A neural wayfinding mechanism adjusts for ambiguous landmark information

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ABSTRACT

Objects along a route can serve as crucial landmarks that facilitate successful navigation. Previous functional magnetic resonance imaging (fMRI) evidence indicated that the human parahippocampal gyrus automatically distinguishes between objects placed at navigationally relevant (decision points) and irrelevant locations (non-decision points). This storage of relevant objects can provide a neural mechanism underlying successful navigation. However, only objects that actually support wayfinding need to be stored. Objects can also provide misleading information if similar objects appear at different locations along a route. An efficient mechanism needs to specifically adjust for ambiguous landmark information. We investigated this by placing identical objects twice in a virtual labyrinth at places with the same as well as with a different navigational relevance. Twenty right-handed volunteers moved through a virtual maze. They viewed the same object either at two different decision points, at two different non-decision points, or at a decision as well as at a non-decision point. Afterwards, event-related fMRI data were acquired during object recognition. Participants decided whether they had seen the objects in the maze or not. The results showed that activity in the parahippocampal gyrus was increased for objects placed at a decision and at a non-decision point as compared to objects placed at two non-decision points. However, ambiguous information resulting from the same object placed at two different decision points revealed increased activity in the right middle frontal gyrus. These findings suggest a neural wayfinding mechanism that differentiates between helpful and misleading information.

Introduction

People spend a great deal of their time navigating through their environment. A neural mechanism supporting successful wayfinding needs to distinguish between helpful spatial information and ambiguous or misleading information. Neuroimaging studies have shown the involvement of the hippocampal formation and the parahippocampal region in spatial memory and navigation (O'Keefe and Nadel, 1978; Maguire et al., 1998a; Burgess et al., 1999; Shelton and Gabrieli, 2002; Hartley et al., 2003; Voermans et al., 2004; Bird and Burgess, 2008; Postma et al., 2008). Additionally, Kumaran and Maguire (2005) found that hippocampal activation is only apparent during navigation in a spatial domain (city), and not in a non-spatial domain (social network). Further studies emphasize the importance of the parahippocampal gyrus for the recognition of spatial environments (Aguirre et al., 1996; Maguire et al., 1998b; Epstein et al., 1999; Bar and Aminoff, 2003; Düzel et al., 2003; Epstein et al., 2003; Rosenbaum et al., 2004; Epstein, 2008; Hassabis et al., 2009). For instance the parahippocampal place area, a functional part of the parahippocampal gyrus, responds more to the visual presentation of

scenes than to the presentation of faces or single objects (Epstein and Kanwisher, 1998).

Previous fMRI studies (Janzen and van Turennout, 2004; Janzen et al., 2007) have shown that the parahippocampal gyrus not only responds to scenes but also to the recognition of single objects which have previously been seen at a navigationally relevant location (objects at decision points). This neural marking of navigationally relevant objects is independent of attentional processes and could be observed immediately after learning a route through a maze. The effect became even stronger after a delay of one day suggesting consolidation of relevant information (Janzen et al., 2007, 2008). This automatic and long-lasting storage in the parahippocampal gyrus of objects previously placed at a relevant location could provide a neural mechanism underlying successful wayfinding and navigation.

To successfully find a way through a maze, helpful information, i.e. an object at a decision point, needs to be distinguished from misleading information, i.e. a similar object at different locations. The present event-related fMRI study investigates whether a neural wayfinding mechanism is able to quickly adapt to ambiguous environmental conditions.

During a study phase, twenty volunteers moved through a complex virtual maze and viewed objects at locations relevant and irrelevant for successful wayfinding (Fig. 1). To examine the specificity of a neural wayfinding mechanism, identical objects were

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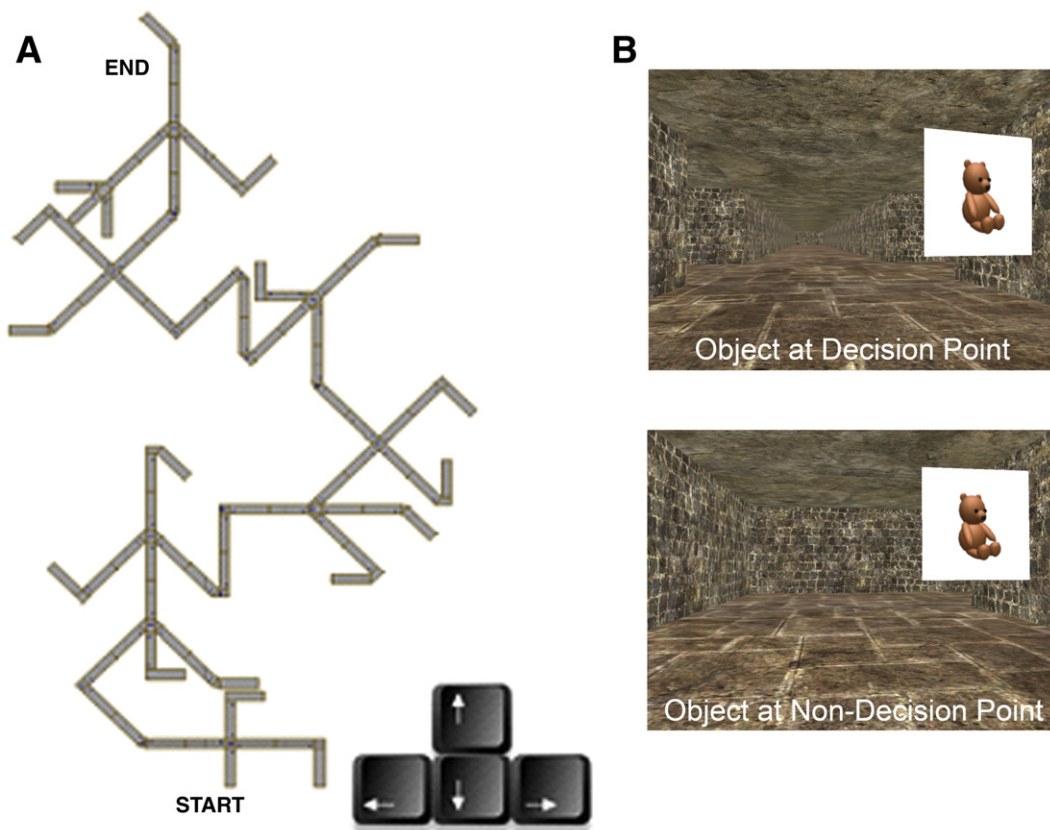 E-mail address: gabriele.janzen@donders.ru.nl (G. Janzen).

Fig. 1. Panel A shows part of the layout of the virtual maze. Participants navigated with button presses from a perspective of a person moving through the maze. Panel B shows two scenes out of the virtual environment that participants viewed in the study phase. The bear was placed at a decision point first and later in the maze at a non-decision point.

placed twice in the maze at places with a different as well as with the same navigational relevance. As the participants moved through the maze, they saw the same object either at two different decision points, at two different non-decision points, or at a decision as well as at a non-decision point. After the study phase, event-related fMRI data were acquired while participants performed an object recognition task with both objects from the maze, and objects they had not seen before.

We expected to find increased activity in the parahippocampal gyrus for objects placed at a decision point only once as compared to objects placed at non-decision points. If a neural wayfinding mechanism exists which adjusts for ambiguous information we expected to find increased activity in areas involved in higher cognitive functions, i.e. the frontal lobe for objects that appear at different decision points as compared to objects that appear at different non-decision points.

Materials and methods

Participants

Twenty healthy human adults (10 female) gave informed written consent before participating in the experiment. All participants were right-handed according to self-report. Mean age was 24.75 years (range 21–30 years). The study was approved by the CMO Committee on Research Involving Human Subjects (Region Arnhem-Nijmegen).

Design and procedure

The experiment was divided into two parts: a study phase outside the scanner, and a recognition phase during which functional images of the whole brain were acquired. Preceding the study task,

participants were trained in a maze not used in the experimental study task. Participants were familiarized with using four buttons to move through the maze. When participants tended to walk into a wrong path they immediately saw a dead end and continued on the correct route. At the end of the training session participants were able to easily move through the maze at a constant speed. Afterwards participants were given a standardized written instruction and the study phase started. All participants walked the route once (mean time 40 min, range 39–41 min). They explored each location only once and never turned around. Each object was passed at comparable speed with a time to view the object for 4–5 s.

Before the learning phase participants were given the following instruction (translated from Dutch): You have been hired as a staff member at the museum for photography. Your boss wants you to get acquainted with the photo-archive, and to report what material is suitable for the next exposition. This will be a photo-exposition on the favourite objects of famous people. You are now sent to the archive that that consists of four floors and holds two copies of each photo. Your assignment is to walk through the archive, to learn the route and to get acquainted with the photos. Afterwards you should be especially familiar with photos that are interesting for children (like toys). Find the way by following the photos. You can walk by pressing the four arrow buttons on the keyboard as learned in the training phase.

The video game software Unreal Tournament (co-developed by Epic Games and Digital Extremes) was used to create the maze presented on a 1.60 GHz-M Pentium 4 personal computer with 512 MB of RAM and a 15.0"XGA LCD-Screen. The virtual museum consisted of four floors in which 144 different pictures with coloured objects were placed at the walls. Each picture was placed twice in the maze which resulted in 288 pictures in total. In real world dimensions, each floor of the maze had a length of 260 ft and was 130 ft wide in relation to a simulated eye level of 5.6 ft (Fig. 1).

In the museum each object appeared twice at two different decision points (D-D objects), at two different non-decision points (ND-ND objects) or once at a decision and once at a non-decision point (D-ND objects and ND-D objects). Decision points were right as well as oblique angled intersections, non-decision points were right as well as oblique angled turns without the possibility to move to the wrong path. Attended objects (toys) and non-attended objects (non-toys) were equally assigned to decision and non-decision points. At half of all objects in the maze, participants either made twice a right or a left turn at the identical object. At the other half of the objects, subjects made different turns, e.g. right turn at the first object and a left turn when the object appeared again. Only participants who walked the correct route and viewed all objects were included.

After maze learning a recognition phase followed and fMRI time series were obtained while participants performed a simple object recognition task. In this recognition phase, participants were instructed to decide as accurately and as quickly as possible whether they had seen the object in the museum by pressing either a yes or a no response key. All objects were shown only once during the recognition phase. Responses were given with the index and the middle finger of the right hand. A trial consisted of a fixation cross centred on the screen, followed by an object for 500 ms shown from a canonical perspective on a white background. Thus, during scanning, no maze-related information was presented. The average inter-stimulus interval was 4000 ms, jittered between 3000 ms and 5000 ms in steps of 250 ms, counterbalanced over conditions. A total number of 252 stimuli were included in the recognition task. All stimuli were presented rapidly, in a randomly intermixed order different for each participant, to prevent participants from anticipating and changing strategies for the different event types.

The entire stimulus material consisted of eight sets of 18 objects each, belonging to the following event types: D-D objects toys, D-D objects non-toys, ND-ND objects toys, ND-ND objects non-toys, D-ND objects toys, D-ND objects non-toys, ND-D objects toys, ND-D objects non-toys. Three sets of 36 objects each were included as distractor objects: novel toys, novel non-toys, and scrambled objects. The scrambled objects were constructed from experimental objects using mosaic scrambling. All sets of objects were matched for word frequency.

Scanning parameters

A 3 Tesla MRI system (Siemens TRIO, Erlangen, Germany) was used to acquire functional images of the whole brain. Using a gradient-echo echo planar scanning sequence 36 axial slices were obtained for each participant (voxel-size $3 \times 3 \times 3$ mm, TR = 2290 ms, field of view = 192, TE = 30 ms, flip angle = 75°). All functional images were acquired in one run that lasted for 18 min. Following the acquisition of functional images a high-resolution anatomical scan (T1-weighted MP-RAGE, 176 slices) was acquired.

Data analysis

FMRI data were analyzed using BrainVoyager QX (Brain Innovation, Maastricht, The Netherlands). Functional images were corrected for motion and slice scan time acquisition. Data were temporally smoothed with a high pass filter removing frequencies below 3 cycles per time course. Functional images were coregistered with the anatomical scan and transformed into Talairach coordinate space using the 9-parameter landmark method of Talairach and Tournoux (1988). Images were spatially smoothed with a FWHM Gaussian kernel of 6 mm.

Statistical analyses were performed in the context of the general linear model, including eleven effects of interests and confounds. Only correct responses were included in the analyses. Event-related hemodynamic responses for each of the different event types were modelled as delta functions convolved with a synthetic hemodynamic response function. Random effects group analyses were performed. The statistical threshold at the voxel level was set at $P<0.001$, uncorrected for multiple comparisons. The statistical threshold for the group analyses was set at $P<0.05$, false discovery rate corrected for multiple comparisons (Genovese et al., 2002).

To test for decision point effects in the parahippocampal gyrus a region of interest analysis was performed as follows: We defined the right posterior parahippocampal gyrus separately for each individual subject in the anatomical scans (Pruessner et al., 2002) and obtained the beta weights (i.e., the regression coefficients) as indexes of effect size separately for all individual subjects out of this region. The regionally averaged beta weights for each of the event types were analyzed in a repeated-measurement ANOVA. Specific effects were tested by applying t-contrasts to the beta weights obtained for the different event types.

For analysis of same and different turns in the middle frontal lobe, we functionally defined the region by selecting all voxels showing an effect of ND-ND and D-D objects in the whole brain group analysis. Then, we obtained the beta weights for all voxels included in this region, separately for all individual subjects, for each of the event types split up in events where same and different turns were made at identical objects.

Results

Behavioural results

Task performance was above chance level (86% correct, see Table 1). Recognition accuracy was calculated as the difference in probabilities of correct decisions for objects included in the mazes (hits) and incorrect decision for distractor items (false alarms; Pr = probability hits − probability false alarm). Because of the low number of false alarms, the overall recognition performance greatly exceeded chance level (Pr = 0.76 ± 0.031 (mean std. error); $t(19) = 21.66$; $P<0.001$).

The accuracy data were entered in an ANOVA with the factors decision point (D-D objects, ND-ND objects, D-ND and ND-D objects), and attention (toys and non-toys). The data showed an effect of decision point during study ($F2,38 = 10.08$, $P<0.001$). Objects presented twice at a non-decision point evoked more errors (15.1%) than objects presented at a non-decision point and a decision point (10.6%; $t19 = 3.34$, $P<0.01$), and less errors than objects presented twice at a decision point (19.0%; $t19 = -2.72$, $P<0.01$). Error rates showed an effect of the attentional manipulation during study ($F1,19 = 9.54$, $P<0.01$). Error rates were lower for toys (15.9%) than for non-toys (22.0%; $t19 = -2.97$, $P<0.01$). No interaction between the factors decision point and attention was observed.

Response times showed an effect of decision point ($F2,38 = 3.58$, $P<0.05$). Response times were significantly faster for objects placed twice at a non-decision point than for objects presented at a non-decision point and a decision point (mean response latencies were 859 and 884, respectively, $t19 = -3.39$, $P<0.01$). The mean response time for objects placed twice at a decision point was 871 ms. Response times showed an effect of attention during study ($F1,19 = 13.44$, $P<0.01$). Response times were faster for toys than for non-toys (mean response latencies were 858 and 891 ms, $t19 = -3.965$, $P<0.001$). No interaction between the factors decision point and attention was observed.

Table 1
Probability of means and standard deviations of recognition performance in the retrieval phase.

Objects from mazes		Distractor objects	
Hits	Misses	Correct rejections	False alarms
0.82 ± 0.10	0.18 ± 0.10	0.94 ± 0.03	0.06 ± 0.03

fMRI

To investigate effects of navigational relevance of object location, we performed a region of interest analysis for the right posterior parahippocampal gyrus (see Materials and methods). An ANOVA of the regionally averaged beta weights obtained from this region of interest showed a main effect of decision point (F3,57 = 4.7, P<0.01) only. T-contrasts showed significantly higher beta weights for ND-D and D-ND compared to ND-ND objects (t19 = −2.05, P<0.05), whereas D-D compared to ND-D and D-ND objects showed significantly lower beta weights (t19 = −3.64, P<0.01). No other main effects and no interactions were observed (see Fig. 2).

To examine how information from objects placed at different navigationally relevant locations is represented, we compared objects placed twice at two different decision points (D-D objects) with objects placed twice at two different non-decision points (ND-ND objects). This comparison revealed increased activity in the right middle frontal gyrus, an area involved in executive functions like cognitive control (Fig. 3). To test for effects of interaction with the factor attention we obtained the beta weights out of this brain area (see Materials and methods). An ANOVA of the averaged beta weights showed no other main effects and no interactions besides the expected increase in activity for D-D objects as compared to ND-ND objects. Interestingly, no activity in the medial temporal lobe including the parahippocampal gyrus was observed.

To investigate the effect of information from different navigationally relevant locations in more detail, we analyzed the regionally averaged beta weights from the right middle frontal gyrus separately for those objects where the same turn (both times right or both times left) was required and where a different turn (right as well as left) was
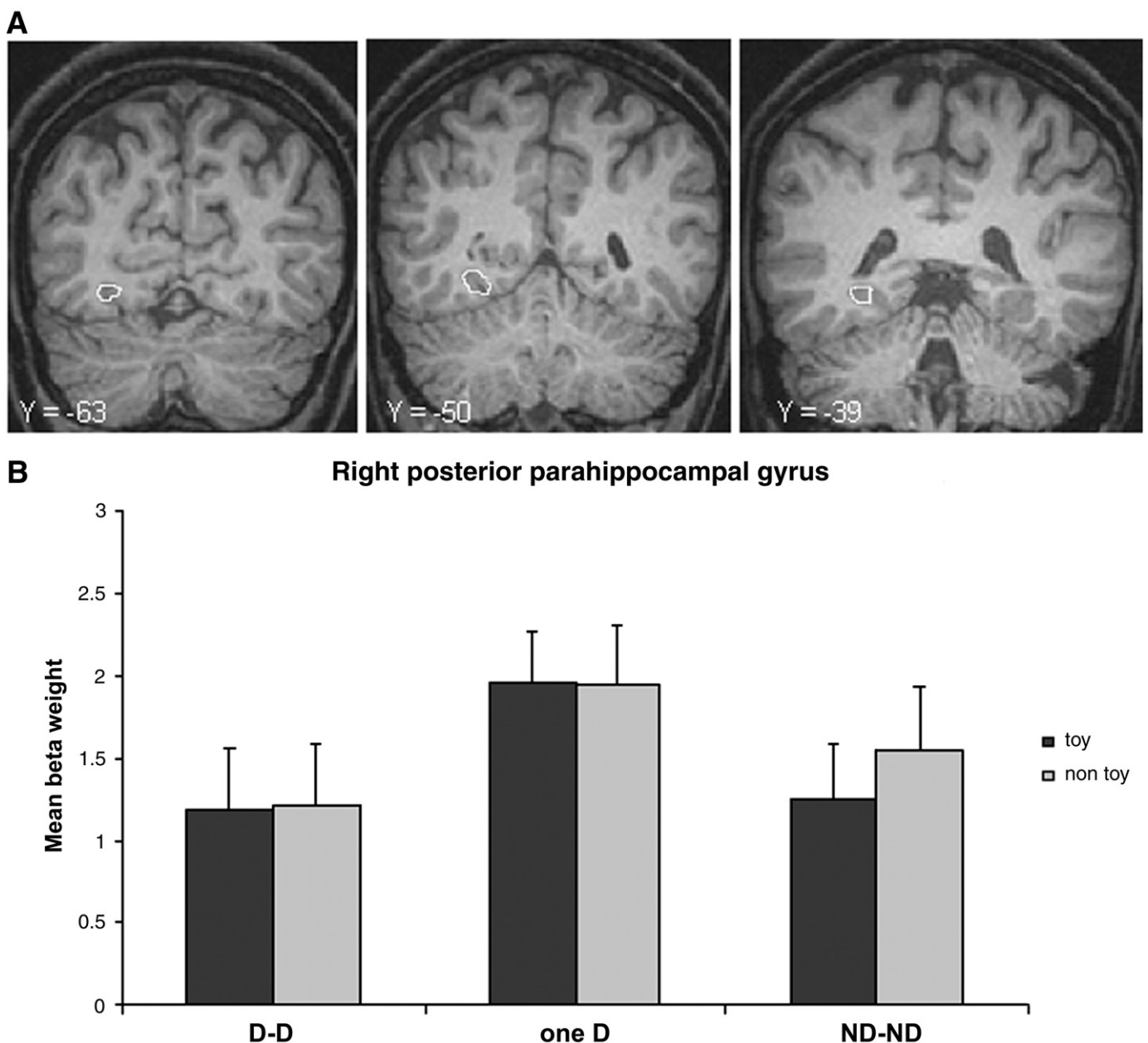

Fig. 2. Panel A shows the anatomical region of the posterior parahippocampal gyrus marked in one individual. Panel B shows the regionally averaged beta weights out of the posterior parahippocampal gyrus as anatomical region of interest. Bars indicate standard errors across participants.
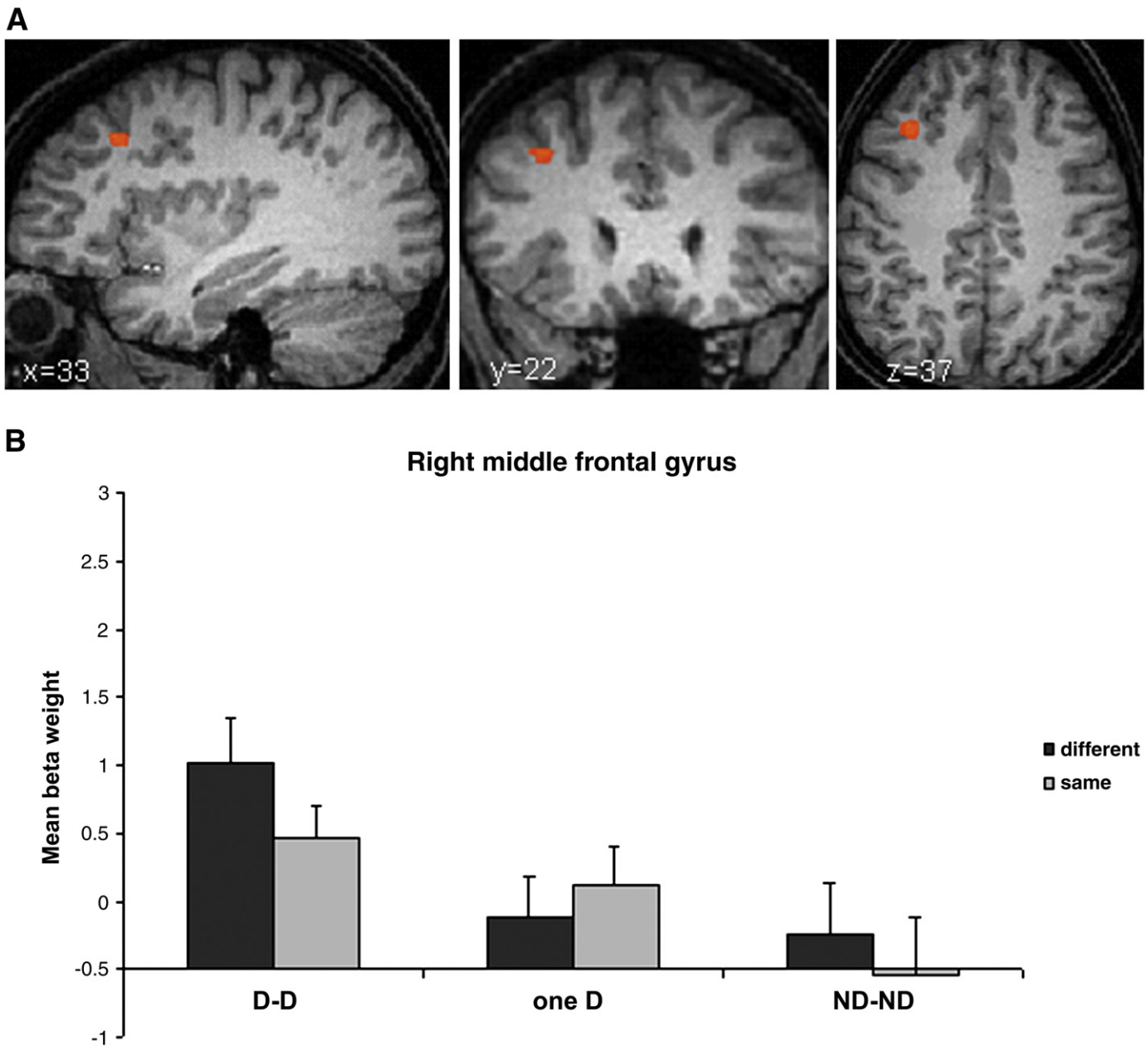
A

B

Fig. 3. Panel A shows the region in the right middle frontal gyrus revealed by contrasting objects seen twice at navigationally relevant locations with objects seen twice at irrelevant locations. Location of peak activation, expressed in millimetres as Talairach coordinates was $x = 33$, $y = 22$, $z = 37$ (FDR $P<0.05$, volume 73 mm^3). Panel B shows the regionally averaged beta weights for the right middle frontal gyrus showing an effect of same and different turns for D-D objects. Bars indicate standard errors across participants.

required. At half of the objects in each condition the same turn and at the other half of the objects a different turn was necessary. The data showed significantly higher beta weights in the right middle frontal gyrus ($t19 = -1.92$, $P<0.05$, Fig. 3) for D-D objects where a different turn was required as compared to objects with the same turn.

To investigate effects of navigational relevance of object location in detail, we compared fMRI responses of objects placed once at a decision and once at a non-decision point (ND-D and D-ND objects) with fMRI responses of objects placed at two non-decision points (ND-ND objects). This comparison revealed an increase in activity for objects seen once at a decision point and once at a non-decision point in the right parahippocampal gyrus ($x = 19$, $y = -27$, $z = -15$, volume 73 mm^3, FDR < 0.05). No other brain regions showed an effect of navigational relevance. Separately for the two conditions with an object viewed once at a decision point, the comparison of

D-ND objects with ND-ND objects revealed an increase in activity in the right parahippocampal gyrus ($x = 20$, $y = -16$, $z = -20$, volume 21 mm^3, $P<0.001$). The comparison of ND-D objects with ND-ND objects showed an increase in the right parahippocampal gyrus ($x = 21$, $y = -27$, $z = -16$, volume 130 mm^3, FDR < 0.05) as well.

Furthermore we compared ND-D and D-ND objects with objects placed at two decision points (D-D objects). This comparison revealed an increase in the right parahippocampal gyrus ($x = 30$, $y = -33$, $z = -12$, volume 40 mm^3, FDR < 0.05). Separately for the two conditions with an object placed once at a decision point, the comparison of D-ND objects with ND-ND objects revealed an increase in activity in the right parahippocampal gyrus ($x = 28$, $y = -40$, $z = -7$, volume 7 mm^3, FDR < 0.05). The comparison of ND-D objects with ND-ND objects showed a strong increase in the right parahippocampal gyrus ($x = 30$, $y = -34$, $z = -12$, volume 282 mm^3, FDR < 0.05) as well.

Comparing event-related fMRI responses to toys with those to non-toys revealed increased activity in the right fusiform gyrus ($x = 23, y = -61, z = -11$, volume 17 mm³, FDR < 0.05). An ANOVA of subjects' averaged beta weights obtained for all voxels in this region showed, besides the expected main effect of attention, no other main effects or significant interactions.

Discussion

In the present event-related fMRI study we investigated whether a neural navigation mechanism can specifically adapt to helpful and misleading environmental situations. In order to successfully find the way through our surroundings we need to adapt flexibly to different as well as changing environments. Objects that can serve as landmarks, e.g. phone booths, mailboxes or gas stations look similar and can appear more than one time along a route. When these objects are encountered at relevant locations, they can be helpful to guide successful navigation. However, if identical objects appear at different relevant locations, the information might be misleading. This is especially the case if different behaviour is required at these locations, e.g. turning right at the first object and turning left at the similar object later along the route. A neural mechanism guiding successful navigation needs to flexibly adapt to possible misleading information.

Consistent with our previous results (Janzen and van Turennout, 2004; Janzen et al., 2007) the present data show that the parahippocampal gyrus selectively responds to objects which have been placed at one navigationally relevant location only. Here, neural marking of navigationally relevant objects in the parahippocampal gyrus was observed for objects that appeared once at a relevant location and once at an irrelevant location as compared to objects that appeared at two different irrelevant locations. This decision point related increase in activity in the parahippocampal gyrus was independent from paying attention to a specific object category during study. This result shows that navigationally relevant objects are represented in the parahippocampal gyrus regardless of whether the same object appears at an irrelevant location in the same maze. This representation is similar to previous results where an object appeared only once at decision points (Janzen and van Turennout, 2004; Janzen et al., 2007, 2008; Janzen and Weststeijn, 2007). Previous results (Janzen and van Turennout, 2004; Janzen et al., 2007) showed that the effect of navigational relevance in the parahippocampal gyrus is bilateral, but stronger in the right hemisphere. The present result shows an increase in the right parahippocampal gyrus only. Increased activity in the left parahippocampal gyrus did not survive the false discovery rate correction for multiple comparisons (see Materials and methods).

When comparing objects placed twice at two different decision points with objects placed twice at two different non-decision points, increased neural activity was observed in the right middle frontal gyrus. This region is part of the prefrontal cortex, a brain area that is involved in executive functions like cognitive control (Goldman-Rakic, 1987; Miller and Cohen, 2001). Neuroimaging studies and a recent case study including a patient with bilateral prefrontal damage have shown the involvement of the prefrontal cortex in spatial navigation tasks (Ghaem et al., 1997; Ciaramelli, 2008; Spiers and Maguire, 2007; Spiers, 2008). The frontal gyrus has been shown to be involved in spatial working memory (Courtney et al., 1998), and plays a special role in monitoring and selecting contextually relevant information (Ridderinkhof et al., 2004). These functions are important for an adaptive cognitive control system. Adaptive control is very efficient because it avoids maintaining high levels of control over a long period of time (Ridderinkhof et al., 2004).

Interestingly, no activity was observed in the parahippocampal gyrus or adjacent areas in the medial temporal lobe for the comparison between objects placed twice at decision points and objects placed twice at non-decision points. However, when objects placed once at a decision point and once at a non-decision point are compared to objects placed twice at a decision point, increased neural activity was again observed in the parahippocampal gyrus. Previous results have shown that this region reflects automatic processing of navigationally relevant objects (Janzen and van Turennout, 2004; Janzen et al., 2007).

For the comparison between objects placed twice at decision points and objects placed twice at non-decision points we observed increased activity in an area involved in cognitive control. This result is comparable to a study from Spiers and Maguire (2006) who observed a shift in activity from temporal regions to prefrontal regions when participants suddenly decided to change their navigational plans. These findings emphasize that a neural wayfinding mechanism is able to quickly adapt to different environmental conditions.

The present result showing increased activity in the prefrontal cortex for objects seen twice at different navigationally relevant locations can be related to adaptive cognitive control functions. The same object marking different relevant locations can be misleading, especially if different behaviour (e.g. turning left at the first decision point, but turning right at the second) is required. To efficiently process this information, a higher level of cognitive control is necessary. This explanation is supported by the result that an object seen at a relevant location once, regardless whether it is seen at irrelevant locations before or afterwards, shows increased activity in the parahippocampal gyrus only. However, for an object seen at two different relevant locations we observed frontal activity only. Besides the role in cognitive control mechanisms the prefrontal cortex is also involved in detecting expectancy violations like mismatch detection and prediction error (e.g. Fletcher et al., 2001; Corlett et al., 2004). Even though all objects appear twice in the maze it might be possible that seeing an object the second time at a different decision point leads to a violation of expectancy especially when a different turn is required. Our results support the existence of a highly specific wayfinding mechanism, which reacts especially sensitive and adaptive if information at navigationally relevant locations is misleading.

Furthermore, the middle frontal gyrus represents whether a similar or a different turn was made at the same objects observed at two relevant locations. Responses were stronger for objects associated with different turns as compared to objects associated with the same turn. This result emphasizes the specificity of a neural wayfinding mechanism.

When comparing previously attended objects (toys) to non-attended objects (non-toys) the brain imaging data showed increased activity in the right fusiform gyrus consistent with previous results (Janzen and van Turennout, 2004; Janzen et al., 2007). This result is in line with studies showing increased neural activity in ventral occipito-temporal regions related to paying attention to objects (Kanwisher and Wojciulik, 2000; Vuilleumier et al., 2001). This increase in the fusiform gyrus was not affected by navigational relevance. The behavioural results showed that the attentional manipulation during study was effective. Importantly, no interaction between the factors navigational relevance and attention was observed.

In conclusion, consistent with our previous results, increased neural activity was observed in the parahippocampal gyrus for objects seen only once at a navigationally relevant location. When observing objects placed twice at two different relevant locations increased neural activity was observed in the prefrontal cortex, an area involved in executive functions like cognitive control. The results show a highly specific and adaptive wayfinding mechanism that reacts to misleading information.

References

Aguirre, G.K., Detre, J.A., Alsop, D.C., D'Esposito, M., 1996. The parahippocampus subserves topographical learning in man. Cereb. Cortex 6, 823–829.

Bar, M., Aminoff, E., 2003. Cortical analysis of visual context. Neuron 38, 347–358.

Bird, C.M., Burgess, N., 2008. The hippocampus and memory: insights from spatial processing. Nat. Rev. Neurosci. 9, 182–194.

Burgess, N., Jeffery, K.J., O'Keefe, J. (Eds.), 1999. The hippocampal and parietal foundations of spatial cognition. Oxford University Press, Oxford.

Ciaramelli, E., 2008. The role of ventromedial prefrontal cortex in navigation: a case of impaired wayfinding and rehabilitation. Neuropsychologia 46, 2099–2105.

Corlett, P.R., Aitken, M.R.F., Dickinson, A., Shanks, D.R., Honey, G.D., Honey, R.A.E., Robbins, T.W., Bullmore, E.T., Fletcher, P.C., 2004. Prediction error during retrospective revaluation of causal associations in humans: fMRI evidence in favour of an associative model of learning. Neuron 44, 877–888.

Courtney, S.M., Petit, L., Maisog, J.M., Ungerleider, L.G., Haxby, J.V., 1998. An area specialized for spatial working memory in human frontal cortex. Science 279, 1347–1351.

Düzel, E., Habib, R., Rotte, M., Guderian, S., Tulving, E., Heinze, H.J., 2003. Human hippocampal and parahippocampal activity during visual associative recognition memory for spatial and nonspatial stimulus configurations. J. Neurosci. 23, 9439–9444.

Epstein, R.A., 2008. Parahippocampal and retrosplenial contributions to human spatial navigation. Trends Cogn. Sci. 12, 388–396.

Epstein, R., Kanwisher, N., 1998. Cortical representation of the local visual environment. Nature 392, 598–601.

Epstein, R., Harris, A., Stanley, D., Kanwisher, N., 1999. The parahippocampal place area: recognition, navigation, or encoding? Neuron 23, 115–125.

Epstein, R., Graham, K.S., Dowing, P.E., 2003. Viewpoint-specific scene representations in human parahippocampal cortex. Neuron 37, 865–876.

Fletcher, P.C., Anderson, J.M., Shanks, D.R., Honey, R., Carpenter, T.A., Donovan, T., Papadakis, N., Bullmore, E.T., 2001. Responses of human frontal cortex to surprising events are predicted by formal associative learning theory. Nat. Neurosci. 4, 1043–1048.

Genovese, C.R., Lazar, N., Nichols, T.E., 2002. Thresholding of statistical maps in functional neuroimaging using the false discovery rate. NeuroImage 15, 870–878.

Ghaem, O., Mellet, E., Crivello, F., Tzourio, N., Mazoyer, B., Berthoz, A., Denis, M., 1997. Mental navigation along memorized routes activates the hippocampus, precuneus, and insula. NeuroReport 8, 739–744.

Goldman-Rakic, P.S., 1987. Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. In: Plum, F., Mouncastle, U. (Eds.), Handbook of physiology. American Physiological Society, Washington, pp. 373–417.

Hartley, T., Maguire, E.A., Spiers, H.J., Burgess, N., 2003. The well-worn route and the path less travelled: distinct neural bases of route following and wayfinding in humans. Neuron 37, 877–888.

Hassabis, D., Chu, D., Rees, G., Weiskopf, N., Molyneux, P.D., Maguire, E.A., 2009. Decoding neural ensembles in the human hippocampus. Curr. Biol. 19, 546–554.

Janzen, G., van Turennout, M., 2004. Selective neural representation of objects relevant for navigation. Nat. Neurosci. 7, 673–677.

Janzen, G., Weststeijn, C., 2007. Neural representation of object location and route direction: an event-related fMRI study. Brain Res. 1165C, 116–125.

Janzen, G., Wagensveld, B., van Turennout, M., 2007. Neural representation of navigational relevance is rapidly induced and long-lasting. Cereb. Cortex 17, 975–981.

Janzen, G., Jansen, C., van Turennout, M., 2008. Memory consolidation of landmarks in good navigators. Hippocampus 18, 40–47.

Kanwisher, N., Wojciulik, E., 2000. Visual attention: insights from brain imaging. Nat. Rev. Neurosci. 1, 91–100.

Kumaran, D., Maguire, E.A., 2005. The human hippocampus: cognitive maps or relational memory? J. Neurosci. 25, 7254–7259.

Maguire, E.A., Burgess, N., Donnett, J.G., Frackowiak, R.S.J., Frith, C.D., O'Keefe, J., 1998a. Knowing where and getting there: a human navigation network. Science 280, 921–924.

Maguire, E.A., Frith, C.D., Burgess, N., Donnett, J.G., O'Keefe, J., 1998b. Knowing were things are: parahippocampal involvement in encoding object locations in virtual large scale space. J. Cogn. Neurosci. 10, 61–76.

Miller, E.K., Cohen, J.D., 2001. An integrative theory of prefrontal cortex function. Annu. Rev. Neurosci. 24, 167–202.

O'Keefe, J., Nadel, L., 1978. The hippocampus as a cognitive map. Clarendon, Oxford.

Postma, A., Kessels, R.P.C., van Asselen, M., 2008. How the brain remembers and forgets where things are: the neurocognition of object-location memory. Neurosci. Behav. Rev. 32, 1339–1345.

Pruessner, J.C., Köhler, S., Crane, J., Pruessner, M., Lord, S., Byrne, A., Kabani, N., Louis Collins, S., Evans, A.C., 2002. Volumetry of temporopolar, perirhinal, entorhinal and parahippocampal cortex from high-resolution MR images: considering the variability of the collateral sulcus. Cereb. Cortex 12, 1342–1353.

Ridderinkhof, K.R., Ullsperger, M., Crone, E.A., Nieuwenhuis, S., 2004. The role of the medial frontal cortex in cognitive control. Science 306, 443–447.

Rosenbaum, R.S., Ziegler, M., Winocur, G., Grady, C.L., Moscovitch, M., 2004. "I have often walked down this street before": fMRI studies on the hippocampus and other structures during mental navigation of an old environment. Hippocampus 14, 826–835.

Shelton, A.L., Gabrieli, J.D.E., 2002. Neural correlates of encoding space from route and survey perspectives. J. Neurosci. 22, 2711–2717.

Spiers, H.J., 2008. Keeping the goal in mind: prefrontal contributions to spatial navigation. Neuropsychologia 46, 2106–2108.

Spiers, H.J., Maguire, E.A., 2006. Thoughts, behaviour, and brain dynamics during navigation in the real world. NeuroImage 31, 1826–1840.

Spiers, H.J., Maguire, E.A., 2007. A navigational guidance system in the human brain. Hippocampus 17, 618–626.

Talairach, J., Tournoux, P., 1988. A co-planar stereotaxic atlas of the human brain. Thieme Medical Publishers, New York.

Voermans, N.C., Petersson, K.M., Daudey, L., Weber, B., van Spaendonck, K.P., Kremer, H.P.H., Fernández, G., 2004. Interaction between the human hippocampus and the caudate nucleus during route recognition. Neuron 43, 427–435.

Vuilleumier, P., Armony, J.L., Driver, J., Dolan, R.J., 2001. Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. Neuron 30, 829–841.