NEURAL CORRELATES OF SPATIAL WORKING MEMORY IN HUMANS: A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY COMPARING VISUAL AND TACTILE PROCESSES

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Abstract—Recent studies of neural correlates of working memory components have identified both low-level perceptual processes and higher-order supramodal mechanisms through which sensory information can be integrated and manipulated. In addition to the primary sensory cortices, working memory relies on a widely distributed neural system of higher-order association areas that includes posterior parietal and occipital areas, and on prefrontal cortex for maintaining and manipulating information. The present study was designed to determine brain patterns of neural response to the same spatial working memory task presented either visually or in a tactile format, and to evaluate the relationship between spatial processing in the visual and tactile sensory modalities. Brain activity during visual and tactile spatial working memory tasks was measured in six young right-handed healthy male volunteers by using functional magnetic resonance imaging. Results indicated that similar fronto-parietal networks were recruited during spatial information processing across the two sensory modalities—specifically the posterior parietal cortex, the dorsolateral prefrontal cortex and the anterior cingulate cortex. These findings provide a neurobiological support to behavioral observations by indicating that common cerebral regions subserve generation of higher order mental representations involved in working memory independently from a specific sensory modality. © 2005 IBRO. Published by Elsevier Ltd. All rights reserved.

Working memory refers to a cognitive system that temporarily maintains an active representation of information for further processing or recall, and supports human cognitive processes by providing an interface between perception, long-term memory and behavioral response (Baddeley, 1986, 2000, 2003). The original framework hypothesized by Baddeley and Hitch (1974) consisted of a number of subsidiary subsystems and a central executive devoted to attentional control and planning. This framework has been recently revised on the basis of the results provided by behavioral and brain functional studies that highlighted the need to consider the working memory system not only as a pattern of separate mechanisms, but mainly as a struc-

ture capable of integrating different types of information provided by distinct sensory modalities and long-term memory systems (Cornoldi and Vecchi, 2003). Recent studies of neural correlates of working memory components have identified both low-level perceptual processes and higher-order supramodal mechanisms through which sensory information can be integrated and manipulated (e.g. Pietrini et al., 2004; Naghavi and Nyberg, 2005; Ranganath and D'Esposito, 2005).

Recently, this line of research focused on the spatial component of working memory (Logie, 1995; Cornoldi and Vecchi, 2003), having recognized common perceptual mechanisms in spatial discrimination (Ganis et al., 2004; Reed et al., 2005), and the relationship between spatial processing and higher-order cognitive tasks, such as imagery or thinking (Logie, 1995). The investigation of the relationship between spatial perception and spatial working memory has become critical to the understanding of two apparently inconsistent findings. On one hand, several investigations have confirmed the critical role of visual perception in spatial processing (e.g. Ganis et al., 2004; Slotnick, 2004). On the other hand, recent behavioral studies in congenitally blind individuals have shown that visual perception and visual experience are not a prerequisite for an efficient spatial working memory (Vecchi, 1998; Vecchi et al., 2004). Therefore, spatial representation may be generated and processed in the absence of visual perception. In addition, other sensory modalities (such as touch) may play a critical role in conveying information from external stimuli for use in spatial processing.

Beyond primary sensory cortices, working memory relies on a widely distributed neural system of higher-order association areas which includes the posterior parietal and occipital areas, and on the prefrontal cortex (PFC) for maintaining and manipulating information (Courtney et al., 1996; Owen et al., 1998; D'Esposito et al., 1999; Smith and Jonides, 1999; Furey et al., 2000a,b).

Various physiological and functional similarities exist across vision and touch (Martino and Marks, 2000; Amedi et al., 2001, 2002; Calvert and Thesen, 2004; Ernst and Bulthoff, 2004; Pietrini et al., 2004), and normally both sensory modalities merge the detection of the surrounding world in an unified percept. Moreover, functional brain studies have recently demonstrated a supramodal representation of object form in the ventral extrastriate cortical pathway of sighted and congenitally blind individuals, thus suggesting that the visual cortical pathways can process information independently from the sensory modality that

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Abbreviations: IPS, intraparietal sulci; LOT, lateral occipito-temporal cortex; PFC, prefrontal cortex; SMA, supplementary motor area.

carries that information to the brain (Pietrini et al., 2004). Beyond this overlapping sensory representation, an efficient perceptual information processing requires a common integrative procedure that relies mainly on working memory.

Though sharing analogous neural mechanisms involved in spatial attention, tactile-based working memory shows a specific activity in the somatosensory, insular, precentral frontal and posterior parietal cortical areas (e.g. Burton and Sinclair, 2000), as compared with visual-based working memory. Because of this differential neural network, tactile-based working memory is thought to involve a selective processing of both the features of the object explored and the spatial coordinates within which the stimuli appear (Smith et al., 1995; Burton and Sinclair, 2000).

These studies emphasize the importance of investigating analogies and differences between spatial processes originating from different sensory inputs, specifically visual and tactile. Previous studies indicated that spatial representation may be generated through tactile perception, although in most cases performance seems to suffer from specific limitations (Vecchi, 1998; Vecchi et al., 2004). Therefore, the present study was designed to determine the neural response to the same spatial working memory task presented either visually or in a tactile format, and to evaluate the relationship between spatial processing in the two sensory modalities. We hypothesized that similar fronto-parietal networks would be recruited across spatial information processing, independent of the sensory modality through which spatial information is acquired. The

expected results would support the theory that working memory processes may derive from the concurrent involvement of both peripheral modality-specific components associated to sensory modalities and more central supramodal structures that process information regardless of its source. In addition, the expected results would support also the hypothesis that information is represented in working memory in a format unrelated to stimulus characteristics but associated to the nature of the mental representation to-be-generated. For example, both visual and tactile stimuli could convey information used to generate spatial images but also linguistic or auditory strings through a higher order network of supramodal cerebral structures.

EXPERIMENTAL PROCEDURES

Subjects

Six right-handed healthy males (mean age±S.D.=28±1 years) volunteered to participate. All subjects received medical, neurological and psychiatric examinations, routine laboratory tests and a structural MR scan of the brain to rule out any disorder that could affect brain function or metabolism. No subject had taken any psychotropic medication or any other medication for at least 4 weeks prior to the study. All subjects had normal visual acuity and intact visual fields, and none of them wore glasses for near or far vision. All subjects gave their written informed consent after the study procedures and potential risks had been explained (protocol n. 1616/2003 approved by the Ethical Committee of the University of Pisa).
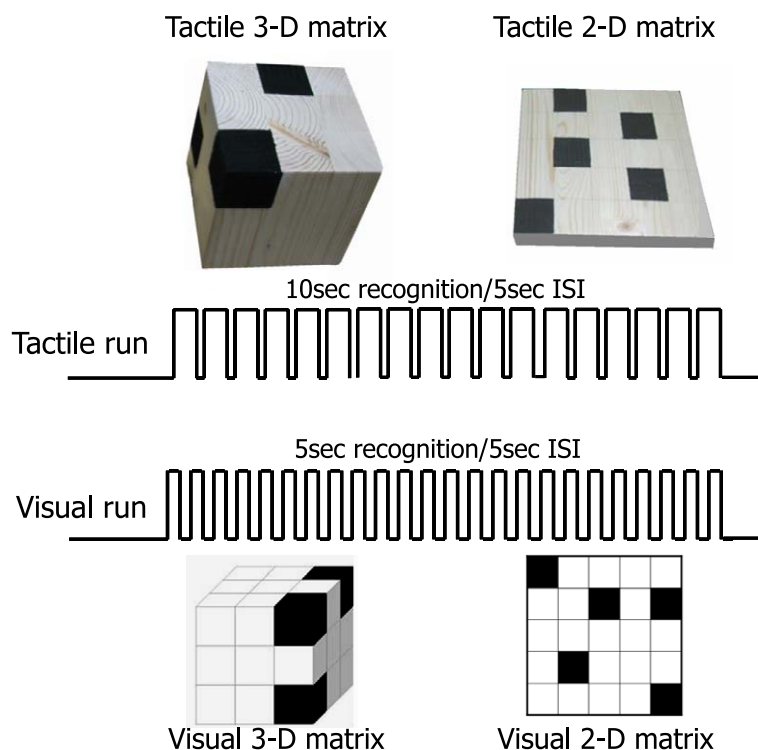

Fig. 1. Examples of two- and three-dimensional stimuli used in the tactile and visual working memory tasks, with the structure and time frame of the fMRI experimental runs (ISI, interstimuli interval).

Image acquisition

Functional magnetic resonance imaging (fMRI) images were acquired to explore brain activity elicited during spatial working memory tasks. We used a Gradient Echo echoplanar (GRE-EPI) sequence with a GE Signa 1.5 Tesla scanner (General Electric, Milwaukee, WI, USA) [repetition time (TR)=2500 ms, field of view (FOV)=24 cm, 22–26 axial slices, slice thickness 5 mm, echotime (TE)=40 ms, flip angle 90°, image plane resolution=64×64 pixels, voxel dimensions=3.75×3.75×5 mm]. For the visual and tactile spatial working memory tasks, six to eight time series, each consisting of 114 brain volumes, were obtained for each subject. High resolution T1-weighted spoiled gradient recall (SPGR) images were obtained for each subject to provide detailed brain anatomy during structural image acquisition.

Experimental paradigm

Brain activity was measured using fMRI while subjects performed, in alternate runs, a one-back spatial discrimination task of visually and tactilely presented matrices (see below). The experimental task adopted in the present study was derived from the procedure originally developed by Cornoldi et al. (1991) to investigate spatial processes in congenitally blind individuals (Vecchi et al., 1995). In this study we used two-dimensional 5×5 matrices and three-dimensional 3×3×3 matrices. The bi-dimensional and the three-dimensional matrices were comparable in terms of number of targets and number of potential combinations of target location.

In order to control for cross-modal priming, or facilitation processes, the presentation of different matrices (2-D vs. 3-D),

number of targets (three vs. five), and modality of presentation of the stimuli (visual vs. tactile) were randomized within and between subjects, so that each person performed all versions of the task.

Tactile stimuli

Wooden squares and cubes with three or five Velcro-covered target-squares/cubes formed the two- and three-dimensional stimuli, respectively (Fig. 1). Each matrix was presented to the subjects by using a wooden pole with a Plexiglas platform on one end upon which the wooden matrix was attached with Velcro. During the one-back tactile recognition task, subjects explored each matrix using both hands and were instructed to keep their eyes closed. Subjects indicated whether the presented matrix was the same or different as compared with the previous one by pressing foot pedals with the right ("same") or left ("different") foot. Based on behavioral pilot studies, matrices were presented for 10 s with an inter-stimulus interval of 5 s. Subjects were allowed to respond at any time between initial presentation of a stimulus matrix and the presentation of the next matrix. Each time series consisted of 16 consecutive matrices with three/five targets in counterbalanced order. The order of presentation of the matrices was randomized for each subject, always including the same number of "same" and "different" judgments. Differences between matrices were obtained by randomizing all possible conditions, namely by mixing matrices differing in one or more targets.

During baseline and inter-stimuli periods, subjects were asked to rest their arms along their side and keep them still.
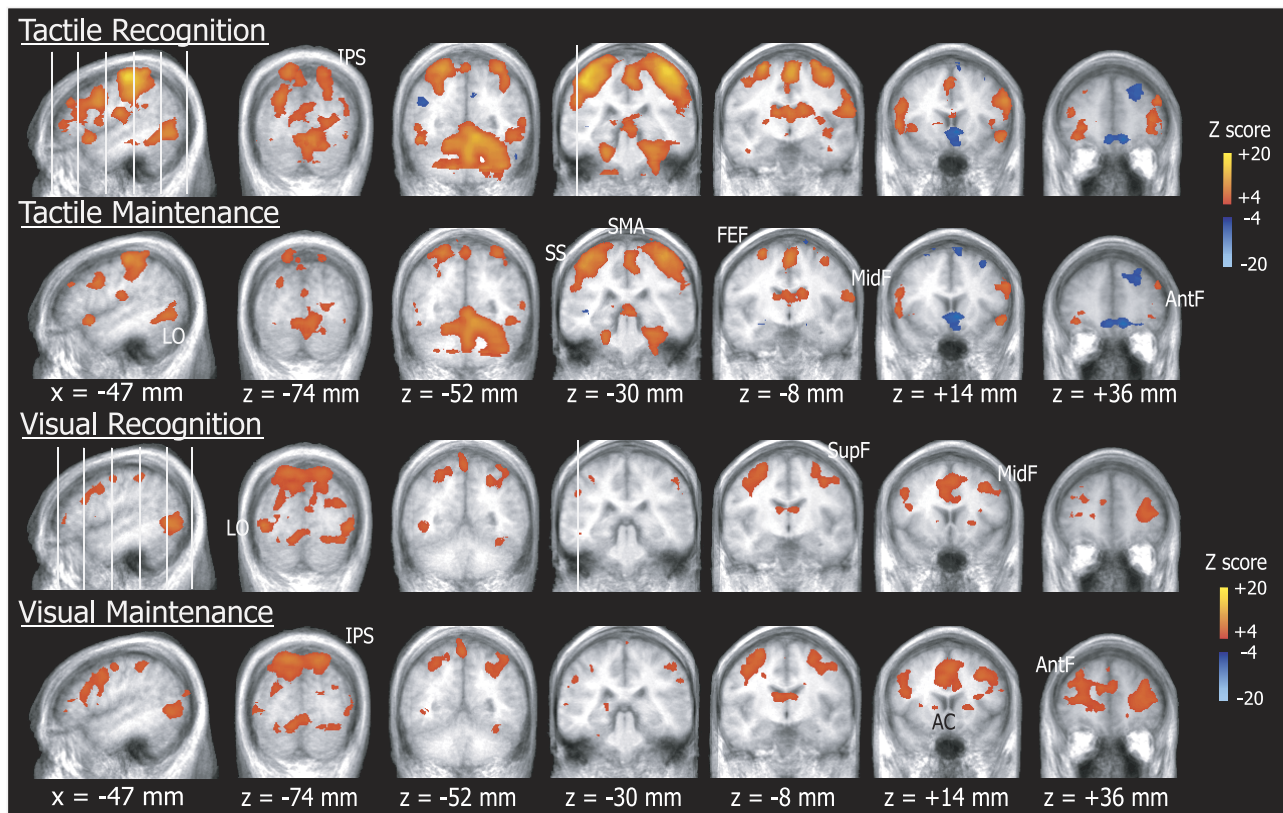
Fig. 2. Brain areas that responded during tactile or visual spatial working memory task. Sagittal and coronal images from group Z-score maps of activated areas are shown. Statistical threshold was established at a P value<10⁻⁴ (z score>3.8) The somatosensory cortex (SS), IPS, SMA, superior (SupF) and middle (MidF) frontal cortices, anterior cingulate (AC), and lateral occipital (LO) cortex activated by tactile and visual matrix recognition and maintenance are indicated. The white lines in the sagittal images correspond to the locations of the coronal slices and, similarly, the white line in the coronal slice indicates the location of the sagittal section. Spatial coordinates are provided according to the Tailairach and Tournoux (1988) atlas.

Table 1. Cortical regions with significant BOLD signal change during the visual/tactile working memory task relative to rest

Brain areas[a]		BA	Tactile[b]				Visual			
			Coordinates[e]			Z score	Coordinates			Z score
			x	y	z		x	y	z	
Prefrontal cortex										
Superior frontal	R	10	21	54	5	6.9				
	R	10	12	73	6	4.3				
	L	10	−21	49	4	4.8				
	R									
Medial frontal	R	6					6	5	70	4.1
	R	6/8	1	25	45	5.2				
	L	6	0	4	52	>7.0	−1	9	50	>7.0
	L	6	−25	−7	65	>7.0				
	L	6	−2	−15	60	>7.0				
Middle frontal	R	6	34	−2	51	>7.0	29	−6	56	6.1
	R	8/9	30	37	37	5.3	42	28	30	6.4
	R	9					48	5	35	>7.0
	R	10/46	37	44	19	>7.0				
	R	10/47	41	57	−8	4.4	34	50	5	5.9
	R	10								
	R	11								
	L	10/47					−44	50	4	6.1
	L	6					−35	−8	45	5.6
	L	6					−51	7	35	5.8
	L	9	−45	36	28	6.3	−34	40	20	>7.0
	L	9								
	L	10	−25	63	21	5.4				
Anterior cingulate	R	24					8	35	4	4.7
	L	24	−3	16	20	4.4	−9	26	13	4.8
	L	24					−16	49	−2	4.3
Cingulate gyrus	R	32					5	24	33	6.6
	R	32								
Inferior frontal	R	44	49	5	19	>7.0	51	8	33	5.9
	R	47	37	34	−8	6.6	40	33	−8	6.7
	L	47					−50	18	−7	>7.0
	L	44	−52	9	29	>7.0	−55	10	29	>7.0
	L	44	−42	50	2	6.5				
Insula	R	13	41	16	1	6.0				
	L	13								
	L	13	−34	24	13	6.6	−29	19	12	5.4
	L	13	−38	1	11	5.6				
Precentral gyrus	R	44					54	9	5	4.5
	R	44					−48	10	8	4.6
	R	4	35	−20	60	>7.0				
	R	4					4	−27	61	4.2
	L	4	−36	−24	61	>7.0				
Parietal cortex										
Postcentral gyrus	R	3	53	−22	32	>7.0	38	−22	46	4.4
	R	2								
	L	3	−16	−35	65	>7.0				
	L	2	−52	−21	37	>7.0				
	L	43								
Paracentral lobule	R	4	7	−36	73	5.9				
	L	31								
Postcentral/inf parietal	R	40	52	−43	35	4.2				
	L	40	−55	−23	16	>7.0	−56	−22	17	4.3
Precuneus	R	7	16	−67	45	>7.0	14	−76	52	>7.0
	R	7	21	−71	19	5.7	27	−71	20	6.0
	R	31	4	−52	59	6.7	1	−60	58	>7.0
	L	31	−21	−80	29	>7.0				
	L	7/19	−9	−83	47	5.5	−7	−83	42	6.4

Tactile maintenance				Visual maintenance				Overlapping[c]				Interactions[d]			
Coordinates			Z score	Coordinates			Z score	Coordinates			Z score	Coordinates			Z score
x	y	z		x	y	z		x	y	z		x	y	z	
29	49	0	5.9					24	50	9	2.7				
12	70	11	5.8												
−18	49	3	4.6	−13	51	5	5.2								
9	52	1	4.7												
				7	4	67	4.9								
2	10	45	4.6					1	−4	57	3.4				
												4	−7	49	4.2
−25	−7	64	5.0												
−2	−16	58	>7.0	−2	−27	69	4.3	2	−25	54	2.3				
27	−8	61	>7.0	30	−5	58	6.6	26	−7	56	3.8	28	−5	62	3.5
				41	30	29	>7.0					13	26	55	−2.7
				47	5	34	>7.0	48	6	23	3.3	13	45	20	−3.8
37	43	19	5.4					38	32	10	3.2				
				32	51	5	6.1					37	44	−11	3.6
				12	48	17	4.2								
												−3	50	−12	−2.5
				−36	51	7	5.9	−39	45	8	3.1				
				−28	−6	54	5.5					−8	8	60	−3.5
				−32	13	36	6.7	−47	12	31	3.1	−32	11	54	−2.4
−45	35	28	5.4	13	26	14	5.0					−48	30	34	5.0
												−35	12	34	−4.6
−25	63	21	5.5	−8	22	14	5.6					−12	46	12	−3.6
								6	12	30	3.2	1	31	−7	−4.1
								−6	27	24	3.2				
								−17	46	9	2.7				
				6	23	33	>7.0					12	19	34	−3.6
				24	−2	38	5.4								
				−38	30	−9	4.2								
				−52	9	24	4.9								
				−53	20	5	4.5								
34	−2	15	4.2												
−32	24	13	5.4	−29	23	13	6.3								
−41	4	14	4.3												
53	5	11	>7.0	50	6	6	4.5					57	5	15	3.0
												−55	5	21	3.3
18	−32	68	6.2					40	−32	57	3.6				
−38	−25	60	>7.0									−37	−19	58	>7.0
53	−22	31	>7.0					40	−32	57	3.6	43	−26	55	>7.0
												52	−23	28	>7.0
−15	−36	66	5.2												
−52	−19	36	>7.0					−46	−29	54	3.5	−55	−24	34	5.7
−62	−11	18	6.4	−63	−18	23	5.3					−49	−16	14	3.6
												4	−35	69	2.8
												−5	−29	45	7.5
52	−45	36	4.6												
22	−61	40	6.0												
				13	−75	52	>7.0					23	−64	31	5.4
								5	−68	48	3.7				
−1	−58	55	7.0	1	−53	59	6.4	4	−51	62	4.4				
−21	−80	29	5.2	−22	−69	52	>7.0					−20	−60	42	4.9
				4	−83	42	4.8	−14	−87	41	2.7	−4	−80	46	3.1

Table 1. Continued

Brain areas[a]		BA	Tactile[b]			Z score	Visual			Z score
			Coordinates[e]				Coordinates			
			x	y	z		x	y	z	
Superior parietal	R	7	24	−52	60	>7.0				
	R	7								
	R	7								
	L	7	−25	−65	49	>7.0	−23	−65	49	6.3
Inferior parietal	R	7					31	−46	47	6.7
	R	40					51	−30	32	4.1
	L	40					−38	−47	47	5.5
Angular gyrus	R	39								
Parahippocarupus	R	36								
	L	36	−42	−20	−12	5.4				
Temporal cortex										
Inferior temporal	R	37/19	46	−62	0	6.5	39	−71	−1	>7.0
	R	20	43	−11	−20	5.2				
	L	37	−52	−57	−6	>7.0	−45	−64	0	>7.0
	L	19								
Middle temporal	R	21								
	L	39	−41	−75	16	6.0	−34	−82	0	5.7
Superior temporal	R	22	59	−10	4	5.2				
	R	22/39					45	−49	10	4.4
	R	38	38	18	−20	4.6				
	L	38	−48	17	−8	>7.0				
Fusiform gyrus	R	37	46	−44	−12	>7.0				
	R	19					28	−41	−14	5.3
	L	37	−40	−42	−14	>7.0	−33	−57	−18	6.4
Occipital cortex										
Lingual gyrus	R	18	18	−100	−5	4.7	12	−76	−13	>7.0
	L	18	−13	−84	−10	>7.0				
	L	18	−22	−69	3	6.7				
	L	18	−28	−100	−2	4.5				
Cuneus	R	18					5	−98	11	6.0
	R	17					14	−79	7	5.1
	R	19								
	L	17/18	0	−89	6	>7.0	−6	−75	15	5.3
	L	18	−1	−78	23	7.0				
Middle occipital	R	19	−41	−75	16	6.0				
Inferior occipital	L	18								
Thalamus	R		14	−23	8	>7.0				
	L		−10	−23	6	6.6				
Caudate	R		9	−1	15	6.4	12	6	15	>7.0
	L		−13	−4	16	>7.0				
Cerebellum	R		15	−45	−40	>7.0				
	R		34	−63	−16	>7.0	32	−77	−24	4.2
	R		18	−52	−11	>7.0				
	L		−20	−42	−17	>7.0				
	L		−36	−52	−35	>7.0				

[a] For each region, coordinates and estimated Brodmann's areas from Talairach and Tournoux atlas (Tailairach and Tournoux, 1988), and Z-values
[b] Statistical significance for the analyses designed to identify regions for each working memory condition for the two sensory modalities was assumed
[c] Statistical significance for group comparisons was restricted to brain regions identified as significant in the within subject task effect analyses
[d] Interactions where tactile maintenance showed higher BOLD increases than visual maintenance are shown in plain font, while brain areas
[e] x=Distance in millimeters to the right (+) or the left (−) side of the midline, y=distance anterior (+) or posterior (−) to the anterior commissure. z=Distance superior (+) or inferior (−) to a horizontal plane through the anterior and posterior commissures.

Visual stimuli

Stimuli were back-projected onto a screen, and subjects looked at the visual matrices through a mirror located inside the head coil of the MRI scanner. White squares and rotating cubes with three or five black target squares/cubes represented the two- and three-dimensional visual stimuli, respectively. The three-dimensional cubes were rotated to give the same possibility to explore five cube faces (six minus the cube base) that subjects had when they explored the wooden cubes in the tactile task. Subjects indicated their response by pressing foot pedals, comparably to the tactile

Tactile maintenance				Visual maintenance				Overlapping[c]				Interactions[d]			
Coordinates			Z score	Coordinates			Z score	Coordinates			Z score	Coordinates			Z score
x	y	z		x	y	z		x	y	z		x	y	z	
24	−49	59	>7.0					28	−49	47	3.9	32	−46	57	3.9
16	−72	58	6.6					24	−69	30	3.1	10	−65	73	3.9
								−33	−48	60	3.8				
−34	−47	63	>7.0									−31	−49	58	6.8
40	−38	52	>7.0	30	−47	47	6.0					31	−37	38	3.5
				51	−35	34	4.7					*43*	*−45*	*22*	*−3.0*
				−36	−47	47	5.9	−38	−47	37	3.2				
				48	−63	35	4.1								
												22	−30	−20	2.8
								−13	−41	−11	2.3	−18	−40	−15	>7.0
				41	−69	0	6.2					46	−52	0	4.4
												−58	−55	−10	5.3
−47	−61	−2	>7.0												
49	−49	4	5.1	30	−70	18	5.0								
−44	−72	15	4.5	−44	−61	3	6.2	−45	−64	−1	4.1				
				60	−25	7	5.4					−57	7	−1	3.1
												47	*−21*	*5*	*−3.1*
38	17	−20	4.5												
								29	−65	−8	3.7	33	−65	−10	2.9
				24	−57	−10	5.3					*22*	*−46*	*−2*	*−3.2*
								−32	−48	−17	4.0				
				10	−79	−10	>7.0	−22	−81	−18	2.7				
−9	−80	−8	>7.0	−18	−87	−15	5.2	0	−76	−6	4.4				
								−3	−56	−1	3.5	−24	−71	3	4.2
0	−91	8	>7.0	4	−98	11	6.4	7	−96	7	4.6	1	−99	22	4.0
				26	−84	37	4.6	3	−94	27	2.7	−31	−85	33	3.1
−18	−70	8	5.6	−20	−74	20	4.3	−22	−73	56	3.3	−12	−93	5	6.1
								−8	−84	13	2.8				
26	−81	14	4.5									−6	−52	−3	>7.0
−31	−94	−12	4.3									−25	−87	−11	2.6
14	−23	8	>7.0	18	−31	3	4.3								
−6	−27	1	6.5	−4	−17	17	6.1					−4	−22	8	3.2
				18	−31	3	5.3								
−13	−4	15	6.8									−12	−5	25	4.0
15	−46	−40	>7.0	24	−56	−31	4.6					−28	−63	−41	2.2
38	−46	−22	6.0	−30	−63	−13	5.4					15	−47	−12	6.4
15	−46	−13	>7.0									19	−40	−41	4.3
−20	−44	−14	>7.0												
−34	−51	−36	>7.0									−27	−43	−39	5.3

of significance are provided.
in the corrected Z-score group maps at Z>3.8, $P<10^{-4}$.
($P<10^{-3}$), and required a cluster of 100 contiguous voxels with a *P*-value<0.05.
responding more to visual than tactile maintenance are reported in italic.

condition. Based on behavioral pilot studies, visual matrices were presented for 5 s with an inter-stimulus interval of 5 s. Each time series consisted of 16 consecutive matrices with three/five targets in counterbalanced order. As for tactile stimuli, the order of presentation of the matrices was randomized for each subject, mixing all the different conditions, including variations of a single target as well as the whole pattern of stimuli. During baseline and inter-stimuli periods subjects looked at a white screen.

Image analysis

To analyze functional data, we used the AFNI software package (http://afni.nimh.nih.gov/afni, Cox, 1996). After reconstruction of raw data, all volume three-dimensional registration to the volume collected nearest in time to the high-resolution anatomy, phase-shifting using Fourier transformation to correct for slice acquisition time, spatial smoothing (isotropic Gaussian filter σ=3.4 mm) and

temporal normalization of the images of each run, the statistical analysis was performed. Normalized data were analyzed with multiple regression by using four regressors to model hemodynamic changes associated with our working memory tasks. For both the tactile and visual conditions, the mean response to each stimulus encoding/recognition and mean response during delays between stimuli were modeled by separate regressors. In addition to these regressors, six regressors of no interest derived from the motion correction post-processing analyses were included to factor out signal changes due to head movement. In order to better identify regions significantly involved in the different components of the two sensorial working memory tasks, cortex that responded significantly during maintenance was identified based on the effect of both the regressors that modeled the responses to each stimulus presentation and during delays between stimuli, while brain areas responding to stimulus encoding were isolated based on the effect of the single regressor modeling for the response to each stimulus presentation ($P < 10^{-3}$). Statistical Z-maps were created for each of the contrasts of interest after threshold correction for false discovery rate in multiple comparison. Individual subject Z-maps were then transformed into the standard Tailairach and Tournoux (1988) atlas coordinate system and resampled to 1 mm³. Group Z-maps were computed by multiplying the cross-subject average of Z-values by the square root of the sample size. Activations were anatomically localized in the averaged data on the Talairach transformed T1-weighted images.

Beta weights for the regressors that modeled the mean responses to the different experimental conditions in each task (visual or tactile encoding or maintenance) were used as estimates of the strength of response relative to rest in each significant voxel ($P < 10^{-3}$). For a group analysis, these responses were used in a one-sample t-test to identify brain areas commonly recruited during both tactile and visual maintenance, and in a mixed-effect model ANOVA for a condition (maintenance vs. recognition)×sensory input (tactile vs. visual) comparison to find cortex responding more to visual or tactile maintenance. For all group comparisons, clusters of voxels with $P < 0.05$ and a minimum volume of 100 μL were considered significant.

RESULTS

During the one-back spatial discrimination task of visually and tactilely presented matrices, all subjects achieved more than 90% accuracy for all the experimental conditions and no significant difference between conditions was found.

The tactile spatial working memory task for matrix recognition evoked activity bilaterally in large areas of the hand region of primary and secondary sensorimotor cortex, that extended to the superior parietal lobe (Brodmann's area BA7), the precuneus and dorsally up to the intraparietal sulci (IPS). Consistently, bilateral supplementary motor areas (SMA; medial frontal areas BA6), frontal eye fields (FEF), lateral occipito-temporal cortex (LOT), cerebellum and PFC areas also were activated. The encoding/recognition phase, that is when subjects were actively exploring the matrices, was associated with a recruitment of bilateral middle (BA6, BA8, BA9) and superior lateral (BA9/10) frontal cortex, and a reduced activity in the orbito-frontal and anterior medial (BA10/11) frontal cortex (Fig. 2 and Table 1).

During the maintenance phase, that is when subjects were holding in mind the spatial configuration of the explored matrix, specific activations as compared with the encoding/recognition condition were seen in dorsolateral

areas of middle and superior frontal gyri, and in the anterior cingulate cortex.

During the visual spatial working memory task, subjects consistently recruited brain areas in the posterior parietal and dorsal occipital cortex, integrated in the dorsal visual extrastriate pathway and, specifically, the bilateral IPS, precuneus and posterior parietal lobe. Additional significant increases in neural responses were found bilaterally in a small region of sensorimotor cortex, in the anterior cingulate cortex, the superior and middle frontal gyri and in the LOT. Similarly, during the maintenance of visuo-spatial information, anterior and dorsal portions of bilateral superior and middle frontal gyri (BA9, BA10, BA46) and the anterior cingulate cortex were significantly recruited across subjects (Fig. 2 and Table 1).

During both visual and tactile maintenance, subjects significantly recruited a common fronto-parietal network that extended bilaterally from dorsal lateral areas of PFC (BA8, 9) and anterior cingulate to fronto-parietal sensorimotor areas, and toward posterior parietal cortices, including precuneus and IPS (Fig. 3 and Table 1).

When brain response to tactile maintenance was compared with brain activity during visual maintenance, a greater activation was present in bilateral inferior and left middle PFC (BA9, 6 and 44), and in bilateral somatosensory cortex, SMA (BA6), and IPS. In contrast, a higher neural response was found in the anterior cingulate cortex (BA24-32), medial and postero-superior PFC (BA8) during visual as compared with tactile maintenance (Fig. 3 and Table 1).

DISCUSSION

In this study, patterns of neural responses were measured with fMRI while subjects performed a one-back spatial discrimination task of visually and tactilely presented matrices that were equivalent in terms of difficulty (memory load) across the two sensory modalities.

We demonstrated that similar fronto-parietal networks are recruited across spatial information processing, specifically the high-order association brain areas that include the posterior parietal cortex and the dorsolateral PFC. Prefrontal and parietal regions are anatomically and functionally associated in spatial discrimination (Corbetta, 1998; D'Esposito et al., 1998; LaBar et al., 1999; Goldman-Rakic and Leung, 2002; Wager and Smith, 2003), and previous functional brain studies clearly isolated fronto-parietal mnemonic processing during spatial vs. nonspatial working memory tasks (Smith et al., 1995; Courtney et al., 1996; Belger et al., 1998). Tactile-based as compared with visually-based spatial working memory, however, relies on specific posterior cortical areas, involving somatosensory and parietal cortices, but also on more anterior brain regions, such as middle and anterior PFC, the precentral motor area, and the anterior cingulate.

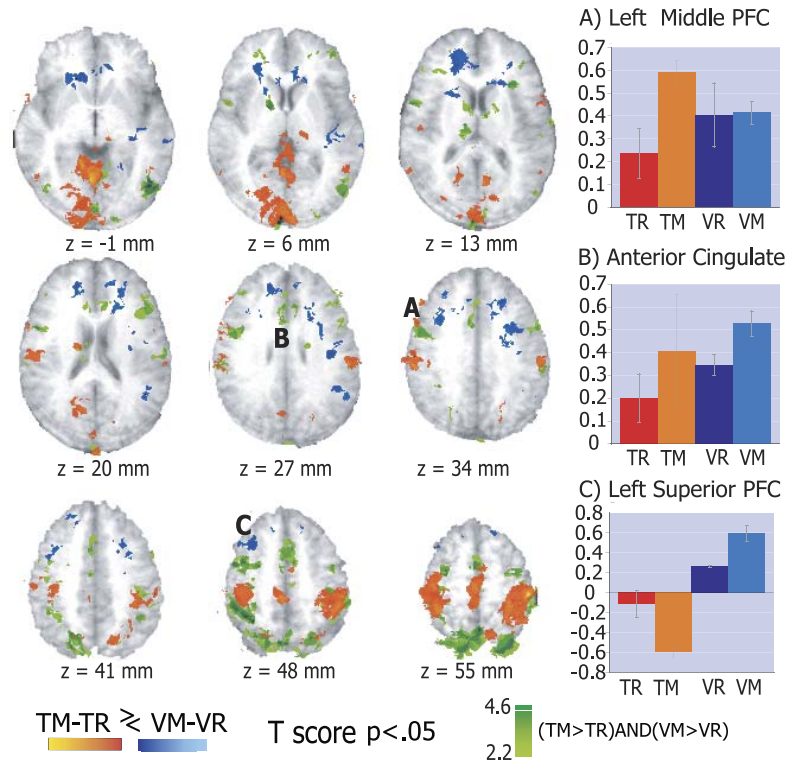Activity in the primary somatosensory cortex seems to be modulated by selective tactile attention, while the

Fig. 3. Condition (maintenance vs. encoding/recognition)×sensory input (tactile vs. visual) comparison. Brain regions showing significant increases in neural activity during tactile or visual maintenance have been superimposed onto nine group-averaged coronal slices in red or blue colors, respectively. Cortical areas commonly activated during both tactile and visual maintenance as compared with encoding/recognition tasks are shown in green. Bar graphs reported group-averaged percent BOLD signal changes±standard errors in three representative brain areas for tactile encoding/recognition (TR—dark red bars) and maintenance (TM—light red bars), or visual encoding/recognition (VR—dark blue bars) and maintenance (VM—light blue bars).

secondary somatosensory cortex modulates selective processing of tactile information and supports sensori-motor integration (Harris et al., 2002; Postle et al., 2004). Parietal cortical areas and secondary somato-sensory cortex in conjunction with ventral premotor cortex have been shown to build the basic circuit for tactile object identification (Binkofski et al., 1999; Amedi et al., 2001; Pietrini et al., 2004). In our study, short-term storage of tactile information for object discrimination relied also on left PFC contribution, consistent with previous findings (Stoeckel et al., 2003). The additional recruitment of the anterior cingulate cortex, that extended to the prefrontal SMA, has been observed also in previous functional studies of response selection and motor planning (Picard and Strick, 1996; Paulus et al., 2002).

These neurophysiological data are consistent with an interpretation of the working memory system that takes into account not only differences between partially independent mechanisms but specific interactions and more complex patterns of activation during working memory tasks (Cornoldi and Vecchi, 2003). Our data on the interaction between tactile and visual stimuli clearly demonstrate that, beyond independent peripheral processes, information processes involved in the generation of higher-order mental representation are sub-

served by a unique integrated neural network. Data show that, during tactile-based spatial processes, areas traditionally associated with both visual imagery and visual perception were activated. There is an interesting analogy with data reported in behavioral studies that investigated spatial images in congenitally blind individuals (e.g. Vecchi et al., 2004). Indeed, the work by Vecchi and colleagues (2004) highlighted that congenitally blind people seem to use similar cognitive mechanisms as sighted individuals while carrying out spatial position tasks, despite differences in performance accuracy and time latencies. Further functional brain studies in sighted and congenitally blind individuals are needed to understand the exact role of visual cortices in spatial detection and spatial imagery task, and behavioral findings indicating that visual experience is not required for spatial working memory to develop. Both tactile and visual stimuli may eventually lead to similar patterns of neural activation as a consequence of the nature of the to-be-generated mental representation, e.g. spatially-based images. These data will in turn support and extend empirical evidence suggesting a supramodal organization in object-based representation (Pietrini et al., 2004). Moreover, these data confirm the need for theoretical models of working memory that address specifically the issue of the interaction between modality-

specific and supramodal mechanisms, involving peripheral independent sensory systems in association with higher-order cognitive structures (Cornoldi and Vecchi, 2003).

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