

To do or not to do: visuomotor processes underlying response conflict.

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Dedication

*A mio padre, per quella sera
che mi insegnò le stelle.*

*A mia madre, per le sue mani
e i suoi baci.*

*A mio fratello,
per la forza che hanno i suoi sogni.*

Abstract

The aim of my thesis was to study the visuomotor processes underlying competing responses in a conflict task. According to the “stimulus-response compatibility effect”, reaction times (RT) to stimuli placed on the same side are faster than to stimuli spatially opposite to the response. This effect is evident also when stimulus side has to be ignored, as in the Simon task. Indeed, the Simon effect refers to the advantage in responding to spatially compatible stimuli, with respect to incompatible ones. After a brief description of anatomical and functional correlates of perception and motor responses, I review the main theories and models on perception and action (Chapter 1), with a particular emphasis on their interaction during conflict tasks. Then I present five different experiments and discuss them along two chapters. The first two experiments propose an analysis of the time-course of the conflict at response stage. First, I tested whether the conflict between competing responses is solved before movement execution (Chapter 2). For this purpose, I analysed the motor evoked potentials (MEP) elicited by different stimuli, from geometrical shapes to directional symbols (arrows). Results show that RT to arrows are faster than to geometrical shapes, both in compatible and incompatible trials. In contrast to RT differences, MEP relative to arrows and to geometrical shapes are similar both in time and shape. Moreover, a negative activity ipsilateral to the responding hand is present at frontal sites before the onset of the response. Remarkably, this ipsilateral frontal activity is present in incompatible trials only, and it can reflect the EEG correlate of the conflict. Indeed, sources reconstruction seems to support this speculation. Dipoles relative to this ipsilateral frontal activity are located in an area belonging to the superior frontal gyrus (GFs), namely in the dorsolateral superior frontal gyrus (DLSFg), which is a region commonly associated with the selection of the task-relevant response in conflict situations.

Thus, RT to arrows result to be faster than to geometrical shapes, whereas MEP waveform and topography are unaffected by the kind of stimuli used. I asked whether directional attributes are encoded at early perceptual stages, rather than at response stage. In a third experiment (Chapter 3), I analysed the visual evoked potentials (VEP)

relative to arrows and to geometrical shapes. A N1 component of the VEP comes out to be selectively modulated by arrows but to be insensitive to non-directional shapes. I interpret these data as the confirm that arrows speed up RT because they are directly “translatable” into right-left responding hand, whereas geometrical shapes cannot elicit such a process. This translation takes place at early visual stages. Indeed, N1 source activity is localised in the parietal lobe, a region belonging to the dorsal stream. Thus, directional attributes are encoded by those dorsal regions that will transform spatial properties into the subsequent related actions. In a fourth experiment (Chapter 3), I aim at detailing the neural substrates of the visuomotor processes previously described in their temporal aspects. The Simon-like task with arrows is replicated, but using a fMRI approach. In particular the core of the fourth experiment was to individuate the neural substrates relative to the frontal ipsilateral activity prior to response and to the visual evoked N1 component elicited by arrows. Confirming EEG results, fMRI analysis show activation both in the inferior parietal (IP) lobe contralateral to the stimulus side and, in incompatible trials only, in the ipsi superior frontal gyrus (GFs). The IP activation is considered to match the parietal N1 visual evoked activity. Indeed, as above mentioned, IP is a dorsal region that functionally subserve the translation of spatial inputs into motor coordinates, that is the translation from arrows direction to right-left responses. On the other hand, GFs is selectively activated in incompatible trials only, and it presumably match the pre-movement activity found at ipsilateral frontal electrodes.

In a fifth experiment I asked whether arrows represent the best cue to speed up responses. Since arrows indicate direction in a symbolic way, I suggest that gaze, which possess an intrinsic biological relevance, can selectively speed up responses as compared to arrows. Contrary to what expected, responses to gaze are slower than to arrows. It is hypothesised that gaze direction requires a time-consuming translation from one frame of reference (the position of the pupils into the eyes) to another (the lateral position of responses), whereas arrows are directly translated into right-left coordinates. An analysis of VEP responses reveals that gaze direction selectively enhances P1 component, with a source in the middle occipital cortex. I concluded that, differently

from the dorsal N1 activation induced by arrows, the P1 gaze-triggered modulation reasonably reflects the activation of a ventral, occipito-temporal pathway.

In conclusion, the main results of my thesis are as follows. When there is a conflict between competing responses to visual stimuli, this conflict is temporally solved before response execution. The solution of the conflict occurs as an active inhibition of the incorrect response. If visual stimuli are also provided with directional information, these are encoded at very early visual stages. This precocious encoding allows responses to directional stimuli to be faster also in conflicting conditions.

Chapter 1

Visuomotor processes and conflict tasks

Thousand times a day we are faced with decisions about the behaviour or the action most appropriate to interact with the world surrounding us. One of the major goals of the cognitive neuroscience is to understand how the brain makes decisions and then generates actions in response to environmental stimulation. Most of our current knowledge on this argument origins from experiments with trained non human primates performing behavioural choices to receive juice rewards. Although these experiments seem to be too artificial, neurophysiological studies on primates have been the basis of experiments on the dynamics of complex human decisions.

A variety of possible behaviours can be chosen in response to environmental stimuli, and the decision about the correct response becomes more difficult as the variables to take into account increase. A particular case is represented by conflict situations, in which it is required to respond to a feature, e.g. the shape of an object, while ignoring other irrelevant features, e.g. its position in space. If, for example, scissors are placed on the left side of our desktop (and we are right-handed), it would be natural for us to reach them with our left hand, because they are on the same side of our arm. Nevertheless the position of the scissors with respect to our body can become totally irrelevant, and thus we have to grasp them with our right hand if we want to work with them.

A similar situation is provided experimentally with a particular type of conflict task, the Simon task. Here, the target is presented peripherally and a spatial response have to be selected according to some non-spatial target features. The Simon effect refers to the advantage in reaction time (RT) in those trials in which the target location spatially corresponds with the response location, although the target location is task irrelevant. (see Simon, 1990 for a review). For example: left or right keypress responses to lateral dots are required, and the target feature is the colour of dots. Left and right responses

are associated with yellow and blue dots, respectively. In this conditions, performance in the incompatible trials (i.e. to respond with the right hand to blue dots on the left side) is compared to that of compatible trials (i.e. to respond with the right hand to blue dots on the right). Generally, responses are longer for the incompatible as compared to compatible trials. It is debated whether the conflict between irrelevant location information and response information, generating the Simon effect, occurs at the stimulus identification stage (Hasbroucq et al., 1991) or at the response-selection stage (Eimer et al., 1995). In any case it is a common assumption that location automatically generates a spatial code which can either facilitate or interfere with response selection (Hommel et al., 1997; Lu et al., 1995). Recent investigations confirm the existence of an automatic, location-based cortical activation (e.g. DeJong et al., 1994; Vallè Inclin et al., 2002), especially in motor areas and during the encoding of visuospatial information. The dorsal pre-motor cortex and the superior and posterior parietal regions appear to be selectively activated whenever the stimulus spatial code conflicts with that of response (Liu et al. 2004, Bush et al., 2003; Dassonville et al., 2001; Fan et al., 2003; Iacoboni et al., 1998; Peterson et al., 2002).

The principal aim of the present study is to address whether the conflict between stimulus position and competing motor response is solved at early stages of visual processing, or close to movement execution. However, before proceeding further, I will briefly review the literature on visual and action processes, and on their anatomical and functional relationship.

1.1 Anatomical and functional aspects of vision and action

Two major cortical pathways carry all the information originated in the primary visual cortex (V1). One “ventral” pathway reaches the inferior temporal cortex (IT) where neurons respond to features as color or shape (caudal IT) or to complex patterns as faces (rostral IT). The second pathway, called “dorsal”, reaches the posterior parietal cortex (PPC). PPC neurons respond either to saccadic control and to visually guided arm movements. Information travels from parietal and temporal regions to the prefrontal cortex where neurons are specialized in planning and organizing actions over extended periods of time.

The ventral or occipito-temporal stream (Ungerleider and Mishkin, 1982) is devoted to object recognition with different sub-areas specifically selective for scenes, tools (Beauchamp et al., 2002; Chao et al., 1999; Martin et al., 1996), places or houses (Aguirre et al., 1998; Epstein et al., 1998; Ishai et al., 1999), faces (Allison et al., 1994; Ishai et al., 1999; Kanwisher et al., 1997; Levy et al., 2001; Puce et al., 1995), animals (Chao et al., 1999; Martin et al., 1996), body parts (Downing et al., 2001; Grossman et al., 2002), and letter strings (Cohen et al., 2000; Hasson et al., 2002; for a review, see Kalanit et al., 2004). The ventral stream connects the primary visual cortex to the IT via a number of routes involving areas V2, the ventral portion of V3, area V4 and area TEO (situated at the posterior border of the IT). The specialization of IT neurons in coding the intrinsic figural and surface properties of visual stimuli is well known from over twenty years (Gross et al., 1972; 1992). Proceeding from early retinotopic areas to high-level specialized areas, the perception of objects involves more and more complex functions. The activity in early retinotopic areas is related with local, low-level aspects of the stimulus. The level of contrast or brightness of a stimulus monotonically increases the strength of the fMRI signal in V1 (Avidan et al., 2002; Boynton et al., 1999) but more higher level areas, as the lateral occipital complex (LO) remains invariant to contrast tunings (Avidan et al., 2002). In monkeys, V1 cells are sensitive to variation in orientation (Hubel & Wiesel, 1968), V2 cells respond to illusory contours (Kourtzi et al.,

2000; Mendola, 1999; Stanley et al., 2003), some V4 cells respond to specific colors or patterns (Gallant et al., 1993; Schein et al., 1990), but only some more high-level ventral areas, as the LO, respond selectively to particular shapes (Booth & Rolls, 1998; Sigala & Logothetis, 2002). Inferotemporal areas are independent of object format, e.g. drawn in gray scale or just with lines (Ishai et al., 2000). Recent investigations have shown that object-selective regions in the ventral stream encode for shapes rather than for contours or for object features (Andrews et al., 2002; Kourtzi et al., 2001; Lerner et al., 2002). Using the Rubin vase-face illusion, it has been found that the face-selective regions in the lateral occipital (LO) and in the ventral occipito-temporal (VOT) regions do not represent figural contours or local features, but the whole percept of a face (Hasson et al., 2001; Andrews et al., 2002). The ventral stream is commonly considered selective for objects recognition. Nevertheless, objects information on shape, orientation and size are also necessary in a variety of dorsal stream-related tasks (Culham et al., 2003; Goodale et al., 1991). Indeed, the ventral stream is interconnected to the dorsal stream by common projections crossing the anterior part of the inferior-temporal cortex. Moreover, objects information on shape, orientation and size activate some specific dorsal sub-regions of the ventral stream during some tasks involving actions (Culham et al., 2003).

The dorsal stream principally projects to the posterior parietal cortex (PPC). PPC receives inputs from a wide range of cortical and subcortical structures. Inputs come from area 19—prestriate cortex, areas 20 and 21—temporal cortex, and from somatosensory and auditory regions (Cavada 1984). PPC is located at the junction of visual, auditory and tactile cortices and subserve the integration of visual, somatosensory, and auditory information. A large amount of PPC activity is related to movement planning. Within PPC it is possible to individuate cells coding preferentially for specific movements (Snyder et al. 1997; Murata et al., 1996; Sakata et al., 1995; Gallese et al., 1994; Murata et al. 2000; Culham, 2002). Besides movement planning, PPC cells also code for other cognitive functions mediating sensorimotor transformations, as decision making (Shadlen et al., 1996; 2001; Platt et al. 1999), salience (Gottlieb et al. 1998), and attention (Goldberg et al., 1990). In particular,

attention allows a subset of inputs to be preferentially selected for further processing. Attention can be stimulus-driven ("bottom-up" processes) when an intrinsic property of the stimulus is sufficiently salient to grab attention from the current focus, or goal-directed ("top-down" processes) when it results from an explicit willing. Recent works suggest that these two attentional mechanisms map onto distinct loci within the parietal cortex (Downar et al., 2001; 2002; Yantis et al., 2002; 2003; Liu et al., 2003; Giesbrecht et al., 2003). In particular, the top-down or goal-directed attention engages the superior parietal lobule (SPL) and the precuneus (PC) (Yantis et al., 2002; 2003; Liu et al., 2003; Giesbrecht et al., 2003). Liu and his colleagues (Liu et al. 2003) asked subjects to attend to moving dots and to shift their attention from one feature to another (color and direction of motion). The attentional shift was related to transient and sustained responses in multiple areas within the SPL and the PC.

Attention is an important cognitive function. When attention is directed to a portion of the visual field, stimuli presented in the attended location enhances activation in the corresponding visual areas, with a retinotopic distribution (Brefczynski et al. 1999; Macaluso et al., 2000; Tootell et al., 2000). Furthermore, actions are faster when are directed towards the portion of space which subjects attend (Craighero et al., 1999; Handy et al., 2003).

1.2 Do perception and action segregate or involve the same neural circuits?

According to Milner and Goodale's two visual systems hypothesis (Milner & Goodale, 1993, 1995; Goodale and Milner, 1992, 2004; for a review see Goodale and Westwood, 2004), perception and action are not only anatomically but also functionally segregated. Vision for perception and vision for action are mediated by distinct cortical networks, represented by the dorsal and the ventral streams. A support for this argument comes from neuropsychological findings.

DF, a young neurological patient, suffered from a profound visual form agnosia following a deep anoxia (Milner et al., 1991). Her primary visual cortex was intact but the ventral lateral region of the occipital lobe was compromised. In particular, at a fMRI investigation DF resulted to be suffering from a greatly reduced activity in those cortical regions normally activated by viewing line drawings, as the lateral occipital complex (LOC), while anterior intraparietal regions were normally activated during visually guided grasping (James et al., 2002). DF was not able to recognise common objects or familiar faces, as those of her friends and relatives. She was, nevertheless, able to correctly identify objects by touching them, and to recognise known persons by hearing their voices. Remarkably, however, DF properly guided her hand and fingers towards objects she attempted to pick up, although she could not identify them. Her grip aperture was correctly wider for larger objects than for smaller ones (Goodale et al., 1991). Similarly, DF was able to execute proper rotation and wrist movements of the hand when reaching out to grasp objects with various orientations, and to place her fingers correctly on the boundaries of objects with different shapes (Goodale et al., 1994; 1991). In other words, DF visual system was no longer able to perceive size, orientation and shape of visually presented objects but, at the same time, her visuomotor system allowed her to program and execute actions towards the same objects. DF deficits represent an example of dissociation between vision for perception and vision for action systems. The case described recently by Le and colleagues (2002), of a 30-year old man suffering since childhood from a bilateral damage to the ventral stream, who was

totally unable to recognise form, colour and texture of objects in front of him, is another proof in favour of the perception/action dissociation. The mirror neurological and behavioural pattern is performed by those patients suffering from optic ataxia, a visuomotor deficit deriving from lesions in the superior regions of the posterior parietal cortex. These patients are unable to direct a grasp or to move towards objects in the near or in the far space, even though they can describe the position of the same objects quite accurately (Perenin et al., 1988). An intriguing but controversial evidence in favour of the two visual streams segregation, comes from studies on optical illusions and related motor actions driven by them (Carey et al. 2001). Aglioti and his collaborators (1995) studied the grip aperture of a hand grasping a disk surrounded by smaller circles and arranged as the size-contrast illusion. The perceptual illusion made the target disk appearing larger than its physical size. Although perception was biased, the hand grasping the target disk was insensitive to the illusion. Grasping aperture exactly matched the real size of the target disk. Thus, the motor system was unaffected by perceptual distortions. Since its publication, the study of Aglioti et al. (1995) has been met with numerous criticism. Two different explanations of the effect found by the authors, were contrasted: the "common source model" (Franz et al., 2000; 2001), and the "obstacle avoidance mechanism" (Haffenden & Goodale, 2000; Haffenden et al., 2001). According to the common source model, the illusion affects both perception and grasping. Indeed, by using large disks surrounding with wide gaps the central disk, Franz and colleagues (2000) found the grasping aperture to be larger than the real size of the target disk. On the other hand, according to the obstacle avoidance mechanism, grasping aperture can be biased only if the surrounding circles are treated as potential obstacles for the fingers, and thus the perceptual illusion is independent from grasping actions (Haffenden et al., 2001).

A different theoretical view, the premotor theory of attention (Rizzolatti et al. 1987; Rizzolatti, Riggio, Dascola & Umiltà, 1987), claims that perception and action do not involve separate but identical anatomical and functional brain structures. During perceptual processes, mechanisms responsible for directing attention to a location in the space are the same that generate motor programs (Rizzolatti & Craighero, 1998). Thus,

any time visual attention is directed to a target a motor program involving ocular shifts is prepared. This hypothesis is supported by anatomical evidences. Different regions of the macaque intra-parietal sulcus (IPs) are sensitive both to ocular shifts and to movement preparatory activity. For example, neurons in the lateral intra-parietal (LIP) region code for incoming saccades, whereas neurons in a more medial area as the parietal reach region (PRR) code for incoming reaching movements (Snyder et al. 1997). Moreover neurons in a more anterior area of the IPs are sensitive to three dimensional objects and also code for preparing grasp (Sakata et al. 1997). Recent brain imaging studies reports both eye- and arm-related activity in the IPs (Kawashima et al. 1995; Petit et al., 1997; Connolly et al. 2000).

Thus, according to the pre-motor theory, any time attention is directed to a spatial location the neural circuits responsible for preparing eye movements are active. Visual spatial inputs are transformed into action by fronto-parietal circuits working in parallel (Colby et al. 1996; Gross et al. 1995; Rizzolatti et al. 1997). These circuits do not encode space according to pre-defined purposes, but according to specific motor requirements (Rizzolatti et al. 1994). In other words, visual attention is nothing more nor less than the facilitation of a particular subset of neurons involved in the preparation of visually guided actions towards a specific portion of space. The theory also predicts that, once the motor program for acting in space has been prepared, it can be delayed. The delay in motor execution is what is introspectively called spatial attention. The delay in execution has the effect to increase motor readiness to act in the region of space towards which the movement was prepared. Moreover the processing of visual inputs coming from that same space region is facilitated. Experimental findings confirm the relation between attention and eye movements (Fischer, 1997; Hietanen et al., 1995; Umiltà et al. 1994; Kustov et al. 1996; Sheliga et al. 1997). Attention activates specific visuomotor structures, including the superior colliculus and the parietal circuits. Experiments with monkeys have found that neurons in separate parts of the premotor cortex, code for near and far egocentric space that also control for, respectively, eye and hand movements. (Rizzolatti et al. 1994). Lesions in these areas produce specific attention disorders as the failure in reaching visual stimuli in near and far space,

respectively. Similar findings are those of Sheliga and coworkers (1994) with humans. Subjects were asked to attend to a spatial location while making a predetermined vertical or horizontal ocular saccade to a target presented at another location. The trajectory of the saccade in response to the target deviated according to where attention was initially allocated. This deviation increased as the attentional demand became stronger. Thus, the spatial attention depends on eye movement programming because of the curvature of the oculomotor saccade: since subjects were instructed not to look at the attended location, the circuits preparing the saccades had to suppress the incipient eye movement towards it, and this caused the shift in the saccade trajectory (Sheliga et al., 1994). Also in monkeys, the trajectory of a saccade evoked by an electrical stimulation of the superior colliculus changes depending on where attention is allocated (Kustov et al. 1996). The collicular excitability is influenced not only by the monkey's ocular saccades but also by manual responses to the target while keeping the eyes fixed on a central point. This means that the oculomotor system is activated by a shift of attention although it is not accompanied by an overt eye movement. Indeed, eye movements can be executed either with the purpose of keeping the salient spatial information into the fovea (target-directed eye movements) , or without such a goal (meaningless and exploratory eye-movements). Single neurons findings show that neurons in some cortical areas, as in the frontal eye fields (FEF), become active during target-directed oculomotor shifts but not during spontaneous exploratory saccades (Bruce & Goldberg, 1985; Burman & Segraves, 1994). This is exactly what the pre-motor theory of attention predicts.

Thus, to summarize, the mere execution of an eye movement is not necessarily accompanied by a spatial motor program, but the selective attention involves goal-directed eye movements. To further confirm this hypothesis, Laila Craighero and coworkers (1999) tested for the attentional consequences of planning actions to graspable objects. Following the premotor theory of attention she predicted that allocating attention to a graspable object would have been translated into preparing a grasping of that same object. Participants planned to grasp a bar that was rotated 45° to the left or to the right. A picture of another bar on a monitor signaled the movement

to be initiated . The orientation of the pictured bar was task-irrelevant. It varied randomly and subjects had to ignore it. Nevertheless, the planned movement was initiated faster if the pictured bar orientation matched the orientation of the bar to be grasped. Thus, the results showed that planning a movement facilitates perceptual processes.

1.3 Perception and action in conflict tasks: the Simon effect

It is a common experience that actions on objects located in the periphery of the visual field are facilitated by using the spatially corresponding arm. The spatial congruence between the position of the stimulus and that of the response is known as “stimulus - response compatibility effect” (SRC) (Fitts & Seeger, 1953), and it takes place although stimulus position is task irrelevant, as it is in the *Simon effect* (Simon & Rudell, 1967; for reviews see Lu and Proctor, 1995; ; Umiltà & Nicoletti, 1990). The classic interpretation of the Simon effect is that it is the result of a natural tendency to respond to the location of the stimulation (Simon & Rudell, 1967). Various hypothesis have been developed to explain the Simon effect, and both behavioral and electrophysiological experiments have been carried out to investigate the phenomenon.

Some cognitive models, as the dual-process models, explain the Simon effect as the result of two stimulus-response (S-R) component processes (De Jong, Liang, & Lauber, 1994; Hommel, 1993, Kornblum, Hasbroucq, & Osman, 1990; O’Leary & Barber, 1993). The idea is that, since in a Simon task responses are assigned to non-spatial features of the stimulus, two alternative choices are available. One is based on target location (task-irrelevant) and one on non spatial stimulus features (task-relevant). Therefore, long-term associations between stimulus location and response location, exist, so as presenting a right (left) stimulus automatically activates a right (left) response, event when the location of the stimulus is task-irrelevant. At the same time, some specific short-term associations are set up as the result of task instructions (“pay attention to

stimulus features!”). The Simon effect occurs as the interference exerted by long-term association on the task-relevant associations at the response level. Hommel (1993) proposes a “temporal overlap” model to explain the response interference induced by the Simon effect. According to this model, the automatic task-irrelevant response activation decays with time, it being time-locked to the presentation of the stimulus. This means that as soon as the target is presented, the tendency to respond to its spatial location is activated, but it is aborted as the task-relevant code is activated (Hommel, 1994). This idea has been incorporated into Kornblum and colleagues’ *dimensional overlap model* (Kornblum, Stevens, Whipple & Requin, 1999). Every experimental factor that increases the temporal distance between the task irrelevant spatial activation and the task relevant activation, has the effect to reduce the Simon effect (decay hypothesis). Practice strengthens the task-relevant S-R links and has an effect in decreasing RT, while the automatic task-irrelevant S-R activation can remain unaltered. The decay hypothesis has been further discussed by Zorzi and Umiltà (1995) in a computational model which assumes that the overall Simon effect is the result of a competition between facilitatory and inhibitory components. A factor influencing the Simon effect is the length of the stimulus onset asynchrony (SOA). If the stimulus onset is varied, so that the temporal interval between two successive stimulation is not fixed, the Simon effect can be huge or weak. As SOA increases, RT decrease to an asymptotic level (Gottssdanker, 1992). The increase of RT as SOA decreases is thought to be the result of inadequate response preparation. The Simon effect is as huge as SOA decreases (Ivanoff, 2003). According to the Kornblum’s model, the activation of the task-relevant code accumulates until reaching a threshold and the overt response is eventually executed. This “accumulator-type” model can be fitted in a Cartesian plot if time and level of activation (ranging from incorrect response-lower level to correct response-higher level of activation) are reported in x and in y axes, respectively. If stimulus and response correspond, the activation of the task-irrelevant spatial code is in the same direction as the task-relevant activation. If stimulus and response location do not correspond, the initial activation of the task-irrelevant code decreases towards the

incorrect response level. Thus, the time-course of response activation and deactivation associated with the task-irrelevant spatial code is shaped like an inverted U.

The automatic spatial code which is activated by long-term S-R associations, is commonly considered as the principal factor in generating the Simon effect. More recently, however, it has been suggested that short-term associations derived from task-instructions, are also strongly involved (De Houwer, 2004; Sturmer et al., 2002, 2003; Tagliabue et al., 2000). This short-term associations are modifiable through practice (Tagliabue et al., 2000) and they can induce RT biases depending on the frequency of corresponding and non corresponding trials preceding the response (Sturmer et al., 2002). Moreover, the Simon effect can be modulated by short-term associations formed at a semantic or abstract representation level of "left" and "right" location (De Houwer, 2004).

In the recent years, the most accounted cognitive model on the Simon effect is the *attention-shift* hypothesis (Nicoletti & Umiltà, 1994) that is based on the "premotor theory of spatial attention" (Rizzolatti, Riggio, Dascola, & Umiltà, 1987; Rizzolatti, Riggio, & Sheliga, 1994; Umiltà, Riggio, Dascola & Rizzolatti, 1991). Attention is engaged by the visual onset of the target. The spatial code of its position is automatically produced, and this in turn will cause the Simon effect. According to the premotor theory (Rizzolatti et al., 1994), covert orienting of attention involves the preparation of saccades with the actual eye movement execution being withheld. The saccade is programmed relative to the spatial location where attention is directed at a given moment; the direction of the saccade becomes the spatial code of the target. The attention-shift hypothesis has been tested in experiments which have shown the relationship between the Simon effect and the direction of attention towards the target. It has, moreover, been showed that no Simon effect occurs when attention remains anchored to a central fixation point (Nicoletti & Umiltà, 1994).

1.4 Aims of this thesis

The work I present in this thesis is aimed at investigating the visuomotor correlates of conflicting responses. In particular, I focus on the temporal and neural aspects of both visual and motor activity in a Simon-type task. I asked whether the conflict is solved at the stimulus onset or later, prior to motor output, and which are the neural substrates underlying the conflict itself.

To study the temporal aspects of the conflict at the response level, I investigate event-related potentials (ERP) elicited by movement onset. In particular, I focus on ERPs evoked by competing responses to geometrical shapes and to directional symbols (arrows).

In order to study the conflict at the early visual stage, I study the visual evoked potentials (VEP) to multi-feature stimuli, from geometrical shapes to horizontal and vertical arrows and to outlines of eyes.

To map the cortical areas underlying the conflict generated by stimuli delivering both positional and directional information, source analysis and fMRI scans are used.

The first part of this thesis reviews studies on vision and action, including anatomical descriptions of the two systems (Chapter 1). Then, a description of the experiments and a discussion of the main results, follows (Chapters 2 and 3). The last chapter (4) is concerned with a general discussion and with the proposal on potential future lines of research.

Chapter 2

What EEG can tell us about the temporal course of events from visual presentation to motor execution?

2.1 Functional imaging techniques and temporal definition of events.

During the last 20 years neuroscientists working on sensorial, motor and cognitive brain functions have massively used non invasive imaging techniques to localise the “online” functions under their investigation. In recent years, the functional magnetic resonance imaging (fMRI) has been largely used, as highlighted by a thorough review by Cabeza and Nyberg (2000). fMRI is considered a “hemodynamic” technique since it allows to investigate neural activity by measuring changes in blood flow (for a review see Buckner & Logan, 2001). It is generally agreed that blood flow is a good index of neural activity. fMRI measures blood flow changes through variations in blood oxygenation: when a brain region is activated, the metabolism of oxy-hemoglobin in that region increases, while the deoxy-hemoglobin concentration decreases. Since the de-oxy-hemoglobin is more paramagnetic than the oxy-hemoglobin, the signal detected with MRI scans refers to the deoxy-hemoglobin level of concentration (BOLD or Blood Oxygenation Level Dependent contrast). In most studies the experimental design (block design) compares blood flow in a target task (for example keypress in response to a word with a specific meaning) and in a reference task (keypress in response to meaningless strings of letters).

Unfortunately, the hemodynamic temporal resolution is limited by the sluggishness of blood flow, since an event lasting a fraction of seconds can elicit a hemodynamic response lasting 20 secs. This temporal limitation has been partially encompassed by a new technique, the event related fMRI (erfMRI). In erfMRI design, the hemodynamic

variations relative to single event-related trials are detected by the scans. Nevertheless, erfMRI gives limited information on the time-course of events (Michel et al., 2001) since it has to be assumed that the brain areas under investigation are activated in a strictly sequential manner and without feedback loops. The resolution of hemodynamic response is limited also spatially (3-6 mm, depending on the smoothing filter employed), and this can compromise any investigation on neuronal or columnar organization. Nevertheless, fMRI is the eligible technique to investigate groups of columns and is particularly useful for revealing cortical and subcortical large-scale distributed brain networks (Cabeza et al., 2000).

Regardless of the type of design adopted, the specific location of observed hemodynamic changes are expressed in three-dimensional coordinates according to the atlas of Talairach and Tournoux (1988). They are x (left/right), y (anterior/posterior), and z (superior/inferior).

2.2 Extraction of the visual and the motor evoked activity from the continuous EEG.

If a pair of electrodes is placed over the human scalp and connected to a differential amplifier, a pattern of voltage variation over time is recorded. This variation in a range from approximately -100 to $+100$ microVolts is known as “electroencephalogram” (EEG). EEG is the result of the voltage difference between each “active” electrode and the reference.

The most used EEG recording procedure is known as “common reference”, with each electrode being connected to a single “reference”, that can be either another electrode or a couple of linked electrodes. The “linked mastoid” reference consists of a pair of linked electrodes, placed on each mastoid bone, located behind the ears. The reference is usually chosen among body parts uninfluenced by the electrical activity under experimental testing. The position of electrodes on the scalp generally refers to the 10-

20 system (Jasper, 1958; see fig. 1). The name of each electrode refers to its proximity to specific regions of the brain (e.g. frontal, central, parietal, occipital, temporal) and to its location in the lateral plane (odd numbers for the left side, even numbers for the right and the subscript z for the midline). Thus, Fz represents a midline electrode over the frontal lobe and T3 defines a left temporal location. Although electrodes are named with the initials of brain areas, they can record the activity of cortical regions far from them. This is because the brain acts as a volume conductor, and activity originating in one region can be recorded at a distant location.

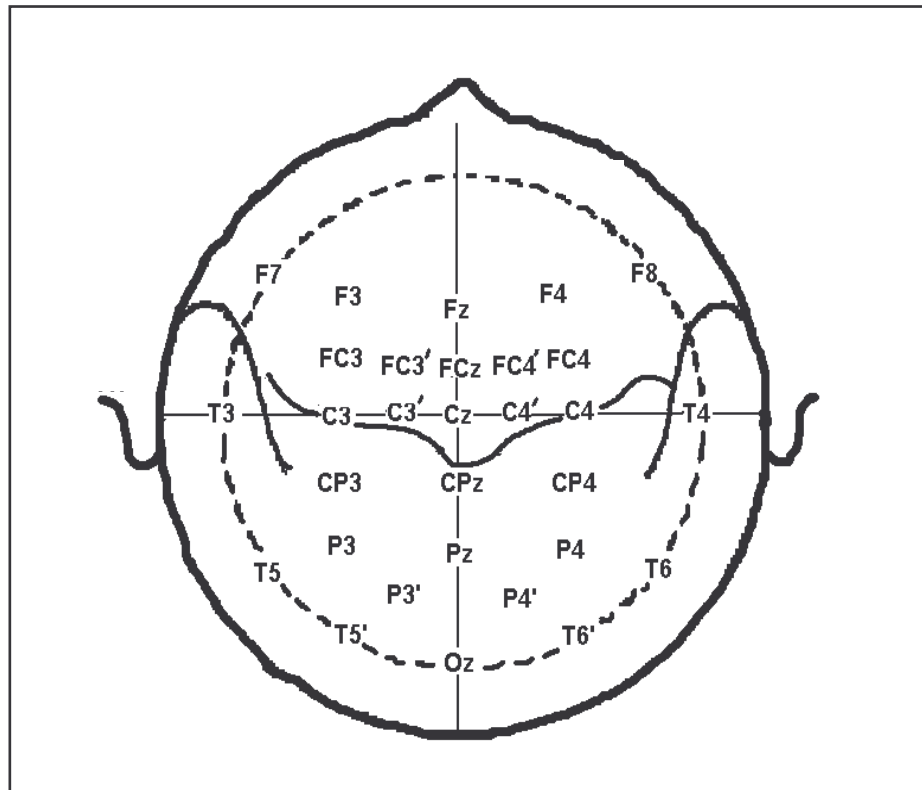


Figure 1: Schematic representation of the electrodes displacement adopted in the present thesis. It is a modified version of the 10-20 system (Jasper, 1958). Reference electrodes were placed over mastoids.

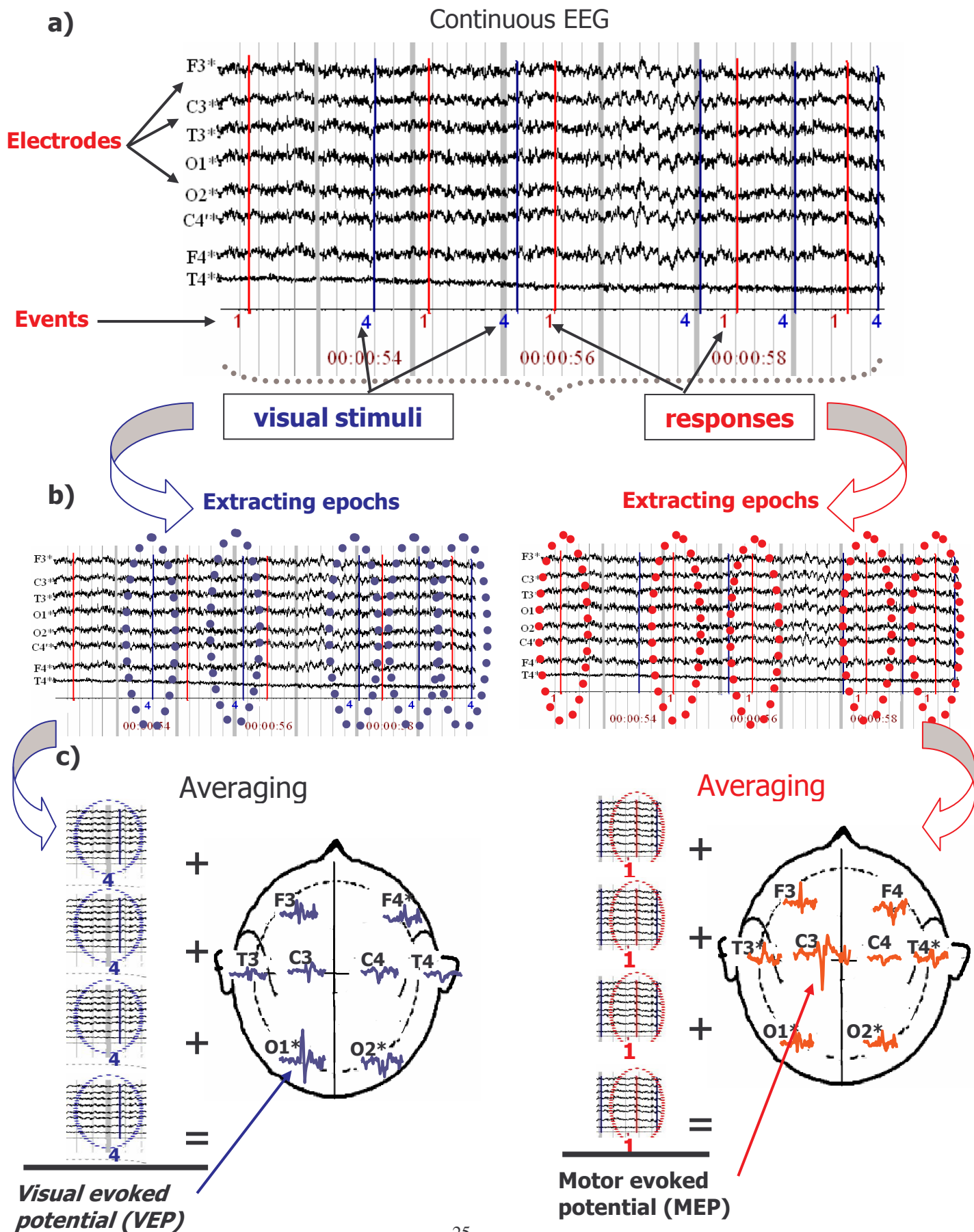
In the recent years a huge number of algebraic algorithms have been elaborated to make more precise inferences about EEG recordings and electrical activity related to specific events (event related potentials: ERPs). In a typical EEG session, a volunteer has to perform an experimental task while his scalp potentials are recorded, for example he can be asked to press a key as soon as a visual target appears on a monitor. The whole recorded continuous EEG can be segmented into several discrete epochs (see fig. 2). An epoch represents a temporal string which can be time-locked to the stimulus onset or to the response onset. For example the epoch can be in phase with the onset of the visual target and can have a length of 500 msec (beginning, for example, 100 msec before the onset of the target and ending 400 msec later). Thus, within this epoch, the time 0 represents the moment of the onset of the visual target, and all the changes in voltage within this epoch reflect specific cortical responses of the brain to the target. If these voltage changes are constant across a huge number of epochs, their average will express the activity of the brain evoked by the onset of that visual target, that is the visual evoked potential (VEP) for that target.

It is assumed that ERPs represent net electrical fields arising from the activity of sizeable populations of neurons. These neuronal populations must be synchronously active and have a specific geometric arrangement to produce the electrical fields recorded at the scalp. It means that the synchronous neuronal activity arises from neurons whose individual electric fields summate to produce a dipolar field. This geometrical configuration, known as "open field", requires that neurons are oriented in a parallel fashion. ERPs reflect the post-synaptic (dendritic) activity of these neurons, and not the axonal action potentials (Allison et al., 1986). Of course, the neuronal activity might be insufficiently synchronous to be recorded at the distance of the electrode placed over the scalp or, although neurons are organized in a parallel fashion, they may not be perpendicular to the scalp surface, so as not to produce a detectable field. Due to these major disadvantages, the whole ERP activity is as complex as difficult to be correctly analyzed.

What is important, working with ERPs, is to exclude that the recorded scalp activity is the result of artifacts and noise arising from sources out of the brain. Of particular

importance in this regard is the high-frequency activity that depends on muscles activity (for example of the jaws). Two major sources of artifacts are gaze movements and eye blinks, which occur at the same frequencies of important ERP waveforms. Post recording filtering can help to remove the contribution of these artifacts (Gratton et al., 1983). As mentioned above, the ERP is the result of constant voltage changes contained within EEG epochs that are in phase with a specific event. In most cases, these changes are too small (on the order of microvolts) to be immediately detected into the EEG waveform (that is on the order of tens of microvolts) containing them. Thus, the ERP signal has to be extracted from the “noise”, that is from the background EEG. The technique of averaging epochs, each of which is time-locked to repetitions of the same event, allows to enhance the signal evoked by the event and to minimize the contribution of noise. It is valid the assumption that EEG activity not related to the event will be casually shifted in time from epoch to epoch. This will allow the background EEG noise to tend to average to zero, while all the activity time-locked to the event will emerge (see fig.2).

Figure 2: Sequences of extracting ERPs from the continuous EEG. a) The ongoing EEG activity (continuous EEG) recorded from each electrode, is depicted. In the bottom the sequence of events is reported, with the blue event (the number 4) representing the onset of the target visual stimulus, and the red event (the number 1) representing the onset of the motor response. b) The continuous EEG is segmented into discrete temporal strings (epochs) each containing visual events or response events. c) Hundreds epochs in phase with the visual or the response event, are averaged. All the signal that is not related to the event (the “not in phase” noise) averages zero and disappears. The remaining potential is the solely activity elicited by the specific event (visual evoked potential, VEP or motor evoked potential, MEP).



2.3 How are ERP sources localized?

Given the fact that EEG possess an intrinsic high temporal resolution but is limited in spatial localisation, it is of crucial importance to define the scalp topography of the electric sources that have generated ERPs. In the last years, a certain number of spatial enhancement algorithms, such as the current source density calculations or deblurring, have been proposed (Babiloni et al., 1996, 2005). It is a common assumption that the only way to localise the electric sources in the brain is by solving the so called “inverse problem”. The inverse problem states that a given electrical signal recorded at the scalp can be determined by an infinite number of intracranial generators. Only specifying a priori constraints about the sources and the volume conductor, it is possible to solve the inverse problem (Fender, 1987; He and Lian, 2002; Baillet et al., 2001). Incorrect assumptions on the positions of electrodes on the scalp also can lead to incorrect source localisation. To avoid this problem it is important to fix the position of some landmarks according to which the position of the rest of electrodes can be reconstructed (Le et al., 1998).

Two basic a priori assumption underlying dipolar model can be made before localising electrical sources. One is the undetermined (distributed) source model, according to which the exact number of dipole sources is not determined before the analysis. The resulting source models comes from a reconstruction of the brain electric activity in each point of a 3D grid of solution points. Each solution point is considered a possible current source, and consequently the source estimate is based on the Minimum Norm (MN) algorithm (Hamalainen et al., 1994). The MN assumes that the 3D current distribution should have minimum overall intensity, and thus a unique solution exists in that a unique combination of intracranial sources can have both the lowest overall intensity and exactly fit the data. The second a priori assumption is the overdetermined (dipolar) model. It assumes that a small number of current sources in the brain can fit the EEG measurement, and in any case the current sources can be less or equal to the number of electrodes that have been used. This limited number of sources can be localised by comparing a model of current propagation (a model on how a dipole at a given position

and orientation propagates signal to the scalp), to the actual recorded map of EEG potential propagation. The algorithm computing the comparison between the model and the real map is based on calculating the averaged squared error between the two maps ("least-square source estimation"). Moreover, this dipole fitting model can incorporate the temporal domain (Scherg et al. 2002) if a dipole location is fitted to a time-varying modulation of its amplitude (this fitting procedure is known as "spatiotemporal multiple source analysis technique").

In this thesis, when localising ERP sources, I adopted the spatiotemporal multiple source analysis technique and I performed estimation of dipolar sources through an additional spatiotemporal decomposition approach (independent component analysis, Kobayashi et al., 2002). All the source estimates I performed in this thesis have been carried out by the multi-modal neuroimaging toolbox Curry (Neuroscan Labs). This software combines functional data (EEG) and anatomical (MRI) data to allow a source localisation that is also extensively used for neuro-surgical purposes.

2.4 Conflicting motor programming during the choice of competing responses.

As described in paragraph 1.3, the choice between competing responses in a conflict task lead to different RTs in incompatible versus compatible trials. A number of imaging studies have identified brain structures (in particular, the anterior cingulate cortex) whose activity is correlated to the choice between competing responses (e.g., Peterson et al., 1999; Carter, Mintun, Nichols, & Cohen, 1997; Carter et al., 1998). It is current opinion that the anterior cingulate is probably the cortical region involved in the monitoring of the conflict (see Gehring & Knight, 2000; Carter et al., 1998). The dorsal pre-motor cortex and the superior and posterior parietal regions are also activated whenever the stimulus position conflicts with that of the response (Liu, Banich, Jacobson and Tanabe, 2004, Bush et al., 2003; Dassonville et al., 2001; Fan et al., 2003; Iacoboni et al., 1998; Peterson et al., 2002). Moreover, the magnitude and the extent of M1 e SMA activation are greater when the responding hand is on the same hemifield as the visual stimulus. (Corbetta, Miezin, Shulman & Petersen, 1991). The effect of stimulus-response compatibility (SRC) has been differently explained.

It has been suggested to be the result of a dimensional overlap between the stimulus side and the effector position (Kornblum, Hasbrouq, & Osman, 1990). Dimensional overlap refers to a perceptual, structural or conceptual similarity between stimulus and response sets (Kornblum, 1999). It is a shared assumption that the SRC effect is the result of an automatic response activation to stimulus location. An electrophysiological marker of this automatic response activation is provided by the lateralized readiness potentials (LRPs) (De Jong et al, 1994; Eimer, 1995). LRP is a measure of EEG negativity (LRP deflection) over the motor cortex contralateral to the responding hand, and it is thought to reflect the automatic response activation to specific stimulus parameters (Coles, et al. 1992; Eimer, 1995; De Jong, Wierda, Mulder & Mulder, 1988; Gratton, Coles, Sirevag, Eriksen & Donchin, 1988). LRPs are extensively used in S1-S2 paradigms, where a warning stimulus (S1) precedes an imperative stimulus (S2). S1 can be more or less informative on the incoming imperative stimulus. LRP is measured

before S2 onset (De Jong et al, 1990; Gratton et al, 1990), or after S2 onset (and culminating in the actual motor keypress). A LRP consists of an asymmetric motor evoked activity developing at electrode C3' and C4 '. Prior to the initiation of spontaneous or stimulus-elicited movement, average EEG activity becomes more negative at the electrode contralateral to the hand to be moved. Therefore, a LRP is the result of a subtraction of the motor evoked response over the contralateral from the ipsilateral electrode. It averages to zero until subject decides which hand to react with, and becomes negative with hand-specific motor preparation (Gratton et al. 1988; Gehring et al. 1992; Coles et al. 1992). LRPs provide a measure of the relative preference for one or the other responding hand, but not of the absolute level of preparation for a specific response (DeSoto et al., 2001, Vidal, 2003). Moreover, LRPs do not provide information about the time-course of the solution of the conflict, nor about the possible simultaneous activation of cortical structures associated with competing motor responses.

In this chapter I will focus on the temporal dynamics underlying the choice between competing motor responses, in a Simon-type paradigm. I will address this issue by using both reaction times (RT) and event related potentials (ERP) to lateral stimuli. Since LRP are not a direct measure of motor evoked activity, they will not be used; rather I will study ERP time-locked to motor execution (MEP) and I will analyse MEP time-course before responses to lateral stimuli.

2.5 Which is the EEG correlate of the conflict? - Experiment 1

This experiment aims at study the time course of the conflict between competing motor responses in a Simon-type paradigm. I will analyse responses to abrupt onset of visual stimuli, instead of using a S1-S2 paradigm. This choice is motivated by the need to obtain a measure of the motor evoked activity in the absence of preparatory or alerting cognitive processes, which might mask the activity related to the conflict itself. I will focus both on compatible trials, in which the task-irrelevant stimulus position corresponds to the side of the response, and on incompatible trials, in which stimulus position is contralateral to the response. Both behavioral and ERP correlates of the task will be examined. I expect faster RT in compatible trials, with respect to incompatible ones. Moreover, I expect MEP topography and amplitude to be affected by the Simon effect.

Method

Participants

Eight right handed subjects participated to the study (4 males, 4 females; age range 26-33, mean age 29.4 years). Handedness was assessed through the Edinburgh Handedness Inventory (Oldfield, 1971) before participants performed the experimental sessions. None of them had prior history of head injury, neurological/psychiatric illness nor were on any medication. All subjects had normal or corrected-to-normal vision. All of them gave informed consent prior to undergo the experiments.

Stimuli and procedure

Participants lied on a bed with reclined back, pressing a key under each hand. A monitor was in front of them at a distance of approximately 70 cm, with a red cross displayed in

the centre (fixation point). Stimuli, consisting of a square (arranged as a chessboard) or a circle (arranged as concentric circles one inside another), appeared randomly to the right or to the left of the fixation point, staying on for 130 msec (Fig. 3). All stimuli had the same luminance. Each stimulus subtended an angle of 4×3 degrees. The central cross subtended an angle of 2×2 degrees, and the distance between the centre of the cross and the centre of each stimulus subtended 4 degrees. Subjects had to release the right key in response to the square and the left key in response to the circle, ignoring their position on the screen. A new visual stimulus was presented 750, 1000 or 1500 msec after key release. 8 blocks of 160 trials each, were presented to each subject. During each trial, subjects were asked to steady fixate the central cross. Reaction time (RT) was measured as the time between stimulus onset and key release. A minimum of 20 practice trials were completed before data acquisition, to ensure that subjects had well understood task instruction and were as fast as they could in responding. They were instructed to give no importance to errors.

EEG was recorded using a 32-channel system (Neuroscan software), from 32 electrodes with the right mastoid used as reference. Midline electrodes (Fz, Cz and Pz) were positioned according to the 10-20 system (Jasper, 1958). The other electrodes were placed according to the 10% system, which is an extended 10/20 system (modified combinatorial nomenclature (MCN); Fisch, 1999). Eye movements were monitored through electrooculogram (EOG) of two electrodes positioned above and below the right eye. Electrodes were placed diagonally with the electrode below the eye positioned towards the outer canthus to detect both horizontal and vertical ocular artefacts (Evinger, et al., 1984). Before each experimental session, I asked subjects to perform blinks and saccades in various directions to ensure that the EOG montage was able to detect both of them. Electrodes were affixed to the scalp by the means of an elastic cap (CuffiaCap, Neuroscan), and impedance were kept below 5 KOhm. Scalp potentials were acquired at a sampling analog to digital rate of 1000 Hz, bandpass filtered at 0.15-200 Hz, with an amplifier gain set to 5000. A Borland C software sent visual stimuli to the PC screen and event-related triggers to the Neuroscan amplifiers. EEG acquisition started when subjects steady fixated the central cross, with 1 sec recording free of visual or

motor activity which served as successive baseline. A Matlab template segmented continuous EEG into discrete sweeps. Only epochs relative to correct responses were taken into account. Epochs length was of 3000 msec. Rejection of both horizontal and vertical eye movements, muscles and amplifier blocking artefacts, was performed before averaging the signal. Artifact elimination consisted in eliminating from EOG channels all the epochs containing signals above +50 or below -50 μV . In a pilot study I verified that the oblique EOG montage I used, was suited to detect both blinks (associated with positive deflections above 50 μV) and small saccades in various directions (associated with slow potential deflections). 130 artefacts-free epochs, corrected for the baseline, were obtained for each condition (left or right hand incompatible trials; left or right hand compatible trials). To further reduce noise, the averaged MEP was further low-pass filtered at 50 Hz and high-pass filtered at 0.2 Hz, with an off-line procedure. Therefore, given the 50-Hz low-pass filter and epoch size of 3 s, the 50 μV criterion in the EOG channels proved to be empirically sufficient for the total elimination of epochs containing both blinks and small horizontal saccades.

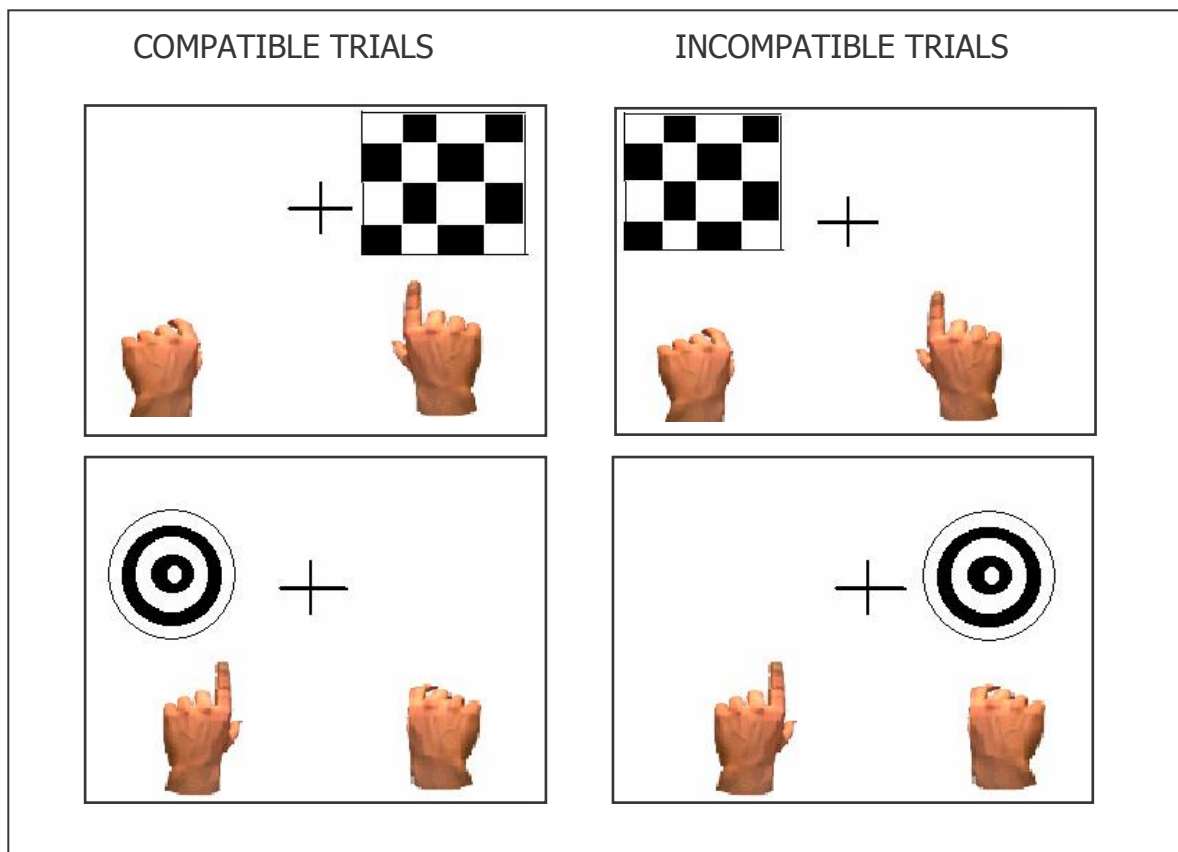


Figure 3: Stimuli of experiment 1. Subjects had to release the right key in response to squares (chessboards), and the left key in response to circles (concentric circles). Stimuli positions had to be ignored. In compatible trials stimulus and response side were the same. In incompatible trials, stimuli were contralateral to the required response.

RESULTS

Behavioural data

RT below 100 ms and above 700 ms were rejected, because clearly unrelated to the task requirements. A repeated measures analysis of variance (ANOVA) using as within subject variables the responding hand and the stimulus location (right vs left) with two levels for each factor, was carried out on correct trials. A main effect of interaction between “stimulus position” and “responding hand” ($F(1, 7) = 90.59$; $p < .001$) was found. Fig. 4 shows RTs in conflict and non-conflict trials for both hands.

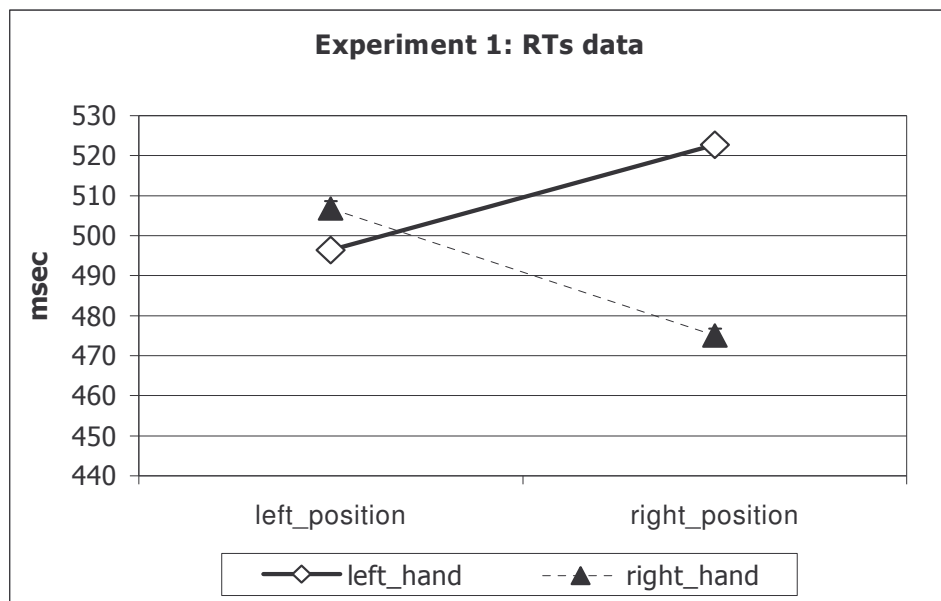


Figure 4: Mean RTs (msec) to right/left presentation of stimuli in experiment 1. When stimulus position and responding hand are on the same side, responses are faster than when they are contralateral. The interaction between stimulus and hand position is significant for $p < .001$.

EEG data

Four types of trials were analysed: right hand compatible and incompatible trials (square on the right/left side, respectively), left hand compatible and incompatible trials (circle on the left/right side, respectively). The right hand MEP on electrode CP3 peaked at –150 msec in compatible and at –87 msec in incompatible trials. This MEP had a higher negative amplitude in compatible than in incompatible trials. At F8, comparing compatible and incompatible right hand trials, a difference in peak amplitudes before movement onset was present at –71 msec (fig.5). The left hand MEP on CP4 peaked at –156 msec in compatible and at –120 msec in incompatible trials. Again, as with right hand, this MEP had a higher negative amplitude in compatible than in incompatible trials. At F7 an amplitude difference between compatible and incompatible trials was present at –58 msec (fig. 6).

Paired-samples t-test were carried out on the peak amplitudes at F7 or F8 electrodes, ipsilateral to the respective responding hand. These electrodes were used in the analysis because they showed the most pronounced pre-movement peak differences. For both right and left hands, the pre-movement peak amplitude at these electrodes was significantly higher in incompatible than in compatible trials. Indeed, both on F8 for the right hand, and on F7 for the left hand, differences in the pre-movement peak between trials was significant for $p < .01$ (d.f. = 7; $t = -4.43$ at F8 and $t = -3.97$ at F7, respectively).

DISCUSSION

This experiment aimed at answering the question whether EEG can help in defining the time course of the conflict between competing motor responses in a Simon-type paradigm. I analysed ERP in phase with response execution (MEP) and found they were temporally modulated during motor programming both in compatible and incompatible

trials. Moreover an ERP correlate of the conflict was present only in incompatible trials, as detailed below.

Behavioural results are in line with the classic Simon effect. Stimulus position influenced motor execution in that responses were faster in compatible than in incompatible trials. Also MEPs topography and amplitude were affected by the Simon effect. In compatible trials MEP amplitude is higher and more negative than in incompatible trials. This result is similar to what previously found with LRPs (De Jong et al, 1990; Gratton et al, 1990). In these studies, the negativity contralateral to the responding hand was found to be more pronounced in compatible than in incompatible trials, and it was assumed to correspond to the readiness potential to respond. The higher negative MEP found in compatible than in incompatible trials was probably related to faster motor execution. In incompatible trials, MEP was weaker probably because it was influenced by the conflict between competing responses. Moreover, it was matched with a frontal negative peak, ipsilateral to the responding hand, that was present only in incompatible trials and that followed the MEP over centro-parietal electrodes. The broad ipsilateral effect was with any doubt unrelated to horizontal eye movements, since the averaging procedure encompassed this problem. This pre-movement peak probably represents the EEG correlate of the conflict and reflects an inhibition of the incorrect response, that is the response automatically activated by the stimulus position. This interpretation is in line with the findings of a couple of studies on choice reaction tasks. The first is a TMS study in which variations in the amplitude of the MEP elicited by the transcranial stimulation show an inhibition of the ipsilateral motor cortex (Leocani et al, 2000). The second is an EEG study using a pre-cue paradigm, in which an inhibition ipsilateral to the responding hand is found over SMA and before contralateral MEP (Carbonell et al., 2004). These results may have some consequences on the issue of the use of the LRPs in choice reaction tasks, since they are blind to the respective contributions of each individual motor cortex (Gratton, 1998; Vidal et al., 2003; De Soto et al., 2001).

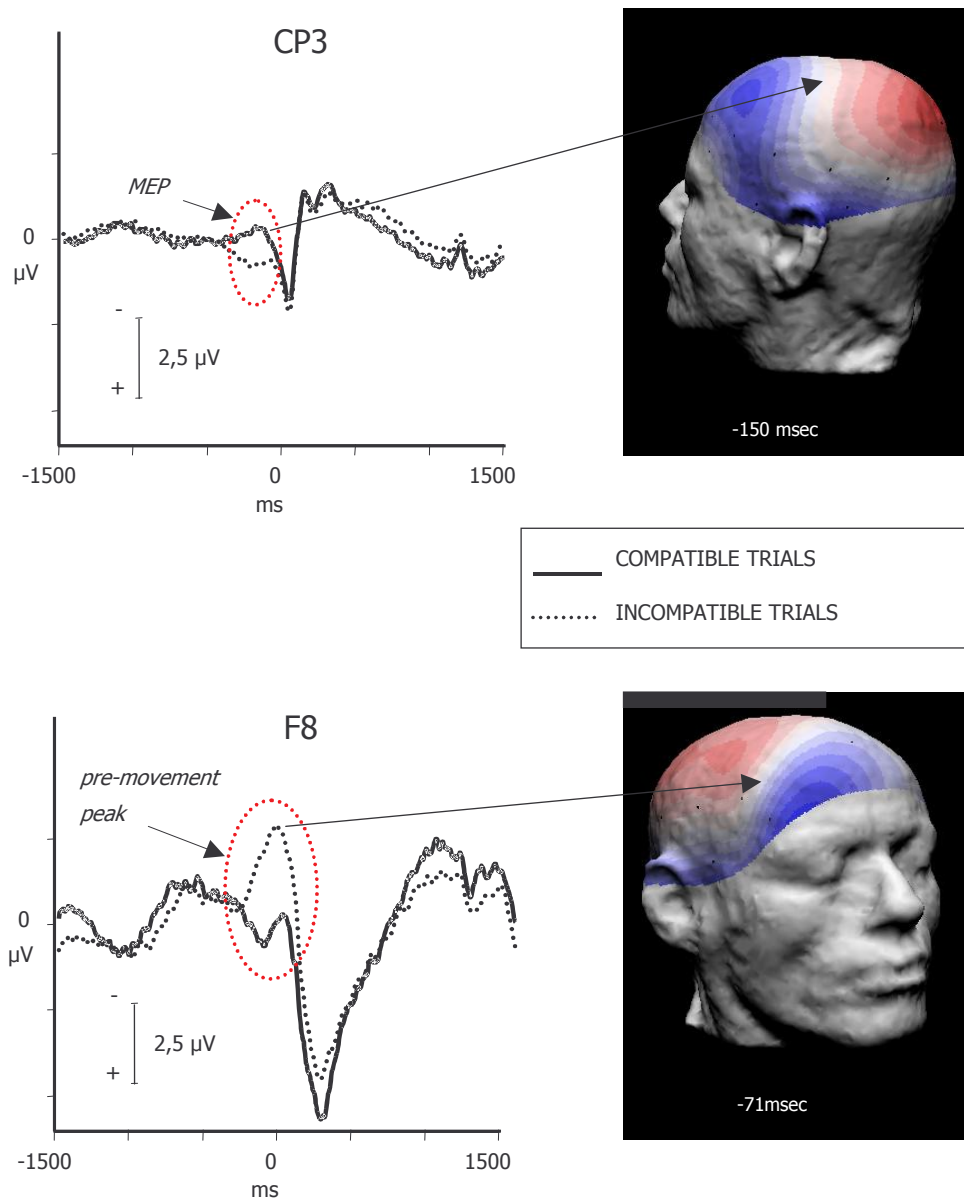


Figure 5: ERPs time-locked to right key-release at electrodes CP3 and F8 (left), and relative maps of isopotentials (right), for both compatible and incompatible trials, in experiment 1. A MEP before key-release onset is present at CP3 (top) for both trials. CP3 is placed over the motor cortex contralateral to the right hand. Before response execution, a frontal negative potential at F8 ipsilateral to the right hand arises only in incompatible trials (the difference between compatible and incompatible trials for this peak is significant for $p < .01$). The maps of isopotentials highlight the distribution of currents over the scalp at the moment in time indicated. Blue and red represent negative and positive distribution of potentials, respectively.

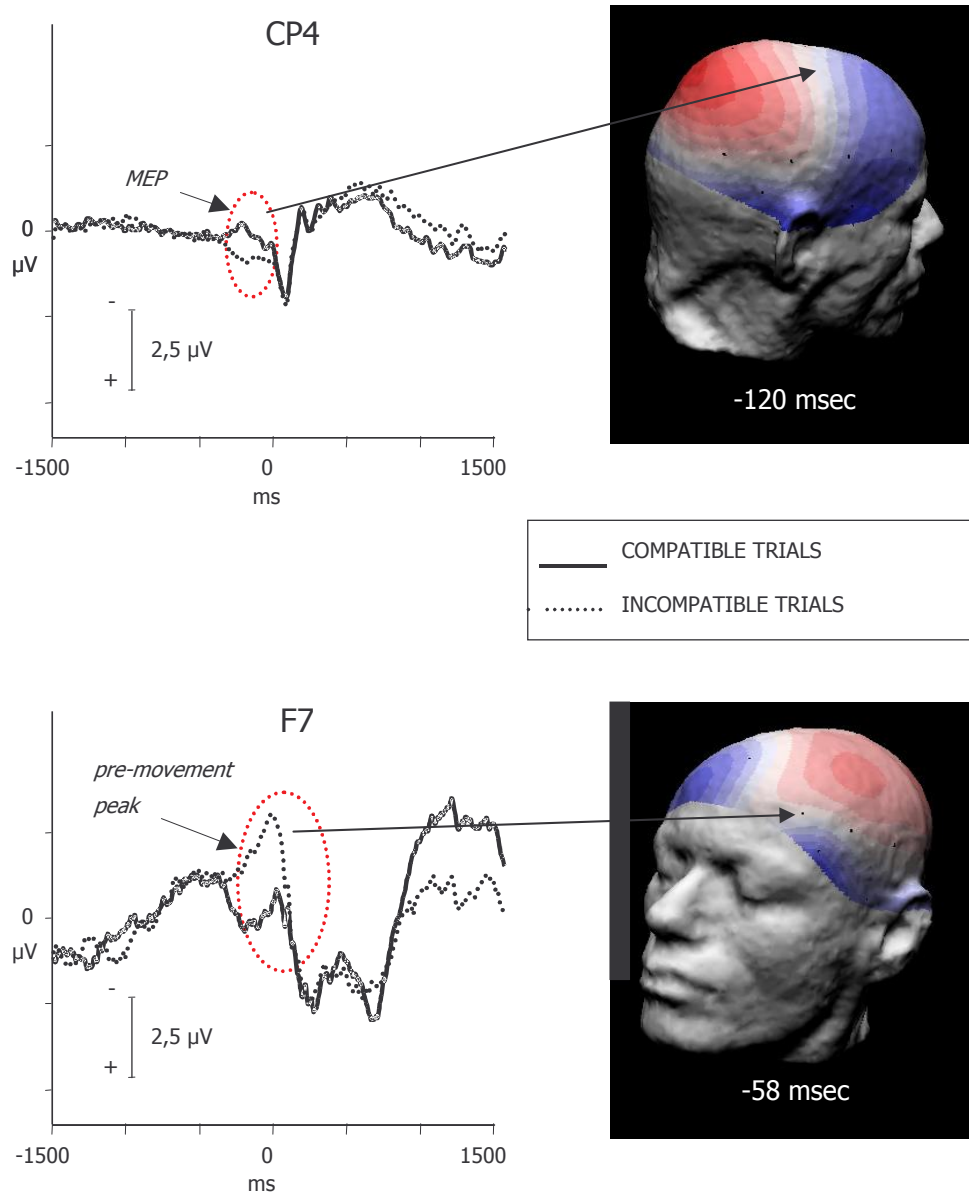


Figure 6: ERPs time-locked to left hand key-release onset at electrodes CP4 and F7 (left), and relative maps of isopotentials (right), for both compatible and incompatible trials, in experiment 1. The MEP is visible at CP4 (top) for both trials. Before response execution, a frontal negative potential at F7 ipsilateral to the right hand arises only in incompatible trials (the difference between compatible and incompatible trials for this peak is significant for $p < .01$). The maps of isopotentials highlight the distribution of currents over the scalp at the moment in time indicated. Blue and red represent negative and positive distribution of potentials, respectively.

Chapter 3

Processing direction versus position¹

In the present chapter I analyse the temporal course of the conflict between competing responses, when the visual cue has also a directional meaning.

According to Kornblum et al., (1990), visual cues automatically provoke some response tendency if there is dimensional overlap between stimulus and response sets, i.e. if stimulus and responses share a common spatial attribute. This means that, for example, a rightward arrow automatically elicits a right-hand response because the direction of the arrow and the side of the responding hand share a common dimension. The automatically elicited motor response can become a conflicting response if the overlap between stimulus and response varies along two common dimensions, such as the left/right side of presentation and the left/right arrowhead pointing direction. An attempt to define the temporal course of the automatic response activation to directional cues has been made by Eimer (1995). In his experiments he used a pre-cueing paradigm with an arrow pointing left or right as S1, and a left-right keypress response as S2. He termed the lateral ERP at about 300-400 msec he found after S1 onset "L-400" and, since it was elicited only by arrows and not by coloured squares having the same meaning, it was concluded that L-400 indicated automatic hand-motor response activation to arrows. Moreover, since it was larger at scalp electrodes over the primary motor cortices than at more posterior electrodes, Eimer (1995) argued that L-400 was a lateralized readiness potential (LRP). L-400 was obtained in further subsequent studies using arrows as visual cues (Yamaguchi et al., 1994; Wauschkuhn et al., 1997; Van der Lubbe et al., 2000). A partially different explanation is provided by Verleger et al. (2000) according to which L-400 does not indicate automatic response activation, but it reflects the encoding of the arrows spatial properties for action.

¹ Parts of this chapter have been submitted as papers to Neuroscience Letters and to Human Brain Mapping.

An fMRI study of Rosen and colleagues (1999) using arrows, found activation in the dorso-lateral pre-motor cortex and in superior and inferior parietal regions related to visual attention. It is possible that arrows induce an automatic shift of attention leading to automatic actions that, in turn, might be further enhanced in compatible situations (Verleger et al., 2000). Given the fact that the compatibility effect is particularly enhanced when there is a relation between responses and the “affordances” produced by the stimulus left-right orientation (Tucker and Ellis, 1998), it is possible that arrows have intrinsic “motoric” features (affordance) eliciting attention to their locations. As a consequence, responses to them are speeded. This point of view is also claimed by the attention-shift hypothesis. (Stoffer, 1991; Umiltà and Nicoletti, 1992). Some spatial attributes of the stimulus (e.g. its lateral position or its direction) elicit an automatic movement of the attentional spotlight. This hypothesis has been tested both by inducing attention shifts with spatial or symbolic cues, and by preventing attention shifts through fixation targets. Using these experimental strategies, the attention-shift hypothesis has been confirmed (Nicoletti et al., 1994; Proctor et al., 1994; Rubichi et al., 1997; Stoffer et al., 1994; Umiltà et al., 1987) or contrasted (Hommel, 1993b; Lamberts et al., 1992; Proctor et al., 1992; Weeks et al., 1996). None of the mentioned studies used abrupt cue onset to stabilise subjects attention.

In this chapter I analyse the temporal course of the conflict between competing responses to directional visual cues, in a Simon-type paradigm. I adopted the experimental strategy of displacing cues with an abrupt onset, in order to avoid problems with attentional shifts (Posner, 1994; Rizzolatti et al., 1987). Response conflicts to visual spatial attributes (i.e. stimuli lateral position and direction) will be analysed both behaviorally and through ERPs. I expect faster RTs in compatible than in incompatible trials. Moreover, I will not specifically focus on modulations of L-400, since I do not adopt a pre-cueing paradigm, but I expect both ERPs latencies and amplitudes to be affected by the conflict between stimulus direction and position.

3.1 Is response conflict influenced by directional cues? - Experiment 2

With this experiment I aimed at study the temporal course of the conflict underlying response selection to lateral cues, in the context of a Simon task where the direction of arrows indicated compatible lateralised motor responses.

Methods





Participants

Eight right-handed healthy subjects (4 males, 4 female; mean age 28 years; range 24-32 years) voluntarily took part to the experiment. The criteria of selection of volunteers were the same as in experiment 1.

Stimuli and procedure

The same experimental procedure, except for stimuli, as in experiment 1 (chapter 2) was used. Stimuli consisted in white arrows pointing to the right or to the left and presented either on the right or on the left of a red central fixation cross. Arrows subtended an angle of 4×3 degrees; the central cross subtended an angle of 2×2 degrees, and the distance between the centre of the cross and the centre of each stimulus subtended 4 degrees. Each stimulus lasted on the screen for 130 msec, and the intervals between two presentations varied randomly (750-1000 -1500 msec). Participants were instructed to release either a left or a right key with the index finger according to the arrow orientation while ignoring its location on the screen. No feedback was provided indicating whether subjects carried out the correct key-release response or not. In non-conflict trials arrow location, direction and hand to be used were on the

same side, while in conflict trials arrow location was opposite to its direction and to the responding hand, as reported in Tab 1. Each block consisted of 160 repetition, randomly build up by 25% of conflict trials for the left hand (arrow presented on the right side but pointing to the left), 25 % of conflict trials for the right hand (arrow on the left but pointing to right), 50% of non-conflict trials both for the right and for the left hand (arrow located and pointing to the same side as the responding hand). Each subject performed at least 8 blocks, in order to collect a sufficient number of artefact-free trials for averaging (mean 320 trials for each condition for each hand).

STIMULUS	CORRECT HAND	CONFLICT
+ 	Right	No
 +	Right	Yes
 -	Left	No
+ 	Left	Yes

Tab. 1: Schematic representation of stimuli presented in experiment 2. Crosses in the left column indicate the central fixation point.

RESULTS

Behavioural data

Subjects performed correctly in 95% and 86% of non-conflict and conflict trials, respectively. A repeated measures analysis of variance (ANOVA) using the responding hand (right Vs left), the stimulus location and the stimulus direction as within subject variables, was carried out on RTs. Reaction times below 100 ms and above 700 ms were rejected. Fig. 7 shows RTs in conflict and non-conflict trials for both hands. I observed a significant stimulus location by response side interaction ($F(1,7) = 40.85$; $MS = 7298.82$; $p = .001$), that expresses the Simon effect. Mean RTs to non directional stimuli (the squares and the circles of experiment 1) and to arrows, are compared in Tab. 2. In the same conditions, (e.g. right hand response-compatible trials), RTs to arrows are of faster than non directional cues of 100 msec or more.

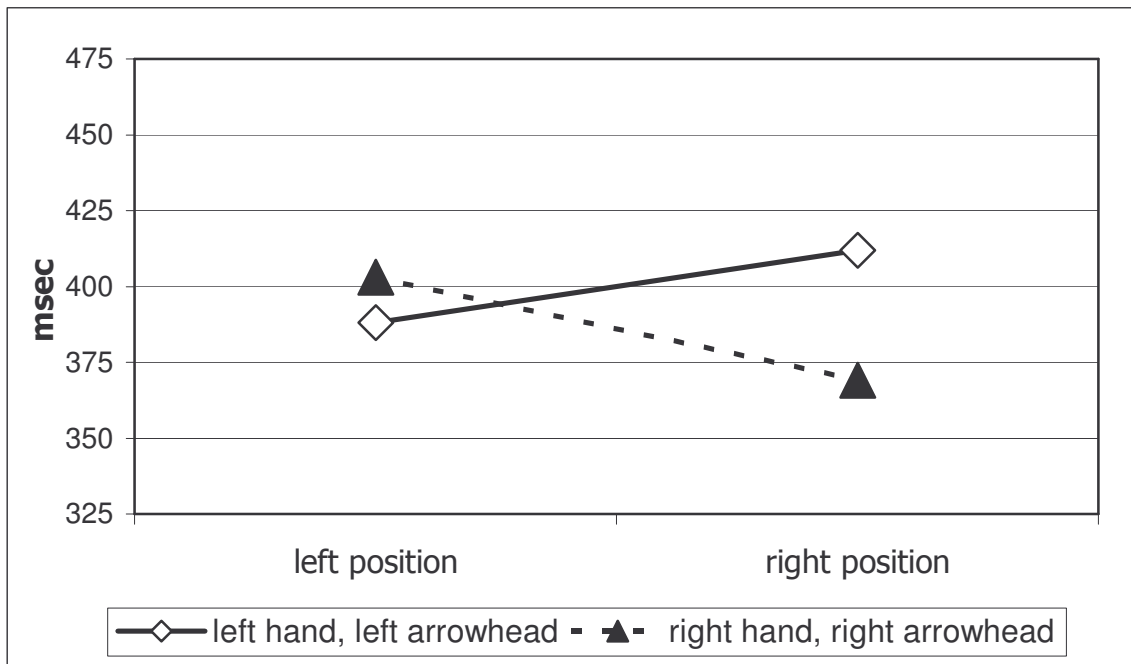


Figure 7: Mean RTs to right/left presentation of arrows, in experiment 1. When stimulus position and responding hand are on the same side, responses are faster than when they are contralateral. The interaction between stimulus and hand position is significant for $p=.001$.

	COMPATIBLE TRIALS (s.e.)	INCOMPATIBLE TRIALS (s.e.)
Squares/right hand	474.99 ms (2.25)	506.82 ms (2.69)
Circles/left hand	496.39 ms (2.20)	522.73 ms (2.73)
Right arrowhead/right hand	369.14 ms (1.86)	408.33 ms (1.88)
Left arrowhead/left hand	368.83 ms (1.94)	395.32 ms (1.77)

Tab. 2: Comparison between mean RTs to directional (the arrows of experiment 2) and non directional cues (the squares and the circles used in experiment 1). Responses are measured in milliseconds and mean standard error is reported in brackets. Pairing off conditions (e.g. right hand-compatible trials), responses to arrows are of faster of about 100 msec or more, than to non directional cues.

EEG data

Grand-average MEPs relative to the right hand recorded at frontal (F7, F8) and central (C3, C4, over motor cortex), and EOG activity, are shown in fig. 8. A summary of the MEP amplitudes at fronto-central, central and temporal electrodes, is reported in Tab. 3. At C3 (motor cortex contralateral to the responding hand) the motor evoked potential peaks at –59 msec in conflict trials and at –63 msec in non-conflict trials. As found in previous experiments using non spatial cues (see exp. 1), a pre-movement peak is present at F8, that is an electrode ipsilateral to the right hand, before response execution and only in incompatible trials (Fig. 8, top right). This ipsilateral peak is significantly different in conflict versus non-conflict trials (repeated measures ANOVA, condition X electrode site interaction effect $F(1, 7) = 25.524$; $MS = 223.133$; $p < .001$). All amplitudes are relative to a 500 msec pre-stimulus baseline; separate analyses of these baselines showed that baseline variances did not statistically differ between conditions of interest. Fig. 9 shows the left hand grand-average MEP. At C4 MEP peaks at – 76 msec in conflict trials, and at –51 msec in non-conflict trials. At ipsilateral frontal F7, before keypress onset, a pre-movement peak is present only in incompatible trials (the difference for this peak in both trials is significant for $p < .001$). Ipsilateral ERPs differences between conflict and non-conflict trials are present also at central and

temporal sites, although they are not statistically significant. For both hands the F7-F8 ipsilateral negative activity temporally follows the MEP over central electrodes.

Dipole analysis

To fit the source model (see paragraph 2.3), event related data, sensors positions and a whole-head MRIs of 8 representative subjects were merged together. Electrode positions were determined during the EEG recording session by means of Polhemus spatial digitizer. The scalp X, Y, Z coordinates of each electrode were referred to three landmarks located at the left and right preauricular points and at the nasion. First, EOG, EMG and referential channels were eliminated from the noise estimate. Then, a linear Fourier filter excluding frequencies above 50 Hz and below 0 Hz was applied. The decomposition of the signal and the dipolar sources estimation was carried out using the Multimodal Neuroimaging Curry (Neuroscan Labs). The interval of analysis was restricted to a time range of the signal from 180 msec before to 115 msec after keypress onset, where ERP difference waveforms were of maximal amplitude (see fig. 8 and 9). For this interval, principal component analysis (PCA) revealed two major components that explained more than 90% of data variance. Then, data were fitted to a 3 concentric shells volume conductor and a single moving dipole was used. In order to estimate the positions of the dipoles on a precise anatomy, the source co-ordinates calculated from 8 subjects ERPs distribution were referred to the structural MRI of a single representative subject and the corresponding regions were identified on standard atlases (Damasio, 1995; Talairach and Tournoux, 1988).

Fig. 10 shows the dipole sources of the ipsilateral peaks (see ERP waveforms in figs. 8 and 9) calculated from 8 subjects MEPs distribution and relative to the right and left hand pre-movement component. Dipoles are projected onto a modelled cortex (left side) and to the coronal (center) and axial (right side) sections of a structural single subject MRI. Dipoles are located in an area belonging to the superior frontal gyrus (GFs), namely in the dorsolateral superior frontal gyrus (DLSFg).

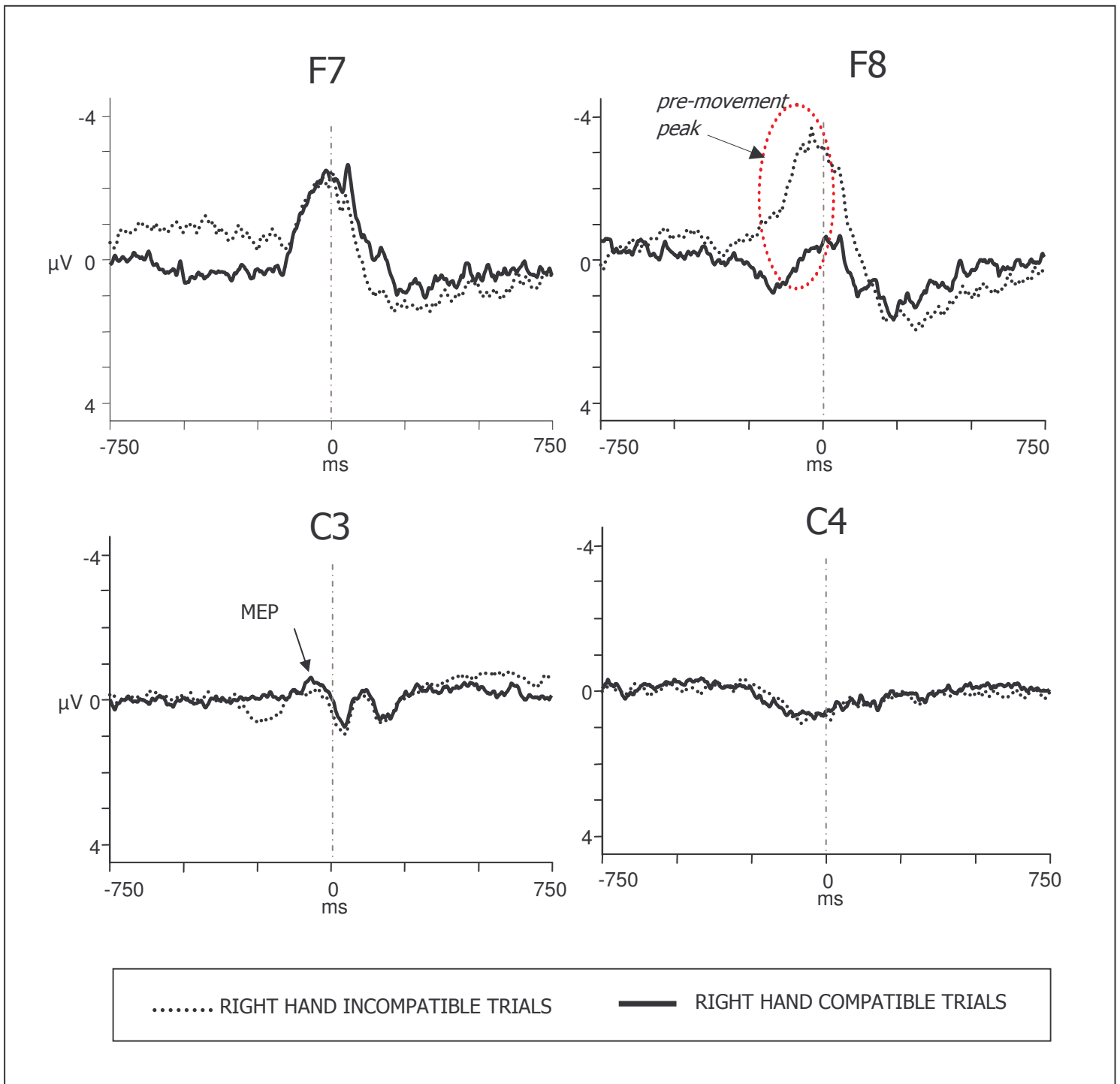


Fig. 8: Grand-average of right hand MEPs at frontal and central electrodes. C3 is placed over the motor cortex contralateral to the right hand, and F8 is ipsilateral. On the top right a peak difference between trials is present. Indeed, only in incompatible trials this peak is significantly higher with respect to compatible ones ($p < .001$). All amplitudes are relative to a 500 msec pre-stimulus baseline.

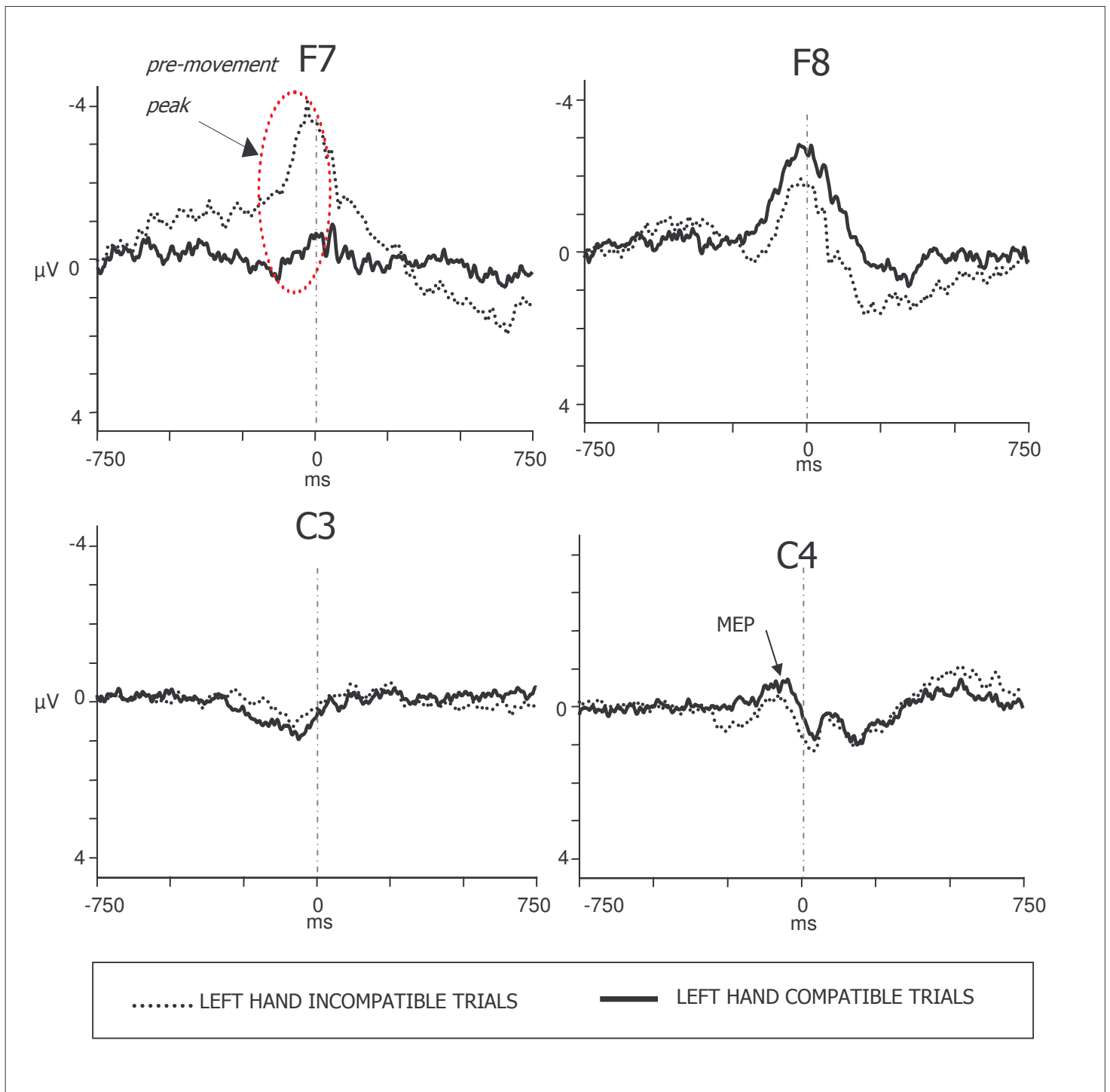


Fig. 9: Grand-average of the left hand MEPs at frontal and central electrodes. C4 is placed over the motor cortex contralateral to the left hand, and F7 is ipsilateral. On the top left a peak difference between trials is present. Indeed, only in incompatible trials this peak is significantly higher with respect to compatible ones ($p < .001$). All amplitudes are relative to a 500 msec pre-stimulus baseline.

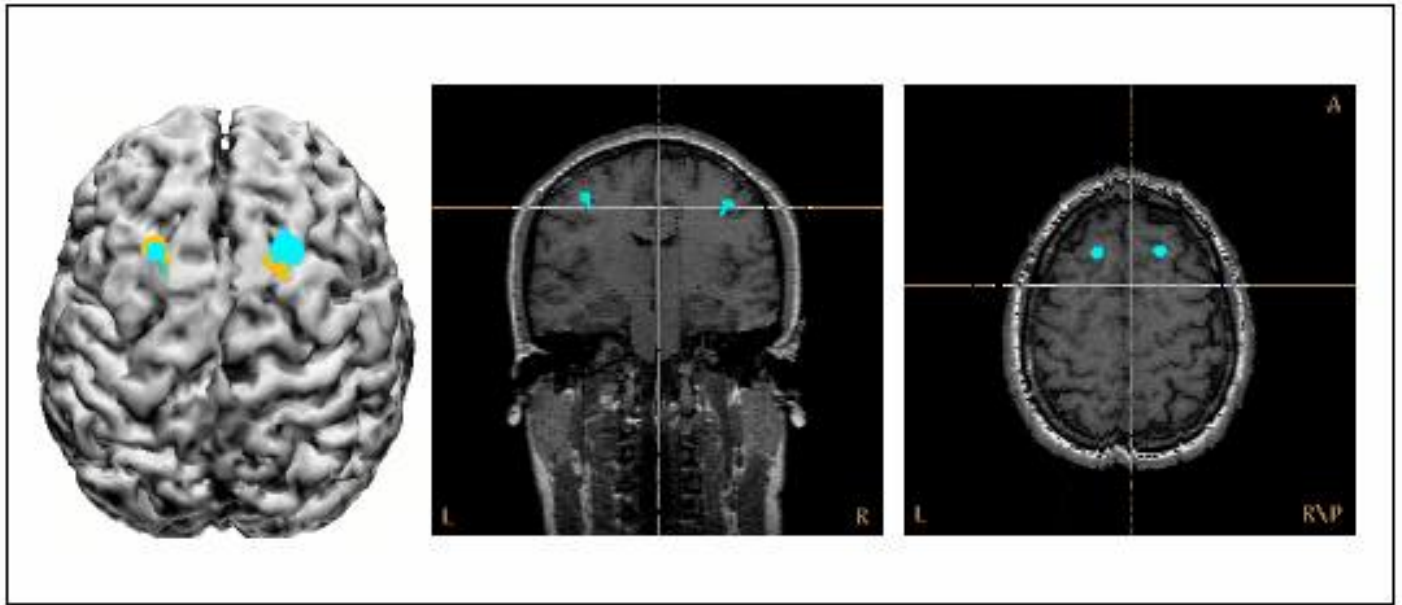


FIG. 10. Reconstruction of dipole sources before right and left keypresses onset from 8 subjects (see ERP waveforms in figs. 3.2 and 3.3). Dipoles are located to the inferior border of the right and left dorsolateral superior frontal gyrus 8DLSFg). Dipoles are projected onto a model of segmented cortex (left side) and to coronal (center) and axial (right side) sections of a structural single subject MRI.

Electrodes	RIGHT HAND		LEFT HAND	
	CONFLICT	NON-CONFLICT	CONFLICT	NON-CONFLICT
	MicroV	MicroV	MicroV	MicroV
F8	-4,8 \pm 1.4	0,2 \pm 0.5	-2,3 \pm 0.7	-2,7 \pm 1.2
T4	-2,1 \pm 0.9	0 \pm 0.6	-1,6 \pm 0.7	-2,2 \pm 0.5
C4	0,4 \pm 0.3	1 \pm 0.2	-0,7 \pm 0.4	-0,3 \pm 0.5
FC4'	-0,2 \pm 0.7	0,7 \pm 0.4	-0,3 \pm 0.5	0,2 \pm 0.3
FZ	-2,3 \pm 0.3	-1 \pm 0.4	-2,1 \pm 0.7	-1,2 \pm 0.5
F7	-2,8 \pm 0.8	-2,9 \pm 0.7	-5,1 \pm 1.1	0,5 \pm 0.7
T3	-1,6 \pm 0.5	-1,8 \pm 0.9	-2,9 \pm 0.7	-0,5 \pm 0.6
C3	-0,5 \pm 0.2	-0,7 \pm 0.1	0 \pm 0.3	1,1 \pm 0.3
FC3'	-1,4 \pm 0.7	-1,5 \pm 0.5	-0,4 \pm 0.7	0,8 \pm 0.7

Tab. 3. Amplitudes of the cortical grand average ERP components peaking before overt movement, averaged across participants (in microVolts \pm s.e.m). Values were measured relative to a 200 msec pre-stimulus baseline.

DISCUSSION

This experiment aimed at studying the cortical processes underlying response selection to stimuli delivering paired or contrasting direction and position information. Stimuli were presented in a Simon type paradigm. Behavioural data show that responses in compatible trials (arrows direction and position on the same side of the response), were faster than in incompatible trials, confirming the classic Simon effect. Moreover, RTs to arrows were faster than RTs to non-directional stimuli (as those presented in experiment 1, see tab. 2). With no doubt, arrows are symbolic cues that speed up compatible lateralised responses more than non directional cues (squares and circles). In contrast to behavioural data, ERPs were not different from those obtained with non directional cues. Before keypress execution, and at electrodes placed over the contralateral motor cortices, MEPs presented more negative amplitudes in conflict than in non-conflict trials, although the difference was not statistically relevant. All studies on the Simon task that have used Lateralised Readiness Potentials (LRPs) have found a different MEP activity in conflict versus non-conflict trials (De Jong et al, 1994; Eimer, 1995). These differences have been variously explained, either as the correlate of subthreshold response activation (e. g. Eimer & Schlagecken, 1998; Heil, Rauch & Hennighausen, 1998; Leuthold & Kopp, 1998; Leuthold, Sommer & Ulrich, 1996; De Jong et al. 1988; Gratton et al. 1988), or as the neural substrate underlying delays in RT (Hackley & Valle-Inclan, 1998, 1999; Miller, 1998; Miller & Ulrich, 1998; Osman & Moore, 1993). I think that the different MEP activity between conflict and non-conflict trials found in present experiments is likely due to the different load of interference between arrows position and pointing direction. As in experiment 1 with non directional cues, a difference in the waveforms between compatible and incompatible trials at ipsilateral frontal electrodes, is present. A peak before movement onset, is significantly higher in amplitude in incompatible trials. This ipsilateral frontal peak might be related to preventing wrong responses execution. It might express a stronger inhibition to move the hand congruent with stimulus position, but incongruent with its direction. Dipole source analysis seems to confirm this speculation. Indeed, it localises this ipsilateral

activity in a frontal area, anterior to the central sulcus, namely in the dorsolateral superior frontal gyrus (DLSFg) which is considered a region involved in controlling the task-relevant response when it is not automatically available (Bunge, et al. 2004; Carter, et al, 1998; MacDonald et al., 2000). It is well known, indeed, from both neuropsychological and neuroimaging studies, that the frontal cortex is involved in monitoring executive functions and, in particular, in guiding controlled behavior (Duncan, 2001; Duncan et al., 2000; Miller & Cohen, 2001; Petrides, 2000). Among the frontal areas, the DLSFg is a key cortical substrate for top-down control over response execution. This region is activated just prior to motor execution to support “response selection” (Banich et al., 2001; Pardo et al., 1991). It is possible that in the present experiment, the DLSFg is engaged in top-down processes controlling whether the response selected is task-appropriate and, possibly, inhibiting any incorrect motor output. According to a recent theoretical view, the DLSFg control serves to reactivate representations that, though recently active, have not been maintained over a delay period (Johnson et al., 2002; 2003). In other words, the DLSFg mechanisms are involved in bringing back to mind representations that were recently active but that have begun to decay. These representations can be, in the case of the Simon task used in the present experiment, the relevant features to be reminded before responding. Such consideration raise the possibility that the DLSFg solves the conflict by biasing or selecting the task-relevant response pathways.

According to a partially different view, the pre-frontal cortex and the anterior portion of the frontal lobes are specialized in managing multiple simultaneous choices (Koechlin, et al., 1999) or in attentional binding of multiple modalities (e.g. what and where) into a single representational entity (Prabhakaran, et al., 2000). In this way, the ipsilateral frontal activity elicited by the present task, is the neural substrate underlying the selection of a response between two alternatives, one based on stimulus position and the other on stimulus feature. The DLSFg, together with the anterior cingulate cortex, is well known to be a correlate of the response conflict (Corbetta, et al., 1991; George, et al., 1994; Peterson, et al., 2002; Cohen, et al, 2000). It is involved in representing and maintaining the attentional demands of the task, thus biasing the task-appropriate

response (MacDonald, et al, 2000). As the DLPFC top-down control increases, the performance in a conflicting task becomes faster and the interference effect decreases (MacDonald et al., 2000).

In the present experiment, subjects are asked to make a response in contrast to a prepotent task-irrelevant tendency, i.e. to respond to the arrowhead direction while ignoring the side of presentation. Thus, the task-irrelevant tendency emerges eliciting the preparation of a response that is ultimately task-irrelevant. The DLPFC might be engaged by the need to control whether the selected response is ultimately task-relevant. This top-down control process operates at the response selection stage, rather than at the stimulus identification stage. Given that the conflict is solved by the top-down control prior to motor output, this lead to an intuitive speculation. Namely, the more effective subjects are in biasing the task-relevant response during the selection stage, the more control (DLSFg activation) they will need to exert before the output, when the initially selected response is ultimately task-irrelevant (that is in incompatible trials).

Since the frontal ipsilateral activity is present either for directional (arrows) and for non directional stimuli (squares and circles), and since RTs to arrows are appreciably faster than to squares and circles, which is the process that speeds up responses to directional cues? Which is the EEG correlate of this process? The third experiment aims at answering these questions.

3.2 Is direction encoded at early stages of the visuomotor processes? A Vep analysis. - Experiment 3

Many theories on the Simon effect claim that the interference effect between the automatic spatial code of stimulus position and that of response, occurs at the response selection stage (Lu et al., 1995; Sturmer et al., 2003). An alternative view argues that the interference effect is due to processes involving stimulus identification (Hasbroucq & Possamai, 1994). Little is known about the conflict generated by cues delivering at the same time both position *and* direction information. The *attention-shift* hypothesis assumes that the spatial code is generated by orienting attention to a location, and thus preparing a saccadic movements towards that location (Nicoletti & Umiltà, 1994; Rubichi, Nicoletti, Iani & Umiltà, 1997; Stoffer, 1991; for a review, see Stoffer & Umiltà, 1997; Stoffer & Yakin, 1994; Umiltà & Nicoletti, 1992). In the case of the Simon task, the direction of this prepared saccade becomes the spatial code of the target. The use of stimuli delivering spatial information (i.e. directional information) should engage attention before overt saccade is performed and it should facilitate (or conflict with) the encoding of the location (spatial) code, more than the use of non directional features. Among the ERPs sensitive to stimuli location, three components of the visual evoked potentials (VEPs) are primarily attention-related: the P1 and the N1 component (positive and negative deflections, respectively, peaking between 80 and 180 msec after visual stimulus onset), depend on whether a stimulus is presented at an attended or an unattended position (Hillyard et al, 1984; Luck, 1995). The third attention-related ERP component is the N2pc (negative component peaking after N1 at electrodes posterior and contralateral to visual stimulus; Luck & Hillyard, 1994a, 1994b).

In the previous experiment, responses to stimuli delivering spatial information (direction) were faster than responses to non directional shapes. Since spatial attributes engage spatial attention (Stoffer & Umiltà, 1997), it is possible that directional features are encoded at early visual stages. This experiment aims at testing this hypothesis. Horizontal arrows will be compared to non directional shapes and to vertical arrows.

Methods

Participants

Fifteen right-handed volunteers, (7 males, 8 females, mean age 28 years) participated in the experiments. Eight subjects carried out experiments A and B on different days; seven subjects performed the vertical arrows experiment only. The criteria of selection of volunteers were the same as in experiment 1.

Stimuli and procedure

Three types of white stimuli, with or without directional attributes (arrows, squares or circles), were separately presented lateralised with respect to a central fixation cross. Three different experiments were carried out, as shown schematically in the inserts A, B, C of Fig. 12. In experiment A, horizontal arrows pointing either to the right or to the left were presented. In experiment B, a square (chessboard) or a disk (concentric circles) was used instead of arrows. In experiment C, vertical arrows were used which pointed either down or upward. In all experiments stimuli were presented in either the left or the right visual field. All stimuli had the same pixel luminance and subtended an angle of 4×3 degrees; the central fixation cross subtended an angle of 2×2 degrees, and the distance between the centre of the cross and the centre of each stimulus subtended 4 degrees. Stimuli were presented on a LCD monitor and lasted 130 msec; the time between two presentations varied randomly among three different intervals (750, 1000 and 1500 msec). In experiment A, subjects were required to release one of two keys with the corresponding hand according to the direction of the arrow, and to ignore its position. In experiment B, subjects were required to release the right key with squares, and the left key with disks, and to ignore their positions. In experiment C, a right key release was required for upward arrows and a left key release was required for downward arrows. Lateralised presentation entailed two types of trials: 1) non-conflict trials, where the stimulus was presented ipsilateral to the required

responding hand; 2) conflict trials, where the stimulus was presented contralateral to the responding hand. Nine blocks of 250 trials each were collected for each experiment. Electroencephalographic (EEG) activity was recorded and analysed as in experiment 1, chapter 2.

RESULTS

Behavioural data.

A repeated measure ANOVA on reaction times was carried out, using the responding hand, the stimulus location and the stimulus type as within subject variables. Fig. 11 shows RT in conflict and non-conflict trials for both hands in the three experiments. A significant stimulus location by response side interaction, which reflects the classical Simon effect, was observed in all experiments (in experiment A: $F(1, 7) = 177.84$; $p < .001$; in experiment B: $F(1, 7) = 90.59$; $p < .001$; in experiment C: $F(1, 6) = 461.334$; $p < .001$).

RT to horizontal arrows was faster than to vertical arrows (the mean difference in non-conflict trials between the two experiments was 33 msec for the left hand and 21 msec for the right hand; the mean difference in conflict trials was 32 msec for the left hand and 15 msec for the right hand). RTs to squares and circles were longer than to horizontal arrows (the mean difference in non conflict trials was 51 msec and 43 msec for the left and right hand, respectively; mean differences in conflict trials was 27 msec and 48 msec for the left and right hand, respectively).

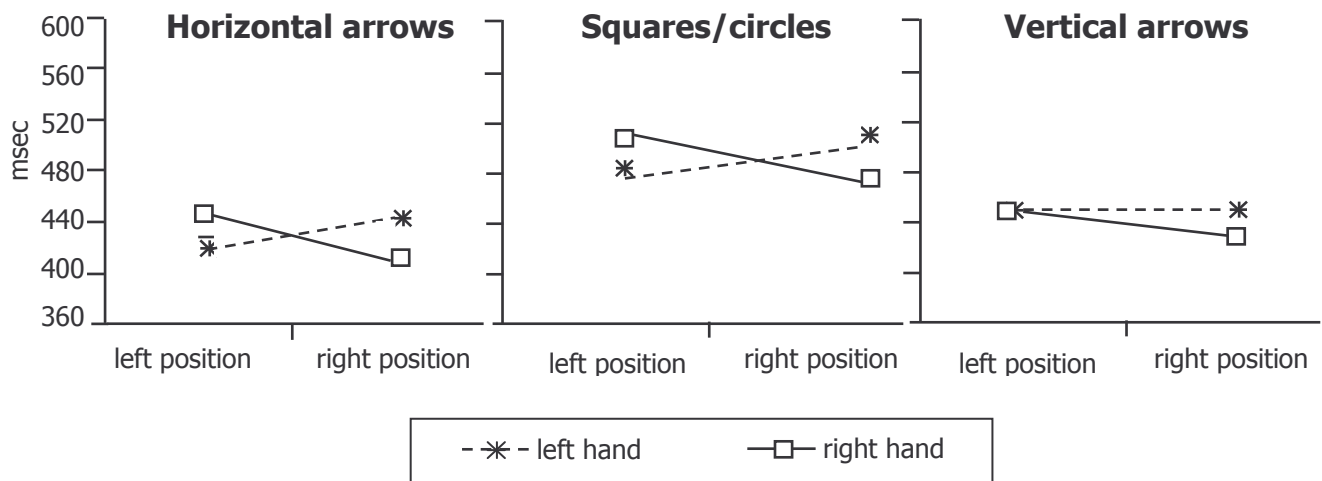


Figure 11: Mean RTs to horizontal arrows, geometrical shapes and vertical arrows. The interaction between stimulus side and hand position is significant for all types of stimuli ($p=.001$). Note that RTs to horizontal arrows are the faster.

	COMPATIBLE TRIALS (s.e.)	INCOMPATIBLE TRIALS (s.e.)
Right arrowhead/right hand	405.43 (1.68)	432.34 (1.93)
Left arrowhead/left hand	412.34 (1.87)	436.49 (1.72)
Squares/right hand	448.11 (1.98)	480.03 (2.03)
Circles/left hand	463.57 (1.80)	476.98 (2.68)
Upward arrows/right hand	426.09 (1.82)	447.08 (1.66)
Downward arrows/left hand	445.67 (1.73)	468.60 (1.92)

Tab. 4: Comparison between mean RTs to directional and non directional cues. Responses are measured in milliseconds and mean standard error is reported in brackets. Pairing off conditions (e.g. right hand-compatible trials), responses to horizontal arrows are the faster.

EEG data

ERPs time locked to visual stimuli revealed a VEP component selectively modulated in amplitude by the presentation of horizontal arrows (all amplitudes were measured from baseline to peak). This component is the N1. The four pairs of electrodes where N1 was higher, were considered for statistical analysis: TO (occipito-temporal electrodes, O1 and O2), TE (temporo-parietal electrodes, TP7 and TP8), OP (occipito-parietal electrodes, PO3 and PO4) and PA (parietal electrodes, P3 and P4). A repeated measure ANOVA on N1 amplitudes in non-conflict trials revealed significant main effects on the experiment type ($F(2, 12) = 21.45, p < .001$), but amplitudes were not dependent on either the hand used ($F(1, 6) = 0.32, p = .59$) or the electrode ($F(3, 18) = 1.302, p = .304$). The main effect on the experiment type was also evident in N1 amplitude in conflict trials ($F(2, 12) = 7.212, p = .009$), while neither the hand used ($F(1, 6) = .080, p = .080$) nor a specific electrode position ($F(3, 18) = 1.88, p = .17$) were statistically significant. Thus, N1 amplitude was differently modulated in the three experiments, irrespectively of the position of stimulus (conflict or non-conflict trials) and hand used (Fig. 12). A subsequent paired-samples t-test, tested for N1 differences among experiments at contralateral O1 or O2. These electrodes were chosen because they showed the most pronounced differences. In all experiments, N1 amplitude was different in condition A versus B, and in A versus C, but not in B versus C. In non-conflict-right trials, N1 was higher in A than in B ($t = -4.2; p = .006$), as well as in A with respect to C ($t = -4.5; p = .004$), although it was not different in B versus C ($t = -1.23; p = .26$). In non conflict-left trials, again, N1 was different in A versus B ($t = -6.8; p = .000$) and in A versus C ($t = -3.95; p = .007$), but no difference was evident in N1 amplitude between B and C experiments ($t = -0.15; p = .88$). In conflict-right trials, N1 amplitude was different in A versus B ($t = -2.6; p = .04$) and in A versus C ($t = -3.6; p = .01$), but not in the B versus C experiment ($t = -0.49; p = .64$). In conflict-left trials, N1 amplitude was different in A versus B ($t = -3.9; p = .008$) and in A versus C ($t = -2.76; p = .03$), but not in B versus C ($t = -1.54; p = .17$).

Dipole analysis

All the data relative to a same subject, his VEP, the sensors location on his scalp and his RMN, were merged to localize the dipole source of the N1 component elicited by horizontal arrows. The dipole fitting procedure I adopted was the same as in paragraph 3.1, section "dipole analysis". I restricted the analysis interval to a time range from 0 msec to 300 msec after stimulus onset, where N1 differences were of maximal amplitude (see fig. 12). For this interval, principal component analysis (PCA) revealed two major components that explained more than 90% of data variance. Hence, data have been fitted to a 3 concentric shells volume conductor and a moving dipole to visualise sources, was used .

Fig. 13 shows the dipoles solution obtained for the waveshapes of the VEP of a representative subject. Depicted are dipole source location and orientation of N1 component relative to horizontal arrows presented on the left hemifield, in compatible trials. The dipole is located dorsally, in the parietal lobe.

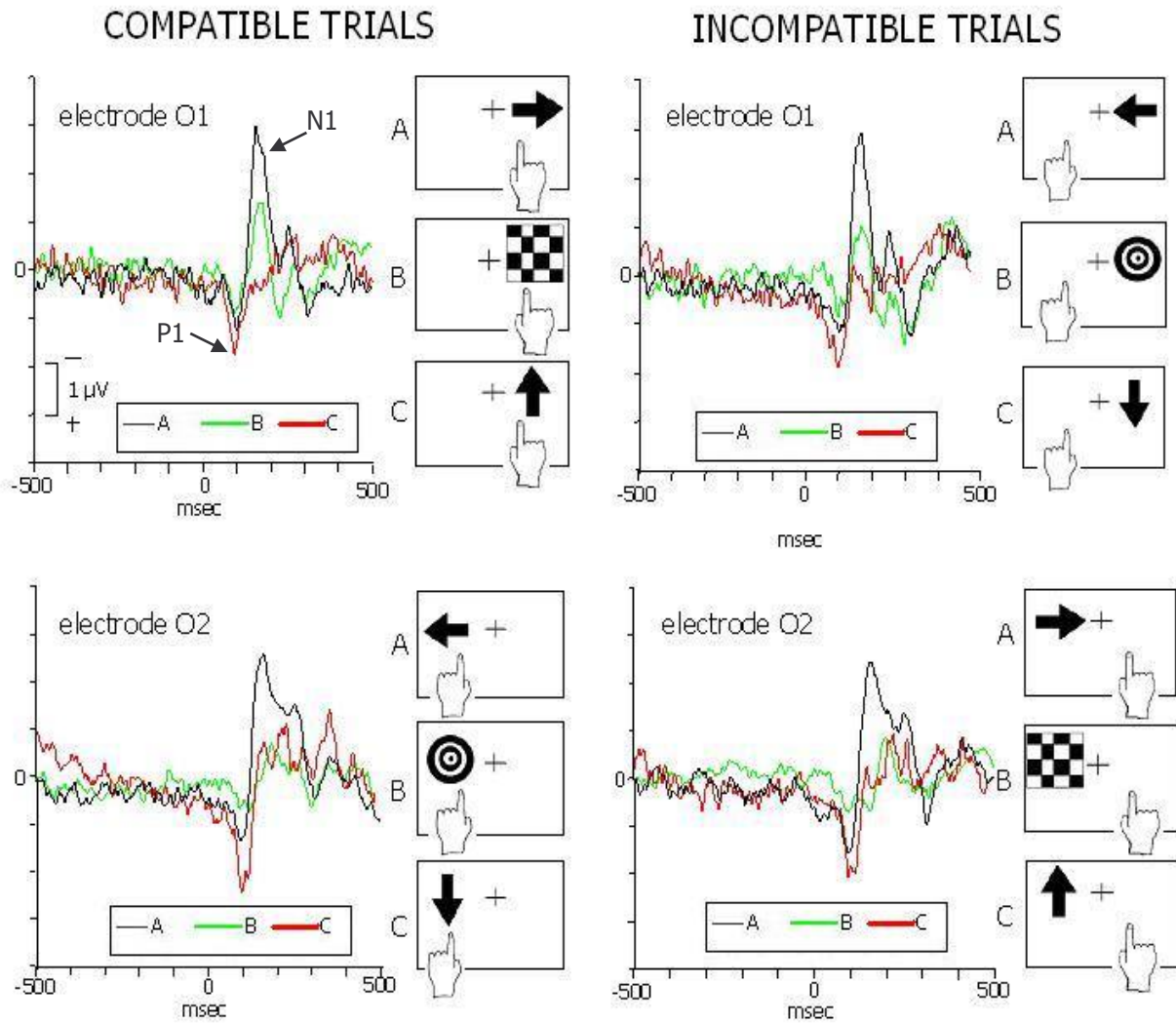


Fig. 12: Grand-average of the VEPs relative to the three types of stimuli of experiment 2 (N = 15). Both in compatible and in incompatible trials, the amplitude of the N1 component was significantly modulated by the horizontal arrowheads pointing direction.

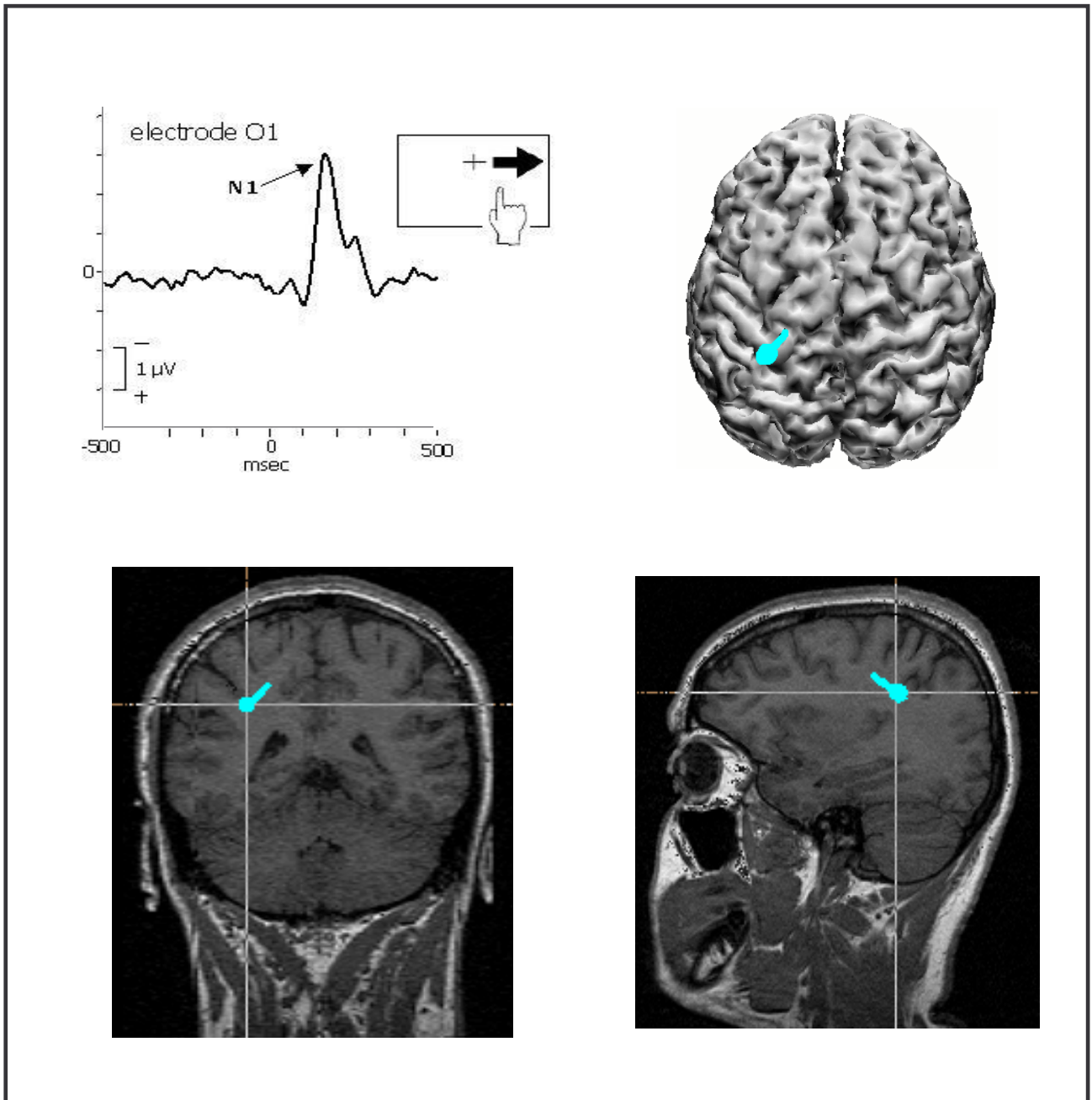


Fig. 13 Source modelling of N1 component relative to right sided horizontal arrows (compatible trials, VEP depicted on the top left). A single subject VEP is plotted over his own MRI. A model of cortex (top right) and both coronal and sagittal MRI sections are reported. The dipole localising N1 is located dorsally, in the contralateral parietal cortex.

DISCUSSION

This experiment aimed at testing whether directional attributes of horizontal left or right pointing arrows are encoded at early stages of visuomotor processes, thus speeding responses to them. Horizontal arrows have been compared to non directional shapes and to vertical arrows (upward and downward pointing).

Behavioural results show that RTs are shorter for horizontal arrows than for squares, circles and vertical arrows, indicating that specific features of the horizontal arrows speed up responses to them. The key-features might be the arrowhead pointing direction, in that it is more directly translatable into left or right hand responses than vertical arrows or non- directed shapes. Indeed, also VEP are selectively modulated by horizontal arrows. Although luminance and spatial frequency are the same in the three experiments, and regardless of the side stimuli are presented on, the N1 component of VEP is selectively modulated by horizontal arrows (Fig. 3.6). The P1 component does not appear to be affected by the type of stimulus, nor by its position (conflict versus non conflict trials). The dipole reconstruction of N1 localises it in the contralateral parietal sulcus, thus in a cortical region located more anterior than the occipital lobe. Similar VEP dipole modelling have been obtained by Di Russo et al. (2001, 2003). These authors recorded a negative component they named N155 at fronto-central electrodes. Although their N155 topography was more anterior than the N1 recorded in the present experiment at occipito-parietal sites, the two VEP components overlap, since source localisation is identical. Indeed, both in the present experiment and in Di Russo et al., (2001), the N155 source was deep in the parietal lobe, medial to the intraparietal sulcus and lateral to the cingulate sulcus. This dipole reconstruction has been further confirmed by fMRI results (Di Russo et al. 2001, 2003). Thus, horizontal arrows speed up RTs probably because they are directly “translatable” into right-left responding hand. The parietal regions where N1 is localised belongs to the dorsal stream, the visual pathway involved in encoding spatial attributes of a stimulus and in transforming them into the appropriate object-related actions (Goodale et al., 2004). The dorsal activation of the present experiment would suggest that arrows induce faster responses with

respect to simple geometrical shapes, since direction is encoded by the same cortical regions that will transform spatial properties into the subsequent related action. Both monkeys and patients studies have shown that the dorsal areas are involved in visuomotor processes (in particular the posterior parietal cortex) and in generating motor-related programs for aimed movements (Andersen et al., 1997; Mattingley et al., 1998; Snyder et al., 2000). Moreover, some results on S-R compatibility tasks using regional cerebral blood flow have suggested that the parietal cortex represents the first interface between sensory and motor-related processes (Iacoboni et al., 1996, 1998). In this sense, the parietal cortex subserves visuospatial perception to bias and regulate the choice of the task-relevant pathway (Liu et al., 2004). Moreover, the inferior parietal cortex is often coactivated with the DLSFg, which is involved in monitoring response output. The activation of the posterior parietal cortex in the present experiment is probably functional to allocate attentional resources before the selection of the overt movement. This visuospatial function is, then, probably hard-wired to the motor circuitry responsible for response control.

3.3 Anatomical localisation of ERP sources: an fMRI study - Experiment 4

Numerous functional imaging studies have attempted to define the neural bases of the interference effects in conflict tasks. These studies suggest that multiple, broadly distributed brain regions are involved in conflict monitoring and in conflict resolution, including the anterior cingulate (ACC) and the prefrontal cortices network (PFC) according to some studies, and the pre-motor (Pm), the supplementary motor (SMA) and the superior parietal cortices (sPC), according to other studies. The prefrontal areas are thought to be involved in top-down modulation during the response selection of the task-relevant information (Botvinick et al., 2001; Cohen et al., 2000; Posner and DiGirolamo, 1998; Badre & Wagner, 2004). The anterior cingulate cortex is frequently coactivated with the dorsolateral pre-frontal cortex (Corbetta et al., 1991; George et al., 1994; Peterson et al., 2002), and a great debate exist about which one of the two areas is responsible for the cognitive monitoring of the response conflict. (Cohen et al., 2000; MacDonald, et al., 2000). One of the most quoted theory is that of Botvinick and colleagues (2001) suggesting that ACC has the function to evaluate conflicts and response errors and to send a request for increased top-down control to dorsolateral pre-frontal cortex (DLPFC). In contrast, DLPFC has the function to modulate the processing in the posterior regions by orienting subjects to the task-relevant information (Badre et al., 2004). However, these theories about the roles of DLPFC and ACC have been contrasted by another series of neuroimaging studies, which have found that activation of DLPFC is relatively independent of ACC activity (Milham et al., 2001; Van Veen et al., 2001). Other investigations on conflict tasks have shown that the left dorsal anterior cingulate (BA 32) and the left prefrontal cortex (BA 10) are extensively involved in monitoring and resolving conflict (Fan, et al., 2003). Similar, although not identical, areas have been found to be activated in tasks involving huge levels of effortful control (Bush et al., 2000; Duncan and Owen, 2000). The PFC and in particular the anterior portion of the frontal lobes, including BA 10, is thought to be specialized for management of multiple simultaneous choices (Koechlin, et al., 1999) or for attentional binding of multiple modalities (e.g. what and where) into a single representational entity

(Prabhakaran, et al., 2000). The lateral premotor and the superior parietal cortices are involved in response selection in incompatible trials (Schumacher and D'Esposito, 2002; Dasonville et al., 2001; Iacoboni et al., 1996; Meyer et al., 1998). In the case the competition between the two potential responses is increased, the lateral premotor cortex is activated, as an index of the uncertainty about which response is correct (Schumacher and D'Esposito, 2002). This latter finding is in line with what found in non-human primates (Fuster, 1995; Wise, 1985). Monkeys with lesions in the lateral premotor cortex are unable to perform a response choice based on a previously learned S-R mapping (Passingham, 1993; Petrides, 1987). A PET study using both the auditory and the visual Simon task has found large, confluent activations of premotor and dorsal parietal cortices in the contralateral conditions (Iacoboni, et al., 1996; 1998). Rosen and colleagues (1999), using directional cues in a Simon task, found an activation of a relatively large portion of the supplementary motor area (SMA; BA 6) that extended inferiorly to include the cingulate gyrus. Peterson and colleagues (2002) compared the Simon and the Stroop task, in order to discriminate the neural substrates underlying the two conflict tasks. They presented volunteers with white arrows pointing either to the left or to the right against a black background, either to the left or right of a central fixation cross. Participants were instructed to press a key to either the left-pointing or right-pointing arrow with the index (relative leftward) or middle (relative rightward) finger of their right hand, respectively. On congruent trials, the direction of the arrow was the same as the location of the arrow relative to the fixation (e.g., a rightward pointing arrow to the right of fixation), whereas on incongruent trials, the direction of the arrow was opposite to the location of the arrow relative to the fixation (e.g., a rightward pointing arrow to the left of fixation). This study found an activation of SMA (BA 6), of the superior parietal (BA 19) and of the superior temporal regions (BA 21) after the presentation of the incongruent event. A smaller portion of the SMA (BA 6; 3-7,53) has been found to be selectively active during conflict conditions (Maclin et al., 2001).

A recent fMRI investigation has attempted to find the common or distinct neural substrates of attentional control in the Simon and Stroop tasks (Liu, et al., 2004).

Participants were presented with upward or downward arrows and they had to respond to upward arrows with the index finger and to the downward one with the middle finger of their right hand. The Simon effect occurred when an arrow was presented in a location incongruent with the finger used to respond (e.g., an upward arrow presented on the right of the fixation, which required response of the index finger—the more leftward of the two fingers). The Simon effect activated many midline areas, including the dorsal ACC, the dorsal pre-motor cortex, and the superior and posterior parietal regions. The same cortical areas were found to be activated by other studies (Bush et al., 2003; Dassonville et al., 2001; Fan et al., 2003; Iacoboni et al., 1998; Peterson et al., 2002).

In order to detail the neural substrates of visuomotor processes I described in their temporal aspects in previous paragraphs, and considering the amount of fMRI results on activation of anterior and posterior cortical areas related to conflict responses, I carried out an fMRI experiment using the Simon paradigm with horizontal arrows. I aimed at verifying the localization of ERP sources found in previous experiments. In particular I expected to find visual and motor activities related to stimulus onset and response execution, respectively. Moreover, I expected to confirm the frontal activation ipsilateral to the responding hand (as in exp. 2) and the contralateral parietal activation (as in exp. 3).

Methods

Participants

Four right-handed volunteers, (2 males, 2 females, mean age 26 years) participated to the experiments. The criteria of selection of volunteers were the same as in experiment 1.

Stimuli and procedure

Horizontal arrows, pointing either to the right or to the left of a central cross, were presented to subjects. Stimuli lasted 130 msec with an interstimulus interval (ISI) randomly varying among intervals of 2500, 3000 and 3500 msec. Three blocks of 30 trials were performed, with stimuli sequenced in a way as to result in equal proportion of compatible and incompatible trials. Furthermore, none of the trial sequences contained exact stimulus repetitions to avoid priming effects. Subjects were instructed to mime a keypress response with their index fingers according to the arrow direction, and to ignore the arrow position. They were asked to maintain their gaze at the central fixation cross. Presentation software (Neurobehavioral Systems) was used to create and deliver stimuli. The task was presented via a back projection onto a Plexiglas screen. Stimuli could be directly viewed by subjects thanks to their reclined neck.

fMRI data acquisition

Images were acquired with a Philips Gioscan Intera 1.5 Tesla scanner with echo planar imaging (EPI) capability. Functional data were acquired along the AC-PC line with a T2*-weighted EPI sequence of 25 contiguous axial slices (TR = 2160, TE = 45, flip angle = 90°, FoV = 210) of 4 mm thickness and 3.28 x 3.28 mm in plane resolution, providing brain coverage from the vertex to upper parts of the cerebellum. Additional high resolution anatomical images were acquired using an inversion recovery (IR) T1 sequence (TE = 15, TR = 1785.557, flip angle = 90°, inversion time (TI) = 350, FoV = 210 and 0.41 x 0.41 mm in plane resolution).

fMRI data analysis

All spatial pre-processing and statistical elaboration were carried out with SPM2 software (Wellcome Department of Imaging Neuroscience, London, UK). Images were spatially realigned to the first volume scanned. The structural T1* scan was co-registered to a

mean image of the realigned functional scans. Functional data were, then, smoothed with a Gaussian kernel using 6 mm (full width half maximum, FWHM) for single subject-analysis. Box-car vectors for each event and condition (4 conditions: left hand compatibility/incompatibility, right hand compatibility/incompatibility) were convolved with the hemodynamic response function with two derivative. The experimental conditions were compared between sessions ($N = 4$) using a conjunction analysis. Voxels within activation sites were considered only if their F values passed a height threshold of $F = 1.435$ ($p < .01$), with a cluster threshold of ≥ 5 voxels.

Results

The maps of activation of a representative subject (the same subject used for dipole source modelling) are presented in Figs. 14 and 15. Regions with common activation in both compatible and incompatible right hand trials are reported in Tab. 5 and include left pre- and post-central gyrus (BA 4 and BA 3, respectively), left inferior parietal (BA 40), left superior and middle frontal (BA 8 and BA 46, respectively), left supplementary motor (BA 6) and bilateral anterior cingulate and paracingulate gyri (BA 24). Selective activation for the right hand conflict trials involve the ipsilateral superior frontal gyrus (BA 8) and the left inferior frontal gyrus (BA 47). For the left hand, common activation in both compatible and incompatible trials involve the right pre and post-central gyri, the right inferior parietal angular gyrus (BA 40), the left supplementary motor area and the bilateral anterior cingulate cortex. Selective activation for left incompatible trials involve the ipsilateral superior frontal gyrus.

Discussion

The Simon task with directional cues activated the same brain regions as previous studies on conflict tasks (Botvinick et al., 2001; Cohen et al., 2000; Posner and DiGirolamo, 1998; Corbetta et al., 1991; George et al., 1994; Peterson et al., 2002; Egner, et al., 2005). Since the basic visual features of the stimuli were well balanced

across trials, fMRI differential brain activation roughly represent the neural substrates involved in the solution of the conflict associated with incompatible compared to compatible stimuli.

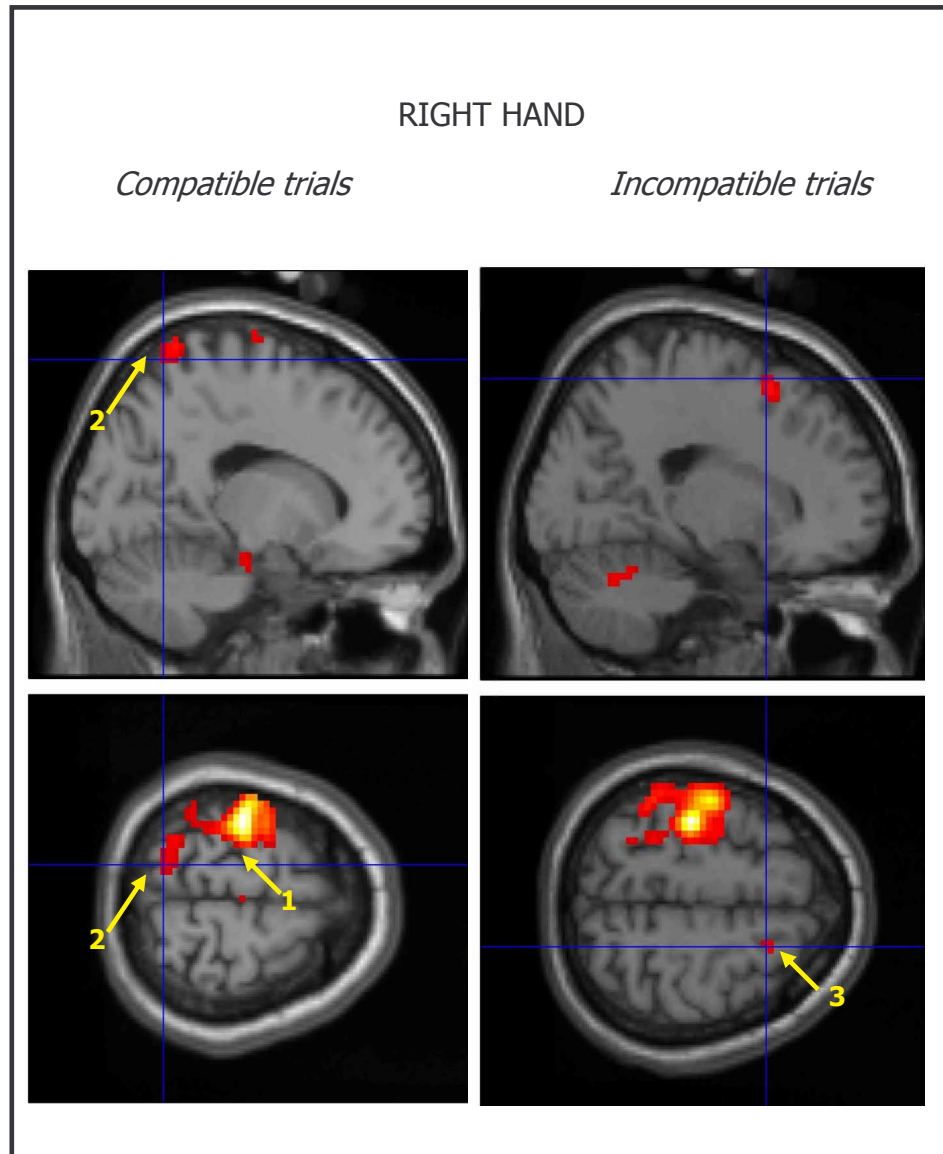


Fig. 14 Maps of activation in compatible and incompatible right hand trials ($p < .01$, corrected; cluster threshold of ≥ 5 voxels). Activity over the left precentral gyrus (1) and over the inferior parietal cortex contralateral to the visual stimulation (2), are present. In incompatible trials the superior frontal gyrus ipsilateral to the hand used to respond (3), is activated.

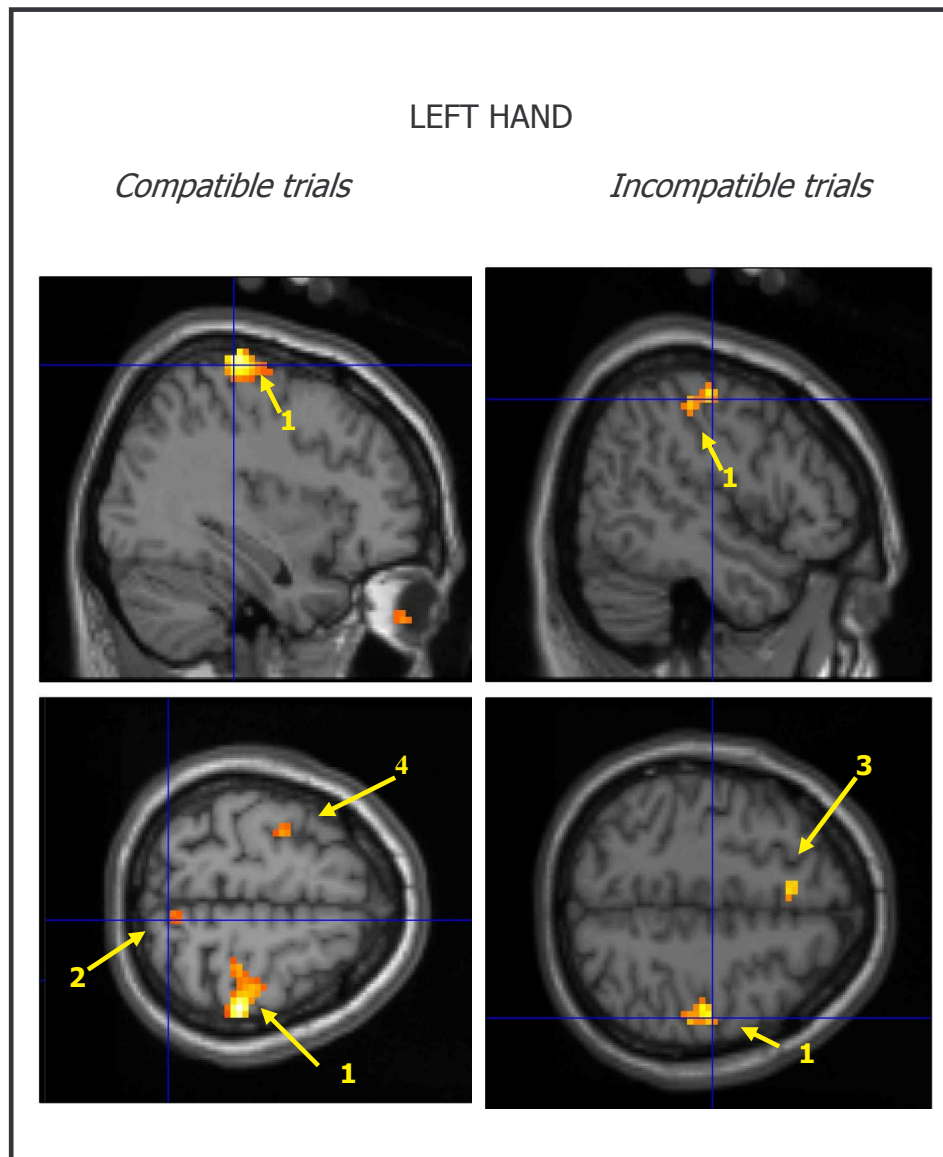


Fig. 15 Maps of activation in compatible and incompatible left hand trials ($p < .01$, corrected; cluster threshold of ≥ 5 voxels). Activity over the right precentral gyrus (1) and over the inferior parietal cortex (L angular gyrus) contralateral to the visual stimulation (2), are present. In compatible trials a right premotor activation is also present (4). In incompatible trials the left superior frontal gyrus ipsilateral to the hand (3) used to respond, is activated.

Increased activation in the parietal and supplementary motor regions likely represent the tuning to features as location and direction (Ivanoff et al., 2000). Moreover, increased activity in the anterior cingulate, superior frontal and parietal regions is associated, according to some authors, to improved task performance and practice (Tracy et al., 2001). The main interest of the present experiment is, however, to identify the brain regions underlying the MEP frontal ipsilateral peak (see paragraph 3.1 experiment 2) and the VEP parietal N1 (see paragraph 3.2 exp. 3), in order to confirm the dipole reconstruction previously obtained. These areas roughly correspond to the ipsilateral superior frontal gyrus (GFs; BA 8) that is activated only in incompatible trials (see figs. 14 and 15 and tab.3) and to the contralateral inferior parietal regions (supramarginal and angular gyri, BA 40), respectively. Firstly, GFs is strongly involved in conflict detection and resolution (Casey et al., 2000; Durtson et al., 2003; Fan et al., 2003; Hazeltine et al., 2003; Milham et al., 2003; Egner et al., 2005). GFs activation fits with MEP frontal ipsilateral activation in incompatible trials. Secondly, the inferior parietal (BA 40) is a visuomotor dorsal region, and it matches the dipole source of N1 component. Its activation might be related to translating spatial inputs from visual-to-motor system, that is from arrows direction to right-left responding hand.

Conditions	Talairach label	Side	BA	Talairach (x,y,z)			Z score
NcRH, CRH	Pre-central gyrus	L	4	-42	-18	60	4.97
NcRH, CRH	Post-central gyrus	L	3	-39	-36	54	4.67
NcRH, CRH	Inf. parietal, supramarg. & ang. gyri	L	40	-51	-51	54	4.08
NcRH, CRH	Superior frontal gyrus dorsolateral	L	8	-24	28	50	4.31
NcRH, CRH	Middle frontal gyrus	L	46	-27	54	33	3.97
NcRH, CRH	Supplementary motor area	L	6	-6	18	48	4.00
NcRH, CRH	Anterior cingulate and paracing. gyri	L, R	24	0	45	9; 4 46 10	3.36
CRH	Superior frontal gyrus dorsolateral	R	8	-28	48	40	4.46
CRH	Inferior frontal gyrus	L	47	-45	36	-15	4.14
NcLH, CLH	Pre-central gyrus	R	4	46	-16	44	3.89
NcLH, CLH	Post-central gyrus	R	3	42	-33	48	5.89
NcLH, CLH	Inf. Parietal angular Gyrus	R	40	48	-50	36	3.57
NcLH, CLH	Supplementary motor area	L	6	-12	-9	75	4.12
NcLH, CLH	Anterior cingulate and paracing. gyri	R, L	24	15	30	24;-3 24 15	3.87
CLH	Superior frontal gyrus dorsolateral	L	8	-14	32	36	3.65

Tab.5. Brain regions activated during the present experiment. Subjects (N = 4) were instructed to release a right/left key in response to the pointing direction of a laterally presented arrow. *Note.* NcRH = Non conflict right hand; CRH = conflict right hand; NcLH = Non conflict left hand; CLH = conflict left hand; R = right; L = left.

3.4 Is an arrow the best cue to speed lateralized hand responses?- Experiment 5

In previous paragraphs, left-right arrows speeded up reaction times to them and it was speculated that this type of stimuli are automatically translated into congruent lateral responses. However arrows are symbols, and they do not possess an intrinsic biological relevance. We learn, after all, what an arrow indicates only by education. A different case is certainly represented by eyes direction. When we see someone else looking to a location in space, our first tendency is to automatically direct our gaze towards the same location. This process involves visual mechanisms that are also important for social interaction, since gaze provides environmental signals and information. Gaze direction is the root of a more general cognitive system that allows interpreting actions, intentions and mental states of other people (Downing et al., 2004). For these reasons gaze direction has been proposed to represent a special form of attention (Kingstone et al., 2003; Langton et al., 2000). Previous studies on this topic have assessed that subjects reflexively orient attention to a gazed-at location, even though gaze does not predict where a target stimulus is likely to appear (Driver et al., 1999). In contrast to the volitional shift of attention triggered by arrows, gaze provoke a reflexive and automatic orienting of attention (Friesen et al., 2004; Zorzi et al. 2003). To test this automatic shift hypothesis, a Simon-type paradigm was designed where directional cues were made by lateralised outlines of eyes gazing to opposite directions. Given the intrinsic biological meaning of eyes direction, I expected gaze to cue faster RTs (as compared to arrows in previous experiments), and to selectively affect VEP topography and temporal course.

Method

Participants

Five right handed subjects participated to the study (2 males, 3 females; mean age 29 years old). The criteria of selection of volunteers were the same as in experiment 1.

Stimuli and procedure

The experimental apparatus and procedure of experiment 2 was replicated, replacing arrows with outlines of eyes pointing to left-right direction, and appearing randomly to the right or to the left of the fixation point. Subjects had to release a key according to the direction of eyes gaze, and to ignore their relative position. EEG recording procedure was the same of experiment 2.

RESULTS

Behavioural data.

Reaction times below 100 ms and above 700 ms were rejected. A repeated measure ANOVA on reaction times was carried out, using the responding hand and the stimulus location as within subject variables. Fig. 16 shows RT in conflict and non-conflict trials for both hands. A significant stimulus location by response side interaction, which reflects the classical Simon effect, was observed ($F(1, 4) = 30.50$ $p < .001$). In Tab.6 mean RT to eyes and horizontal arrows, are compared. Pairing off conditions (e.g. right hand response-compatible trials), RTs to arrows are faster than eyes of about 50 msec or more.

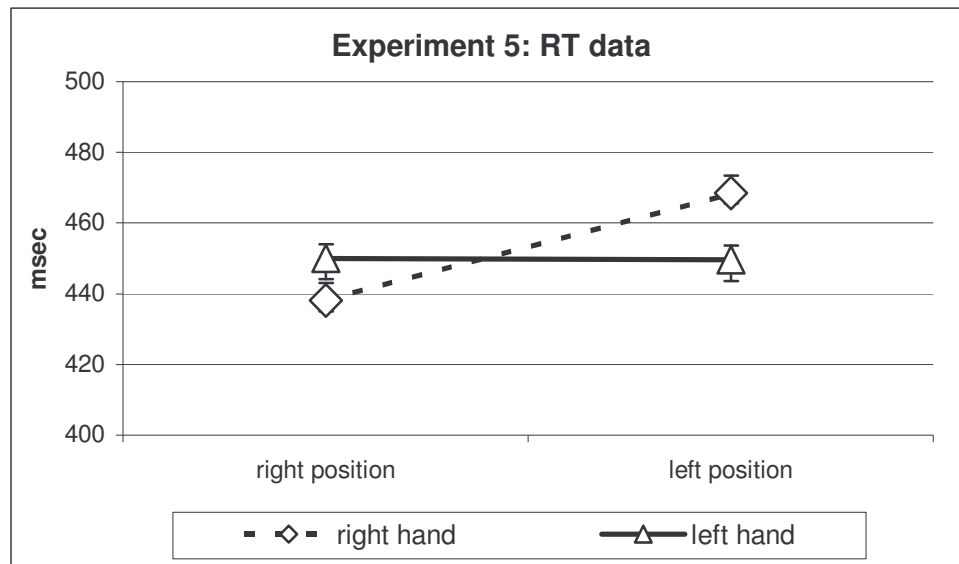


Figure 16. Mean RTs to right/left presentation of eyes, in experiment 5. Vertical bars represent standard error. When stimulus position and responding hand are on the same side, responses are faster than when they are on opposite sides. The interaction between stimulus and hand position is significant for $p < .001$.

	COMPATIBLE TRIALS (s.e)	INCOMPATIBLE TRIALS (s.e.)
Right arrowhead/right hand	369.14 (1.86)	408.33 (1.88)
Left arrowhead/left hand	368.83 (1.94)	395.32 (1.77)
Eyes pointing right/right hand	438,01 (1.82)	468,52 (1.99)
Eyes pointing left/left hand	450,06 (1.75)	449,63 (2.05)

Tab. 6: Comparison between mean RTs to the arrows of experiment 2 (chapter 3) and the eyes of the present experiment. Pairing off conditions (e.g. right hand-compatible trials), responses to arrows are of faster of about 50 msec or more, than to eyes.

EEG data.

ERPs time locked to visual stimuli onset revealed the P1 of VEP component to be selectively modulated by the presentation of eyes (fig. 17). A paired-samples t-test, tested for P1 differences among eyes (fig. 17, insert A), shapes (fig. 17, insert B) and horizontal arrows (fig. 17 insert C) at contralateral O1 or O2. These electrodes were chosen because they showed the most pronounced differences. In all experiments, P1 amplitude was different in condition A versus B, and in A versus C, for $p < .01$ or less.

Dipole analysis

All the data relative to a same subject, his VEP, the sensors location on his scalp and his RMN, were merged to localize the dipole source of the P1 component elicited by gaze direction. The dipole fitting procedure I adopted was the same as in paragraph 3.1, section "dipole analysis". I restricted the analysis interval to a time range from 0 msec to 300 msec after stimulus onset, where P1 differences were of maximal amplitude (see fig. 17). For this interval, principal component analysis (PCA) revealed two major components that explained more than 95% of data variance. Hence, data have been fitted to a 3 concentric shells volume conductor and a moving dipole to visualise sources, was used .

Fig. 18 shows the dipoles solution obtained for the waveshapes of the VEP of a representative subject. Depicted are dipole source location and orientation of P1 component relative to gaze presented on the left hemifield, in compatible trials. The dipole is located ventrally, in the middle occipital cortex.

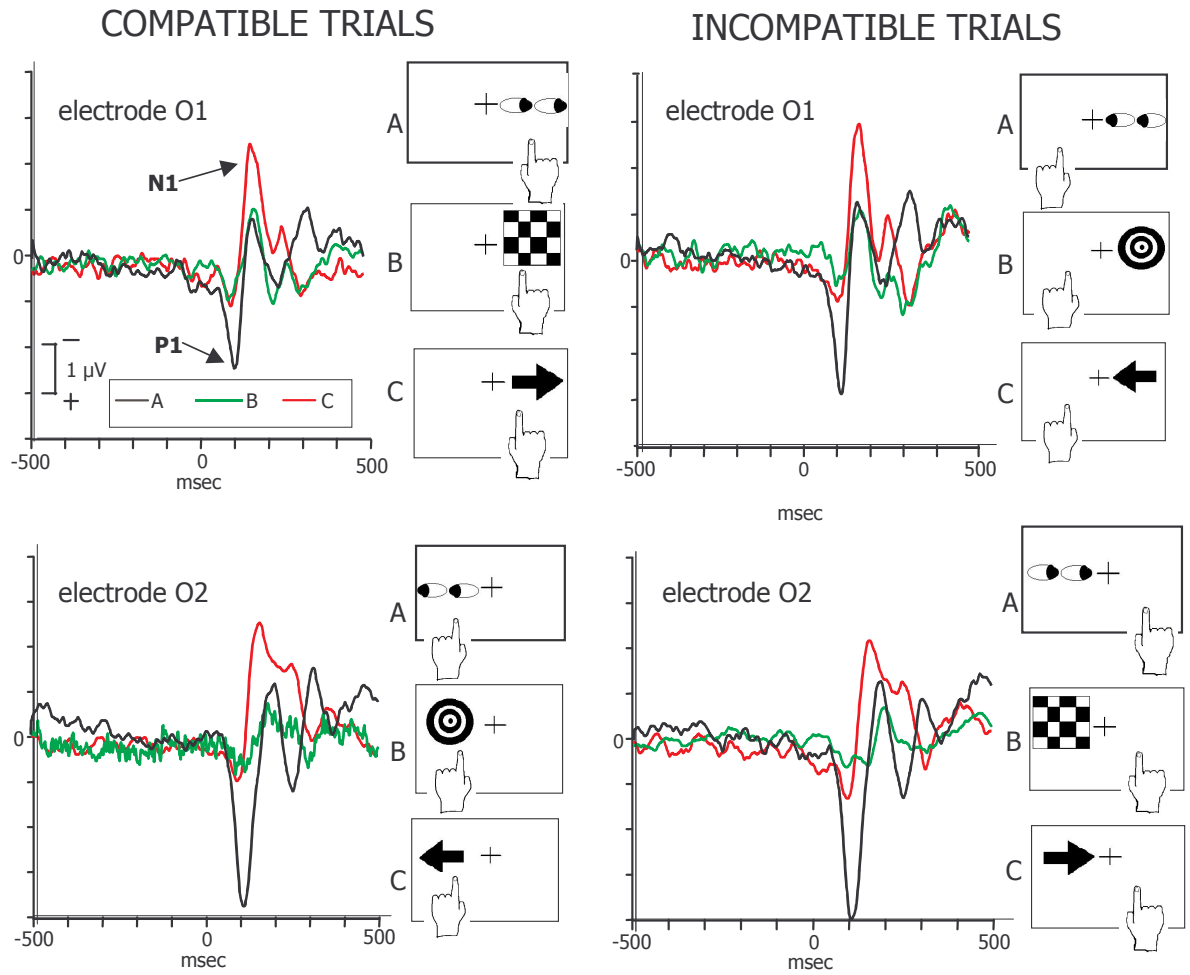


Fig. 17: Grand-average of the VEPs comparing eyes to arrows and shaped stimuli. Both in compatible and in incompatible trials, the amplitude of the P1 component is significantly modulated by the eyes pointing direction.

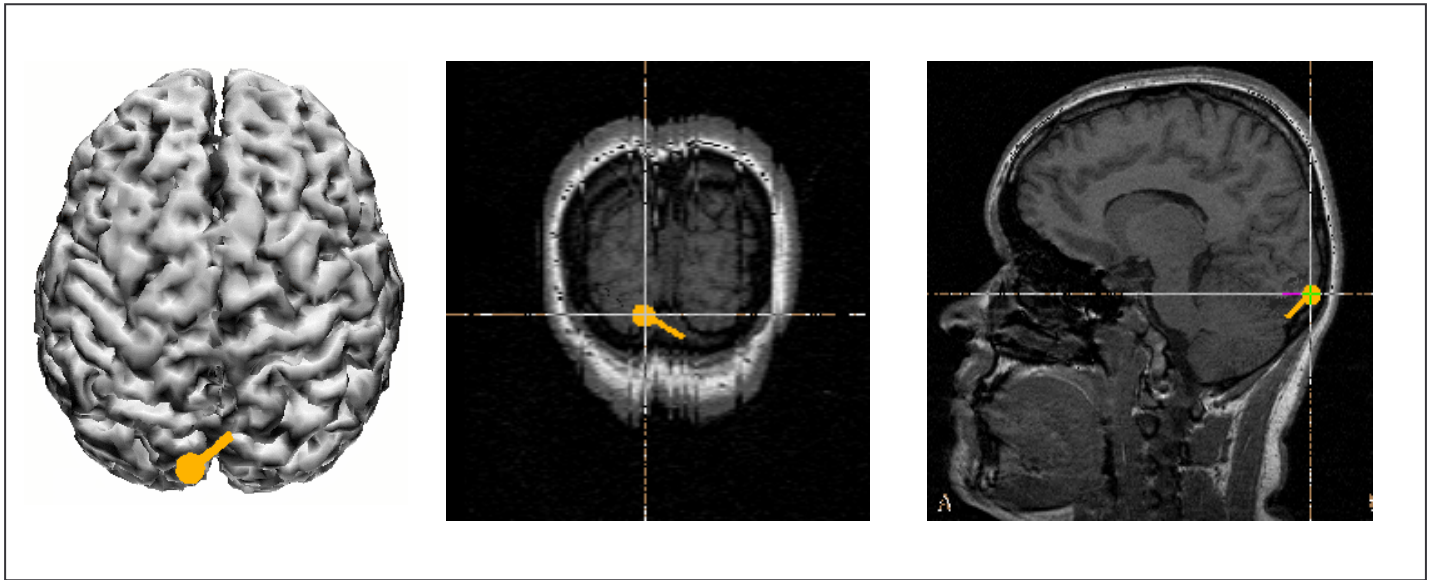


Fig. 18. Source modelling of P1 component relative to right sided eyes looking right (compatible trials). A single subject VEP is plotted over his own MRI. A model of cortex (left) and both coronal and sagittal MRI sections are reported. The dipole localising P1 is located ventrally, in the contralateral middle occipital cortex.

Discussion

This experiment aimed at studying whether gaze provokes an automatic shift of attention that speeds up RT more than arrows. Moreover, I expected early visual evoked potential components to be selectively affected by gaze direction.

In contrast to what foreseen, responses to eyes direction were slower than to arrows. Gaze direction seems not to facilitate RT. These data can be interpreted as the result of a time-consuming translation from one frame of reference to another (see Pisella & Rossetti, 2002). Gaze direction is firstly coded with respect to a context-relative spatial content (i.e. the position of irises into the eye). Then, it has to be translated into the observer-relative hand position. The former is an additional process that takes place

because gaze has a great biological intrinsic value, providing important social signals depending on where someone else is looking to. In contrast, the symbolic direction indicated by arrows is directly translated into R-L observer-relative co-ordinates. Previous studies with precueing paradigm found that RT facilitation to gaze direction was obtained only for SOA (the onset asynchrony between the cue and the target) greater than 100 msec (Driver et al., 1999). The task used in this experiment provides an abrupt onset of the cue, thus corresponding to the shorter SOA one can imagine. Thus, the resulting slower RT are in line with these previous reports. Anyway, although processing gaze direction is relatively slow, it does not conflict with its interpretation as an automatic process (Ansorge, 2003). Indeed, gaze direction is processed even when this is not explicitly required (Ansorge, 2003).

The ERP analysis reveals a selective gaze-induced P1 modulation, both in incompatible and compatible trials. This P1 activity is, probably, related to the automatic shift of attention that gaze cues provoke, and has a scalp topography that is different from the negative VEP component (i.e. the N1) elicited by arrows cues. Indeed, as shown by dipole reconstruction, P1 is located over the contralateral middle occipital cortex, whereas N1 is more parietally located. These data also fit with previous findings on P1 localization (Di Russo et al., 2001; 2003). It has been proposed that gaze engage attention differently from those processes encoding for symbolic direction, with cells in the occipito-temporal cortex processing for eye information and cells in the parietal cortex shifting attention to stimuli-cued spatial location (Kingstone et al., 2000). The P1 gaze-triggered modulation can reasonably reflect this occipito-temporal pathway of activation. Indeed, encoding for gaze direction probably requires object recognition processes that are different from those involved in symbolic directional encoding. Gaze direction conveys a great variety of social signs, and thus encoding for eyes direction may represent a special form of attention, as suggested by other studies (Friesen et al., 1998; Kingstone et al., 2003; Langton et al., 2000). The reflexive orienting to the location indicated by gaze direction is not supported by the fronto-parietal pathway that underlies volitional orienting (Friesen et al., 2004). The ventral activation to gaze direction of the present experiment is in line with previous findings (Kingstone et al.,

2000). To summarise, gaze and arrow cues can trigger qualitatively different behavioral and neural effects, with the attentional orienting to gaze direction being reflexive and with orienting to symbolic directional cues being volitional.

Chapter 4

General Discussion

The aim of my thesis was to address whether, in a response-choice task, the conflict between target position and competing responses is solved at early perceptual stages or prior to motor execution. Moreover I aimed at detailing the temporal processes and the neural substrates underlying this conflict. Taken together, the main results of this thesis suggest that the conflict is solved at the response stage by means of an active suppression of the incorrect response. Moreover, if stimuli are provided with directional attributes which strengthen the conflict, these attributes are coded at early perceptual stages, and this facilitates the solution of the conflict.

In Chapter 1 I presented a review of recent studies on perception and action, and on their relationship in conflict tasks. In Chapter 2 the time-course of programming conflict responses to shaped stimuli, was investigated. In Chapter 3 the conflict generated by both symbolic (arrows) and “biological” (eyes gaze) directional stimuli was studied. The temporal course of the conflict was investigated both prior to response execution and after visual onset. Moreover, the anatomical substrates underlying response conflict were described.

In the next two sections I will discuss the main results reported in previous chapters.

4.1 Programming conflicting responses

In Chapter 2, I investigated the time course of the conflict between competing responses using lateralised shapes (in a Simon-type paradigm). In it responses had to be performed according to specific shapes while ignoring their left/right position. ERP in phase with response execution (MEP) revealed the moment in which the cortical motor areas were activated. Moreover, in incompatible trials (i.e. in trials in which stimulus and response side were opposite) a selective ERP correlate of the conflict emerged. Indeed,

a frontal negative activity ipsilateral to the hand used to respond popped out in incompatible trials only. This ipsilateral activity probably reflects the suppression of the incorrect response, that is the response automatically evoked by stimulus position. This interpretation is in line with results obtained by previous studies with TMS (Leocani et al., 2000) and MEP (Carbonell et al., 2004).

A second experiment investigated whether the ipsilateral frontal ERP was also present if symbolic directional stimuli (arrows) were used instead of geometrical shapes. Responses to arrows were faster than to simple shapes but ERPs did not differ between the two tasks. Indeed, a frontal activity ipsilateral to response was in the same way elicited by spatially incompatible arrows. The source of this activity is located, as confirmed by a following fMRI localisation (experiment 4), in the superior frontal lobe, an area typically activated in conflict detection and resolution (Casey et al., 2000; Durston et al., 2003; Fan et al., 2003; Hazeltine et al., 2003; Egner et al., 2005).

If directional stimuli have the intrinsic property to speed up compatible lateralised responses, but this process is not related to a specific cortical marker, it is probably because directional attributes are not encoded at response but at early perceptual level.

4.2 Visuomotor coding of directional attributes

In a third experiment, ERP elicited by directional and non directional stimuli were compared. The visual evoked potential (VEP) revealed that arrows selectively modulate N1 amplitude when triggering compatible lateralised responses. This N1 component was enhanced by the presentation of horizontal but not of vertical arrows, nor of geometrical shapes. N1 dipole source was localised in the inferior parietal cortex, confirmed by fMRI activation (experiment 4) and in agreement with previous findings (Di Russo et al., 2001, 2003). This parietal region belongs to the dorsal stream, that is involved in encoding spatial attributes of a stimulus and in transforming them into the appropriate stimulus-related actions (cfr. Goodale et al., 2004). Thus, directional attributes seems to

be encoded by the same cortical regions that will translate spatial properties into the subsequent related action.

In the case stimulus direction is not indicated by a symbolic but by a “biologically relevant” cue as it is the gaze, RT are slower. This phenomenon is probably due to a translation from a frame of reference (the position of irises into the eye) to another (the observer’s hand position), which is not required by arrows (as suggested by Pisella et al. 2002). Nevertheless, a gaze-induced P1 modulation of the VEP is present both in compatible and incompatible trials. The source of the P1 component is located over the middle occipital cortex, which is a visuomotor ventral area. Thus, gaze engage early perceptual processes differently from arrows, with cells in the ventral areas processing for eye information (as proposed by Kingstone et al., 2000), and cells in the dorsal areas encoding for symbolic direction.

4.3 To do or not to do: neural processes underlying response conflict.

In everyday life, our behavior is guided by both cognitive (top-down) factors, such as knowledge, expectation and current goals, and by bottom-up factors that reflect sensorial stimulation. The results of this thesis suggest that the processes underlying response conflict involve two partially segregated neural systems.

One system, which involves the dorsal inferior parietal and superior frontal cortex, is engaged by the selection of sensory information and responses. In particular, the inferior parietal (stimulus-driven) activation might probably serve as the early visuomotor interface between visual encoding and motor-related programs for aimed actions. In this sense, the spatial features of the arrows are directly translated into congruent actions. Therefore, the activation of the inferior parietal cortex might be functional to allocate attentional resources before selecting for the overt movement. The inferior parietal cortex is often co-activated with the DLSFg, which is engaged by (top-down) monitoring of the target response. The DLSFg top-down bias is exerted by controlling whether the response selected is ultimately task-appropriated and, possibly,

by inhibiting incorrect outputs. Thus, the inferior parietal cortex represents a sort of pre-program of the spatial response, and the frontal circuit controls whether the initially selected response is ultimately task relevant.

The second system, which is centered on the ventral (occipito-temporal) pathway, is recruited during the detection of biologically relevant sensory events. This ventral activation is stimulus-driven, and is engaged by a reflexive, rather than volitional, orienting of attention. The reflexive nature of attentional resource also accounts for the very precocious encoding for stimuli provided with biological relevance.

4.4 Future directions

The proposed functional interactions between neural systems for stimulus-driven processes and top-down monitoring for action, raises many questions for future research. One issue concerns the anatomical relationship between regions of the inferior parietal cortex and motor areas for attending to objects eliciting grasping actions (e.g. ergonomic tools). Specifying these relationships will involve detailed studies on single cases (patients suffering from damages to the inferior parietal areas). Another issue concerns the functional relationship between dorsal and ventral streams during bottom-up orienting. For example, topographical mapping in both the middle occipital and in the inferior parietal areas might indicate the relative role of each in encoding for location attributes. Understanding the mechanisms underlying spatial encoding might also help in clarifying the pathophysiology of neglect. It might be also important to integrate these functional descriptions with neuropsychological and pharmacological studies, in order to better understand top-down (cholinergic system) and bottom-up (noradrenergic system) attentional mechanisms in acquired (strokes, traumas) or developmental (attention deficit) disorders of attention.

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References

- Aglioti, S., De Souza, J.F., Goodale, M.A. (1995). Size-contrast illusions deceive the eye but not the hand. *Current Opinion in Biology*, 5, 679-685.
- Aguirre, G.K., Zarahn, E., D'Esposito, M. (1998). An area within human ventral cortex sensitive to "building" stimuli: evidence and implications. *Neuron*, 21, 373-383.
- Allison, T., McCarthy, G., Nobre, A., Puce, A., Belger, A. (1994). Human extrastriate visual cortex and the perception of faces, words, numbers, and colours. *Cerebral Cortex*, 4, 544-554.
- Allison, T., Wood, C.C., and McCarthy, G. (1986). The central nervous system. In M.G.H. Coles, E. Donchin, and S.W. Porges (Eds.) *Psychophysiology: systems, processes and applications*, Guilford, New York (pp.5-25).
- Andersen, R.A., Snyder, L.H., Bradley, D.C., Xing, J. (1997). Multimodal representation of space in the PPC and its use in planning movements. *Annual Review of Neuroscience*, 20, 303-330.
- Andrews, T.J., Schluppeck, D., Homfray, D., Matthews, P., Blakemore, C. (2002). Activity in the fusiform gyrus predict conscious perception of Rubin's vase-face illusion. *NeuroImage*, 17, 890-901.
- Ansorge, U. (2003). Spatial Simon effects and compatibility effects induced by observed gaze direction. *Visual Cognition*, 10, 363-383.
- Avidan, G., Harel, M., Hendler, T., Ben-Bashat, D., Zohary, E., Malach, R. (2002). Contrast sensitivity in human visual areas and its relationship to object recognition. *Journal of Neurophysiology*, 87, 3102-3116.

- Babiloni, F., Babiloni, C., Carducci, F., Fattorini, L., Onorati, P., Urbano, A. (1996). Spline Laplacian estimate of EEG potentials over a realistic magnetic resonance-constructed scalp surface model. *Electroencephalography and Clinical Neurophysiology*, 98, 363-373.
- Babiloni, F., Cincotti, F., Babiloni, C., Carducci, f., Mattia, D., Astolfi, L., Basilisco, A., Rossini, P.M., Ding, L., Ni, Y., Cheng, J., Christine, K., Sweeney, J., and He, B. (2005). Estimation of the cortical functional connectivity with the multimodal integration of high-resolution EEG and fMRI data by directed transfer function. *NeuroImage*, 24, 118-131.
- Badre, D., Wagner, A.D. (2004). Selection, integration, and conflict monitoring: Assessing the nature and generality of prefrontal cognitive control mechanisms, *Neuron* 41, 473-487.
- Baillet, S., Mosher, J.C., Lahey, R.M. (2001). Electromagnetic brain mapping. *IEEE Signal Processing Magazine*, Nov., 14-30.
- Banich, M. T., Milham, M.P., Atchley, R., Cohen, N.J., Webb, A., Wszalek, T., Kramer, A.F., Liang, Z.P., Wright, A., Shenker, J., and Magin, R. (2001). FMRI studies on the Stroop tasks reveal unique roles of anterior and posterior brain systems in attentional selection. *Journal of Cognitive Neuroscience*, 12, 988-1000.
- Beauchamp, M.S., Lee, K.E., Haxby, J.V., Martin, A. (2002). Parallel visual motion processing streams for manipulable objects and human movements. *Neuron*, 34, 149-159.
- Booth, M.C., Rolls, E.T. (1998). View-invariant representations of familiar objects by neurons in the inferior temporal visual cortex. *Cerebral Cortex*, 8, 510-523.

- Botvinick, M.M., Braver, T.S., Barch, D.M., Carter, C.S., Cohen, J.D. (2001). Conflict monitoring and cognitive control. *Psychological Review*, 108, 624-652.
- Boynton, G.M., Demb, J.B., Glover, G.H., Heeger, D.J. (1999). Neuronal basis of contrast discrimination. *Vision Research*, 39, 257-269.
- Brefczynski, J.A., De Yoe, E.A. (1999). A physiological correlate of the "spotlight" of visual attention. *Nature Neuroscience*, 2, 370-374.
- Bruce, C.J., & Goldberg, M.E. (1985). Primate frontal eye field: I. Single neurons discharging before saccades. *Journal of Neurophysiology*, 53, 603-635.
- Buckner, R.L., & Logan, J.M. (2001). Functional neuroimaging methods: PET and fMRI. In R. Cabeza & A. Kingstone (Eds.), *Handbook of functional neuroimaging of cognition*, Cambridge, MA: MIT Press.
- Bunge, S.A, Burrows, B., Wagner, A.D. (2004) Prefrontal and hippocampal contributions to visual associative recognition: interaction between cognitive control and episodic retrieval, *Brain Cognition* 56, 141-152.
- Burman, D.D., & Segraves, M.A. (1994). Primate frontal eye field activity during natural scanning eye movements. *Journal of Neurophysiology*, 71, 1266-1271.
- Bush, G., Luu, P., & Posner, M.I. (2000). Cognitive and emotional influences in the anterior cingulate cortex. *Trends in Cognitive Sciences*, 4, 215-222.
- Bush, G., Shin, L.M., Holmes, J., Rosen, B.R., Vogt, B.A. (2003). The multi-Source interference Task: validation study with fMRI in individual subjects. *Molecular Psychiatry* 8, 60-70.
- Cabeza, R., Nyberg, L. (2000). Imaging cognition. II. An empirical review of 275 PET and fMRI studies. *Journal of Cognitive Neuroscience (Review)*, 12, 1-47.

- Carbonell, L., Hasbroucq, T., Grapperon, J., Vidal, F. (2004). Response selection and motor areas: a behavioral and electrophysiological study. *Clinical Neurophysiology*, *115*, 2164-2174.
- Carey, D.P. (2001). Do action systems resist visual illusions? *Trends in Cognitive Sciences*, *5*, 109-113.
- Carter, C.S., Braver, T.S., Barch, D.M., Botvinick, M.M., Noll, D., & Cohen, J.D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science*, *280*, 747-749.
- Carter, C.S., Mintun, M., Nichols, T., & Cohen, J.D. (1997). Anterior cingulate gyrus dysfunction and selective attention deficits in schizophrenia: [¹⁸F]-FDG PET study during single-trial Stroop task performance. *American Journal of Psychiatry*, *154*, 1670-1675.
- Casey, B.J., Thomas, K.M., Whelsh, T.F., Badgaiyan, R.D., Eccard, C.H., Jennings, J.R., Crone, E.A. (2000). Dissociation of response conflict, attentional selection, and expectancy with functional magnetic resonance imaging. *PNAS, USA*, *97*, 8728-8733.
- Cavada, C. (1984). Transcortical sensory pathways to the prefrontal cortex with special attention to the olfactory and visual pathways. In: Reinoso-Suares F., & Ajmone-Marsan, C. (Eds.). *Cortical Integration*, Raven Press, NY, (pp. 317-328).
- Chao, L.L., Haxby, J.V., Martin, A. (1999). Attribute-based neural substrates in temporal cortex for perceiving and knowing about objects. *Nature Neuroscience*, *2*, 913-919.
- Cohen, L., Dehaene, S., Naccache, L., Lehericy, S., Dehaene-Lambertz, G. et al., (2000). The visual word form area: spatial and temporal characterization of an initial stage

of reading in normal subjects and posterior split-brain patients. *Brain*, 123, 291-307.

Colby, C., & Duhamel, J. R. (1996). Spatial representations for action in parietal cortex. *Cognitive Brain Research*, 5, 105-115.

Coles, M. G. H. , Gehring, W.J., Gratton, G., & Donchin, E. (1992). Response activation and verification: A Psychophysiological analysis. In G.E. Stelmach & J. Requin (Eds), *Tutorials in motor behaviour II*. Amsterdam: Elsevier, 779-792.

Connolly, J.D., Goodale, M.A., Desouza, J.F., Menon, R.S., & Vilis, T.A. (2000). A comparison of frontoparietal fMRI activation during anti-saccades and anti-pointing. *Journal of Neurophysiology*, 84, 1645-1655.

Corbetta, M., Miezin, F.M., Dobmeyer, S., Shulman, G.L., Petersen, S.E. (1991). Selective and divided attention during visual discriminations of shape, color and speed: functional anatomy by positron emission tomography. *Journal of Neuroscience*, 11, 2383-2402.

Craighero, L., Fadiga, L., Rizzolatti, G., & Umiltà, C.A. (1999). Action for perception: a motor-visual attentional effect. *Journal of Experimental Psychology: Human Perception and Performance*, 25, 1673-1692.

Culham, J.C. (2002). Parietal cortex. *Encyclopaedia of Cognitive Sciences*, 2002, 451-457.

Culham, J.C., Danckert, S.L., Souza, J.F., Gati, J.S, Menon, R.S., Goodale, M.A. (2003). Visually guided grasping produces fMRI activation in dorsal but not ventral stream areas. *Experimental Brain Research*, 153, 180-189.

- Damasio, H. (1995). Human brain anatomy in computerized images. New York: Oxford University Press.
- Dassonville, P., Lewis, S.M., Zhu, X.H., Ugurbil, K., Kim, S.G., Ashe, J. (2001). The effect of stimulus-response compatibility on cortical motor activation. *NeuroImage*, 13, 1-14.
- De Houwer, J. (2004). Spatial Simon effects with non spatial responses. *Psychonomic Bulletin & Review*, 11, 49-53.
- De Jong, R., Coles, M.G.H., Logan, G.L., & Gratton, G. (1990). In search of the point of no return.: The control of response processes. *Journal of experimental Psychology: Human Perception and Performance*, 16, 164-182.
- De Jong, R., Liang, C.-C., & Lauber, E. (1994). Conditional and unconditional automaticity: A dual process model of effects of spatial stimulus-response correspondence. *Journal of Experimental Psychology: Human Perception and Performance*, 20, 731-750.
- De Jong, R., Wierda, M., Mulder, G., & Mulder, L.J.M. (1988). Use of partial information in response processing. *Journal of Experimental Psychology, human Perception and Performance*, 14, 682-692.
- De Soto, M.C., Fabiani, M., Geary, D.C., & Gratton, G. (2001). When in doubt, do it both ways: Brain evidence of the simultaneous activation of conflicting motor response in a spatial Stroop task. *Journal of Cognitive Neuroscience*, 13, 523-536.
- Di Russo, F., Martinez, A., Sereno, M.I., Pitzalis, S., Hillyard, S.A. (2001). Cortical sources of the early components of the visual evoked potential, *Human Brain Mapping*, 15, 95-111.

- Di Russo, F., Martinez, A., Hillyard, S.A. (2003). Source analysis of event-related cortical activity during visuo-spatial attention, *Cerebral Cortex*, *13*, 486-499.
- Downar, J., Crawley, A.P., Mikulis, D.J., Davis, K.D. (2001). The effect of task relevance on the cortical response to changes in visual and auditory stimuli: An event-related fMRI study. *Neuroimage*, *14*, 1256-1267.
- Downar, J., Crawley, A.P., Mikulis, D.J., Davis, K.D. (2002). A cortical network sensitive to stimulus salience in a neutral behavioural context across multiple sensory modalities. *Journal of Neurophysiology*, *87*, 615-620.
- Downing, P.E., Jiang, Y., Shuman, M., Kanwisher, N. (2001). A cortical area sensitive for visual processing of the human body. *Science*, *293*, 2470-2473.
- Downing, P.E., Dodds, C.M., Bray, D. (2004). Why does the gaze of others direct visual attention? *Visual Cognition*, *11*, 71-79.
- Driver, J., Davis, G., Ricciardelli, P., Kidd, P., Maxwell, E., & Baron Cohen, S. (1999). Gaze perception triggers visuospatial orienting by adults in a reflexive manner. *Visual Cognition*, *6*, 509-540.
- Duncan, J., & Owen, A.M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends in Neuroscience*, *23*, 475-483.
- Duncan, J. (2001). An adaptive coding model of neural function in prefrontal cortex. *Nature Review Neuroscience*, *2*, 820-829.
- Durston, S., Davidson, M.C., Thomas, K.M., Worden, M.S., Tottenham, N., Martinez, A., Watts, R., Ulug, A.M., Casey, B.J. (2003). Parametric manipulation of conflict and response competition using rapid mixed-trial event-related fMRI. *NeuroImage*, *20*, 2135-2141.

- Egner, T., Hirsch, J. (2005). The neural correlates and functional integration of cognitive control in a Stroop task. *NeuroImage*, 24, 539-547.
- Eimer, M., Hommel, B., & Prinz, W. (1995). S-R compatibility and response selection. *Acta Psychologica*, 90, 301-313.
- Eimer, M. & Schlaghecken, F. (1998). Effects of masked stimuli on motor activation: Behavioral and electrophysiological evidence. *Journal of Experimental Psychology: Human Perception and Performance*, 24, 1737-1747.
- Epstein, R., Kanwisher, N. (1998). A cortical representation of the local visual environment. *Nature*, 392, 598-601.
- Evinger, C., Shaw, M. D., Peck, C. K. , Manning, K. A. and Baker, R. (1984). Blinking and associated eye movements in humans, guinea pigs, and rabbits. *Journal of Neurophysiology*, 52, 323-339.
- Fan, J., Flombaum, J.I., McCandliss, B.D., Thomas, K.M., Posner, M.I. (2003). Cognitive and brain consequences of conflict. *NeuroImage*, 18, 42-57.
- Fender, D.H. (1987) Source localization of brain electrical activity. In: Gevins, A.S., Remond, A. (Eds.). *Handbook of electroencephalography and clinical neurophysiology, Vol. 1. Methods of analysis of brain electrical and magnetic signals*. Amsterdam: Elsevier (pp. 355-399).
- Fisch, B.J. (1999) EEG Primer: Basic Principles Of Digital And Analog EEG. 3rd Revised And Enlarged Edition. Elsevier Science B.V, Amsterdam.
- Fischer, M.H. (1997). Attention allocation during manual movement preparation and execution. *European Journal of Cognitive Psychology*, 9, 17-51.

- Fitts, P.M., & Seeger, C.M. (1953). S-R compatibility: Spatial characteristics of stimulus and response codes. *Journal of Experimental Psychology*, 46, 199-210.
- Franz, V.H., Fahle, M., Bulthoff, H.H., Gegenfurtner, K.R. (2001). Effects of visual illusions on grasping. *Journal of Experimental Psychology: Human Perception and Performance*, 27, 1124-1144.
- Franz, V.H., Gegenfurtner, K.R., Bulthoff, H.H., Fahle, M. (2000). Grasping visual illusions: no evidence for a dissociation between perception and action. *Psychol Sci* 11, 20-25.
- Friesen, C.K., Ristic, J., Kingstone, A. (2004). Attentional effects of counterpredictive gaze and arrow cues. *Journal of Experimental Psychology: Human Perception and Performance*, 30, 319-329.
- Friesen, C.K., Kingstone, A. (1998). The eyes have it! Reflexive orienting is triggered by nonpredictive gaze. *Psychonomic Bulletin & Review*, 5, 490-495.
- Fuster, J.M. (1995). Memory in the cerebral cortex. Cambridge: MIT Press.
- Gallant, J.L., Braun, J., Van Essen, D.C. (1993). Selectivity for polar, hyperbolic, and Cartesian gratings in macaque visual cortex. *Science*, 259, 100-103.
- Gallese, V., Murata, A., Kaseda, M., Niki, N., & Sakata, H. (1994). Deficit of hand preshaping after muscimol injection in monkey parietal cortex. *Neuroreport*, 5, 1525-1529.
- Gehring, W., Gratton, G., Coles, G.H., and Donchin, E. (1992). Probability effects on stimulus evaluation and response processes. *Journal of Experimental Psychology: Human Perception and Performance*, 18, 1, 198-216.

- Gehring, W.J., & Knight, R.T. (2000). Prefrontal cingulate interactions in action monitoring. *Nature Neuroscience*, *3*, 516-520.
- George, M.S., Ketter, T.A., Parekh, P.I., Rosinsky, N., Ring, H.A., Casey, B.J., et al. (1994). Regional brain activity when selecting a response despite interference: an O-15 PET study of the Stroop and an emotional Stroop. *Human Brain Mapping*, *1*, 194-209.
- Giesbrecht, B., Woldorff, M.G., Song, A.W., Mangun, G.R. (2003). Neural mechanisms of top-down control during spatial and feature attention. *Neuroimage*, *19*, 496-512.
- Goldberg, M.E., Colby, C.L., & Duhamel, J.R. (1990). Representation of visuomotor space in the parietal lobe of the monkey. *Cold Spring Harb. Simp. Quant. Biol.*, *55*, 729-739.
- Goodale, M.A., Meenan, J.P., Bulthoff, H.H., Nicolle, D.A., Murphy, K.J., Racicot, C.I. (1994). Separate neural pathways for the visual analysis of object shape in perception and prehension. *Current Opinion in Biology*, *4*, 604-610.
- Goodale, M.A., Milner, A.D. (1992). Separate visual pathways for perception and action. *Trends in Neuroscience*, *15*, 20-25.
- Goodale, M.A., Milner, A.D. (2004). Sight unseen: an exploration of conscious and unconscious vision. Oxford: Oxford University Press.
- Goodale, M.A., Milner, A.D., JaKobson, L.S., Carey, D.P. (1991). A neurological dissociation between perceiving objects and grasping them. *Nature*, *349*, 154-156.
- Goodale, M.A., Westwood, D.A. (2004). An evolving view of duplex vision: separate but interacting cortical pathways for perception and action. *Current Opinion in Neurobiology*, *14*, 203-211.

- Gottlieb, J.P., Kusunoki, M., & Goldberg, M.E. (1998). The representation of visual salience in monkey parietal cortex. *Nature*, *391*, 481-484.
- Gottsdanker, R., & Shragg, G. P. (1985). Verification of Donders' subtraction method. *Journal of Experimental Psychology: Human Perception and Performance*, *11*, 765-776.
- Gratton, G. (1998). The contralateral organization of visual memory: a theoretical concept and research tool. *Psychophysiology*, *35*, 638-647.
- Gratton, G., Bosco, C.M., Kramer, A. F., Coles, M.G.H., Wickens, C.D., & Donchin, E (1990). Event related brain potentials as indices of information extraction and response priming. *Electroencephalography and Clinical Neurophysiology*, *75*, 419-432.
- Gratton, G., Coles, M.G.H., and Donchin, E. (1983). A new method for off-line removal of ocular artifacts. *Electroencephalography and Clinical Neurophysiology*, *55*, 468-484.
- Gratton, G., Coles, M.G., Sirevaag, E.J., Eriksen, C. W. & Donchin (1988). Pre- and poststimulus activation of response channels: A psychophysiological analysis. *Journal of Experimental Psychology: Human Perception and Performance*, *14*, 331-344.
- Gross, C.G. (1992). Representation of visual stimuli in inferior temporal cortex. *Phyl. Trans. R. Soc. Lond.*, *B335*, 3-10.
- Gross, C.G., & Graziano, M. S. A. (1995). Multiple representations of space in the brain. *Neuroscientist*, *1*, 43.

- Gross., C.G., Rocha-Miranda, C.E., and Bender, D.B. (1972). Visual properties of neurons in the inferotemporal cortex of the macaque. *Journal of Neurophysiology*, 35, 96-111.
- Grossman, E.D., Blake, R. (2002). Brain areas active during visual perception of biological motion. *Neuron*, 35, 1167-1175.
- Hackley, S.A. & Valle-Inclán, F. (1998). Automatic alerting does not speed late motoric processes in a reaction-time task. *Nature*, 391, 786-8.
- Hackley, S.A. & Valle-Inclán, F. (1999). Accessory stimulus effects on response selection: does arousal speed decision making? *Journal of Cognitive Neuroscience*, 11, 321-329.
- Haffenden, A.M., Goodale, M.A. (2000). Independent effects of pictorial displays on perception and action. *Vision Research*, 40, 1597-1607.
- Haffenden, A.M., Schiff, K.C., Goodale, M.A. (2001). The dissociation between perception and action in the Ebbinghaus illusion: nonillusory effects of pictorial cues on grasp. *Current Opinion in Biology*, 11, 177-181.
- Hamalainen, M.S., Ilmoniemi, R. J. (1994). Interpreting magnetic fields of the brain- minimum norm estimates. *Med Biol Eng Comput*, 32, 35-42.
- Handy, T.C., Grafton, S.T., Shroff, N.M., Ketay, S., & Gazzaniga, M.S. (2003). Graspable objects grab attention when the potential for action is recognized. *Nature Neuroscience*, 6, 421-427.
- Hasbroucq, T., & Guiard, Y. (1991). Stimulus-response compatibility and the Simon effect: toward a conceptual clarification. *Journal of Experimental Psychology: Human Perception and Performance*, 17, 246-266.

- Hasbroucq, T., & Possamai, C.A. (1994). What can a precue enhance-an analysis of the experiments of Proctor, Lu and Van Zandt (1992). *Acta Psychologica*, *85*, 235-244.
- Hasson, U., Hendler, T., Ben Bashat, D., Malach, R. (2001). Vase or face? A neural correlate of shape-selective grouping processes in the human brain. *Journal of Cognitive Neuroscience*, *13*, 744-753.
- Hasson, U., Levy, I., Behrmann, M., Hendler, T., Malach, R. (2002). Eccentricity bias as an organizing principle for human high-order object areas. *Neuron*, *34*, 479-490.
- Hazeltine, E., Bunge, S.A., Scanlon, M.D., Gabrieli, J.D.E. (2003). Material-dependent and material-independent selection processes in the frontal and parietal lobes: an event-related fMRI investigation of response competition. *Neuropsychologia*, *41*, 1208-1217.
- He, B., Lian, J. (2002). High-resolution spatio-temporal functional neuroimaging of brain activity (Review). *Crit Rev Biomed Eng*, *30*, 283-306.
- Heil, M., Rauch, M., & Hennighausen, E. (1998). Response preparation begins before mental rotation is finished. Evidence from event-related brain potentials. *Acta Psychologica*, *99*, 217-232.
- Hietanen, J. H., & Rama, p. (1995). Facilitation and interference occur at different stages of processing in the Simon paradigm. *European Journal of Cognitive Psychology*, *7*, 183-199.
- Hillyard, S.A., & Munte, T.F. (1984). Selective attention to color and location: an analysis with event-related brain potentials. *Perception and Psychophysics*, *36*, 185-198.

- Hommel, B. (1993). The relationship between stimulus processing and response selection in the Simon task: evidence for a temporal overlap. *Psychological Research, 55*, 280-290.
- Hommel, B. (1993b). The role of attention for the Simon effect. *Psychological Research, 55*, 208-222.
- Hommel, B. (1994). Spontaneous decay of response code activation. *Psychological Research, 56*, 261-268.
- Hommel, B., & Prinz, W. (1997). *Theoretical issues in stimulus-response compatibility*. Amsterdam: Elsevier.
- Hubel, D.H., Wiesel, T.N. (1968). Receptive fields and functional architecture of monkey striate cortex. *Journal of Physiology, 195*, 215-243.
- Iacoboni, M., Woods, R.P., Mazziotta, J.C. (1996). Brain-behaviour relationships: evidence from practice effects in spatial stimulus-response compatibility. *Journal of Neurophysiology, 76*, 321-331.
- Iacoboni, M., Woods, R.P., Mazziotta, J.C. (1998). Bimodal (auditory and visual) left frontoparietal circuitry for sensorimotor integration and sensorimotor learning. *Brain, 121*, 2135-2143.
- Ishai, A., Ungerleider, L.G., Martin, A., Haxby, J.V. (2000). The representation of objects in the human occipital and temporal cortex. *Journal of Cognitive Neuroscience, 12*, 35-51.
- Ishai, A., Ungerleider, L.G., Martin, a., Schouten, J.I., Haxby, J.V. (1999). Distributed representation of objects in the human ventral visual pathway. *Proceedings of the National Academy of Sciences USA, 96*, 9379-9384.

- Ivanoff, J. (2003). On spatial response code activation in a Simon task. *Acta Psychologica, 112*, 157-179.
- Ivanoff, J., Peters, M. (2000). A shift of attention may be necessary, but is not sufficient, for the generation of the Simon effect. *Psychological Research, 64*, 117-135.
- James, T.W., Humphrey, G.K., Gati, J.S., Menon, R.S., Goodale, M.A. (2002). Differential effects of viewpoint on object-driven activation in dorsal and ventral streams. *Neuron, 35*, 793-801.
- Jasper, H.H. (1958). Report of the Committee on Methods of Clinical Examination in Electroencephalography, Electroencephalogr. *Clin. Neurophysiol. 10*, 370-371.
- Johnson, M.K., Reeder, J.A., Raye, C.L., and Mitchell, K.J. (2002). Second thoughts versus second looks: an age related deficit in reflectively refreshing just-activated information. *Psychological Science, 13*, 64-67.
- Johnson, M.K., Raye, C.L., Mitchell, K.J., Green, E.J., and Anderson, A.W. (2003). FMRI evidence for an organization of prefrontal cortex by both type of process and type of information. *Cerebral Cortex, 13*, 265-273.
- Kalanit, G.S., & Malach, R. (2004). The human visual cortex. *Annual review of Neuroscience, 27*, 649-677.
- Kanwisher, N., Mc Dermott, J., Chun, MM (1997). The fusiform face area: a module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience, 17*, 4302-4311.

- Kawashima, R., Roland, P. E., & O'Sullivan B. (1995). Functional anatomy of reaching and visuomotor learning: a positron emission tomography study. *Cerebral Cortex*, 5, 111-122.
- Kingstone, A., Friesen, C.K., & Gazzaniga, M.S. (2000). Reflexive joint attention depends on lateralized cortical connections. *Psychological Science*, 11, 159-165.
- Kingstone, A., Smilek, D., Ristic, J., Friesen, C.K., & Eastwood, J.D. (2003). Attention, researchers! It is time to take a look at the real world. *Current Directions in Psychological Science*, 12, 176-180.
- Kobayashi, K., Akiyama, T., Nakahori, T., Yoshinaga, H., Gotman, J. (2002). Systematic source estimation of spikes by a combination of independent component analysis and RAP-MUSIC. I. Principles and simulation study. *Clinical Neurophysiology*, 113, 713-724.
- Koechlin, E., Basso, G., Pietrini, P., Panzer, S. & Grafman, J. (1999). The role of the anterior prefrontal cortex in human cognition. *Nature*, 399, 148-151.
- Kornblum, S., Hasbroucq, T., & Osman, A. (1990). Dimensional overlap: cognitive basis for stimulus-response compatibility- a model and taxonomy. *Psychological Review*, 97, 253-270.
- Kornblum, S. Stevens, G.T., Whipple, A., Requin, J. (1999). The effects of irrelevant stimuli: 1. The time-course of stimulus-stimulus and stimulus-response consistency effects with Stroop-like stimuli, Simon-like tasks, and their factorial combinations. *Journal of Experimental Psychology, Human Perception and Performance*, 25, 688-714.

- Kourtzi, Z., Kanwisher, N. (2000). Cortical regions involved in perceiving object shape. *Journal of Neuroscience*, 20, 3310-3318.
- Kourtzi, Z., Kanwisher, N. (2001). Representation of perceived object shape by the human lateral occipital complex. *Science*, 293, 1506-1509.
- Kustov, A.A., & Robinson, D.L. (1996). Shared neural control of attentional shifts and eye movements. *Nature*, 384, 74-77.
- Lamberts, K., Tavernier, G. & D'Ydewalle, G. (1992). Effects of multiple reference points in spatial stimulus response compatibility. *Acta Psychologica*, 79, 115-130.
- Langton, S.R.H., Watt, R.J., & Bruce, V. (2000). Do the eyes have it? Cues to the direction of social attention. *Trends in Cognitive Sciences*, 4, 50-59.
- Le, J. Lu, M., Pellouchoud, E., Gevins, A. (1998). A rapid method for determining standard 10/20 electrode positions for high resolution EEG studies. *Electroencephalography and Clinical Neurophysiology*, 106, 554-558.
- Le, S., Cardebat, d., Boulanouar, K, Henaff, M.A., Miche, F., Milner, D., Dijkerman, C., Puel, M., Demonet, J.F. (2002). Seeing, since childhood, without ventral stream: a behavioural study. *Brain*, 125, 58-74.
- Leocani, L., Cohen, L.G., Wasserman, E.M., Ikoma, K., Hallet, M. (2000). Human corticospinal excitability evaluated with transcranial magnetic stimulation during different reaction time paradigms. *Brain*, 123, 1161-1173.
- Lerner, Y., Hendler, T., Malach, R. (2002). Object completion effects in the human lateral occipital complex. *Cerebral Cortex*, 12, 163-177.
- Leuthold, H., & Kopp, B. (1998). Mechanisms of priming by masked stimuli: Inferences from event-related potentials. *Psychological Science*, 9, 263-269.

- Leuthold, H., Sommer, W., & Ulrich, R. (1996). Partial advance information and response preparation: Inferences from the lateralized readiness potential. *Journal of Experimental Psychology: General*, 125, 307-323.
- Levy, I., Hasson, U., Avidan, G., Hendler, T., Malach, R. (2001). Centre-periphery organization of human object areas. *Nature Neuroscience*, 4, 533-539.
- Liu, X., Banich, M.T., Jacobson, B.L., & Tanabe, J.L. (2004). Common and distinct neural substrates of attentional control in an integrated Simon and spatial Stroop task as assessed by event-related fMRI. *NeuroImage*, 22, 1097-1106.
- Liu, T., Slotnick, S.D., Serences, J.T., Yantis, S. (2003). Cortical mechanisms of feature-based attentional control. *Cerebral Cortex*, 13, 1334-1343.
- Lu, C.-H., & Proctor, R.W. (1995). The influence of irrelevant location information on performance: A review of the Simon and spatial Stroop effects. *Psychonomic Bulletin & Review*, 2, 174-207.
- Luck, S.J. (1995). Multiple mechanisms of visual-spatial attention: recent evidence from human electrophysiology. *Behavioral Brain Research*, 71, 113-123.
- Luck, S.J., Hillyard, S.A. (1994a). Electrophysiological correlates of feature analysis during visual search. *Psychophysiology*, 31, 291-308.
- Luck, S.J., Hillyard, S.A. (1994b). Spatial filtering during visual search: evidence from human electrophysiology. *Journal of Experimental Psychology, Human Perception and Performance*, 20, 1000-1014.
- Macaluso, E., Frith, C.D., Driver, J. (2000). Modulation of human visual cortex by crossmodal spatial attention. *Science*, 289, 1206-1208.

- MacDonald, A. W., Cohen, J. D., Stenger, V. A., Carter, C. S. (2000). Dissociating the role of dorsolateral prefrontal cortex and anterior cingulate cortex in cognitive control, *Science* 288, 1835-1838.
- MacLin, E.L., Gratton, G., & Fabiani, M. (2001). Visual spatial localization conflict: an fMRI study. *NeuroReport*, 12, 3633-3636.
- Martin, A., Wiggs, C.L., Ungerleider, L.G., Haxby, J.V. (1996). Neural correlates of category specific knowledge. *Nature*, 379, 649-652.
- Mattingley, J.B., Husian, M., Rorder, C., Kennard, C., Driver, J. (1998)., Motor role of human inferior parietal lobe revealed in unilateral neglect patients. *Nature*, 392, 179-182.
- Mendola, J.D., Dale, A.M., Fischl, B., Liu, A.K., Tootell, R.B. (1999). The representation of illusory and real contours in human cortical visual areas revealed by functional magnetic resonance imaging. *Journal of Neuroscience*, 19, 8560-8572.
- Meyer, D.E., Evans, J., Lauber, E.J., Gmeind, L., Rubinstein, J., Junck, L., Koeppe, R.A. (1998). The role of dorsolateral prefrontal cortex for executive cognitive processes in task switching. *Journal of Cognitive Neuroscience*, (Suppl.), 106-106.
- Michel, C.M., Thut, G., Morand, S., Khateb, A., Pegna, A.J., Grave de Peralta, R., Gonzales, S., Seeck, M., Landis, T. (2001). Electric source imaging of human cognitive brain functions (Review). *Brain Research Review*, 36, 108-118.
- Milham, M.P., Banich, M.T., Claus, E. D., Cohen, N.J. (2003). Practice related effects demonstrate complementary roles of anterior cingulate and prefrontal cortices in attentional control. *NeuroImage*, 18, 483-493.

Milham, M.P., Banich, M.T., Webbe, A., Barad, V., Cohen, N.J., Wszalek, T. et al. (2001).

The relative involvement of anterior cingulate and prefrontal cortex in attentional control depends on nature of conflict. *Brain Res Cognitive Brain Research*, 12, 467-473.

Miller, E.K., and Cohen, J.D. (2001). An integrative theory of prefrontal cortex function.

Annual Review of Neuroscience, 24, 167-202.

Miller, J. O. (1998). Effects of stimulus-response probability on choice reaction time:

Evidence from the lateralized readiness potential. *Journal of Experimental Psychology: Human Perception and Performance*, 24, 1521-1534.

Miller, J. O., & Ulrich, R. (1998). Locus of the effect of the number of alternative

responses: Evidence from the lateralized readiness potential. *Journal of Experimental Psychology: Human Perception and Performance*, 24, 1215-1231.

Milner, A.D., Goodale, M.A. (1993). Visual pathways to perception and action. In: Hicks,

T.P., Molotchnikoff, S., Ono, T. (eds.). *The visually responsive neuron: From basic physiology to behaviour. Progress in brain research*. Vol. 95. Amsterdam: Elsevier (pp. 317-338).

Milner, A.D., Goodale, M.A. (1995) The visual brain in action. Oxford: Oxford University Press.

Murata, A., Gallese, V., Kaseda, M., & Sakata, H. (1996). Parietal neurons related to

memory-guided hand manipulation. *Journal of Neurophysiology*, 75, 2180-2186.

Milner, A.D., Perret, D.i., Johnston, R.S., Benson, P.J., Jordan, T.R., Heley, D.W.,

Bettucci, D., Mortara, F., Mutani, R., Terazzi, E., Davidson, D.L.W. (1991). Perception and action in "visual form agnosia". *Brain*, 114, 405-428.

- Murata, A., Gallese, V., Luppino, G., Kaseda, M., & Sakata, H. (2000). Selectivity for the shape size, and orientation of objects for grasping in neurons of monkey parietal area AIP. *Journal of Neurophysiology*, *83*, 2580-2601.
- Nicoletti, R., & Umiltà, C. (1994). Attention shifts produce spatial stimulus codes. *Psychological Research*, *56*, 144-150.
- O'Leary, M., J., Barber, P.J. (1993). Interference effects in the Stroop and Simon paradigms. *Journal of Experimental Psychology: Human Perception and Performance*, *19*, 830-840.
- Oldfield, R.C. (1971). The assessment and analysis of handedness: the Edinburgh Inventory. *Neuropsychologia*, *9*, 97-113.
- Osman, A., & Moore, C.M. (1993). The locus of dual-task interference: psychological refractory effects on movement-related brain potentials. *Journal of Experimental Psychology: Human Perception and Performance*, *19*, 1292-1312.
- Pardo, J.V., Pardo, P.J., Janer, K.W., and Raichle, M.E. (1991). The anterior cingulate cortex mediates processing selection in the Stroop attentional conflict paradigm. *Proceedings of the National Academy of Sciences USA*, *87*, 256-259.
- Passingham, R.E. (1993). The frontal lobes and voluntary action. Oxford: Oxford Psychology Series.
- Perenin, M.T., Vighetto, A. (1988). Optic ataxia: a specific disruption in visuomotor mechanisms. I. Different aspects of the deficit in reaching for objects. *Brain*, *111*, 643-674.

- Peterson, B.S., Kane, M.J., Alexander, G.M., Lacadie, C., Skudlarski, P., Leung, H.C., et al.,(2002). An event-related functional MRI study comparing interference effects in the Simon and Stroop tasks. *Brain Res. Cognitive Brain Research*, 13, 427-440.
- Peterson, B.S., Skudlarski, P., Gatenby, J.C., Zhang, H., Anderson, A.W., & Gore, J.C. (1999). An fMRI study of Stroop Word-Color interference: evidence for cingulate subregions subserving multiple distributed attentional systems. *Biological Psychiatry*, 45, 1237-1258.
- Petit, L., Clark, V.P., Ingeholm, J., & Haxby, J.V. (1997). Dissociation of saccade-related and pursuit-related activation in human frontal eye fields as revealed by fMRI. *Journal of Neurophysiology*, 77, 3386-3390.
- Petrides, M. (1987). Conditional learning and the primate frontal cortex. In: Perecman E. (Ed.). *The frontal lobes revisited*. New York: IRBN Press (pp. 91-108).
- Petrides, M. (2000). Dissociable roles of mid-dorsolateral prefrontal and anterior inferotemporal cortex in visual working memory. *Journal of Neuroscience*, 20, 7496-7503.
- Pisella, L., & Rossetti, Y. (2002). Several "vision for action" systems: A guide to dissociating and integrating dorsal and ventral functions. In: W. Prinz & B. Hommel (Eds.), *Attention and Performance, XIX: Common mechanisms in perception and action*, Oxford, UK: University Press (pp. 62-119).
- Platt, M.L., & Glimcher, P.W. (1999) Neural correlates of decision variables in parietal cortex. *Nature*, 400, 233-238.
- Posner, M.I., & Dehaene, S. (1994). Attentional networks, *Trends in Neuroscience*, 17 75-79.

- Posner, M.I., DiGirolamo, G.J. (1998). Executive attention: conflict, target detection, and cognitive control. In: Parasuraman, R (Ed.), *The Attentive Brain*, MIT Press, Cambridge, MA.
- Prabhakaran, V., Narayanan, K., Zhao, Z., Gabrieli, J.D. et al..(2000). Integration of diverse information in working memory within the frontal lobe. *Nature Neuroscience*, 3, 85-90.
- Proctor, R.W., & Lu, C-H. (1994). Referential coding and attention-shifting account of the Simon effect. *Psychological Research*, 56, 185-195.
- Proctor, R.W., & Lu, C-H., & Van Zandt, T. (1992). Enhancement of the Simon effect by response precuing. *Acta Psychologica*, 81, 53-74.
- Puce, A., Allison, T., Gore, J.C., McCarthy, G. (1995). Face-sensitive regions in human extrastriate cortex studied by functional MRI. *Journal of Neurophysiology*, 74, 1192-1199.
- Rizzolatti, G., Camarda, R. (1987). Neural circuits for spatial attention and unilateral neglect. In M. Jeannerod (Ed.). *Neurophysiological and neuropsychological aspects of spatial neglect*. Amsterdam: North-Holland (pp. 289-313).
- Rizzolatti, G., Craighero, L. (1998). Spatial attention: mechanisms and theories. In M. Sabourin, F. Craik, & M. Roberts (Eds.), *Advances in psychological science: Vol. 2. Biological and cognitive aspects*. East Sussex, England: Psychology Press (pp. 171-198).
- Rizzolatti, G., Fadiga, L., Fogassi, G., & Galese, L. (1997). The space around us. *Science*, 277, 190-191.

- Rizzolatti, G., Riggio, L., Dascola, I., & Umiltà, C. (1987). Reorienting attention across the horizontal and vertical meridians: evidence in favour of a premotor theory of attention. *Neuropsychologia*, *25*, 31-40.
- Rizzolatti, G., Riggio, L., & Sheliga, B.M. (1994). Space and selective attention. In C. Umiltà & M. Moscovitch (Eds.), *Attention and Performance XV*. Cambridge, MA: MIT Press (pp. 231-265).
- Rosen, A.C., Rao, S.M., Caffarra, P., Scaglioni, A., Bobholz, J.A., Woodley, S.J., Hammeke, T.A., Cunningham, J.M., Prieto, T.E., Binder, J.R. (1999). Neural basis of endogenous and exogenous spatial orienting: a functional MRI study. *Journal of Cognitive Neuroscience*, *11*, 135-152.
- Rubichi, S., Nicoletti, R., Iani, C. & Umiltà, C. (1997). The Simon effect occurs relative to the direction of an attention shift. *Journal of Experimental Psychology: Human Perception and Performance*, *23*, 1353-1364.
- Sakata, H., Taira, M., Kusunoki, m., Murata, A., & Tanaka, Y. (1997). The parietal association cortex in depth perception and visual control of hand action. *Trends in Neuroscience*, *20*, 350-357.
- Sakata, H., Taira, M., Murata, A., & Mine, S. (1995). Neural mechanisms of visual guidance of hand action in the parietal cortex of the monkey. *Cerebral Cortex*, *5*, 429-438.
- Schein, S.J., Desimone, R. (1990). Spectral properties of V4 neurons in the macaque. *Journal of Neuroscience*, *10*, 3369-3389.

- Scherg, M., Ille, N., Bornfleth, H., Berg, P. (2002). Advanced tools for digital EEG review: virtual source montages, whole-head mapping, correlation, and phase analysis. *Journal of Clinical Neurophysiology*, 19, 91-112.
- Schumacher, E., & D'Esposito, M. (2002). Neural implementation of response selection in humans as revealed by localized effects of stimulus-response compatibility on brain activation. *Human Brain Mapping*, 17, 193-201.
- Shadlen, M.N., & Newsome, W.T. (1996). Motion perception: seeing and deciding. *Proceedings of the National Academy of Sciences USA*, 93, 628-633.
- Shadlen, M.N., & Newsome, W.T. (2001). Neural basis of a perceptual decision in the parietal cortex (area LIP) of the rhesus monkey. *Journal of Neurophysiology*, 86, 1916-1936.
- Sheliga, B.M., Craighero, L., Riggio, L. & Rizzolatti, G. (1997). Effects of spatial attention on directional manual and ocular responses. *Experimental Brain Research*, 114, 339-351.
- Sheliga, B.M., Riggio, L. & Rizzolatti, G. (1994). Orienting of attention and eye movements. *Experimental Brain Research*, 98, 507-522.
- Sigala, N., Logothetis, N.K. (2002). Visual categorization shapes feature selectivity in the primate temporal cortex. *Nature*, 415, 318-320.
- Simon, J.R. (1990). The effects of an irrelevant directional cue on human information processing. In R. W. Proctor & T. G. Reeve (Eds.), *Stimulus-response compatibility: an integrated perspective*, Vol. 65 (pp. 31-86). North-Holland, Amsterdam: Advances in Psychology.

- Simon, J.R., & Rudell, A.P. (1967). Auditory S-R compatibility: the effect of an irrelevant cue on information processing. *Journal of Applied Psychology*, *51*, 300-304.
- Snyder, L.H., Batista, A. P., & Andersen, R. A. (1997). Coding of intention in the posterior parietal cortex. *Nature*, *386*, 167-170.
- Snyder, L.H., Batista, A.P., Andersen, R.A. (2000). Intention-related activity in the posterior parietal cortex: a review. *Vision Research*, *40*, 1433-1441.
- Stanley, D.A., Rubin, N. (2003). FMRI activation in response to illusory contours and salient regions in the human lateral occipital complex. *Neuron*, *37*, 323-331.
- Stoffer, T.H. (1991). Attentional focussing and spatial stimulus-response compatibility. *Psychological Research*, *53*, 127-135.
- Stoffer, T.H., & Umiltà, C. (1997). Spatial coding with reference to the focus of attention in S-R compatibility and the Simon effect. In B. Hommel & W. Prinz (Eds.). *Theoretical issues in S-R compatibility*. Amsterdam: North-Holland (pp. 181-208).
- Stoffer, T.H., Yakin, A.R. (1994). The functional role of attention for spatial coding in the Simon effect. *Psychological Research*, *56*, 151-162.
- Sturmer, B., Leuthold, H., Soetens, E., Schroter, H., Sommer, W. (2002). Control over location-based priming in the Simon task: behavioral and electrophysiological evidence. *Journal of Experimental Psychology: Human Perception and Performance*, *28*, 1345-1363.
- Sturmer, B., Leuthold, H. (2003). Control over response priming in visuomotor processing: a lateralized event related potential study. *Experimental Brain Research*, *153*, 35-44.

- Tagliabue, M., Zorzi, M., Umiltà, C., Bassignani, F. (2000). The role of long-term-memory and short-term-memory links in the Simon Effect. *Journal of Experimental Psychology: Human Perception & Performance*, 26, 648-670.
- Talairach, J., Tournoux, P. (1988). A co-planar stereotactic atlas of the human brain. Stuttgart, Germany: Thieme.
- Tootell, R.B., Hadjikhani, N. (2000). Attention-brains at work! *Nature Neuroscience*, 3, 206-208.
- Tracy, J.I., Faro, S.S., Mohammed, F., Pinus, A., Christensen, H., Burkland, D. (2001). A comparison of "Early" and "late" stage brain activation during brief practice of a simple motor task. *Cognitive Brain Research*, 10, pp. 303 – 316.
- Tucker, M., and Ellis, R. (1998). On the relations between seen objects and components of potential actions. *Journal of Experimental Psychology: Human Perception and Performance*, 24, 830-846.
- Umiltà, C., Liotti, M. (1987). Egocentric and relative spatial codes in S-R compatibility. *Psychological Research*, 49, 81-90.
- Umiltà, C., Mucignat, C., Riggio, L., Barbieri, C. & Rizzolatti, G. (1994). Programming shifts of spatial attention. *European Journal of Cognitive Psychology*, 6, 23-41.
- Umiltà, C., & Nicoletti, R. (1990). Spatial stimulus-response compatibility. In R.W. Proctor & T.G. Reeve (Eds.). *Stimulus-response compatibility: An integrated perspective. Advances in psychology*. (Vol. 65, pp. 89-116). Amsterdam, The Netherlands: North-Holland.

- Umiltà, C., & Nicoletti, R. (1992). An integrated model of the Simon effect. In J. Alegria, D. Holender, J. Junca de Morais, & M. Radeau (Eds.), *Analytic approaches to human cognition*, Amsterdam: North Holland (pp. 331-350).
- Umiltà, C., Riggio, L., Dascola, I., & Rizzolatti, G. (1991). Differential effects of central and peripheral cues on the reorienting of spatial attention. *European Journal of Cognitive Psychology*, 3, 247-267.
- Ungerleider, L.G., and Mishkin, M. (1982). Two cortical visual systems. In *Analysis of visual behaviour*, (ed. D.J. Ingle, M.A. Goodale, and R.J.W. Mansfield), pp. 549-586. MIT Press, Cambridge, MA.
- Valle-Inclán, F., Hackley, S.A., & de Labra, C. (2002). Does stimulus-driven response activation underlie the Simon effect? In B. Hommel & W. Prinz (Eds.), *Common mechanisms in perception and action: Attention and performance XIX* (pp. 474-493). Oxford, England: Oxford University Press.
- Van Der Lubbe, R.h.J., Wauschkuhn, B., Wascher, E., Niehoff, T., Kompf, D., Verleger, R. (2000). Lateralization with directional information for the preparation of saccades and finger movements. *Experimental Brain Research*, 131,
- Van Veen, V., Cohen, J.D., Botvinick, M.M., Stenger, V.A., Carter, C.S. (2001). Anterior cingulate cortex, conflict monitoring, and levels of processing. *NeuroImage*, 14, 1302-1308.
- Verleger, R., Wauschkuhn, B., Van Der Lubbe, R.h.J., Jaoekowski, P., Trillenber, P. (2000). Posterior and anterior contributions of hand movement preparation to Late CNV. *Journal of Psychophysiology*, 14, 69-86.

- Vidal, F., Grapperon, J., Bonnet, M., Hasbroucq, T. (2003). The nature of unilateral motor commands in between-hand choice tasks as revealed by surface Laplacian estimation. *Psychophysiology*, 40, 796-805.
- Wauschkuhn, B., Wascher, E., Verleger, R. (1997). Lateralized cortical activity due to preparation of saccades and finger movements: A comparative study. *Electroencephalography and Clinical Neurophysiology*, 102, 114-124.
- Weeks, D.J., Chua, R., & Hamblin, K. (1996). Attention shifts and the Simon effect: a failure. *Psychological Research*, 58, 246-253.
- Wise, S.P. (1985). The primate premotor cortex fifty years after Fulton. *Behavioral Brain Research*, 18, 79-88.
- Yamaguchi, S., Tsuchiya, H., Kobayashi, S. (1994). Electroencephalographic activity associated with shifts of visuospatial attention. *Brain*, 117, 553-562.
- Yantis, S., Schwarzbach, J., Serences, J.T., Carlson, R.L., Steinmetz, M.A., Pekar, J.J., Courtney, S.M. (2002). Transient neural activity in human parietal cortex during spatial attention shifts. *Nature Neuroscience*, 5, 995-1002.
- Yantis, S., Serences, J.T., (2003). Cortical mechanisms of space-based and object-based attentional control. *Current Opinion in Neurobiology*, 13, 187-193.
- Zorzi, M., & Umiltà, C. (1995). A computational model of the Simon effect. *Psychological Research*, 58, 193-205.
- Zorzi, M., Mapelli, D., Rusconi, E., Umiltà C. (2003). Automatic spatial coding of perceived gaze direction is revealed by the Simon effect. *Psychonomic Bulletin & Review*, 10, 423 -429.