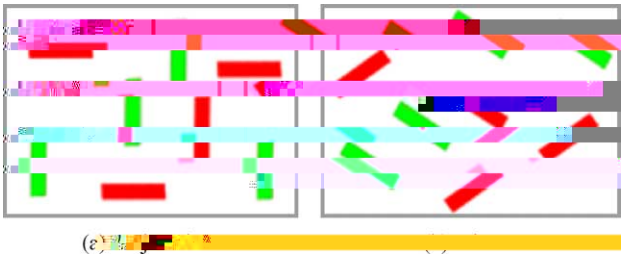

Fig. 1. Diagrammatic representation of the visual search tasks used in the study.

302; 1194) and the experiment protocol was approved by the local research ethics committee.

Each participant completed two types of visual search tasks. One was a conjunction task, where the target was a vertical red bar and the distracters were green vertical and red horizontal bars (Fig. 1a), i.e., two feature classes (e.g. color and orientation) are present in the array and spatial attention and feature binding are required. The other was a subset task, where again two features are present but only one of them is needed in order to group stimuli together (the subset) to allow parallel processing without the need for feature binding [9]. In which the target was a red bar of a particular orientation, among green distracters of the same orientation and red distracters of a different orientation (Fig. 1b). The orientations (0–90° in 10 steps) of the bars changed randomly from trial to trial with a minimum difference of 30° between the two orientations present on any trial. The target was therefore the red bar with the odd-one-out orientation. The visual display subtended a maximum size of 12° horizontally and 8° vertically. Three stimulus set sizes (i.e., the number of bars in each stimulus view) (4, 8 and 12) were randomly varied from trial to trial and the target was present in 50% of trials.

Each task condition was performed in a separate run during brain imaging. The functional scan followed a classic block design where the stimuli were presented in six blocks (54 s of each block with 12 trials), alternating with fixation periods of 27 s. In both conditions, a single trial proceeded as follows: a central fixation cross (+) was presented for 500 ms, followed by the array of visual stimuli for 3000 ms. A blank interval of 1000 ms intervened between trials. In all task conditions, participants were required to detect predefined target stimuli amid an array of distracting items and respond with a right-hand button press. Participants were instructed to respond as quickly as possible, while avoiding errors. Reaction time (RT) and accuracy were recorded. Before experiment the participants were given enough practice and familiarized with the procedures.

The fMRI experiment was performed using a 1.5-T MRI system (Siemens Sonata, Germany). For functional imaging, 16 slices [(slice thickness = 5 mm, slice gap = 1 mm; flip angle (FA) = 90°; matrix size = 64 × 64; field of view (FOV) = 220 mm × 220 mm)], were acquired using a gradient-echo echo-planar imaging (GE-EPI) sequence with a repetition time (TR) of 4500 ms, and an echo time (TE) of 50 ms. Each functional time series consisted of 108 volumes and lasted 486 s. Additionally, structural three-dimensional data sets were acquired in the same session using a T1-weighted sagittal MP-RAGE sequence (TR = 1900 ms, TE = 3.93 ms; matrix = 448 × 512; thickness = 1.70 mm, gap = 0.85 mm; FOV = 250 mm × 250 mm).

Table 1
Reaction times (mean ± S.D.) and accuracy (percent correct) in the conjunction and subset task in the two subject groups

	Patients	Controls	Between-group significance (P)
Accuracy			
Conjunction	90.36	96.27	<0.01
Subset	87.43	92.29	<0.01
Repeated measure	ns	$P < 0.05$	
RT(ms)			
Conjunction	1241.5 ± 96.4	987.6 ± 84.7	<0.01
Subset	1548.3 ± 87.3	1123.9 ± 78.5	<0.01
Repeated measure	$P < 0.05$	$P < 0.05$	

ns: no significance ($P > 0.05$).

SPM 99 was used for imaging data preprocessing and statistical analysis [10,11]. Functional images were co-aligned with a high-resolution anatomical scan taken in the same session (3D-MPRAGE). Images were transformed into Talairach space [28] and smoothed (effective smoothing for group: 12 mm). The statistical effects of task conditions and subjects were estimated according to the general linear model applied to each voxel in brain space. Statistical comparisions between experimental factors were based on the random-effects model. The different activations between groups and within each group were analyzed using two-way ANOVA. The common brain areas engaged by each search conditions were identified by group analysis between the significant activation in each visual task relative to its baseline. Subsequently a direct voxel-by-voxel t-statistic comparison was performed between the Alzheimer's patients and the healthy elderly. The statistical threshold was set at $P < 0.001$ uncorrected.

Behavioral data: Behavioral accuracy and reaction time (RT) data were summarized in Table 1. The two groups showed higher accuracy in the conjunction task than the subset task ($P < 0.01$), but post hoc comparison revealed that the

Table 2
Anatomical regions activated during the conjunction task ($P > 0.001$)

Age-matched controls					AD patients				
Region (Brodman area)	Voxels	*X*	*Y*	*Z*	Region (Brodman area)	Voxels	*X*	*Y*	*Z*
L-precuneus (BA18)	27717	−26	−68	44	L-superior parietal lobule (BA7)	13813	−36	−42	62
L-superior parietal lobule (BA7)	27717	−32	−56	50	L-inferior occipital gyrus (BA18)	13813	−20	−104	0
L-postcentral gyrus	27717	−50	−32	50	R-superior parietal lobule (BA7)	5280	32	−66	50
R-superior parietal lobule (BA7)	8070	32	−60	48	R-medial occipital gyrus (BA19)	5280	34	−94	6
R-frontal eye fields (BA6)	4030	32	−6	64	R-inferior parietal lobule (BA40)	5280	38	−48	44
R-inferior frontal gyrus (BA47)	4030	56	16	2	R-medial frontal gyrus (BA 10)	1090	44	50	−4
L-basal ganglia	1444	−16	−14	14	L-medial frontal gyrus (BA 46)	476	−48	42	20

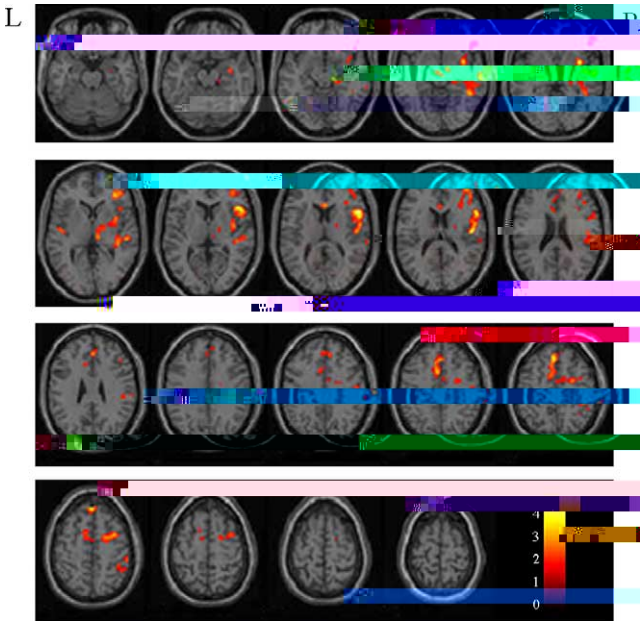

Fig. 3. Cortical activation for the conjuction task compared to the subset task in the controls. Note: R designates the right hemisphere and L designates the left hemisphere.

etal involvement during visual search are possible. Firstly, the parietal cortex could be involved in directing attention serially toward successive locations for the purpose of integrating the constituent features of individual items. In this interpretation, parietal activation reflects both spatial attention and feature binding mechanisms [27,29]. Secondly, the right parietal cortex is not responsible for both selective attention and feature binding, but rather is involved in selecting spatial locations which contained a particular feature variable (such as the color red). When target items can be segmented from neighboring distracters via similarity grouping, detection may not rely on spatial integration. These effects of distracter similarity are reflective of the role of perceptual grouping in visual search and constitute new evidence that it is not the mere search for conjunction targets that activates the superior, posterior parietal lobe [16,32]. Rather, it is the failure of grouping mechanisms to preattentively segment target from distracter items and the subsequent need for feature binding that engages superior parietal cortex. In the absence of these grouping relations, search is mediated by superior parietal-motor regions associated with spatial selection [23]. The binding of features itself is presumably mediated by other areas such as the temporal cortex of the ventral processing stream, which has been suggested to be involved in object representation. Thus, the posterior parietal lobe in visual search may not be bind-specific but rather reflect more general attentional mechanisms.

Other possibly relevant brain regions are the anterior cingulate cortex, thought to be involved in selecting target information from distracting information [17,23] and frontal lobes, thought to be involved in resolving response conflict, both of which may also be abnormal in AD. Disconnection between frontal and posterior parietal areas may mediate the selective disruption of attentional function in AD.

We also compared the conjunction search with subset search. In this comparison, the normal controls showed a higher amplitude in the right prefrontal lobe, temporal cortical regions and parietal lobes compared with the ADr8.6(406.4(imilaria

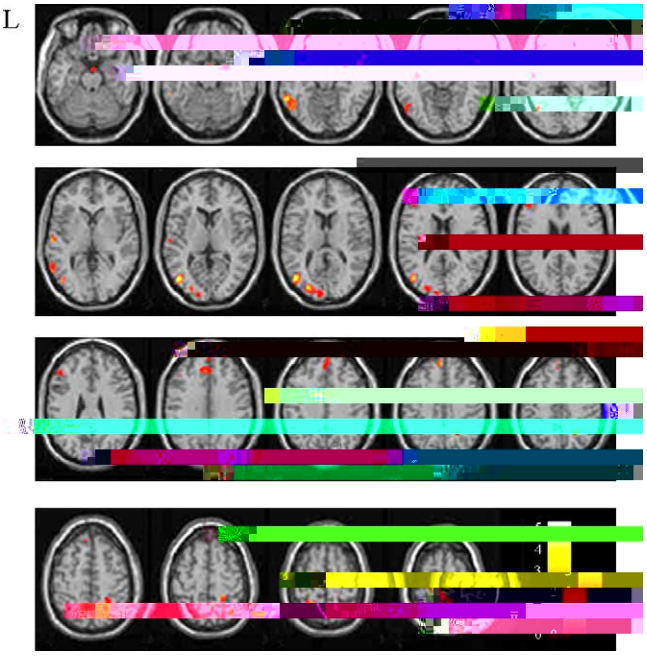

Fig. 4. Cortical activation for the conjuction task compared to the subset task in AD patients. Note: R designates the right hemisphere and L designates the left hemisphere.

increased activation of cortical regions subserving task processing or to the additional activation of regions initially not involved in the task [25,26].