reduced activation might reflect indirect effects of emotional self-regulation during increased concentration or effort.

Broca's region

Left inferior gyrus activation was increased by increased response time/effort, regardless of task and regardless of subject performance (Table 2), yet those that perform well activate this area even more as a function of increased effort, compared to poor performers (Table 4, Fig. 4). This effect is task independent, which is in concordance with studies showing that this region is involved in short-term memory processes related to linguistic processing

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695 (Baddeley and Hitch, 1974; Smith and Jonides, 1998; Dapretto and
696 Bookheimer, 1999; Fiebach et al., 2005).

697 Conclusion

698 Previous studies in animals and humans have shown that
699 multiple neural memory systems interact in learning and recall, a
700 short-term spatial mapping system, a long term habitual system of
701 generalized knowledge and procedures, a “verbal” short-term
702 memory system, and a system for modulating incentive. We have
703 shown how language in the form of verbally cued recall can
704 modulate all these systems in differential ways. This is a very
705 important part of language processing, since language relies on
706 contextual specification, as can be seen from the generic nature of
707 our most commonly used words, e.g., personal pronouns (see
708 Introduction). Activation in dorsal precuneus is strongly correlated
709 with performance measures both within and between subjects
710 during spatial recall, and this modulation is highly task specific.
711 Caudate, on the other hand, showed task-specific between-subjects
712 differences of activation, during the nonspatial age judgement task,
713 in concordance with this region being involved in processing of
714 classification tasks based on learning by generalization. Amygdala
715 showed task-independent performance-related deactivations, inter-
716 preted as performance-mediating emotional control, and finally, we
717 find that Broca’s region increases its activity as a function of
718 increased effort, especially in good performers, supporting theories
719 claiming a role for this region in verbal short-term memory.

720 Acknowledgments

721 This work was supported by an EU NEST grant on “Way-
722 finding”, the Medical Research Council, U.K., The Faculty of
723 Humanities at University of Aarhus, and by The Danish National
724 Research Foundation’s grant to Center for Functionally Integrative
725 Neuroscience. The authors wish to thank John O’Keefe, Christian
726 F. Doeller, Tom Hartley, John King, Torben Ellegaard Lund and
727 Kim Mouridsen for their kind help and expertise during the course
728 of this experiment.

730 Appendix A. Supplementary data

731 Supplementary data associated with this article can be found, in
732 the online version, at doi:10.1016/j.neuroimage.2006.05.002.

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