

Activation of the hippocampal complex during tactile maze solving in congenitally blind subjects

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ABSTRACT

Despite their lack of vision, congenitally blind subjects are able to build and manipulate cognitive maps for spatial navigation. It is assumed that they thereby rely more heavily on echolocation, proprioceptive signals and environmental cues such as ambient temperature and audition to compensate for their lack of vision. Little is known, however, about the neural mechanisms underlying spatial navigation in blind individuals in settings where these cues are absent. We therefore measured behavioural performance and blood oxygenation-level dependant (BOLD) responses using functional magnetic resonance imaging (fMRI) in congenitally blind and blindfolded sighted participants while they navigated through a tactile multiple T-maze. Both groups learned the maze task at a similar pace. In blind participants, tactile maze navigation was associated with increased BOLD responses in the right hippocampus and parahippocampus, occipital cortex and fusiform gyrus. Blindfolded sighted controls did not show increased BOLD responses in these areas; instead they activated the caudate nucleus and thalamus. Both groups activated the precuneus during tactile maze navigation. We conclude that cross-modal plastic processes allow for the recruitment of the hippocampal complex and visual cortex in congenital blindness.

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1. Introduction

The capacity to navigate efficiently in an environment depends on one's sense of direction and the ability to establish our position relative to space in a precise manner. Although many sensory inputs contribute to the sense of orientation, vision is unique as it reunites spatial cues that are simultaneously present. Due to their lack of vision, blind people have to rely on auditory, proprioceptive and haptic cues. It has been hypothesized that this stronger dependence on non-visual senses explains why congenitally blind individuals exhibit superior performance in various tactile (Alary et al., 2009; Chebat, Chen, et al., 2007; Van Boven, Hamilton, Kauffman, Keenan, & Pascual-Leone, 2000; Wong, Gnanakumaran, & Goldreich, 2011), auditory (Röder et al., 1999; Starlinger & Niemeier, 1981) and

olfactory (Beaulieu-Lefebvre, Schneider, Kupers, & Ptito, 2011) tasks. Nonetheless, blind individuals are able to learn a route and build and manipulate cognitive maps efficiently (Kupers, Chebat, Madsen, Paulson, & Ptito, 2010; Passini, Proulx, & Rainville, 1990). The vast majority of the navigation studies in blind participants were conducted inside life-size mazes (Chebat, Schneider, Kupers, & Ptito, 2011; Fortin et al., 2008) or in ecological environments (Passini et al., 1990; Rieser, Hill, Talor, Bradfield, & Rosen, 1992) and showed that congenitally blind subjects outperform their blindfolded sighted counterparts. However, we recently showed that when limiting access to allothetic cues, blind subjects lose their competitive advantage (Gagnon, Kupers, Schneider, & Ptito, 2010).

Neuroanatomical studies using voxel-based morphometry and diffusion tensor imaging techniques revealed that blind subjects not only show structural changes in their visual system but also in brain areas that are involved in navigation (Chebat, Rainville, Kupers, & Ptito, 2007; Noppeney, 2007; Ptito, Schneider, Paulson, & Kupers, 2008). Indeed, the posterior hippocampus, a structure involved in spatial cognitive mapping (O'Keefe & Conway, 1978), is reduced in size in congenitally blind individuals (Chebat, Rainville,

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Table 1
Demographic data of the blind participants.

Sex	Age (years)	Education (years)	Handedness	Etiology of blindness	Onset
F	26	16	R	Retinopathy of prematurity	Birth
M	56	15	R	Retinopathy of prematurity	Birth
F	21	12	R	Retinopathy of prematurity	Birth
M	21	12	R	Retinopathy of prematurity	Birth
F	41	14	R	Retinopathy of prematurity	Birth
M	23	14	L	Retinopathy of prematurity	Birth
M	19	10	R	Retinopathy of prematurity	Birth
M	42	19	R	Bilateral retinoblastoma	Birth
F	27	14	R	Retinopathy of prematurity	Birth
M	57	17	R	Retinopathy of prematurity and cataract	6 months
M	35	12	R	Unknown	<3 months

Abbreviations: M, male; F, female; R, right; L, left.

et al., 2007). Interestingly, this brain structure is enlarged in sighted subjects with supra-normal navigational capacities, such as London taxi drivers (Maguire et al., 2000). Furthermore, the better navigational skills of congenitally blind subjects within human-size mazes have been attributed to the observation that they have an enlargement of the anterior hippocampus (Fortin et al., 2008).

Only a few studies have investigated the neural correlates of navigation in the absence of vision. For example, Fiehler, Burke, Bien, Roder, and Rosler (2009) showed that active navigation within small-scale space such as controlled drawing, strongly activates both the visual cortex and the dorsal visual stream in congenitally blind individuals. In a previous study, we trained blind and blindfolded subjects to use the tongue display unit (TDU) in an active route learning task. The TDU is a sensory substitution device that translates a visual image into electro-tactile pulses that are applied to the tongue. Following training, subjects participated in a fMRI experiment during which they had to recognize previously learned routes that were presented with the TDU. Our fMRI data showed that trained blind but not blindfolded sighted control subjects activate their right parahippocampus and large parts of the visual cortex during this route recognition task (Kupers et al., 2010). To further extend these neuroimaging results, we used fMRI to measure BOLD responses during an active navigation task in which participants used their index finger to navigate through a complex tactile maze. This task is devoid of environmental cues that blind subjects would normally use during navigation in real world situations, thereby putting them at equal level with sighted controls. In line with results on tactile abilities (Chebat, Chen, et al., 2007; Wong et al., 2011) and cross-modal plastic processes (Kupers, Pietrini, Ricciardi, & Ptito, 2011; Ptito, Moesgaard, Gjedde, & Kupers, 2005), we hypothesized that congenitally blind subjects would recruit structures involved in spatial navigation in normal sighted subjects such as the occipital cortex and the medial temporal lobe (Kupers et al., 2010).

2. Materials and methods

2.1. Participants

Eleven congenitally blind subjects (7 males; range: 21–57 y; mean 33 ± 4 y) and 14 blindfolded sighted controls (7 males; range: 21–46 y; mean 29 ± 2 y) participated in the study. All blind subjects were recruited through the Danish Institute for the Blind and the Partially Sighted and a major Danish University Hospital. Demographic data of the blind subjects are given in Table 1. All participants were right-handed except for one blind subject who was trained on the maze task with his non-dominant hand (Edinburgh Handedness Inventory). The local Ethics Research Committee of the Capital region of Denmark (H-KF-01 328723) approved the experimental protocol and all participants gave their written informed consent before participation.

2.2. Apparatus

A multiple T-maze with 12 decision points (Fig. 1A) was made out of a transparent acrylic platform, measuring 27.0×13.5 cm. The black acrylic walls were

0.3 cm wide and 0.8 cm high. The hallway width was 1.6 cm and the dead-end lengths were 2.0 cm. In order to allow continued navigation after a trial was over, the start and the end positions of the maze were placed next to each other. A raised circle was added on the maze path to indicate the starting position. A square of 6×6 cm without navigational decision points was positioned to the left of the maze and served as the control condition. The square was designed to control for all possible movements done inside the active maze condition. Participants were asked to continuously move up, right, down and left within the square, following a clockwise pattern. Although this is a much simpler than the active navigation task, it has the advantage that it is devoid of any decisional points.

Prior to the onset of the fMRI session, all participants were trained to solve tactile multiple T-mazes as described in a previous behavioural study (Gagnon et al., 2010). Participants were also familiarized with responding to the auditory cues, moving within the control square and finding the starting position of the maze (see below).

2.3. fMRI data acquisition

The fMRI scans were acquired on a 3T Siemens Magnetom Trio scanner equipped with an 8-channel head coil. In order to prevent head movement during scanning, soft padding was placed between the head and the coil. The platform containing the transparent tactile maze and square was installed perpendicularly to the subject's abdomen. This installation was optimal for task completion and allowed a good

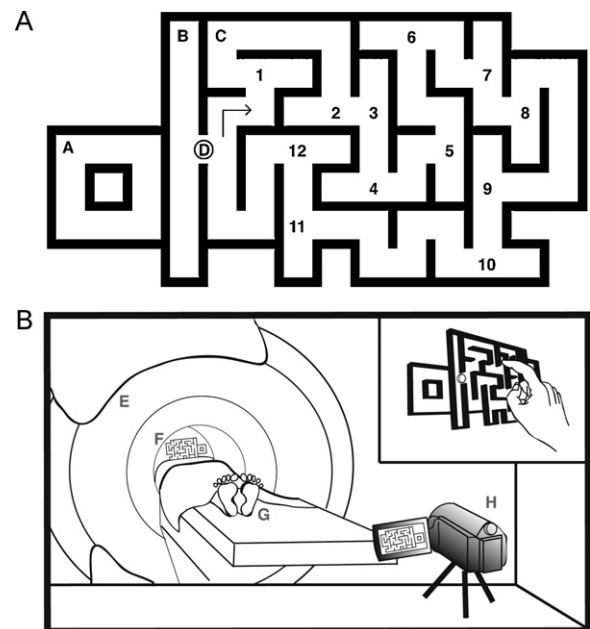


Fig. 1. Maze design and experimental setting. **A.** Each decision point in the maze is numbered from 1 to 12. The letters refer to the square (A), the maze (C) and the starting point (D). The arrow points to the direction to follow. The simple alley (B) was not used in this experiment. **B.** In the experimental setting, a participant (G) is lying in the scanner (E) with the transparent maze platform (F) fixed on his abdomen, while a camcorder (H) placed behind the window in the control room recorded the performance. In the right top corner, navigation within the maze with the right index finger is illustrated.

quality of video recording of the subject's behaviour (Fig. 1B, upper right corner). Participants were instructed to complete the tactile multiple T-maze as quickly as possible, thereby avoiding dead-ends and without stepping back. None of the sighted subjects had seen the mazes before testing and no haptic exploration was allowed prior to the onset of the fMRI study.

A T1-weighted structural MRI scan (MPRAGE) was obtained for each participant with the following acquisition parameters: TR/TE/TI/FA 1.55 s/3.04 ms/800 ms/9°, 256 × 256 matrix, resolution of 1 × 1 × 1 mm³. The T2*-weighted echo planar (EPI) images were acquired using the following parameters: TR/TE/FA 2.95 s/30 ms/90°, 64 × 64 matrix, total readout time 38.4 ms and resolution of 3 × 3 × 3 mm³. A total of 45 slices covering the entire brain were collected continuously in an oblique orientation, 30° to the commissural plane. Three functional runs were acquired, each lasting 622 s, consisting of 211 EPI volumes. The functional scans were followed by a field mapping sequence (FLASH, TR/TE short/TE long/FA 500 ms/5.19 ms/7.25 ms/60°, 64 × 64 matrix with a resolution of 3 × 3 × 3 mm³, 45 slices) in order to correct for static magnetic field inhomogeneities.

2.4. fMRI paradigms

The three conditions (MAZE, SQUARE and REST) were performed in 20 s blocks, each repeated 8 times per run. During the MAZE condition, participants used their right index finger to navigate as accurately and fast as possible through the maze. When a participant solved the maze in less than 20 s (time limit of 20 s/trial), he/she restarted the maze until the total time had elapsed. There were 24 trials in total. The square was used as somatosensory-motor control condition. During this condition, subjects moved their right index finger through the square until the 20 s time limit had elapsed. A verbal cue ("maze", "control" or "rest") announced the beginning of each trial, while a ring tone indicated its end. This was followed by a 5-s pause during which participants returned to the starting point, positioned between the maze and the square. The condition order was semi-randomized across subjects.

Navigation in the maze was videotaped and scored offline by two independent observers. We calculated the number of correct choices (dead-ends avoidance) for the 12 decision points. In case of discordance, both observers re-evaluated the performance until they reached agreement. A two-way (2 groups × 3 runs) mixed design analysis of variance (ANOVA) was carried out on the mean number of correct choices (dead-end avoidance) inside the maze for each run and each participant using a Bonferroni correction.

2.5. Processing and statistical analysis of the fMRI data

We used SPM 8 (statistical parametric mapping 8; www.fil.ion.ucl.ac.uk/spm/) for image processing and statistical analyses. We calculated task-induced percent signal changes using *rfxplot* (Glascher, 2009). The first two scans of each functional run were discarded from further analysis to eliminate non-equilibrium effects of magnetization. In order to address the susceptibility-by-movement interaction, we used the FieldMap Toolbox of SPM 8 and the reconstructed phase and magnitude images of the FLASH sequence described above. An unwrapped field map was calculated and then converted to a voxel displacement map (VDM) (Hutton et al., 2002; Jezzard & Balaban, 1995) that was co-registered to the first EPI volume of each fMRI session. EPI time-series were corrected for head movements and unwrapped using the VDMs (Andersson, Hutton, Ashburner, Turner, & Friston, 2001). The resulting images were spatially normalized, resampled to 3 mm isotropic voxel size, high-pass filtered (128 s) and spatially smoothed using a Gaussian kernel of 8-mm full width half maximum.

Statistical analysis was performed on a voxel-by-voxel basis with the general linear model formulation of SPM 8. We used three models to estimate the effects associated with the experimental design. In the first model, we evaluated BOLD signal changes associated with the contrast active tactile navigation (MAZE) compared to the control task (SQUARE) devoid of decision points (dead-ends). Following single subject analyses, we performed a random-effects analysis at the group level using the individual contrast estimates for each functional run. Sex was added as a covariate to control for gender differences (Grön, Wunderlich, Spitzer, Tomczak, & Riepe, 2000). In the second model, we introduced a parametric modulation at the first level using individual performance scores during the maze trials to identify BOLD signal changes associated with tactile maze performance. As there are no decisional points in the square condition, linear contrasts were used to test the effect of interest (MAZE vs. REST) for each fMRI run. Next, we performed a random-effects analysis at the group level using the individual contrast estimates of each functional run. Sex was added as a covariate to control for gender differences. We first conducted a whole brain analysis applying an uncorrected threshold of $P < 0.05$. In a next step, we applied small volume correction (SVC) using the centre of mass of the activations reported in our previous navigation study in congenital blindness (Kupers et al., 2010). In order to assess the role of the hippocampus in tactile learning, we defined spherical regions-of-interest (ROIs) with a 1 cm diameter, covering the head, body and tail of the two hippocampi (Chebat, Rainville, et al., 2007). For both the SVC and ROI analysis, P -values ≤ 0.05 , corrected for multiple comparisons using the family-wise error (FWE) method, were considered as statistically significant. Finally, in the third model, we evaluated BOLD signal change associated with the sensorimotor control task (SQUARE) compared to baseline (REST). Following the

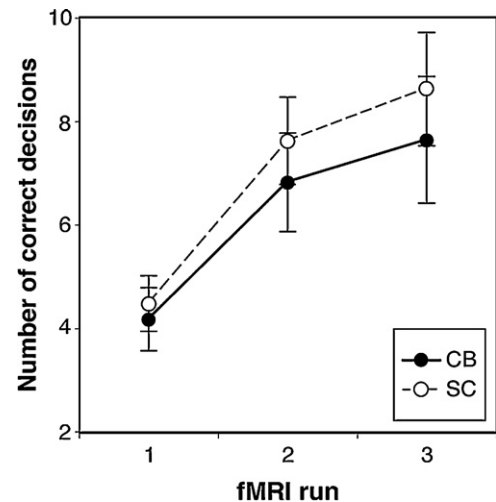


Fig. 2. Maze learning curves expressed as the mean number of correct decisions as a function of runs. Statistical analysis revealed a significant effect of runs but no significant group effect, neither a group × run interaction. The standard error of the mean (S.E.M.) is indicated with vertical lines. Abbreviations: CB = congenitally blind; SC = sighted controls.

single subject analysis, we performed a random-effect analysis at the group level using the individual contrast estimates for each functional run. Sex was added to control for gender differences (Grön et al., 2000). We first conducted a whole brain analysis ($P < 0.05$, uncorrected), followed by an SVC and ROI analysis ($P < 0.05$, FWE).

3. Results

3.1. Behaviour

The two-way (group × run) mixed ANOVA showed significant main effects of runs [$F_{2,46} = 45.4$, $p < 0.0001$] on the number of correct choices, indicating that subjects improved their performance with practice (Fig. 2). We found neither a significant group effect [$F_{1,23} = 0.343$, $p = 0.564$], nor a group × run interaction [$F_{2,46} = 0.362$, $p = 0.699$], indicating that both groups performed equally well inside the scanner. Pair-wise comparison confirmed continuous learning throughout the experiment in both groups: performance increased significantly from the first to the second ($p < 0.0001$) and further from the second to the third run ($p = 0.038$).

3.2. fMRI

The direct comparison of active tactile navigation (MAZE) with the control task (SQUARE) did not show significant BOLD response increases in any of the pre-defined ROIs. This may be due to the fact that this analysis does not take into account within-subject differences in learning. This is confirmed by the results of the parametric analysis (contrast "MAZE vs. REST"; Fig. 3, Table 2) that models differences in behavioural performance. This analysis reveals that blind but not blindfolded sighted control subjects show significant BOLD signal increases in the body and tail of the right hippocampus and in the right parahippocampus during tactile navigation (Fig. 4A). As shown in Fig. 4B, the BOLD signal increased linearly over the three successive runs in the hippocampal body and the parahippocampus, whereas activation in the posterior part of the hippocampus plateaued after the second run. When using a more lenient statistical criterion ($p \leq 0.05$ with false discovery rate (FDR) correction), a significant BOLD response increase was also observed in the head of the right hippocampus. Blind subjects showed additional activations in the medial and right inferior occipital gyri (BA 18), left lingual gyrus (BA 18), bilateral superior parietal lobule (BA 7), right fusiform gyrus (BA 37) and cuneus

Table 2
BOLD signal increases associated with tactile maze learning (MAZE-REST).

Brain region	BA	Search volume ^a			Congenitally blind				Sighted controls			
		x	y	z	Cluster size	Peak <i>P</i>	Peak <i>T</i>	Local maximum ^b	Cluster size	Peak <i>P</i>	Peak <i>T</i>	Local maximum ^b
								x y z				x y z
<i>Occipital cortex</i>												
Medial occipital gyrus	R	18	24	−87	12	16	0.018	2.90	24	−85	13	
	L	18	−21	−78	21	14	0.036	2.58	−18	−79	25	
Cuneus	L	17	0	−78	3	13	0.036	2.59	−3	−79	7	
Inferior occipital gyrus	R	18	36	−84	3	10	0.017	2.93	33	−82	4	
Lingual gyrus	L	18	−12	−75	−9	18	0.007	3.28	−12	−76	−11	
<i>Parietal cortex</i>												
Inferior parietal lobule	R	40	45	−48	51	15	0.016	2.94	42	−49	49	
Superior parietal lobule	R	7	18	−63	54	13	0.016	2.94	21	−64	52	
	L	7	−18	−57	54	18	0.005	3.39	−18	−58	58	
Precuneus	R	7	9	−72	39	16	0.013	3.03	12	−70	40	16 0.009 3.16 9 −70 43
	L	7	−9	−72	39	18	0.026	2.74	−9	−76	37	19 0.010 3.15 −9 −73 37
<i>Temporal cortex</i>												
Medial temporal gyrus	R	21	57	−45	−9	12	0.019	2.86	54	−46	−8	
Inferior temporal gyrus	R	37	54	−54	−12	11	0.024	2.76	51	−55	−8	
Fusiform gyrus	R	37	42	−51	−9	19	0.004	3.52	45	−52	−5	
Parahippocampus	R	36	33	−42	−12	18	0.009	3.16	36	−43	−14	
Hippocampus (body)	R		32	−25	−10	17	0.035	2.59	30	−25	−8	
Hippocampus (tail)	R		34	−34	−2	19	0.026	2.74	33	−34	1	
<i>Subcortical</i>												
Thalamus	R		9	−18	−6				8	0.039	2.55	9 −16 −8
Caudate nucleus	R		12	6	0				17	0.007	3.27	12 5 −2
	L		−6	3	3				8	0.032	2.63	−9 2 1

^a Montreal Neurological Institute (MNI) coordinates for the center of the region of interest (10-mm sphere).

^b MNI coordinates of the local maximum. Peak *P* reflects the probability of the peak voxel of the cluster using the FWE correction for multiple tests. The cluster size is expressed in voxels; BA, Brodmann's area.

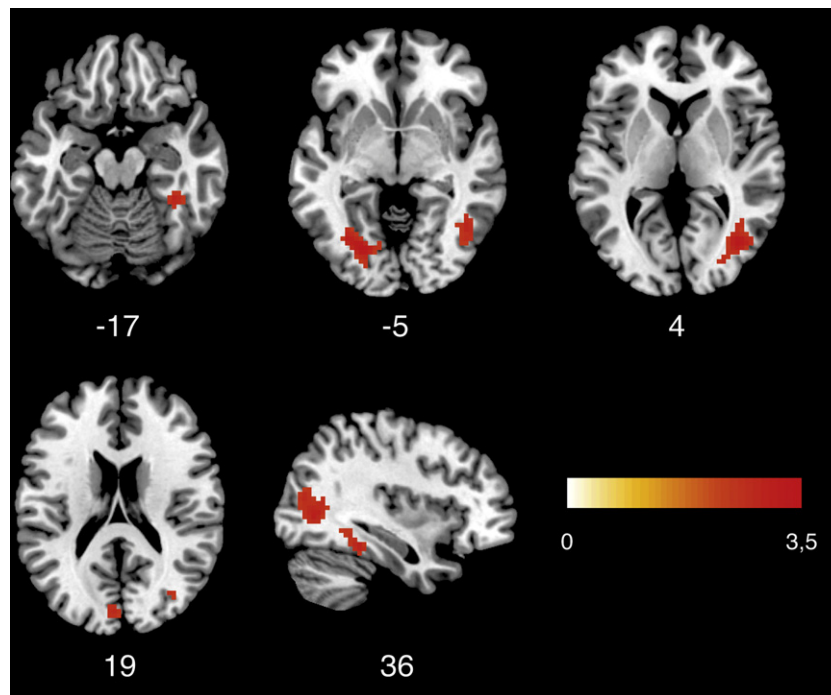


Fig. 3. T-statistical map showing areas where BOLD signal increases for the contrast "MAZE-REST" were significantly larger in congenitally blind compared to sighted control subjects. The visualization threshold is set to $P < 0.01$, uncorrected, cluster size $k > 5$ voxels, and activation maps are displayed on the single subject T1-template provided in SPM8. Blind subjects show stronger BOLD responses in the occipital cortex and parahippocampal area. The numbers (mm) below the slices refer to the dorso-ventral (z-dimension, axial slices) or medio-lateral (x-dimension, sagittal slice) positioning of the slices in stereotactic (Montreal Neurological Institute, MNI) space.

(BA 17) (Table 2 and Fig. 5). In sharp contrast, blindfolded sighted control subjects activated bilateral precuneus (BA 7), caudate nucleus and right thalamus. A direct group comparison revealed that the BOLD signal increases in the right parahippocampus, right

fusiform gyrus, left lingual gyrus and right medial occipital gyrus were significantly stronger in blind subjects (Table 3).

Interestingly, activity in the anterior intraparietal area showed a group $\times$ run interaction during tactile maze learning. Sighted

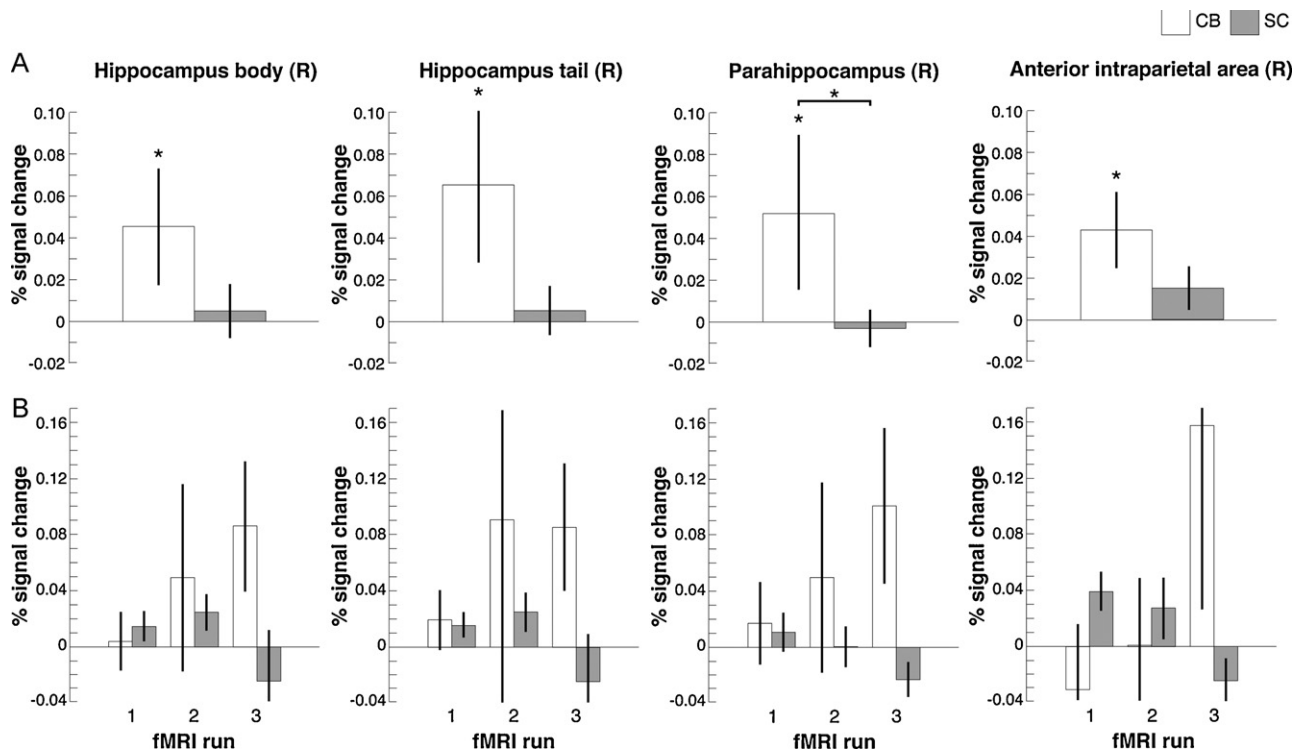


Fig. 4. A. Average percentage BOLD signal changes ($\pm$ S.E.M.) in the hippocampus/parahippocampus complex and the right anterior intraparietal area during tactile navigation for the three runs. The asterisks indicate the level of statistical significance ($P < 0.05$). B. Evolution of the BOLD signal changes over the three successive runs. Abbreviations: CB = congenitally blind; SC = sighted controls. L = left; R = right.

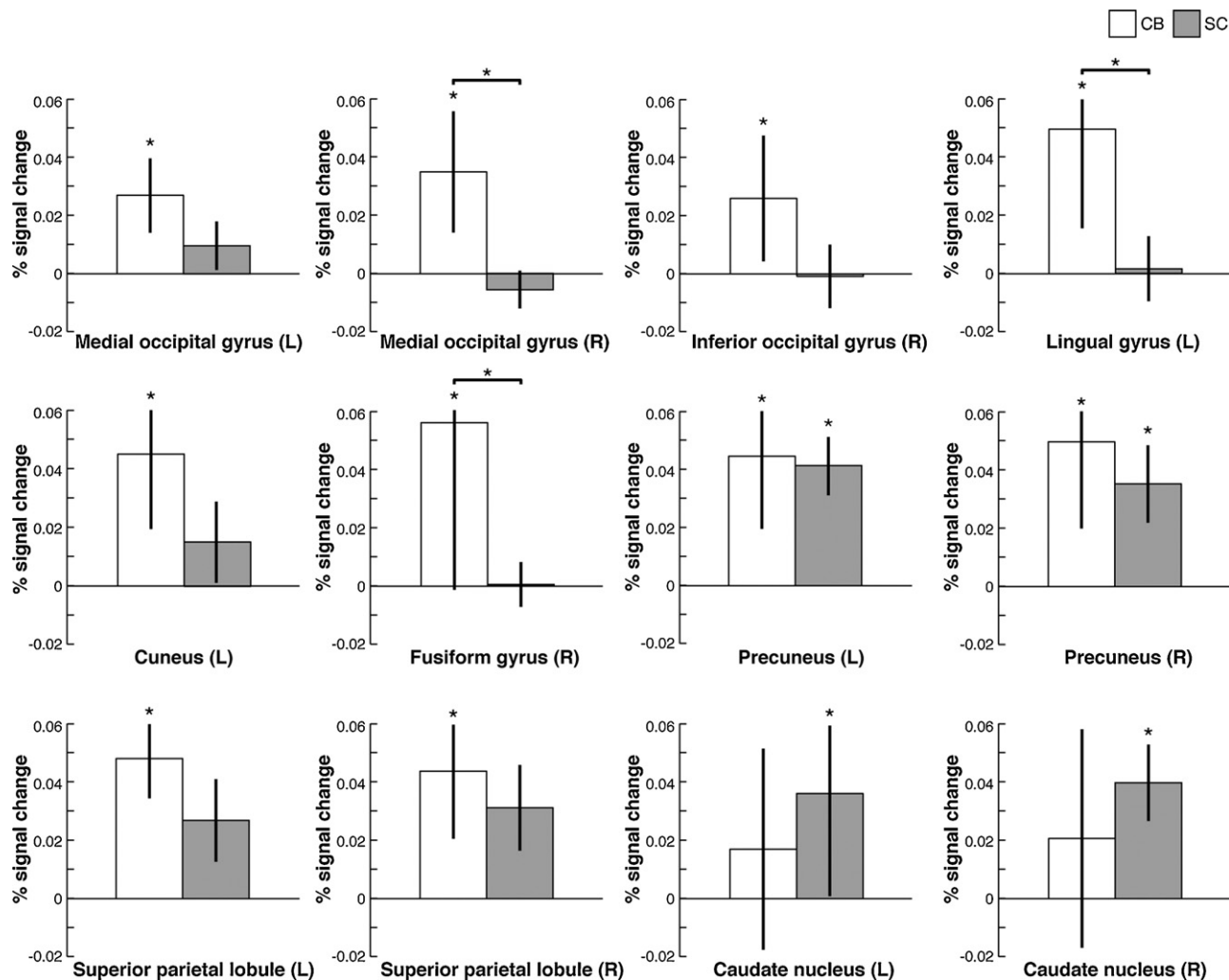


Fig. 5. Average percentage BOLD signal changes ($\pm$ S.E.M.) associated with tactile navigation in occipital cortex, precuneus, superior parietal lobules and caudate nucleus. Abbreviations: CB = congenitally blind; SC = sighted controls. L = left; R = right.

subjects recruited the anterior intraparietal sulcus (MNI coordinates: 39, -43, 49; cluster size = 210 voxels; peak $T = 3.58$) at the beginning but not at the end of tactile maze learning. Conversely, blind subjects showed an increase in regional activity in this area during tactile maze learning (Fig. 6).

In the sensorimotor control task (SQUARE-REST), both groups activated mainly right-hemispheric sensorimotor areas. The SVC and ROI analysis reveal that blind subjects activated the right medial and inferior temporal gyri, right fusiform gyrus and right cerebellum. In contrast, blindfolded sighted control subjects recruited the right inferior temporal gyrus, right fusiform gyrus,

right inferior and left superior parietal lobules, and right cerebellum (Supplementary Table S1).

4. Discussion

Our results show that during tactile maze navigation in which visual and other sensory inputs are absent, congenitally blind and blindfolded sighted control subjects activate different cortical networks. Whereas congenitally blind subjects recruited a neural network including the right hippocampus, right parahippocampus,

Table 3
Group differences (congenitally blind > sighted control) in BOLD signal increases associated with tactile maze learning (MAZE-REST).

Brain region		BA	Search volume ^a			Cluster size	Peak <i>P</i>	Peak <i>T</i>	Local maximum ^b		
			<i>x</i>	<i>y</i>	<i>z</i>				<i>x</i>	<i>y</i>	<i>z</i>
<i>Occipital cortex</i>											
Medial occipital gyrus	R	18	24	−87	12	15	0.047	2.45	24	−85	13
Lingual gyrus	L	18	−12	−75	−9	16	0.045	2.48	−12	−73	−5
<i>Temporal cortex</i>											
Fusiform gyrus	R	37	42	−51	−9	19	0.036	2.58	45	−52	−5
Parahippocampus	R	36	33	−42	−12	14	0.033	2.62	36	−46	−11

^a Montreal Neurological Institute (MNI) coordinates for the center of the region of interest (10-mm sphere).
^b MNI coordinates of the local maximum. Peak *P* reflects the probability of the peak voxel of the cluster using the FWE correction for multiple tests. The cluster size is expressed in voxels; BA, Brodmann's area.

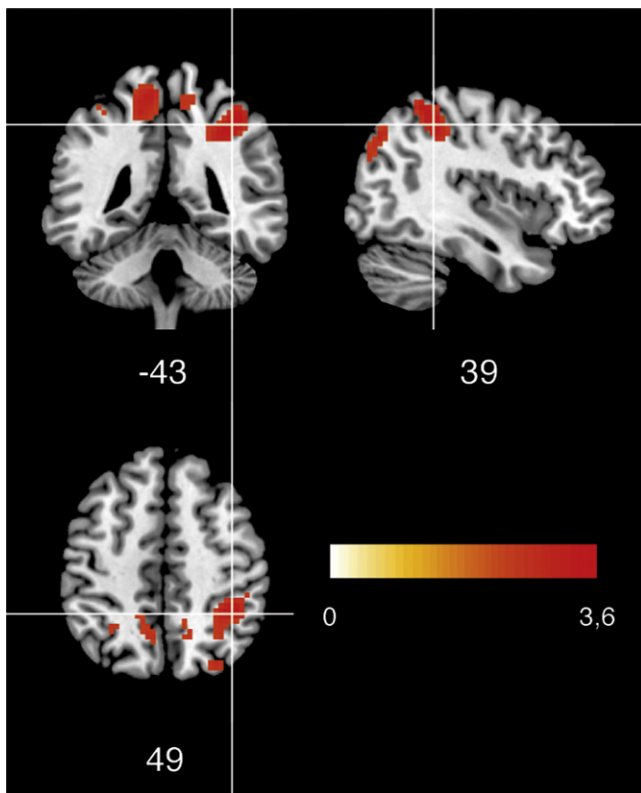


Fig. 6. T-statistical map showing areas where BOLD signal increases for the group $\times$ run interaction contrast of “MAZE minus REST” (run3 – run1) were significantly larger in congenitally blind compared to sighted control subjects. The visualization threshold is set to $P < 0.01$, uncorrected, cluster size $k > 5$ voxels, and activation maps are displayed on the single subject T1-template provided in SPM8. Blind subjects show stronger BOLD responses mainly in the anterior intraparietal area. The numbers (mm) refer to the rostro-caudal (y-dimension, coronal slice), medio-lateral (x-dimension, sagittal slice) or dorso-ventral (z-dimension, axial slice) positioning of the slices in stereotactic (Montreal Neurological Institute, MNI) space.

superior parietal cortex, striate and extrastriate visual cortex, blindfolded sighted control participants activated the precuneus, thalamus and caudate nucleus. Since both groups performed equally well on the maze task, the observed differences in brain activation patterns cannot be explained by differences in behavioural performance. Our results therefore suggest that blind and sighted participants use different cognitive strategies during tactile maze solving.

Some earlier behavioural studies showed that compared to blindfolded sighted controls, congenitally blind subjects perform better in several navigation tasks (Passini, Delisle, Langlois, & Proulx, 1986; Passini, Proulx, & Rainville, 1988; Passini et al., 1990; Passini, Rainville, & Paiement, 1991). In line with the results from our previous behavioural study on navigation within a small-scale environment (Gagnon et al., 2010), we did not find superior performance in our blind subjects. Compared to navigation in life-size (artificial) environments, navigation inside a small-scale maze relies much less on allothetic (spatial orientation cues that are external to the body such as visual, olfactory and auditory information) and more on idiothetic (vestibular, proprioceptive, motor efference copy) cues. Indeed, we previously reported that when allothetic cues are reduced or eliminated, sighted controls actually outperform congenitally blind subjects (Gagnon et al., 2010). We attribute the absence of a group difference in behavioural performance in the current study to the fact that our participants were previously trained in solving a variety of multiple T-mazes (Gagnon et al., 2010).

4.1. Hippocampal complex

The role of the hippocampus in navigation and spatial memory in sighted individuals is well established (Bilkey, 2007; Ekstrom et al., 2003). We show here that the hippocampus is also involved in navigation in the absence of visual input. In our previous study in which blind participants learned to navigate through a virtual maze using a sensory-substitution device, we failed to find hippocampal activation (Kupers et al., 2010). We hypothesized that this lack of activation was due to the fact that the subjects were already trained before scanning. This is confirmed by the present findings showing the recruitment of right hippocampus during the learning process. To the best of our knowledge, the present data provide the first evidence substantiating the functional role of the hippocampus in navigation in human congenital blindness.

The hippocampus is involved in both the formation and the retrieval of allocentric maps (Iaria, Chen, Guariglia, Ptito, & Petrides, 2007; Maguire, 2001; Van Horn et al., 1998; Wolbers & Buchel, 2005). Iaria and colleagues (2007) hypothesized that the anterior portion of the hippocampus is strongly involved in the *formation* of new cognitive maps, whereas the posterior part is responsible for *using* these maps. Our present findings show that tactile navigation activates the body and tail of the right hippocampus in congenitally blind subjects. When using a more lenient statistical threshold (FDR-correction), increased BOLD activation was also found in the head of the hippocampus. Since there is evidence for the existence of place cells in the hippocampus in early blind rats whose properties are very similar to those in sighted rats (Save, Cressant, Thinus-Blanc, & Poucet, 1998), it is reasonable to assume that early vision is not necessary for normal functioning of place cells. It seems therefore that the hippocampus in congenitally blind subjects is involved in both the formation and the use of cognitive maps during tactile maze navigation.

Besides the hippocampus, a number of other brain structures are critically involved in spatial navigation, including the parahippocampus, superior parietal lobule, precuneus and ventral occipital and occipito-temporal cortices. Cells that respond to places (O’Keefe & Dostrovsky, 1971) are not only found in the hippocampus but also in the posterior parietal cortex and the parahippocampus (Whitlock, Sutherland, Witter, Moser, & Moser, 2008). In addition, the parahippocampus also contains “spatial view” cells, i.e. cells that respond when looking at a specific part of the environment (Rolls, Robertson, & Georges-François, 1997). We should of course be cautious in assuming a direct relationship between brain imaging findings in humans and response characteristics of these place cells and view cells recorded in animals.

In sighted individuals, the parahippocampus is recruited while navigating under full vision in virtual environments (Aguirre, Detre, Alsop, & D’Esposito, 1996; Weniger et al., 2010), processing of visual scenes (Epstein & Kanwisher, 1998; Epstein, Higgins, & Thompson-Schill, 2005), mental navigation (Ghaem et al., 1997; Rosenbaum, Ziegler, Winocur, Grady, & Moscovitch, 2004) and scene recognition (Committeri et al., 2004; Epstein & Kanwisher, 1998; Iaria et al., 2007; Maguire et al., 1998). It seems therefore that the hippocampus and parahippocampus have different functions in navigation, the former being more involved in allocentric spatial representations (Burgess, Maguire, & O’Keefe, 2002; Iaria, Petrides, Dagher, Pike, & Bohbot, 2003; Maguire et al., 1998) and the latter in egocentric spatial learning (Weniger et al., 2010). Besides the hippocampus, our blind subjects also activated their right parahippocampus. This finding confirms recent results from our laboratory showing that blind subjects activate this structure during route recognition with a sensory substitution device (Kupers et al., 2010). Anatomical studies in human and non-human primates indicate that the parahippocampus has strong reciprocal connections with sensory-specific and multimodal association

cortices, allowing the reception and feed-back control of unimodal and multimodal inputs (Blatt, Pandya, & Rosene, 2003). With respect to the present findings, it is worth mentioning that direct projections have been demonstrated between extrastriate visual areas, the parietal and the superior temporal sulcus and the parahippocampus both in the macaque (Martin-Elkins & Horel, 1992) and the human brain (Powell et al., 2004). We previously suggested that the activation of the parahippocampus in our blind subjects is probably due to an increased connectivity with the ventral extrastriate cortex and/or the posterior parietal cortex (Kupers et al., 2010). The fact that our blind subjects activated the hippocampus/parahippocampus complex suggests that they can use both allocentric and egocentric strategies to solve the navigation task.

4.2. Caudate nucleus and thalamus

In contrast with the results obtained in blind subjects, blindfolded sighted controls activated bilateral caudate nucleus, right thalamus and bilateral precuneus during tactile navigation. This is in line with results from our previous study showing that blindfolded sighted controls but not congenitally blind subjects activate this area during tactile navigation with a sensory substitution device (Kupers et al., 2010). Whereas the hippocampus has been traditionally associated with spatial strategies, the caudate nucleus plays a role in non-spatial (Iaria et al., 2003) or stimulus-response types of navigation (White, 2009). This is supported by the results of a morphometric study showing that normal sighted individuals who use a non-spatial strategy in a visual radial maze task have a significantly larger caudate nucleus compared to subjects using a spatial strategy (Bohbot, Lerch, Thorndyck, Iaria, & Zijdenbos, 2007). Thus, it is possible that our sighted participants used a sequence of actions coded in time instead of space, such as a verbal-guided plan “continue up, turn right, go down, etc.” during navigation. The equal performance in blind and sighted participants suggests that both spatial and non-spatial strategies are as effective in tactile navigation. With respect to the thalamus, head direction cells have been found in its anterodorsal division (Taube & Muller, 1998). The anterior thalamus is connected with the retrosplenial cortex, a structure that is critically involved in spatial navigation (Epstein, 2008). The anterodorsal thalamus receives self-movement related motor and vestibular input from subcortical structures such as the dorsal tegmental and the lateral mammillary nuclei, hence providing idiothetic spatial orientation cues.

4.3. Visual cortex

Only congenitally blind subjects activated striate and extrastriate visual structures during tactile maze navigation such as the cuneus, right medial and inferior occipital gyri and left lingual gyrus. We explain the increased occipital activity in the blind group by cross-modal plasticity in an *active* navigation task. In a previous study (Kupers et al., 2010), we also found increased activation in the occipital lobe when blind participants performed a *passive* route discrimination task using a sensory substitution device. Our results therefore add to a growing number of studies that have shown that blind subjects recruit their occipital cortex in a wide variety of sensory and cognitive tasks (reviewed in Sadato, 2005; Kupers et al., 2011). A recent study by Fiehler and co-workers (2009) showed that the occipital cortex of congenitally blind individuals is involved in the retrieval of mental representations in order to guide behaviour, a result that is in line with the present data. It might also be that the occipital cortex of the blind contributes to form the maze representation, and plays a major role in spatial cognition microgenesis.

4.4. Anterior intraparietal area

Both groups activated the anterior intraparietal sulcus yet displaying an inverse temporal dynamics during tactile maze learning. Blind subjects recruited this area only at the end whereas sighted controls activated this structure only at the beginning of the tactile maze task. Neuroimaging studies in healthy subjects have shown that the anterior parietal area is part of a tactile shape-processing network. In sighted individuals, this area is activated when subjects have to discriminate three-dimensional shapes by active and passive touch (Bodegaard, Geyer, Grefkes, Zilles, & Roland, 2001) or have to construct or recognize three-dimensional objects with their hands (Jäncke, Kleinschmidt, Mirzazade, Shah, & Freund, 2001). More importantly, this area subserves the cross-modal transfer of three-dimensional information between the visual and haptic modality (Grefkes, Weiss, Zilles, & Fink, 2002). In the present study, blindfolded normally sighted subjects might have initially recruited the anterior intraparietal area because they processed the maze as a three-dimensional shape and transferred this haptically obtained shape information into the visuospatial domain. This strategy attenuated over time as sighted subjects became more proficient in navigation resulting in a decay of task-related anterior parietal activity. In contrast, blind subjects did not activate this area at the beginning of tactile maze learning suggesting that the absence of vision impairs the use of such a strategy at the early learning phase. However, it seems that this haptic mode of processing gained importance during the course of maze learning. Previous work (Mellet et al., 2000) demonstrates that learning the configuration of a maze using a survey point of view recruits the para/hippocampus to a lesser degree than when using a route point of view. The inverse temporal dynamics in AIP suggest that SC might have used a survey point of view in the visual domain, whereas CB resorted to a route point of view in the tactile domain, a conjecture that may partly explain the absence of para/hippocampal activation in the SC group.

4.5. Concluding remarks

We provide here the first evidence that congenitally blind subjects activate the hippocampal complex to solve a spatial navigation task when environmental cues that are present in more naturalistic settings are largely reduced. This suggests that the formation and the manipulation of an allocentric representation as well as a high level of spatial understanding are not limited to people with visual experience. The activation of the occipital cortex in congenitally blind subjects during tactile maze navigation indicates cross-modal recruitment by higher cognitive tasks such as navigation.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neuropsychologia.2012.03.022.

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