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NeuroImage 41 (2008) 511–524

# Neural correlates of age-related visual search decline: A combined ERP and sLORETA study

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Received 13 November 2007; revised 13 February 2008; accepted 19 February 2008
Available online 6 March 2008

**Differences in the neural systems underlying visual search processes for young (n = 17, mean age 19.6 ± 1.9) and older (n = 22, mean age 68.5 ± 6) subjects were investigated combining the Event-Related Potential (ERP) technique with standardized Low-Resolution brain Electromagnetic Tomography (sLORETA) analyses. Behavioral results showed an increase in mean reaction times (RTs) and a reduction in hit rates with age. The ERPs were significantly different between young and older subjects at the P3 component, showing longer latencies and lower amplitudes in older subjects. These ERP results suggest an age-related decline in the intensity and speed of visual processing during visual search that imply a reduction in attentional resources with normal aging. The sLORETA data revealed a significantly reduced neural differentiation in older subjects, who recruited bilateral prefrontal regions in a nonselective manner for the different search arrays. Finally, sLORETA between-group comparisons revealed that relative to young subjects, older subjects showed significantly reduced activity in anterior cingulate cortex as well as in numerous limbic and occipitotemporal regions contributing to visual search processes. These findings provide evidence that the neural circuit supporting this cognitive process is vulnerable to normal aging. All these attentional factors could contribute to poorer performance of older compared to young subjects in visual search tasks.**


*Keywords:* Aging; Visual Search; Event-related potentials (ERPs); Standardized low-resolution brain electromagnetic tomography (sLORETA)

## Introduction

Visual selective attention is a fundamental human cognitive function that can be defined as the ability to enhance the processing of visual information relevant to our goals and to inhibit the processing of what is irrelevant. This ability is essential for everyday functioning since a large part of natural visual processing involves the discrimination of stimuli that appear at unpredictable locations in complex scenes, surrounded by irrelevant but potentially distracting stimuli. Since visual search tasks capture these qualities of visual scenes, they have been extensively used in studies of selective attention in humans (Luck and Ford, 1998; Luck and Hillyard, 1995). In these tasks, subjects view arrays of stimuli and must indicate whether a predefined target stimulus is present or absent among a variable number of nontarget distractors.

An age-related decline in visual selective attention has been well documented in the behavioral and neuroimaging literature (Kok, 2000; Madden et al., 2005; Raz, 2000), suggesting that older subjects are less able to selectively focus on relevant stimuli than young subjects. In particular, during visual search tasks, it has been reported that older subjects often have substantially more difficulties than young subjects in locating and identifying targets defined by a conjunction of features among heterogeneous distractors, and with increasing number of distractors (Hommel et al., 2004; Madden and Whiting, 2004; McDowd and Shaw, 2000). Influential theories of cognitive aging have attributed decrements in performance with advancing age to a generalized decline in the speed at which information is processed (Salthouse, 1996, 2000). However, it has been also proposed that the age-related deficits in visual search can be accounted for by a decline in inhibitory control functions of selective attention with aging, leading to an age-related decrease in the ability to focus attention to relevant stimuli and to ignore or inhibit the irrelevant distractors (Colcombe et al., 2003; Madden and Whiting, 2004). Additionally, other studies have pointed to more specific mechanisms, such as an age-related decrease in target detectability (Madden et al., 1999), or a reduction in the flexibility of reorienting attention in the visual field (Greenwood and Parasuraman, 1999).

Taking into account that the exact nature of the age-related attentional decline and its neural substrate is not clear, the general

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

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doi:10.1016/j.neuroimage.2008.02.041

aim of the present study was to characterize the age-related changes in selective attention processes involved in the execution of a visual search task, whose electrophysiological correlates have been previously described in young subjects (Luck and Hillyard, 1994). In a previous Event-Related Potential (ERP) study (Lorenzo-López et al., in press), we evaluated for the first time the effects of normal aging on the main visual search-related ERP component, the N2pc (N2-posterior-contralateral), during a feature detection task. Our results showed that this component, which has been validated as an electrophysiological correlate of the allocation of visuospatial attention during visual search (Luck and Hillyard, 1994; Woodman and Luck, 1999, 2003), was significantly delayed and attenuated in older subjects compared to young subjects, suggesting a specific impairment in the allocation of visuospatial attention with advancing age. These findings led us to propose that the age-related deficits in visual search may be partially explained by a specific slowing in the allocation of attention itself, rather than by a generalized slowing of information processing with age. Now, we attempt to extend our previous results by exploring the effects of normal aging on a late ERP component, the P3, which has been shown in previous studies to be sensitive to aging (Iragui et al., 1993; Kutas et al., 1994; Pfefferbaum and Ford, 1988; Pfefferbaum et al., 1984; Polich, 1997). P3 is a large positive waveform with posterior-parietal maximum amplitude and a peak latency of about 300-400 ms in young subjects (for a review see Hruby and Marsalek, 2003). It is closely related to stimulus evaluation processes underlying attention and memory tasks (Polich, 1996, 2003). In our opinion, the study of age-related changes in this component is relevant given that the human visual system consists of several processing streams that operate in parallel (Goodale and Milner, 1992), and it is possible that a deficit in the specific process reflected by the N2pc component is not propagated to different processes at later time points.

Considering the previous arguments, the specific aims of the present study were (i) to localize brain regions predominantly involved in the generation of the P3 component during a feature search task, and (ii) to examine possible age-related differences in P3 neural activation during the processing of different search arrays. For this purpose, EEG was recorded from a group of young and older healthy subjects during the execution of a visual search task, and cortical sources of the P3 component were modeled by the standardized low-resolution brain electromagnetic tomography software (sLORETA; Pascual-Marqui, 2002).

The application of the ERP technique in combination with sLORETA may help understand the contributions of specific selective attention deficits to the observed age-related behavioral decrements in visual search, providing the opportunity to connect directly cognitive behavior to brain function. In particular, the sLORETA method allows the examination of specific sites of neural activation while different visual search arrays are being processed.

## Methods

### *Subjects*

Seventeen young (10 females, mean age 19.6±1.9 years, range 18-24) and 22 older subjects (11 females, mean age 68.5±6 years, range 60-84) took part in the study. All the subjects underwent a semi-structured interview to ensure that they were free from depressive and other psychiatric symptoms and antecedents, and not limited in their activities of daily living. This interview revealed that all were healthy well-functioning subjects without a history of neurological or psychiatric disorder. All had normal or corrected-to-normal visual acuity of at least 20/30, and reported normal color vision. None of the older subjects had received a diagnosis of glaucoma or cataracts, and they performed the Mini-Mental State Examination (MMSE, Folstein et al., 1975) showing normal scores (>28). The experiment was undertaken with the understanding and written informed consent of all subjects, and they were paid for their participation.

### *Stimuli and experimental procedure*

Recordings were made in an electrically shielded and sound attenuated room. Subjects sat on a comfortable armchair at 100 cm viewing distance from a computer screen with a black background and a continuously visible fixation white cross. Subjects were instructed to maintain central fixation on this cross while they performed a visual search task consisting in detecting a singleton target stimulus presented among an array of distractors (stimuli and experimental task were based on those described by Luck and Hillyard, 1994). In each trial, a multi-element search array was presented being composed of eight colored bars subtending a visual angle of 0.3°×0.9°, which were located at random positions in an imaginary rectangle of 9.2°×6.9° of visual angle around the fixation cross. Three types of search arrays were randomly presented: homogeneous arrays, arrays containing a singleton pop-out target defined by orientation, and arrays containing a singleton pop-out nontarget (i.e., an irrelevant distractor singleton that was deviant in a different feature dimension, namely color). Homogeneous arrays ($P$=0.6) consisted of eight blue-horizontal (RGB 0,0,255) identical bars. Target arrays ($P$=0.2) consisted of seven blue-horizontal bars and one blue-vertical bar. Nontarget arrays ($P$=0.2) consisted of seven blue-horizontal bars and one red-horizontal (RGB 255,0,0) bar. The pop-out stimuli (both target and nontarget) were equally likely to appear in the right or left visual hemifield and their location was unpredictable. Each search array was presented for 750 ms, followed by a variable intertrial interval of 900 to 1100 ms during which only the fixation cross was present. The same visual feature (orientation) defined the target across all trials and the subjects were not informed about the appearance of the irrelevant color singleton. All the stimuli and search arrays were created, presented, and controlled using the Presentation software application (Neurobehavioral Systems, Inc., version 0.76). The experimental session was divided into six blocks of trials. Each block consisted of at least 10 orientation pop-out arrays and at least 10 color pop-out arrays presented to each hemifield, and at least 80 homogeneous arrays, to a maximum of 250 arrays in total. The task of the subjects was to indicate as rapidly and accurately as possible whether the target stimulus (a vertical bar) was present or absent in each search array, pressing a button with one hand for target-present trials and another button with the other hand for target-absent trials. Thus, the nontarget arrays required the same response as the homogeneous arrays. Response buttons were counterbalanced across subjects.

The duration of the experiment ranged from 40 to 45 min depending on individual resting periods between experimental blocks.

### *EEG recordings*

The electroencephalogram (EEG) was recorded with a NeuroScan system using scalp electrocaps (ECI, Inc.) with 30 electrodes placed at FP1, FP2, FPz, Fz, Cz, Pz, POz, Oz, F7, F8, F3, F4, C3, C4, T3, T4, PO3, PO4, FCz, CPz, CP3, CP4, T5, T6, P3, P4, FC3, FC4, O1 and

O2 (Extended 10-20 International System). All the active electrodes were referred to the nose tip and grounded with an electrode placed at nasion. Vertical and horizontal EOG activity was recorded bipolarly from above and below the left eye and from the outer canthi of both eyes. Electrode impedances were kept below 10 kΩ. EEG signals were continuously amplified and digitized at a rate of 500 Hz, and filtered on-line with a band pass of 0.05-100 Hz.

### *Data analysis*

#### *Behavioral analysis*

RTs were on-line recorded for the three types of search arrays in all experimental blocks. Only RT values associated with correct responses were considered for data analyses. Hit rates were calculated as the percentage of correct responses with RTs no longer than 1100 ms. A log-transformation was applied to the correct RTs to obtain normally distributed data. These log-transformed RT data were then compared across groups using a mixed design analysis of variance (ANOVA) with age (young, older) as the between-subjects factor and search array (target, nontarget, and homogeneous arrays) as the within-subject factor. Hit rates were also compared across groups using one-way ANOVA with age (young, older) as the between-subjects factor.

#### *ERP analysis*

All EEG data were analyzed using the NeuroScan software (Edit, Version 4.1). The EEG was digitally filtered off-line with a 0.1-30 Hz bandpass filter and segmented into epochs of 1000 ms from 100 ms before array onset (baseline) until 900 ms thereafter. Epochs exceeding ±100 μV and those containing blinks, horizontal or vertical eye movements, or incorrect responses were rejected and excluded from analysis. Average ERPs time locked to target, nontarget and homogeneous arrays were computed for each participant separately. The average number of artifact-free EEG epochs entered into the analyses was 91.8±8.8 for target arrays and 77.6±5 for nontarget arrays in young subjects, and 87.4±14.6 for target arrays and 72.2±12 for nontarget arrays in older subjects. The amplitude of the P3 component was then measured as the maximum positive voltage peak between 300 and 600 ms post-stimulus, relative to the 100 ms baseline in each group of subjects. These amplitude values were subjected to a mixed ANOVA with age (young, older) as the between-subjects factor, and search array (target, nontarget, homogeneous array), localization (anterior, central, posterior), and electrode (anterior: F3, Fz, F4, FC3, FCz, FC4; central: C3, Cz, C4, CP3, CPz, CP4; posterior: P3, Pz, P4, PO3, POz, PO4) as the within-subject factors.

The P3 latency values were determined with respect to the largest positive voltage at the Pz electrode within the same time interval used for measuring amplitude, and subjected to a mixed ANOVA with age (young, older) as the between-subjects factor, and search array (target, nontarget, homogeneous) as the within-subject factor. An alpha level of 0.05 was used for all statistical tests. Whenever appropriate, degrees of freedom were corrected by the conservative Greenhouse-Geisser estimate. When necessary, post-hoc comparisons were performed using the Bonferroni adjustment for multiple comparisons.

#### *sLORETA analysis*

On the basis of the scalp-recorded electric potential distribution, sLORETA was used to compute the cortical three-dimensional distribution of current density at individual P3 latencies for target, nontarget and homogeneous arrays in both age groups. This method finds a particular solution to the non-unique EEG inverse problem by assuming similar activation of neighbouring neuronal sources, followed by an appropriate standardization of the current density, producing images of electric neuronal activity without localization bias (Greenblatt et al., 2005; Pascual-Marqui, 2002; Sekihara et al., 2005).

The previous version of sLORETA (LORETA, Pascual-Marqui et al., 1994) has received considerable validation from studies combining LORETA with other more established localization methods as functional Magnetic Resonance Imaging (fMRI, Mulert et al., 2004; Vitacco et al., 2002), structural MRI (Worrell et al., 2000), Positron Emission Tomography (PET, Dierks et al., 2000; Pizzagalli et al., 2004; Zumsteg et al., 2005), and invasive implanted electrode recordings (Zumsteg et al., 2006). These results serve also as validation for sLORETA, since it is an improved version of the original LORETA method. It is worth emphasizing that deep structures such as the anterior cingulate cortex (ACC, Pizzagalli et al., 2004) and mesial temporal lobes (Zumsteg et al., 2006) can be correctly localized with this method.

Computations were made in a realistic head model (Fuchs et al., 2002), using the MNI152 template (Mazziotta et al., 2001), with the three-dimensional solution space restricted to cortical gray matter. The intracerebral volume is partitioned in 6239 voxels at 5 mm spatial resolution. Anatomical labels as Brodmann areas are reported using an appropriate correction from MNI to Talairach space (Brett et al., 2002). Thus, sLORETA images represent the electric activity at each voxel in neuroanatomic Talairach space (Talairach and Tournoux, 1988) as the squared standardized magnitude of the estimated current density.

The grand mean P3 sLORETA images were computed by calculating in a first step the sLORETA solution for each subject, and in a second step by averaging the current density values across all subjects for each age group and search array, separately. This procedure makes it possible to explore the effects of aging on the patterns of brain activity related to the different search arrays.

The sLORETA software was then used to perform voxel-by-voxel between-group comparisons of the P3 current density distribution. Specifically, in order to identify possible differences in the brain electrical activity between groups (older compared to young), nonparametric statistical analyses of functional sLORETA images (Statistical non-Parametric Mapping; SnPM) were performed for each search array employing a log-F-ratio statistic for independent groups. The results correspond to maps of log-F-ratio statistics for each voxel, for corrected $P<0.05$. As explained in the review by Nichols and Holmes (2002), the SnPM methodology corrects for all multiple comparisons, and at the same time does not require any assumption of Gaussianity.

Table 1
Mean reaction times (RT, in ms) and hit rates (%) and their corresponding standard deviations (in parentheses) as a function of search array in young and older subjects

| Search array | RT | | Hit Rates | |
|---|---|---|---|---|
| | Young | Older | Young | Older |
| Target | 507.6 (51.4) | 628.9 (88.4) | 98 (1.8) | 90.8 (13.1) |
| Nontarget | 463.1 (57.7) | 590.8 (95.8) | 97.8 (2.2) | 91.5 (12.3) |
| Homogeneous | 448.2 (56) | 581.7 (95.9) | 97.9 (2) | 91.3 (12.7) |

## Results

### *Behavioral results*

Mean RTs and hit rates are summarized in Table 1. There was a significant main effect of age on mean RTs ($F(1,37)=31.39$, $P<0.0001$), with slower values in the older group (young: 473±52.9 ms; older: 600.5±90 ms). The effect of the array type on mean RTs was also significant ($F(2,74)=62.19$, $P<0.0001$, $\varepsilon=0.56$), showing that RTs were slowest for target arrays, intermediate for nontarget arrays, and fastest for homogeneous arrays in both age groups (see Table 1). Pairwise comparisons (Bonferroni corrected) revealed that the mean RTs for target, nontarget, and homogeneous arrays were all significantly different from each other ($P<0.0001$). A significant main effect of age was also observed on hit rates ($F(1,37)=4.92$, $P<0.03$; young: 98±1.8%; older: 91.2±12.5%), revealing a lower performance level for the older subjects in the search task.

### *Electrophysiological results*

The ERPs elicited by the three search arrays in young and older subjects are displayed in Figs. 1 and 2 respectively, at anterior, central, and posterior electrode sites.

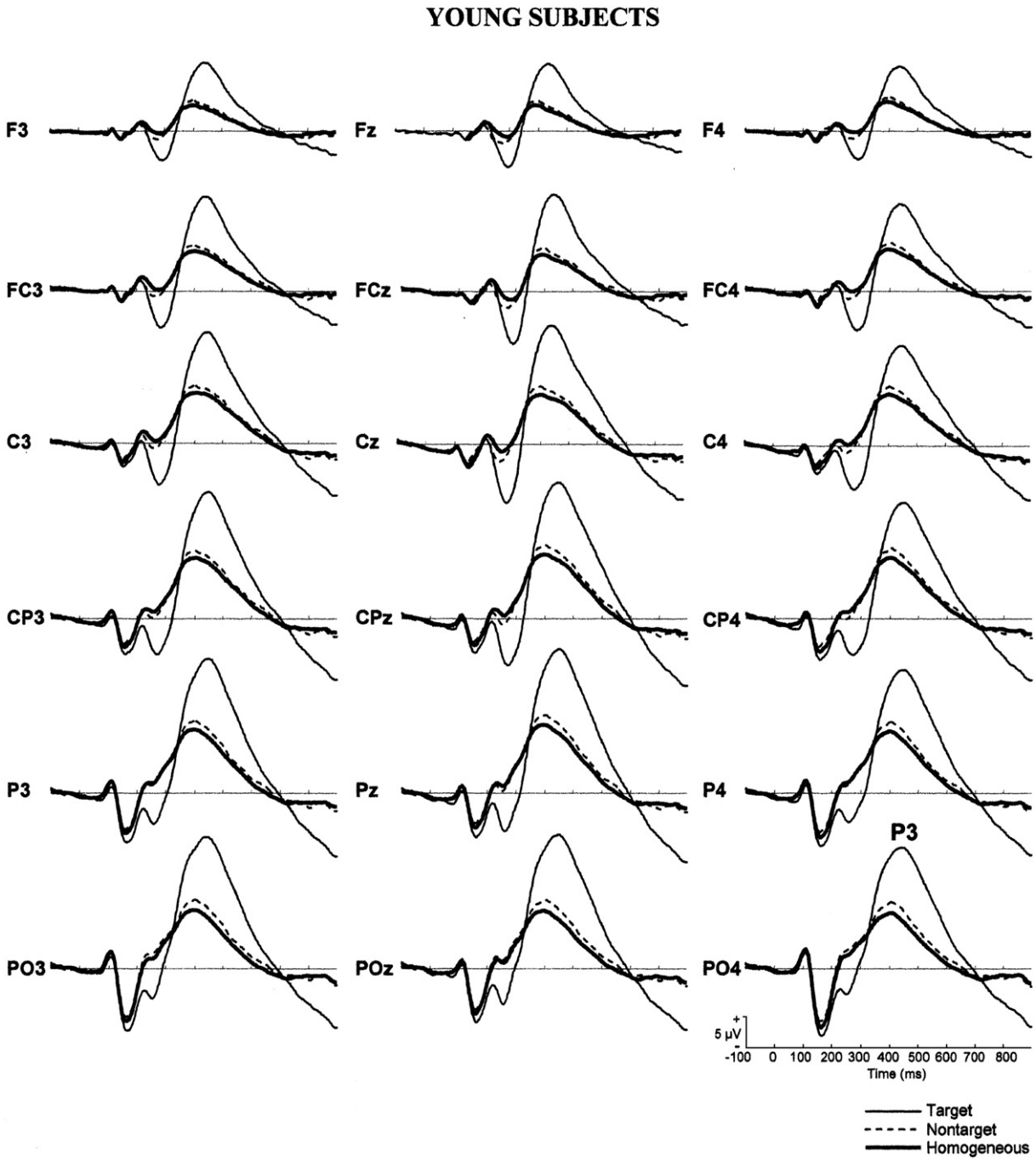


Fig. 1. Grand average ERPs elicited by target, nontarget and homogeneous arrays in the young subjects (n=17) at anterior, central, and posterior electrode sites.

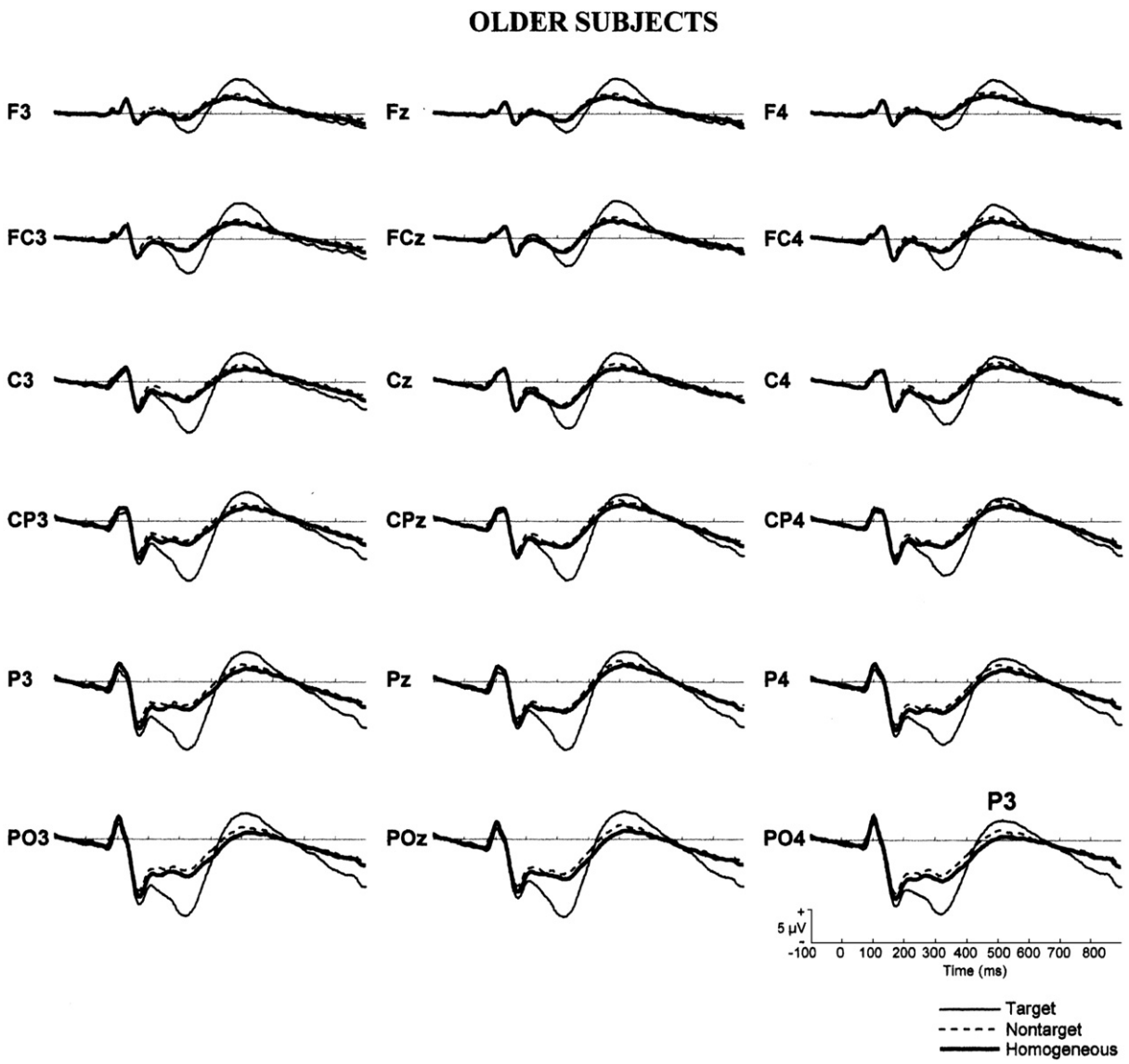


Fig. 2. Grand average ERPs elicited by target, nontarget and homogeneous arrays in the older subjects (n=22) at anterior, central, and posterior electrode sites.

As can be seen in these figures, mean latency of the P3 component was significantly prolonged in older subjects (509.1±38.9 ms) compared to young subjects (420.6±28.6 ms) regardless of search array ($F(1,37)=61.92$, $P<0.0001$), suggesting that the time needed to evaluate all the visual search arrays was significantly increased with age (see Table 2). Additionally, the "age X search array" interaction was also significant ($F(2,74)=6.36$, $P<0.003$). Pairwise comparisons revealed that in young subjects the P3 latency was significantly larger for target arrays than for nontarget ($P<0.007$) and homogeneous ($P<0.002$) arrays, without significant differences between the last two array types ($P=1$). However, P3 latency of older subjects did not differ significantly as a function of search array (target-nontarget arrays: $P=1$, target-homogeneous arrays: $P=1$, nontarget-homogeneous arrays: $P=0.1$).

Table 2
Mean P3 latency in ms (standard deviation) as a function of search array in young and older subjects

| Search array | P3 Latency | |
|---|---|---|
| | Young | Older |
| Target | 444.06 (34.4) | 508.91 (39.2) |
| Nontarget | 410.47 (33.9) | 501.86 (50.3) |
| Homogeneous | 407.29 (30.1) | 516.45 (50.1) |

P3 amplitude was significantly lower in older (3.7±2.3 µV) than in young (11.8±3.2 µV) subjects ($F(1,37)=83.69$, $P<0.0001$), as is apparent from Figs. 1 and 2. Additionally, a significant "age X localization" interaction ($F(2,74)=58.63$, $P<0.0001$) indicated that the P3 voltage distribution across the scalp significantly differed between groups. Pairwise comparisons confirmed that young subjects presented a significant difference of P3 amplitude between anterior, central and posterior scalp locations, with maximal P3 amplitudes at posterior, intermediate at central, and minimal at anterior electrodes (anterior-central: $P<0.0001$; anterior-posterior: $P<0.0001$; central-posterior: $P<0.008$). However, the P3 amplitude of older subjects did not differ significantly between anterior, central

and posterior brain areas ($P=1$), thus being equally distributed over the scalp. Statistical analyses of P3 amplitude also revealed a significant "age X search array" interaction ($F(2,74)=30.99$, $P<0.0001$). Pairwise comparisons showed that in young subjects the P3 amplitude was maximal for target, intermediate for nontarget, and minimal for homogeneous arrays ($P<0.0001$). In older subjects the P3 was larger for target arrays than for either nontarget ($P<0.01$) or homogeneous ($P<0.006$) arrays, without significant difference between nontarget and homogeneous arrays ($P=0.09$).

*sLORETA results*

*sLORETA brain activity patterns at P3 latency*

Fig. 3 displays the sLORETA brain maps representing cortical regions where young subjects showed activation at P3 latency in each of the three search arrays. Table 3 lists the anatomical description and the MNI coordinates corresponding to these regions. As can be seen in Fig. 3, target arrays (A) activated several widely distributed brain regions including frontal (Brodmann areas BA 9/10/25/31), temporal

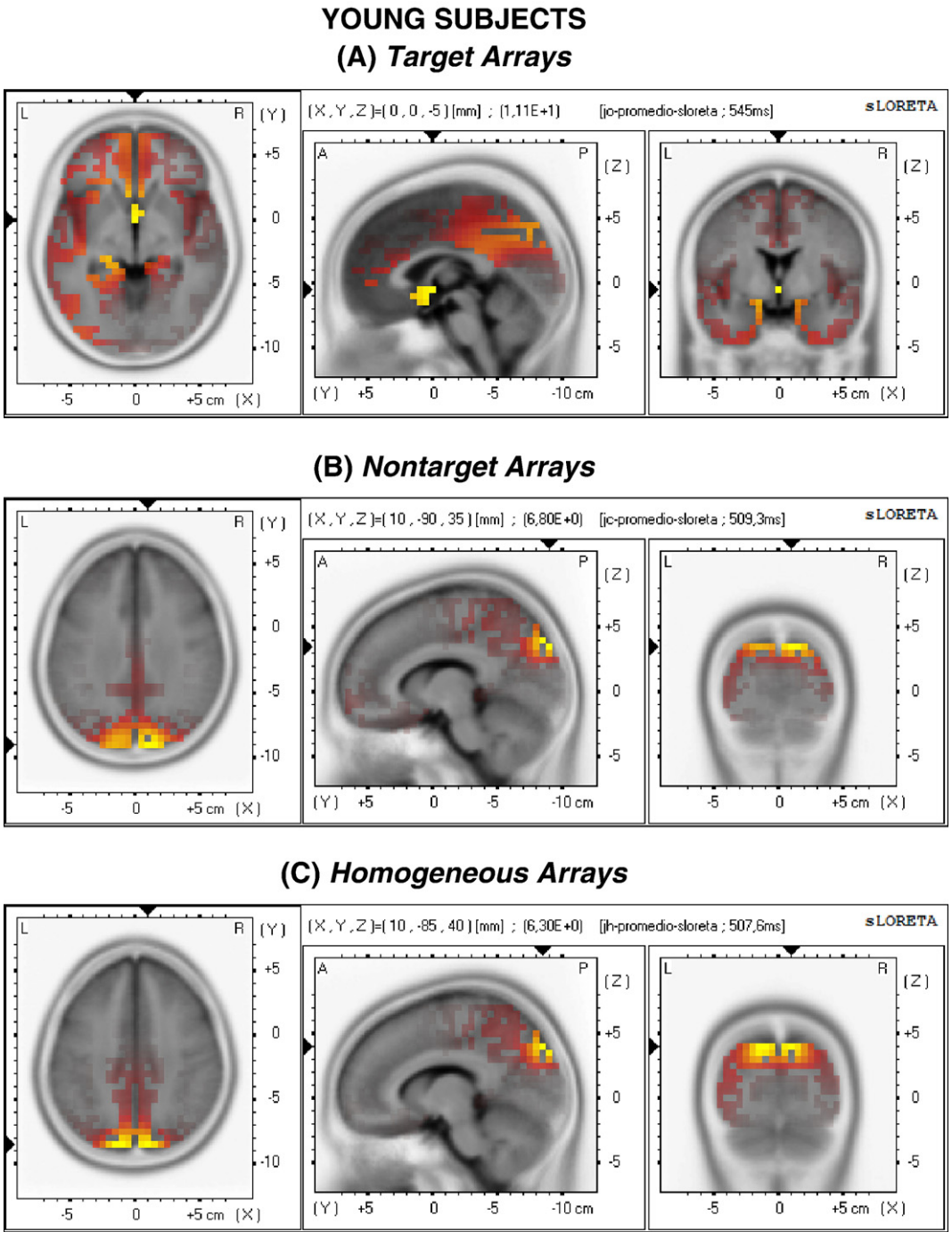


Fig. 3. Grand average P3 sLORETA images showing standardized current density maxima of young subjects (n=17) for target (A), nontarget (B) and homogeneous (C) arrays. Each map consists of axial, sagittal, and coronal planes showing the same activation areas. Maxima are color coded as yellow.

Table 3
Locations of P3 current-density activity maxima observed in young subjects as a function of search array

| Anatomical region (BA) | MNI Coordinates |
|---|---|
| *(A) Target* | |
| Anterior Cingulate (25) | (0, 0, −5) |
| Middle Frontal Gyrus (9/10) | (0, 40, 30) |
| | (5, 65, 5) |
| Superior Frontal Gyrus (10) | (−5, 60, −5) |
| Subcallosal Gyrus (25) | (0, 10, −15) |
| Paracentral Lobule (31) | (0, −20, 45) |
| Superior Temporal Gyrus (21) | (−55, −15, −5) |
| Parahippocampal Gyrus (37/35) | (−25, −45, −10) |
| Superior Parietal Lobule (7) | (30, −55, 50) |
| Precuneus (7/31) | (0, −65, 30) |
| Medial Occipital Gyrus (18) | (−30, −95, 5) |
| Cuneus (19/23) | (−10, −80, 35) |
| | (−15, −75, 10) |
| *(B) Nontarget* | |
| Cuneus (19) | (10, −90, 35) |
| *(C) Homogeneous* | |
| Precuneus (19) | (10, −85, 40) |

BA: Brodmann area; MNI: Montreal Neurological Institute coordinates.

(BA 21/35/37), parietal (BA 7/31) and occipital areas (BA 18/19/23), with the highest level of activation localized in the anterior cingulate cortex (ACC; BA 25). However, for nontarget (B) and homogeneous (C) arrays strong activations were estimated by sLORETA around bilateral occipital regions corresponding to visual extrastriate cortex (BA 19).

On the other hand, Fig. 4 displays the sLORETA maps corresponding to older subjects in each search array, and Table 4 lists the anatomical description and the MNI coordinates of activated regions. As can be seen in Fig. 4, the maximal neural activation was localized in prefrontal cortex (BA 11), which was active during the whole task regardless of search array type.

*sLORETA between-group comparisons*

Fig. 5 shows sLORETA statistical nonparametric maps comparing electric neuronal activity of young and older subjects for target (A), nontarget (B) and homogeneous (C) arrays at P3 latency. Note that these maps represent log-F-ratio statistics computed on each search array comparing young and older subjects. Blue colored areas are indicative of brain areas that were significantly less activated at $P<0.05$ in older subjects compared with young subjects. A significant age-related increase of activation was not observed in any cerebral region. Table 5 lists brain regions, with MNI coordinates, where the SnPM log-F-ratio statistic for independent groups achieved statistical significance for each search array. As can be seen in Fig. 5 and Table 5, for target arrays (A), sLORETA between-group comparisons revealed significantly less current density (activation) for older subjects in several brain areas (log-F ratio = −1.36, corrected $P<0.05$), predominantly including the occipitotemporal visual pathway and the frontal cortex. Specifically, the older subjects showed a significant bilateral hypoactivation in limbic regions corresponding to parahippocampal gyrus (BA 27/28/30/35/36) as well as in occipitotemporal regions corresponding to lingual (BA 19) and fusiform gyrus (BA 37). An age-related hypoactivation of left temporal areas including middle (BA 21/22/37) and superior (BA 22) gyrus was also observed. Finally, an age-related hypoactivation was observed affecting ACC (BA 24/25/32).

As illustrated in Fig. 5 and Table 5, for nontarget (B) and homogeneous (C) arrays, between-group comparisons revealed significantly (nontarget: Log-F-ratio = −1.06, $P<0.05$; homogeneous: Log-F-ratio = −1.27, $P<0.05$) less activation for older subjects, predominantly in left occipitotemporal regions including parahippocampal gyrus (BA 36), and middle (BA 21/37), superior (BA 41), and inferior (BA 21/37) temporal gyrus.

## Discussion

In the present study, ERPs were recorded from a group of young and older healthy subjects during the execution of a feature search task, and the cortical sources of the P3 visual component were modeled by sLORETA software. The specific aims here were to localize the brain regions involved in the generation of this component during visual search, and to examine possible age-related differences in P3 neural activation during the processing of different search arrays (target, nontarget and homogeneous arrays).

*Behavioral execution*

The observed age-related delay in RTs and reduction in hit rates irrespective of the search array are in line with previous behavioral studies showing that older subjects are slower and less accurate than young subjects in visual search tasks (Hommel et al., 2004; Madden and Whiting, 2004; McDowd and Shaw, 2000).

*Latency and amplitude of P3 component*

Latency and amplitude of the P3 component have been considered useful electrophysiological indices for quantifying the effects of age on neural function and processing resources that are activated during cognitive task performance. In particular, P3 latency has been considered an indicator of the speed of cognitive processing (Coles et al., 1995; Kutas et al., 1977; McCarthy and Donchin, 1981), and P3 amplitude as an index of the allocation of attentional brain resources (Kok, 1997; Polich, 1996; Polich and Kok, 1995).

It is important to note that the experimental task used in the present study differs from the traditional oddball paradigm typically used to elicit P3. In this regard, although there are some similarities between the visual three-stimulus oddball paradigm and the present visual search task (both imply infrequent target detection and include the presentation of infrequent irrelevant nontarget stimuli), the nature of the tasks and their response requirements are different. Specifically, the classic oddball task implies the sequential presentation of a repetitive (standard) stimulus and an infrequent stimulus that is designated as the target to which subjects must respond while ignoring the standard (which does not require any response). However, in visual search tasks subjects must rapidly shift their spatial attention among stimuli that are presented simultaneously on the visual display (multiple-elements stimulus arrays). The subjects are instructed to detect a predefined target surrounded by a variable number of competing irrelevant stimuli (distractors), and to press one button for target-present arrays and another button for target-absent arrays (i.e., all the search arrays require an overt response).

Despite the mentioned differences in task paradigm, the age-related effects on P3 component are in good agreement with those previously reported. Thus, in accordance with many previous studies

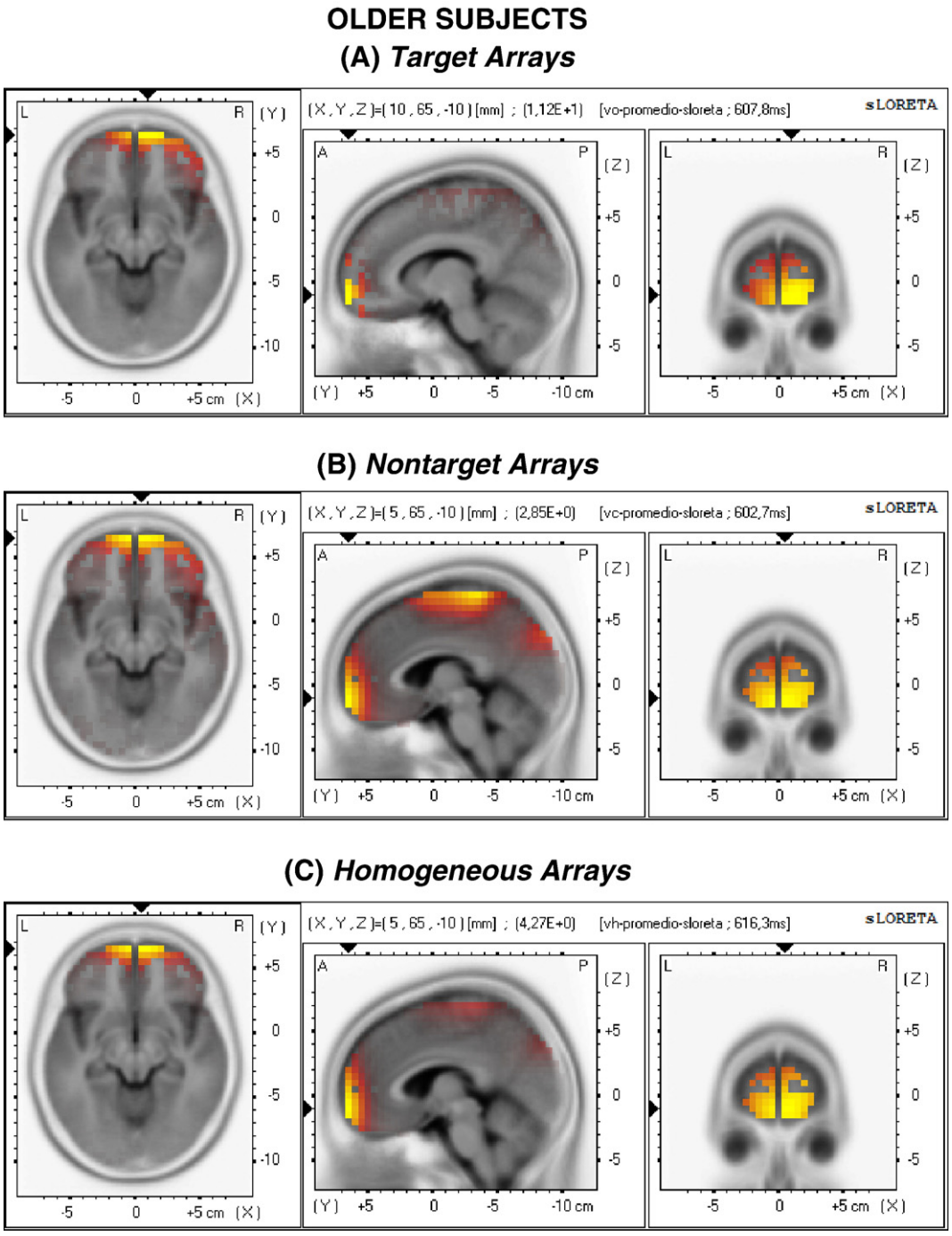


Fig. 4. Grand average P3 sLORETA images showing standardized current density maxima of older subjects (n=22) for target (A), nontarget (B) and homogeneous (C) arrays. Each map consists of axial, sagittal, and coronal planes showing the same activation areas. Maxima are color coded as yellow.

(Iragui et al., 1993; Kutas et al., 1994; Pfefferbaum and Ford, 1988; Pfefferbaum et al., 1984; Polich, 1997), P3 latency was significantly prolonged with age regardless of search array. Since, as previously stated, P3 latency has been considered a sensitive measure of the time needed to evaluate the visual stimuli, we can conclude that older subjects showed a significantly slower speed than young subjects in evaluating each search array. This result therefore suggests that delayed RTs observed in searching visual stimulus may be partially due to an age-related delay in the time needed to evaluate the stimuli.

With regard to P3 amplitude, in agreement with previous studies (Pfefferbaum and Ford, 1988; Polich, 1997), we observed a significant reduction with age irrespective of search array, suggesting a possible decline in the attentional resources in older subjects during the entire task. Since we did not perform single-trial analysis of our data, we cannot discard the possibility that higher latency-jitter in older subjects could contribute in part to the observed P3 amplitude differences between age groups. Nevertheless, it is important to note that in previous electrophysiological studies in which

Table 4
Locations of P3 current-density activity maxima observed in older subjects as a function of search array

| Anatomical region (BA) | MNI Coordinates |
|---|---|
| *(A) Target* | |
| Orbital Gyrus (11) | (4, 50, −19) |
| Superior Frontal Gyrus (11) | (10, 65, −10) |
| *(B) Nontarget* | |
| Orbital Gyrus (11) | (5, 51, −19) |
| Superior Frontal Gyrus (11) | (5, 65, −10) |
| *(C) Homogeneous* | |
| Orbital Gyrus (11) | (5, 45, −21) |
| Superior Frontal Gyrus (11) | (5, 65, −10) |

BA: Brodmann area; MNI: Montreal Neurological Institute coordinates.

P3 amplitudes were measured on single-trials (Ford and Pfefferbaum, 1991; Lorenzo-López et al., 2007), similar P3 reductions have been reported in old age regardless of the existence of higher age-related latency variability. Thus, it is unlikely that the significant age-related P3 reductions can be entirely due to greater latency variability with age.

Finally, target arrays elicited enlarged P3 component compared to nontarget and homogeneous arrays in both age groups. This significant P3 amplitude reduction for nontarget and homogeneous arrays suggests that these arrays were not processed as fully as the target arrays.

The significant RT and latency prolongation, and the amplitude reduction of P3 component observed in older subjects, suggest an age-related decline in the intensity and speed of visual cognitive processing that imply a reduction in attentional resources and a slowing down of evaluation time with aging during visual search. These results extend our previous findings on the effects of normal aging on feature visual processing during visual search (Lorenzo-López et al., in press), suggesting that the age-related search decline appears to imply both an alteration in the visuospatial attention shift to target location (N2pc) and in the later stimuli evaluation processes (P3).

### *sLORETA functional images of P3 neuronal electrical activity*

P3 sLORETA images showed evidence of a clear neural differentiation in young subjects, who presented a high degree of specificity in their brain activity patterns depending on the search array presented. Specifically, strongest brain activation was found for target arrays. In fact, the main activity of the P3 component for these arrays was localized in the ACC, with contribution of multiple widely distributed brain regions, including frontal (middle frontal gyrus, superior frontal gyrus, subcallosal gyrus, paracentral lobe), temporal (superior temporal gyrus, parahippocampal gyrus), parietal (superior parietal lobe, precuneus), and occipital (middle occipital gyrus, cuneus) areas. This finding is in line with the results of several neuroimaging and neuropsychological studies demonstrating the existence of a complex network of several distributed and interconnected cortical and subcortical brain areas that plays a key role in the control of visual selective attention in humans, and that includes critical components in frontal areas (Cabeza and Nyberg, 2000; Corbetta et al., 2000; Kastner and Ungerleider, 2000; Posner and Dehaene, 1994; Woldorff et al., 2004). Moreover, the ACC has been proposed to be an important component of the anterior attentional control system (Posner and Petersen, 1990), and its involvement in selective attention to visual stimulation has received substantial theoretical and experimental support (Cabeza and Nyberg, 1997; Mangun and Hillyard, 1995; Posner and Raichle, 1994). In this regard, the ACC could play a relevant role in visual search processes, which involve the selective attention to specific predefined relevant features as well as the inhibition of other irrelevant features (Pardo et al., 1990; Posner and Raichle, 1994; Vogt et al., 1992).

As noted above, sLORETA revealed intracerebral sources of P3 electric activity to target arrays in a widely distributed brain network, including frontal, temporal, parietal, and occipital regions. These locations of activity considerably overlap with brain regions that have previously been suggested to be involved in discriminating visual features under conditions of selective attention (Cabeza and Nyberg, 1997, 2000; Corbetta et al., 1991). Furthermore, these data support the suggestion that there are multiple generators of scalp-recorded visual P3. In fact, the majority of these brain regions are similar to those identified in previous fMRI studies in which the neural generators of the P3 component have been explored during visual oddball tasks (Ardekani et al., 2002; Bledowski et al., 2004; Clark et al., 2000). Thus, our study partly uncovers similar results, which are extended by the new finding of the parahippocampal activation associated to P3 generation during visual search. In this regard, taking into account the spatial nature of the search arrays presented to the subjects and the involvement of the parahippocampal gyrus in working memory processes during spatial tasks (Campo et al., 2005a,b; Ranganath and D'Esposito, 2001), this activation might be related to working memory mechanisms activated by young subjects, which are necessary to correctly evaluate the stimuli during visual search (i.e., the generation and active maintenance of a neural template of the stimulus features to be searched, followed by the posterior comparison of each search array with this neural representation).

For both nontarget and homogeneous arrays, the maximal P3 activity was, however, localized in bilateral extrastriate visual areas, which have been related to visuoperceptual processing. This supports the notion that in these arrays, the search process was primarily guided by information available in the visual cortex without the involvement of attentional control processes outside visual areas.

In older subjects, the neural activity patterns elicited by different search arrays were less distinctive than in young subjects. In particular, the maximal neural activation was localized in bilateral prefrontal cortex corresponding to Brodmann area 11, which was active during the whole task regardless of search array. These findings suggest the existence of less neural specialization or functional differentiation for search array types with normal aging. In this regard, there is previous evidence from functional neuroimaging studies that older subjects show less specificity or differentiation in brain recruitment while performing cognitive tasks. For example, Park et al. (2004) demonstrated that neural structures become significantly less functionally differentiated and specialized with age in ventral visual cortex to different visual categories (faces, houses, pseudowords, and chairs).

Previous functional neuroimaging data have also provided evidence that older subjects recruit additional brain regions (particularly in prefrontal cortex; PFC), different from those activated by the young, in order to correctly perform cognitive tasks (Cabeza, 2002; Cabeza et al., 2002; Grady et al., 1992, 1994; Madden et al., 1997). This paradoxical neural pattern has been interpreted in terms of

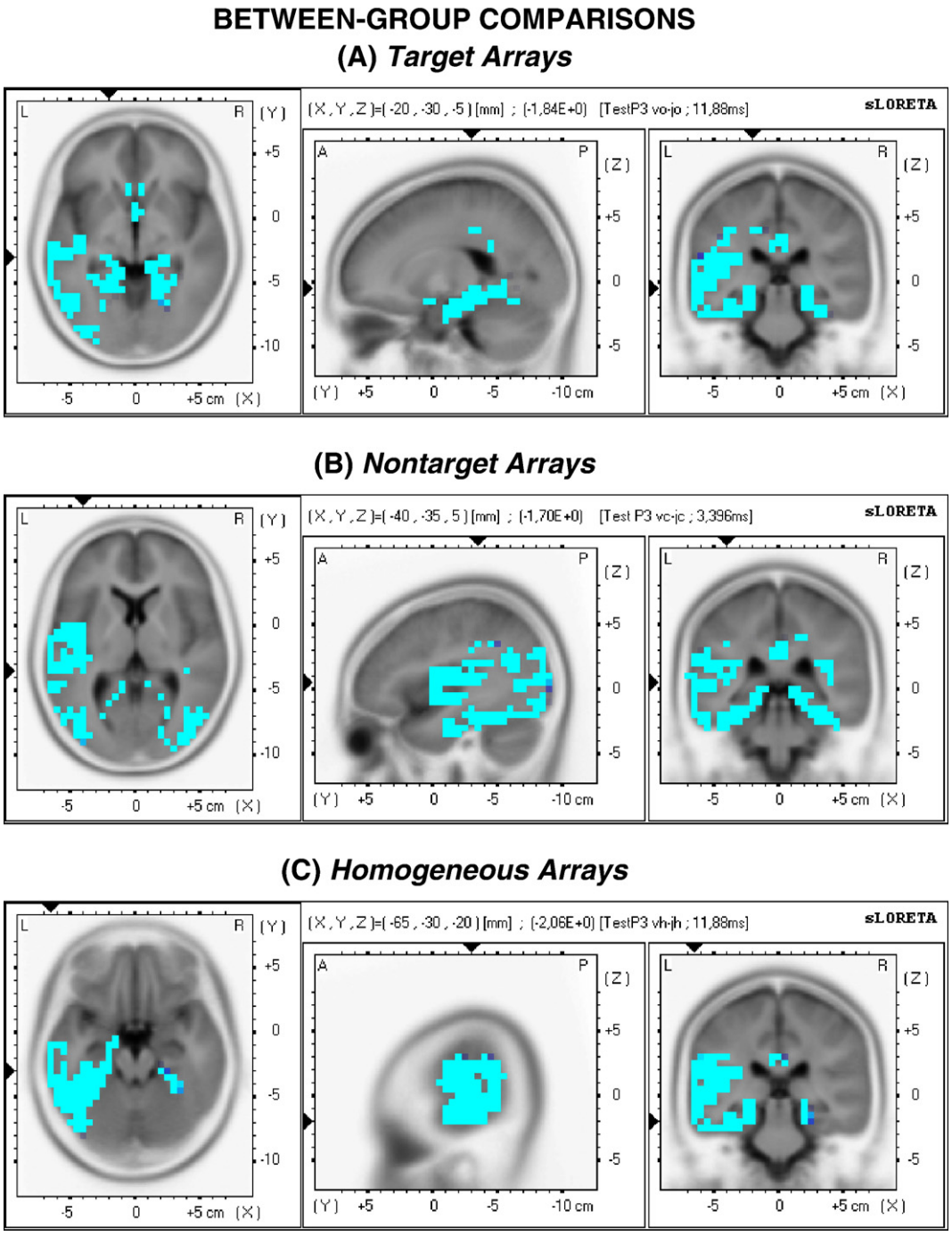


Fig. 5. sLORETA-based statistical nonparametric maps (SnPM) comparing the standardized current density values between young (n=17) and older (n=22) subjects for target (A), nontarget (B) and homogeneous (C) arrays at P3 latency. Significantly reduced activation (corrected $P<0.05$) for older subjects compared to young subjects is displayed in blue color. L=left, R=right, A=anterior, P=posterior.

functional compensation for a decline in the efficiency of processing in task-relevant neural regions (Cabeza, 2001, 2002; Cabeza et al., 2004; Gutchess et al., 2005). Thus, the compensation view suggests that this age-related PFC activation may be beneficial for cognitive performance (Reuter-Lorenz, 2002; Reuter-Lorenz et al., 2000). The strongest evidence in favor of this hypothesis comes from comparisons between high- and low-performing older subjects, which have suggested that an increased prefrontal activation was related to superior performance (Cabeza et al., 2002; Reuter-Lorenz, 2002). However, these additional prefrontal activations in older subjects have been alternatively interpreted in terms of a difficulty in recruiting specialized neural mechanisms needed for task execution (dedifferentiation hypothesis; Logan et al., 2002; Lorenzo-López et al., 2007; Milham et al., 2002). In this regard, it is important to note that in the present study the performance of older subjects during the visual search task was significantly worse than that of the young. Therefore, the presence of maximal prefrontal P3 activity throughout the three search arrays could not be interpreted as a compensatory recruitment.

Table 5
Brain regions that showed significant differential activation between age groups as a function of search array

| Anatomical region (BA) | MNI Coordinates | *Log-F-ratio* |
|---|---|---|
| *(A) Target* | | |
| Older<Young | | |
| L Parahippocampal Gyrus (27/28/35/30/36) | (−20, −30, −5) | −1,84** |
| | (−20, −25,−10) | −1,83** |
| | (−20, −25, −20) | −1,79** |
| | (−15, −40, −10) | −1,77** |
| | (−30, −30, −25) | −1,75** |
| L Fusiform Gyrus (37) | (−30, −45, −20) | −1,74** |
| L Lingual Gyrus (19) | (−15, −45, −5) | −1,68** |
| R Parahippocampal Gyrus (35/28/36) | (20, −35, −10) | −1,62** |
| L Middle Temporal Gyrus (37) | (−45, −60, −5) | −1,55* |
| L Superior Temporal Gyrus (22) | (−45, −20, −5) | −1,54* |
| L Middle Temporal Gyrus (21/22) | (−65, −35, −5) | −1,51* |
| R Fusiform Gyrus (37) | (25, −50, −15) | −1,50* |
| R Lingual Gyrus (19) | (25, −65, 0) | −1,42* |
| Anterior Cingulate (25/32/24) | (0, 15, −10) | −1,59* |
| | (5, 20, −10) | −1,48* |
| | (5, 25, −5) | −1,42* |
| Older > Young | No significant activation differences | |
| *(B) Nontarget* | | |
| Older<Young | | |
| L Parahippocampal Gyrus (36) | (−20, −40, −10) | −1,78** |
| L Superior Temporal Gyrus (41) | (−40, −35, 5) | −1,70** |
| L Middle Temporal Gyrus (21/37) | (−65, −30, −10) | −1,54** |
| | (−60, −45, −10) | −1,48** |
| Older > Young | No significant activation differences | |
| *(C) Homogeneous* | | |
| Older<Young | | |
| L Middle Temporal Gyrus (21) | (−65, −30, −20) | −2,06** |
| L Inferior Temporal Gyrus (21/37) | (−60, −35, −20) | −2,01** |
| | (−45, −45, −20) | −1,88** |
| L Parahippocampal Gyrus (36) | (−45, −50, −20) | −1,80** |
| L Superior Temporal Gyrus (41) | (−40, −35, 5) | −1,70** |
| Older > Young | No significant activation differences | |

**=corrected $P<0.01$, *=corrected $P<0.05$, R=right, L=left.
BA: Brodmann area; MNI: Montreal Neurological Institute coordinates.

As noted, sLORETA data indicated that a different set of brain structures was active at P3 latency in young and older subjects. It is possible that these changes in sLORETA P3 source distribution between age-groups may be ascribed to changes in the strategy used for solving the search task. In this regard, older subjects appear to use a more effortful task strategy that relied on the controlled processing abilities of prefrontal cortex. Functional neuroimaging data have provided compelling evidence that the prefrontal areas are crucial for the executive control of attention to environmental events, playing an important neurophysiological role in both the retrieval and the maintenance of information in working memory (Cabeza et al., 1997). Thus, a possible interpretation is that the age-related prefrontal maximal activity reflects the recruitment of executive processes, which, for older subjects have to be continuously engaged in order to manage the working memory demands of the search task (to encode, store, compare, and retrieve information). In this regard, aging has been consistently associated with a decline in visuospatial working memory processes (Jonides et al., 2000; McEvoy et al., 2001).

### *sLORETA between-group comparisons*

Between-group comparisons of sLORETA data revealed an age-related hypoactivation of several brain areas activated by young subjects that may be crucial in visual feature search. First, for target arrays, the statistical nonparametric analysis showed a significant age-related hypoactivation of bilateral limbic regions of temporal-medial lobe corresponding to the parahippocampal gyrus, which has been shown to be involved in the processing of visuospatial scenes (Bar and Aminoff, 2003; Epstein and Kanwisher, 1998). This parahippocampal hypoactivation might be related to structural brain changes in medial temporal areas with aging. In this respect, the parahippocampal region has been shown to be particularly subject to volume and neuronal loss with aging (De Leon et al., 1995; Raz, 2000), and this volumetric decline has been considered to be a predictor of memory deficits with advancing age (Rodrigue and Raz, 2004). These findings suggest that some of the memory processes that support visual search might be affected by normal aging.

Second, a bilateral hypoactivation of other occipitotemporal structures (lingual and fusiform gyrus) was also observed for target arrays in older subjects. These associative visual areas have been previously found to be involved in object discrimination and recognition (Anllo-Vento et al., 1998; Corbetta et al., 1991; Esposito et al., 1999; Haxby et al., 1991), and the activation of these areas has been widely documented under visual selective attention (for a review see Cabeza and Nyberg, 2000), depending the specific activated areas on the stimulus feature to be attended (Corbetta et al., 1990, 1991). Thus, the hypoactivation observed in the present study may be related to the loss of volume that these areas undergo concomitant to normal aging (Raz, 2000).

Finally, older subjects evidenced a significant hypoactivation in the ACC for target arrays, which could reflect an age-related failure to appropriately engage the attentional control mechanisms needed to select these arrays and to correctly perform the visual search task. The age-related decline in the activation of this region is in line with previous results reporting a significant hypoactivation of cingulate cortex as well as of prefrontal dorsal areas in older subjects compared to young subjects during letter search tasks (Madden et al., 1997).

For nontarget and homogeneous arrays, SnPM showed a significant age-related hypoactivation in left occipitotemporal regions including parahippocampal gyrus, and middle, superior, and inferior temporal gyrus. Thus, a common finding for the three search arrays in the present study was an age-related decreased activation in temporal-medial structures that affected mainly the left hemisphere. In this regard, some studies of visual search in primates have suggested the implication of temporal cortex in the representation and classification of the visual stimulation in natural scenes (Culham, 2001; Sheinberg and Logothetis, 1997, 2001). In addition, in several human PET studies (for a review see Cabeza and Nyberg, 1997) the activation of ventral temporal areas during the perception of visual objects has been documented, consistent with the implication of the occipitotemporal ventral pathway in the processing of visual features.

In line with our results, previous functional neuroimaging (PET and fMRI) studies of cognitive aging have consistently yielded evidence of an age-related decline in cortical regions mediating

visual sensory input, characterized by a significant decrease in the occipitotemporal activity (Buckner et al., 2000; Cabeza et al., 1997, 2000; Esposito et al., 1999; Grady et al., 1994; Huettel et al., 2001; Madden et al., 1996, 1997, 2002; Park et al., 2003). In general, this age-related hypoactivation has been attributed to inefficient sensory processing in the occipitotemporal visual pathway with age (Cabeza et al., 2004).

As previously mentioned, a parallel age-related increase in frontal and parietal cortex activity has been also documented across a variety of tasks, which has been typically interpreted in terms of functional compensation for a declining neural system (Cabeza et al., 2004; Grady et al., 1992, 1994; Madden et al., 1996). It is important to note that in the present study a significant age-related increase of activation was not observed in any cerebral region.

In summary, sLORETA between-group comparisons suggested that several brain areas activated by the young subjects were not recruited as robustly by the older subjects. Since these brain regions are part of a neural network associated with selective attention processes (Cabeza and Nyberg, 1997, 2000; Corbetta et al., 1991), these results indicate an age-related difficulty in engaging and activating the appropriate or specialized brain networks to a level that would be sufficient to successfully perform the visual search task. These findings led us to conclude that normal aging affects the neural mechanisms supporting visual search performance, at least during simple feature search tasks as applied in the present study. Future studies will be necessary to investigate if these age-related findings are generalized to conjunction search tasks.

Taken all together, our sLORETA data provided evidence for two separate age-related changes in neural correlates of visual search: a reduced neural specialization and a significant hypoactivation of specific search-related brain areas. In order to obtain a more complete understanding of age-related changes in visual search processes, it will be useful in the future to consider not only regional decreases or increases in neural activation but also age-related changes in brain connectivity.

## Conclusion

The main results of the present research indicate that the decrement in performance in searching visual stimulus in older subjects may be partially due to an age-related selective attentional deficit characterized by (1) a delay in the evaluation times of the stimulus, (2) a less efficient allocation of attentional resources, (3) a reduced neural specialization, and finally (4) an hypoactivation of several brain structures critically involved in selective attention performance.

Understanding fundamental age-related deficits in visual processing during visual search may lead to future interventions that restore search capabilities with the goal of enhancing cognitive ability and daily function in older subjects.

## Acknowledgments

This work was supported by Grants SEJ-01377 (partially supported by FEDER funds) and PGIDIT05PXIC21101PN from the Ministerio de Educación y Ciencia, and Xunta de Galicia respectively.

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