A Magnetoencephalographic Study of Brain Dynamics Associated with Conflict in Selective Attention

Jesús M. Alvarado, Carmen Santisteban & Manuel Cortijo

Universidad Complutense de Madrid. Madrid, Spain.

Correspondence: Jesús M. Alvarado. Instituto de Estudios Biofuncionales, Universidad Complutense de Madrid, Paseo Juan XXIII, 1, 28040 Madrid, Spain. Tel: +34 91 3943241, Fax: +34 91 3943245. E-mail: alvarado@psi.ucm.es

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Summary

The activity time-course of the principal cerebral areas involved in processing different levels of conflict was studied by magnetoencephalography (MEG). Participants carried out an Eriksen's flanker task having negligible conflict, some stimulus conflict and considerable response conflict in the congruent, neutral and incongruent trials, respectively. The intensities peaked at practically the same time under all three conditions assayed, suggesting that the brain was using the same circuits to evaluate the information in all three cases. The highest intensities were observed in the visual areas and thalamus during the first 200 ms, followed by the parietal cortex (which detected the conflict in our neutral trials) at around 272 ms, the anterior cingulated cortex (which detected any type of conflict) at around 331 ms and the prefrontal cortex at around 378 ms (activated in the incongruent trials around 100 ms before the mean of the response times). Our results agree with the hypothesis of a sequential "wiring" circuit controlling the conflict situations in this selective-attention process, where, after an initial filtering in the thalamic areas, the parietal cortex may be responsible for embodying a response, which could be modulated in the anterior cingulated cortex. Lastly, the prefrontal cortex might be recruited when necessary to select between competing responses, sending executive orders to the pre-supplementary and supplementary motor areas. The results also concur with the idea that a competitive bias begins in any part of the system, probably in the visual areas, and then spreads to "higher" and "lower" levels.

Keywords: Flanker task, visual selective attention, conflict evaluation, MEG.

Un Estudio Magnetoencefalográfico de la Dinámica Cerebral Asociada con Conflicto en la Atención Selectiva

Resumen

Mediante magnetoencefalografía (MEG) se ha estudiado el curso temporal de la activación de las principales áreas cerebrales involucrada en el procesamiento del conflicto. Los sujetos participantes en el estudio realizaron una tarea de flancos basada en el paradigma de Eriksen con tres niveles de conflicto: nulo o prácticamente nulo, pequeño conflicto estimular y fuerte conflicto de respuesta, producidos respectivamente en las condiciones de ensayos congruentes, neutrales e incongruentes. Los picos de intensidad observados, aproximadamente, en los mismos tiempos bajo las condiciones ensayadas sugieren un mismo circuito cerebral de activación en la evaluación de las tres condiciones. Las mayores intensidades fueron observadas en las áreas visuales y el tálamo durante los primeros 200 ms, seguidos por el cortex parietal (el cual detecta el conflicto estimular provocados por nuestros ensayos neutrales) alrededor de los 272 ms, el cortex cingulado anterior (el cual detecta todo tipo de conflicto, estimular y de respuesta) alrededor de los 331 ms y finalmente, el cortex prefrontal alrededor de los 331 y 378 ms (que se activa en los ensayos incongruentes alrededor de 100 ms antes del promedio de los tiempos de reacción). Nuestros resultados apoyan la hipótesis de un circuito "conectado" de control secuencial que evalúa las situaciones de conflicto en los procesos de atención selectiva, en el que después de un filtrado inicial en las áreas talámicas, el cortex parietal es el responsable de iniciar una respuesta que sería modulada en el cortex cingulado anterior. Finalmente, el cortex prefrontal actuaría en caso de necesario para seleccionar entre respuestas que entran en competición, enviando órdenes ejecutivas a las áreas motoras presuplementarias y suplementarias. Nuestros resultados también son compatibles con la idea de que se produce un sesgo competitivo en alguna parte del sistema, probablemente en las áreas visuales, y de allí se difunde a otros niveles de procesamiento.

Palabras clave: Tarea de flancos, atención visual selectiva, evaluación del conflicto, MEG.

Introduction

An understanding of the neural mechanisms underlying the control of brain processes is of paramount interest for neuropsychologists and neurophysiologists, but it also has important, immediate consequences in practical applications for the study and treatment of many mental disorders as well as in many daily aspects of modern life. For example, decision making is a topic of great interest in economics, which has led to a new important discipline, that of neuroeconomy. A great variety of mental processes are being studied using simple tasks in the hope that they may only influence a few areas of the brain, although the highly complex interconnections in the human brain are tending to prove this thesis untenable. Notwithstanding this complexity, present interest is directed towards the understanding of basic cognitive processes involving deep brain areas more than sensorial events, mainly processed by very well known cerebral cortices. One of the more appealing studies is directed towards the understanding of conflict processes, which underlie many cognitive processes. Decision making, for example, must solve some conflict steps, although many other

factors play important roles, such as impulsivity, aggression and so on, as is reported in a recent issue of *Science* devoted to this subject (Stern, 2007). The inability to resolve conflict (e.g., identifying similar letters with opposite orientations such as q and p) may also be involved in some learning disabilities, such as dyslexia (Eden et al., 2004; Paulessu et al., 2001; Seymur, Aro & Erskine, 2003). We only focus here upon the conflict in a visual selective attention process.

The importance of selective attention in psychology is currently being subject to considerable scrutiny. The neural mechanisms involved in visual attention have often been studied by behavioral, neurophysiological and imaging techniques via a great variety of tasks. Multidimensional stimuli are presented to participants whose responses may also be multidimensional. Nevertheless, only one stimulus dimension (target) and one response dimension are normally designed to be relevant, and the participants are instructed to pay attention and respond to it alone, whilst the other stimuli (distractors) and response dimensions are designed to be irrelevant, and the participants are instructed to ignore them. There is little consensus concerning the terminology used when referring to these tasks, words such as congruency, congruity, compatibility, consistency and correspondence often being accepted as synonymous. We will use the following terms: A trial is referred to as being congruent (CO) when all the stimuli presented to the participant belong to the same category and are mapped to the same response, whilst the trial is incongruent (IN) when the target and the other stimuli belong to different categories and the distractors are mapped to the opposite response to the target. Neutral trials (NT) are those in which the distractors are also different from the target but are not mapped to any response (Alvarado, Santalla, & Santisteban, 1999; Bunge, Hazeltine, Scanlon, Rosen, & Grabieli, 2002; Egner, Delano, & Hirsch, 2007; Eriksen & Eriksen, 1974; Eriksen & Schultz, 1979; Fan, Flombaum, Mccandliss, Thomas, & Posner, 2003; Hübner & Léele, 2007; Liston, Matalon, Hare, Davidson, & Casey, 2006; Roelofs, van Turennout, & Coles, 2006; van Veen, Cohen, Botvinick, Stenger, & Carter, 2001).

Typical compatibility tasks in experimental psychology are the flanker task, Simon task and Stroop task. There is a growing agreement that similar mechanisms control the conflicts generated in all these tasks (Kornblum, Hasbroucq, & Osman, 1990; Kornblum, Stevens, Whipple, & Requin, 1999; Zhang, Zhang, & Kornblum, 1999), although the neural mechanism of the underlying cognitive control processes remains largely unexplained, as has been pointed out by Wittfoth, Buck, Fahle, & Herrmann (2006). Neuroimaging techniques, mainly functional magnetic resonance imaging (fMRI), have led to the identification of the several areas involved in selective attention, the most relevant being the visual areas (VA), the dorsal thalamus (DT), the anterior cingulated cortex (ACC), the prefrontal cortex (PFC), the superior and inferior parietal cortices (PC) and the pre-supplementary and supplementary motor areas (pre-SMA/SMA) (Botvinick, Cohen, & Carter, 2004; Braver, Barch, Gray, Molfese, & Snyder, 2001; Bunge, Hazeltine, et al., 2002; Bunge, Dudukovic, Thomason, Vaidya, & Grabieli, 2002; Egner et al., 2007; Harrison et al., 2005; Hazeltine, Poldrack, & Grabieli, 2000; Liston et al., 2006; Roelofs et al., 2006; van Veen & Carter, 2005; Ward & Danziger, 2004). Cognitive control intervenes in selective attention, resolving the conflict established between contradictory information, which

requires the coordinated intervention of several brain structures. The conflict-monitoring theory maintains that the ACC plays an important role in the cognitive control of conflict (Botvinick, Braver, Carter, Barch, & Cohen, 2001; Botvinick, Nystrom, Fisell, Carter, & Cohen, 1999). Results obtained from many compatibility tasks have shown that ACC activity is higher in incongruent than in congruent trials (review in Botvinick et al., 2004). The relationship between the ACC and other areas involved in conflict resolution has not been clearly established, although some authors are of the opinion that the PFC may be involved, activating a top-down control mechanism (Barch et al., 2001; Casey et al., 2000; Corbetta & Shulman, 2002; Durston et al., 2003; Fan et al., 2003; Kranczioch, Debener, Schwarzbach, Goebel, & Engel, 2005) and that the PC may also intervene (Banich et al., 2000a, 2000b; Chafee & Goldman-Rakic, 2000; Milham et al., 2001; Milham et al., 2002). Other authors have shown that the ACC, the PFC and the PC are all sensitive to changes in the level of conflict (Bunge, Hazeltine, et al., 2002; Casey et al., 2000; Durston et al., 2003; Nieuwenhuis, Yeung, van der Wildenberg, & Ridderinkhof, 2003; Ridderinkhof, Nieuwenhuis, & Bashore, 2003; van Veen et al., 2001). Several authors assert that the ACC and the PC are sensitive to distinct forms of conflict, with both structures regulating PFC activity by signaling the need for greater control (Liston et al., 2006; MacDonald, Cohen, Stenger, & Carter, 2000; Milham et al., 2001; Roelofs et al., 2006). In general, therefore, agreement exists that the ACC and PC are involved in the resolution of conflict but their roles in IN or NT conditions are still moot.

In this study the participants undertook a slightly modified version of Eriksen's paradigm flanker task (Alvarado et al., 1999; Santisteban, Alvarado, & Cortijo, 2005), which reveals the association of the orientation of the stimuli to the response. We used letters, as many other authors have done (Eriksen & Eriksen, 1974; Eriksen & Schultz, 1979; Kornblum et al., 1990; van Veen et al., 2001; van Veen & Carter 2002; Zhang et al., 1999), although in this case orientated to some extent, in the same way as the arrows used by authors such as Botvinick et al. (1999), Botvinick et al. (2001), Casey et al. (2000), Fan et al. (2003) and Lau, Rogers & Passingham (2006). We believe that the excellent temporal resolution of MEG may provide useful information about the dynamics of the activated areas by showing when and how long their activations take place in each type of trial, which in turn may lead to a better understanding of the conflict problems involved. Therefore, we report here on an MEG analysis of brain activation using a flanker task to study the several areas involved in the processing of the different levels of conflict, their relative activities and the time course in each of these regions.

Material and Method

We first of all optimized the stimuli, designs and procedures to be used in the MEG experiments, making several assays under behavioral conditions to attain the desired statistical relevance. Thus we previously assayed several possible MEG designs, using the 3Ddeconvolve program (with the -nodata option) of the AFNI software package (Cox, 1996) to achieve the highest statistical power. We then tested the experiments in a sound-proof room in order to distinguish the values of the behavioral variables among the three conditions. As we explain below, the experiments carried out were minor modifications of the flanker-task paradigm

developed by Eriksen & Eriksen (1974), which has been extensively studied by many researchers, including the authors themselves (Eriksen & Eriksen, 1979; Eriksen & Hoffman, 1973; Eriksen & Schultz, 1979; Eriksen & St.James, 1986; Yeh & Eriksen, 1984). In summary, three consecutive experiments were conducted: the first two were behavioral and took place in a sound-proof room whilst the third was run in the MEG room, recording the number of correct responses, the RTs and the MEG signals.

Participants

The participants were twelve undergraduate and doctoral students (aged 21-37, mean age 24.7, SD = 4.35) in Experiment 1, and thirteen different doctoral students (aged 22-35, mean age 28.1, SD = 4.77) in Experiment 2. Eight participants (aged 23-30, mean age 28.5, SD = 3.74) were selected from this second experiment to take part in Experiment 3. All the participants, from the Complutense University of Madrid (Spain), were healthy, right-handed and had normal or corrected-to-normal vision. They gave informed consent prior to the experiments.

Stimuli, designs and procedures

The participants' task was to identify a central target letter flanked by two flanker (distractor) letters and to press either the left button of the mouse when the target was **q** or the right one when it was **p** (or two keys of a specific sensor in the MEG experiment)**.** The participants were instructed to respond only to the target letter that appeared in the centre of the display and to respond as quickly as possible whilst avoiding errors. The target and flanker letters appeared simultaneously. The two flanker letters were always identical to each other. The letters **p** and **q** were also used as flankers for the CO trials (identical letter to that of the target and mapped to the same response, **p p p** or **q q q**) and for the IN trials (different letter from that of the target and mapped to the opposite response, **p q p** or **q p q**). For the NT trials we used different flanker letters from the target (not mapped towards any response). We chose the flanker letter **x** in the NT trials (**x q x** or **x p x**) for Experiment 1 and the letter **o** for the NT trials (**o q o** or **o p o**) in Experiments 2 and 3. All the letters were white, curvilinear (except **x)**, lower-case (luminance: 116 cd/m^2) and presented on a black background (luminance: 1 cd/m^2). All the stimuli subtended a visual angle of 0.40º x 0.40°. The distance between the centre of the target and each flanker letter was 0.65º.

· *Experiment 1*

The participants performed this behavioral experiment in a sound-proof room with their heads resting on a chin-rest 90 cm from the computer screen. Each trial started with a fixation cross at the centre of the monitor screen for 1000 ms at the same point where the target was to appear. The trial displays shown immediately afterwards remained on screen until the participants gave their response. The next trial was started by pushing the space bar. The letters **p** and **q** appeared in the trials, as has been described above. The letter **x** was used as flanker in the NT trials. A total of 709 trials (CO, IN and NT) were presented at random with equal probability. Stimulus presentation and response recording were controlled by the DEVAT program (Alvarado & Santisteban, 2000). RTs were measured and analyzed following the methods explained in previous publications (Alvarado et al., 1999; Santisteban et al., 2005). The participants started with a practice session consisting of 90 trials randomly selected from the 709 trials available. The responses recorded in this practice session were not used in the data analyses.

· *Experiment 2*

The second behavioral experiment was carried out in the same way as the first except for the following changes: The letter **o** was used as flanker in the NT trials. Each trial started with a central fixation cross for 300 ms, followed by the simultaneous presentation of the target and the flankers for a further 600 ms. There was an interval of 600 ms between trials. A total of 600 trials were presented to each participant in NT-CO-IN and NT-IN-CO random sequences.

· *Experiment 3*

This third experiment was conducted inside the MEG room. All procedures, stimuli and designs were identical to those used in Experiment 2 except for the following changes: The participants did not undergo a practice session because they had previously participated in Experiment 2. The stimuli were generated with Matlab and presented using Superlab software. They were projected onto a screen via an LCD video projector (Sony VPL-X600E) placed outside the shielded room and a set of mirrors located inside it. The final mirror was suspended 90 cm above the participant's face, who was lying supine throughout the experiment. The MEG recordings were taken with a whole-head neuromagnetometer (Magnes 2500 WH, 4-D Neuroimaging, San Diego) consisting of 148 magnetometer coils. The instrument was housed in a magnetically shielded room designed to reduce any environmental magnetic noise that might interfere with the biological signals. Data was continuously recorded at a sampling rate of 254.31 Hz and filtered online with a 0.1-100 Hz band-pass filter. Periods of blinking, eye movement, instrumental artifacts or amplifier saturation were rejected offline before averaging with Brain Electrical Source Analysis (BESA 5.1) software. Waveforms were filtered with a 24.5 Hz notch filter and a 40 Hz low-pass filter. Time signals were analyzed from 300 ms before to 600 ms after the presentation of each stimulus and the baseline windows set from -300 ms to 0 ms relative to the presentation of each stimulus using BESA 5.1.

Results

Behavioral experiments

· *Response times*

The mean RTs measured for correct responses are set out in Table 1, where higher values for the incongruent trials were always observed, as might be expected. The within-subject repeated-measurement ANOVAs showed significant main effects in the three experiments studied [$F_{(2,22)}$= 8.75, p = 0.002; $F_{(2,24)}$= 36.76, p = 0.000; and $F_{(2,14)}$= 54.85, p = 0.000]. *Post hoc* Bonferroni analyses were also made to find out whether there were any statistically significant differences between the values measured in the CO, NT and IN trials. The results of these comparisons are also shown in Table 1, where a clear difference can be seen between the results obtained in Experiment 1 and the other two experiments. There were no significant differences between the RTs measured for the congruent and neutral trials in Experiment 1, when the letter **x** was used as flanker. Nevertheless, it is noteworthy that there were significant differences between the RTs for the NT and CO trials in the other two experiments, when the letter **o** was used as flanker. There were significant differences between the RTs measured for the congruent and incongruent trials as well as for the incongruent and neutral conditions in all three experiments.

· *Percentages of incorrect responses*

The percentages of correct responses were very high in all cases, as might be expected given the previous training of all

the participants and the simplicity of the task. The results are also given in Table 1, where it is clear that the percentage of error was higher in the incongruent than in the other two trials in all three experiments. The within-subject repeated-measurement ANOVAs showed significant main effects in the three experiments studied [$F_{(2,22)}$= 12.55, p = 0.000; $F_{(2,24)}$= 21.08, p = 0.000; and $F_{(2,14)}$= 22.13, p = 0.000]. *Post hoc* Bonferroni analyses were also made to discover whether there were any statistically significant differences for the CO, NT and IN trials. No significant differences between the percentages of error in the congruent and neutral trials were found in any of the three experiments (Table 1). Nevertheless, there were significant differences between the percentages of incorrect responses for the congruent and incongruent trials, as well as for the incongruent and neutral trials in all three experiments.

Table 1.
Mean reaction times (RTs) and percentage of incorrect responses

Experiment	Measurement	CO	NT	IN	CO vs. NT	CO vs. IN	NT vs. IN
1	RTs (ms)	438 (68)	438 (59)	467 (55)	1.000	0.025	0.003
	Errors (%)	0.6 (0.3)	0.9 (0.4)	5.9 (1.6)	1.000	0.009	0.018
2	RTs (ms)	436 (30)	443 (33)	467 (34)	0.000	0.000	0.001
	Errors (%)	1.8 (2.7)	2.6 (4.3)	7.0 (8.7)	0.242	0.001	0.002
3	RTs (ms)	445 (29)	450 (28)	472 (26)	0.029	0.000	0.000
	Errors (%)	2.7 (9.4)	3.6 (9.1)	8.4(12.1)	0.280	0.008	0.003

Note: Numbers in the three last columns refer to the p values (Bonferroni) for two-tailed t tests comparing average values obtained for the three conditions studied (CO, NT and IN). Values in brackets indicate standard deviations.

In summary, behavioral data analyses reveal that there were statistically significant differences between the RTs for the three conditions studied: CO < NT < IN when the letter **o** was used as flanker, whilst these differences were only significant between the values corresponding to the IN and the other two conditions, IN > (NT ≈ CO) when the letter **x** was used as flanker. The percentages of incorrect responses were always very small but there were significant differences between the experimental values corresponding to the IN and the other two conditions, IN > (NT ≈ CO), using either letter **o** or **x** for the flankers in the NT trials.

Due to the significant differences observed between the RTs in the CO and NT trials we concluded that the letter **o** should be used as flanker for the MEG experiment in the hope of also seeing differences in the MEG recordings with both trials. It is noteworthy that essentially the same behavioral results were obtained for Experiments 2 and 3, indicating the negligible influence of the minor procedural changes introduced and the simultaneous recording of the MEG signal while Experiment 3 was being run.

The MEG experiment

The analysis was started by filtering the MEG recordings subject by subject and then calculating the grand-average signal for all the participants. This allowed us to obtain very stable activation patterns. Subsequently we made three analyses: a) of the residual variance within each type of trial studied (CO, NT or IN), attempting in each case to identify the brain areas showing the highest activity while the participants performed the task; b) of the time course of brain activation, in an attempt to ascertain the moment at which each of the cerebral areas involved showed highest activity; and c) of the variance, to look for any possible significant difference between the results obtained for each experimental condition.

a) Identification of the activation sources

We started the analyses by simultaneously fitting all the MEG recordings from all the participants for each of the three conditions assayed (CO, NT and IN), using the residual variances as criteria to choose the best model. We studied several time windows and different numbers of regional sources and came to the conclusion that the most relevant time window was from 100 to 400 ms after stimulus presentation. With this window we found that six regional sources were needed to obtain adequate fittings (residual variances lower than 5%, which did not improve significantly with a larger number of regional sources). The locations of the regional sources, bearing in mind the low spatial resolution of this technique, roughly corresponded to the VA-DT, PC, left and right Pre-SMA, ACC and PFC (Table 2). This model explains the 96.13%, 96.08% and 95.12% of the total variances for the CO, NT and IN trials respectively. The effect on the residual variances when one of each regional source was removed from the analysis is also shown in the Table 2.

Table 2.
Locations of the six regional sources and residual variances found

Area involved	xyz - Talairach coordinates	CO	NT	IN
VA-DT	0.4, - 38.0, - 6.7	9.02	10.23	10.34
PC	0.3, - 69.8, 24.3	11.26	10.87	13.41
ACC	- 0.1, 4.4, 39.6	4.59	5.62	7.81
PFC	- 17.1, 41.8, 2.9	4.62	4.68	6.65
Pre-SMA right	29.1, - 13.2, 37.5	5.28	5.49	8.26
Pre-SMA left	- 25.2, - 20.1, 35.9	7.23	7.73	9.99
Whole model		3.77	3.92	4.88

Values of the residual variances for the six-regional-sources model are given in the whole-model row. Other values are residual variances for the five-regional-sources models resulting from the elimination of one regional source (that corresponding to each row).

b) Analysis of the time-course of brain activities

The average time courses observed for the CO, NT and IN conditions are shown at the bottom of Figure 1. Note that at any given time some channels are registering negative intensities and others positives ones. The time peaks at around 100 ms show similar patterns, although of lower

intensity, than the following high peaks at around 158 ms.

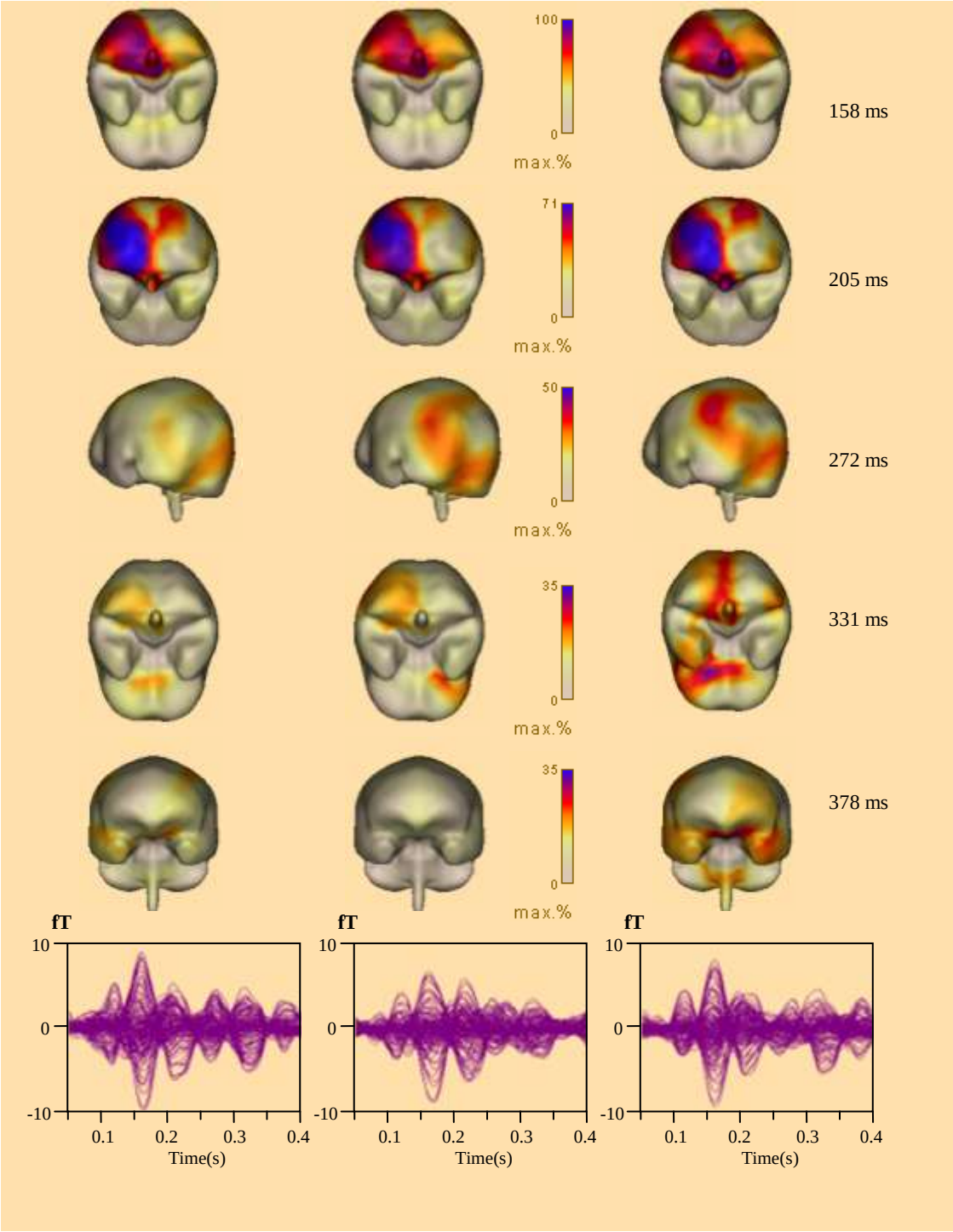

Figure 1. Average time courses (bottom panels) measured for the three conditions studied: CO (left), NT (middle) and CI (right). Brain activities at the five highest peaks are depicted in the upper panels.

c) ANOVA analyses in the areas involved in the conflict processing

Activities at each time peak in some of the several brain areas appear to be different for the three conditions studied (Figure 1), a fact that was confirmed by ANOVA analysis for each of the main areas involved in the conflict. Thus we measured the intensities of the eight different channels that were mainly registering the activities of each area at the times corresponding to the five highest peaks (those shown at the bottom of Figure 1 and in brackets in the first column of Table 3). The intensities were measured from 25 ms before until 25 ms after each peak. The average intensities and their standard deviations are set out in Table 3. The repeated-measurement ANOVA indicates significant main effects in all the areas in question [$F_{(2,14)}$= 27.16, $F_{(2,14)}$= 54.27, $F_{(2,14)}$= 44.54, $F_{(2,14)}$= 24.87 and $F_{(2,14)}$= 29.08 for VA-DT at 158 ms, VA-DT at 205 ms, PC at 272 ms, ACC at 331 ms and PFC at 378 ms respectively, with $p < 0.001$ in all cases]. *Post hoc* Bonferroni analyses show significant differences between some values of the average intensities. The right-hand columns in Table 3 show the p values of these comparisons. The fact that the activities peaked at practically the same time under all three conditions strengthens the relevance of these comparisons. These p values indicate that the intensities in all measured areas, except PFC, are significantly different in the CO versus NT trials. The differences between the intensities measured in the CO and IN trials are also significantly different in all areas, except in the PC, in which we find no statistically significant differences between either of these two trials. The intensities measured in neutral and incongruent trials are significantly different in the VA-DT (at 205 ms), PC and PFC, but not in the ACC.

Table 3.

Average intensities for the three conditions studied (CO, NT and IN)

Area involved	CO	NT	IN	CO vs. NT	CO vs. IN	NT vs. IN
VA-DT (158)	1.59 (0.90)	0.77 (0.69)	1.12 (0.97)	0.000	0.010	0.102
A-DT (205)	- 1.91 (0.85)	- 0.67 (0.70)	- 2.25 (0.86)	0.000	0.012	0.000
PC (272)	0.46 (0.39)	- 0.44 (0.35)	0.78 (0.55)	0.000	0.121	0.001
ACC (331)	0.16 (0.41)	0.59 (0.42)	0.76 (0.59)	0.007	0.001	0.264
PFC (378)	0.05 (0.17)	- 0.01 (0.14)	0.43 (0.31)	0.495	0.001	0.003

Note: Numbers in the three last columns refer to the p values (Bonferroni) for two-tailed t tests comparing average intensities, which were measured (in fT) at the channels that were mainly registering the activities of the indicated areas. Values in brackets indicate standard deviations, except for the first column, where they represent the times (in ms) at which the intensities of each area were measured.

The VA-DT activities are positive at 158 ms and negative at 205 ms. Their absolute values are lower for the NT than for the IN and CO conditions at both times, although the differences for the IN and NT trials at 158 ms are not statistically significant (p = 0.10). The differences between the activities for the CO, NT and IN trials are statistically significant in these areas at 205 ms, i.e., the three conditions can be distinguished. The greatest activities around 272 ms are observed in the PC and are significantly different in the NT trials (negative intensities) from the other

two conditions (positive intensities not significantly different). Fractionally later, at around 331 ms, the greatest activity took place in the ACC and under the CO condition was significantly lower than under the NT or IN conditions (no significant different between them). The greatest activity at 378 ms was observed at the PFC, being almost negligible for the CO and NT trials.

Discussion

Our behavioral results agree in general with previous ones obtained using the flanker paradigm (Alvarado et al., 1999; Eriksen & Eriksen, 1974; Eriksen & Eriksen, 1979; Eriksen & Hoffman, 1973; Eriksen & Schultz, 1979; Santisteban et al., 2005; van Veen et al., 2001; van Veen & Carter, 2002; Yeh & Eriksen, 1984). Many of these studies were carried out using repeated trials (several consecutive trials of either CO, or NT, or IN). This is particularly evident in fMRI experiments, where block designs were almost exclusively used. These repetitions may lead to sequential modulations (Hommel, 2003; Kerns et al., 2004; Kunde, 2003) affecting the conflict with benefit or at a cost whatever their origin, whether it be a conflict-adaptation effect (Botvinick et al., 2001) or a repetition priming (Logan, 2002; Mayr, Awh & Laury, 2003; Mayr, Niedeggen, Buchner & Pietrowsky, 2003). We avoided any repetition in the second and third experiments, by allowing only random NT-CO-IN and NT-IN-CO possibilities in the sequence of stimuli and using an event-related design with intertrial black-screen breaks, although we designed a random presentation of the three types of trial for the first experiment. In any case, we can clearly distinguish between the three types of trial used in Experiments 2 and 3, which was our purpose.

Yeh & Eriksen (1984) reported that "previous research using the response competition paradigm typically has found that when the target letter is flanked by noise letters that are identical to the target, RT is essentially the same as when the target is presented alone without accompanying noise letters (no-noise control)". We have found the same results in those cases investigated over the last ten years and so it is reasonable to expect negligible interference or conflict for the CO trials. It is well known from Eriksen and co-workers' publications (several of which are cited above) that name-codes and physical features are involved in discrimination between letter forms, the latter of these two effects playing the dominant role. Thus in our previous publications (e.g. Alvarado et al., 1999; Santisteban et al., 2005) we have used curvilinear lower-case letters for our stimuli and the letter x for the flankers in the NT trials in an attempt to provide orthographic disparity and thus obtain great visual discrimination and a low "confusability" effect (Eriksen & Eriksen, 1974; Eriksen & St. James, 1986). We have now also assayed the letter **o** for the NT trials in an attempt to achieve better visual discernment because this letter shows similar physical features to both targets, although it is not mapped to any direction and it might be expected than the RT values obtained for the NT trials could fall somewhere between those obtained in the CO (a control trial with negligible conflict) and IN trials, given the similar features of the target and the flankers. This was in fact the case, as we have described in the Results section. Therefore, some conflict must occur in the neutral trials, although less so than under the IN conditions. Thus it may be concluded that some stimulus-conflict (also known in the literature as "perceptual-conflict") is occurring in the NT trials at an early stage, perhaps during the

objective-detection or stimulus-evaluation step, whilst an important response conflict may be surmised for the IN trials at a later stage, which may be reinforced by the influence of the same conflict generated by the presentation of the stimuli, which cannot be ruled out, given that both letters, **q** and **p,** are part of the stimulus set. Our time-course measurements by MEG appear to confirm our assumptions, given that the PC, which could be mainly in charge of detecting the conflict for our NT trials, is activated 60 ms before the ACC, which could be mainly detecting any conflict in our NT and IN trials (see last paragraph of the Results section).

Analyses of our MEG recordings indicate that six regional sources were principally involved in the brain activation pattern while the participants performed the task. This result was always observed whatever the type of trial studied, CO, NT or IN. These regional sources roughly correspond to the following brain areas: VA-DT, PC, ACC, PFC and right and left pre-SMA, the activation of which while the participants performed similar tasks has been widely reported in the literature (Badre & Wagner, 2004; Bench et al., 1983; Botvinick, et al., 1999; Botvinick et al., 2001; Botvinick, et al., 2004; Bunge, Dudukovic, et al., 2002; Bunge, Hazeltine, et al., 2002; Carter et al., 2000; Casey et al., 2000; Chalupa, 1977; Corbetta & Shulman, 2002; Diamond, 1990; Kranczioch et al., 2005; LaBerge & Buchsbaum, 1990; Liston et al., 2006; Milham, & Banich, 2005; Petersen, Robinson, & Keys, 1985; Petersen, Robinson, & Morris, 1987; Roelofs et al., 2006; van Veen et al., 2001; van Veen & Carter, 2005; Ward & Danziger, 2004; Weissman, Giesbrecht, Song, Mangun, & Woldorff, 2003). Our results do not, however, rule out the possibility that other brain areas might also be involved, although their contributions to the MEG recordings should be slight under our experimental design. In any case, MEG has a low spatial resolution and the location of neural activations is better approached by other techniques such as fMRI or PET. Notwithstanding the low resolution of MEG for the exact location for the observed activations, some conclusions may be inferred from the average intensities measured: a) The VA-DT areas clearly distinguish between the CO, NT and IN trials (significantly different intensities among all of them) at around 205 ms but not before. This result confirms those of previous studies specially designed to study the early steps in attention processes (Di Russo, Martinez, & Hillyard, 2003; Martinez, et al., 1999; Noesselt et al., 2002; O'Connor, Fukui, Pinsk, & Kastner, 2002; Pauli, Braun, Wiech, Birbaumer, & Bourne, 2005). These authors presented checkerboard stimuli, which induce higher activations in the visual areas than our stimuli and allowed them to use only four sensors to analyze the differences instead of the eight sensors we had to use, resulting in better spatial resolution than in our trials. Nevertheless, we observed the delayed feedback reported by these authors at the same times and with the same inversion of polarity for later (205 ms) and earlier (158 ms) peaks. These agreements strengthen the significance of all the other results that we obtained at later times in others areas; b) The stimulus-conflict was detected by the PC after around 272 ms, whilst both conflicts (stimulus and response-conflicts) were detected by the ACC at around 331 ms. In other words, the PC detects the NT trials (with negative intensities) around 60 ms earlier than the ACC detects any type of conflict; and c) The greatest activation of the PFC is observed for the IN trials at 378 ms (around 100 ms before the mean RTs of the participants), which is compatible with the idea that the decision is taken in

this area, after the conflicts are detected in the PC and ACC.

We now discuss the time course observed by MEG, which is the main advantage of this technique over fMRI and PET. The intensities peaked at almost the same time under the three conditions assayed (CO, NT and IN), which suggests that the brain was using the same circuits to evaluate the information in all three cases and implies that a given area may be more or less active in the visual conflict presented but is always involved. Thus, when we say that a certain area detects a given type of visual conflict we mean that its neurons are firing with greater activity in this case than in other circumstances. The highest intensities can be seen in the visual areas and thalamus during the first 200 ms, followed by the parietal cortex at around 272 ms, the ACC at around 331 ms and the prefrontal cortex at around 378 ms. These findings could be interpreted as demonstrating the existence of a sequential "wiring" circuit controlling the conflict situations in selective-attention processes, where, after an initial filtering in the thalamic areas, the parietal cortex may be responsible for embodying a response, which could be modulated in the ACC through a relatively "dumb" system continuously extracting an index of information-processing conflicts (Botvinick et al., 2001). Lastly, the prefrontal cortex might be recruited when necessary to select between competing responses, either through a dual pathway (from the PC or the ACC) or a single consecutive pathway, sending executive orders to the pre-SMA and the SMA. It must be emphasized, however, that Figure 1 clearly indicates that all the areas involved are more or less active throughout the whole task, which implies the functioning of more complicated circuits than a simple sequential one. What might well be happening is a permanent activation and inhibition of neurons from one area to the neurons of other areas, which is compatible with a greater involvement of some of them at certain times, reflected in the intensity of consecutive peaks such as those we have observed. Therefore the results shown in Figure 1 also concur with the idea than a competitive bias begins in some part of the system (probably the visual areas in our task) and then spreads to "higher" and "lower" levels, as has been recently suggested by Duncan (2006). We might also speculate upon the existence of a permanent interaction (activations and inhibitions) between all the areas involved throughout the whole task, which should be studied by other techniques for a firmer proof. The sequential steps described in resolving visual conflict have been observed using a flanker task, but they may be the same with other tasks, such as Simon or Stroop tasks. Therefore, similar MEG studies to those described here should be carried out with other tasks to generalize our findings.

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