



UNIVERSITÀ DEGLI STUDI DI VERONA

**DIPARTIMENTO DI SCIENZE NEUROLOGICHE E
DELLA VISIONE
- SEZIONE DI FISIOLOGIA -**

**DOTTORATO DI RICERCA IN
SCIENZE PSICOLOGICHE E PSICHIATRICHE**

XXI ciclo

***Interaction between mechanisms of attention selection in
space and time:
Behavioural and electrophysiological evidence***

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ABSTRACT

The study of mechanisms involved in spatial attention is one of the most investigated field in modern neuroscience, but in the last years a growing interest has been devoted to unveil the mechanisms concerning also the temporal aspects of attention. In this thesis three experiment are reported that tried to cast more light on the temporal aspects of attention and on the relationship between spatial and temporal attentional mechanisms.

In the first experiment the relationship between spatial and temporal deficit in selective visual attention has been investigated in a group of neglect patients using a temporal order judgement task (TOJ). The main finding is a stronger impairment in temporal selection for spatial position in which the attention selection is more impaired, suggesting an interaction between the two aspects in the modulation of the deficit.

The second and the third experiment investigated temporal expectations generated by a regular rhythm. In particular, the impact of exogenous and endogenous temporal expectation has been compared in a discrimination task, revealing the pervasive effect of regularity of movement and speed in orienting attention in time. Moreover, it has been confirmed the combined effect of spatial and temporal expectations in modulation of electrophysiological response.

These results suggest the existence of an interaction between spatial and temporal mechanisms of attention.

ABSTRACT

I meccanismi attentivi consentono di selezionare dall'ambiente circostante le informazioni utili allo svolgimento di un determinato compito. Negli ultimi trenta anni, i processi coinvolti nella selezione di informazioni di natura spaziale sono stati ampiamente investigati, mentre rimangono ancora da chiarire i meccanismi coinvolti negli aspetti di selezione temporale. I tre esperimenti riportati all'interno di questa tesi sono volti ad indagare alcuni degli aspetti legati alla capacità di selezionare gli eventi nel tempo ed in che modo gli aspetti temporali e quelli spaziali interagiscono tra loro.

Nel primo esperimento è stato impiegato un compito di Giudizio di Ordine Temporale (TOJ) per investigare la relazione esistente tra disturbi di selezione nello spazio e nel tempo in pazienti con eminegligenza spaziale unilaterale. Una forte compromissione dei meccanismi di selezione nel tempo è stata rilevata per le coppie di stimoli presentate in porzioni dello spazio in cui il deficit spaziale è più marcato, suggerendo l'esistenza una relazione tra gli aspetti spaziali e quelli temporali nella modulazione del deficit.

Nel secondo e nel terzo esperimento è stato investigato l'orientamento dell'attenzione nel tempo utilizzando stimoli che, grazie ad un movimento con velocità regolare o irregolare, rendono possibile il generarsi di aspettative temporali e di verificare cosa avviene quando tali aspettative vengono disattese. La regolarità del movimento si è rivelato essere un indice importante nel generare aspettative temporali che a loro volta influenzano profondamente la performance diminuendo sensibilmente la velocità di risposta del soggetto. Inoltre, la registrazione dei potenziali evocati ha evidenziato come aspettative spaziali e temporali interagiscano influenzando l'analisi dello stimolo fin dalle prime fasi di elaborazione.

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CHAPTER 1

1.1 Introduction

“Every one knows what attention is. It is the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains [p. 404] of thought. Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others, and is a condition which has a real opposite in the confused, dazed, scatterbrained state...” (James, 1890 pp.403-404)

The definition of attention proposed by James is one of the most famous and cited definition and, even though it is quite old, is still actual. Attention is a complex cognitive function. It is articulated in many different subcomponents and constantly influences our behaviour and mental state.

The study of attention has been one of the core topic investigated by neuroscience in the last 30 years. A great amount of energy has been invested to unveil the mechanisms of attention selection, the effect of attentional deployment on behaviour and the interaction between attention and other cognitive functions. Electrophysiological and modern neuroimaging techniques have been extensively employed to reveal the neural mechanisms of attention and the cerebral structures that are involved in attentive processes.

A particular type of attention is selective attention. It serves as an important filter that regulates the impact of external stimulation on behaviour. When subjects are confronted with multiple sources of stimulation, selective attention is responsible for choosing which objects or events is relevant with respect to the actual goal. Mechanisms of selective attention are thought to bias the competition between different objects or events favouring the information that is most important for the actual behaviour (Desimone & Duncan, 1995).

Spatial attention, a subtype of selective attention, is one of the most studied attentional mechanisms and refers to the ability of directing attention towards a specific portion of space relevant for the current behaviour. The present study is concerned with temporal attention, a

process that only in the last years has started to be investigated. Coull & Nobre (1998) reasoned that temporal information about stimuli could provide useful information to select important stimuli in a dynamic world. It is well established that to know in advance where one stimulus will appear increase the level of performance. So far, many studies have tried to unveil the mechanisms involved in temporal orienting of attention and the brain area devoted to the code of temporal information. In particular, some studies have compared the mechanism of spatial and temporal attention in order to understand if the two processes are completely distinct or if they share some common aspects (Coull & Nobre, 1998; Griffin et al., 2002). A growing interest is also being devoted to the study of how temporal and spatial mechanisms interact in influencing the behaviour (Doherty et al., 2005).

The experiments presented in this thesis try to cast more light on the processes involved in attention to space and time and how these two functions interact influencing the neural activity and the behaviour.

1.2 Thesis outline

During the 3 years of my PhD course I collaborated to distinct projects covering different aspects of the mechanisms related to conscious processing of spatial and temporal visual information.

The three experiments reported here cover quite different topics in the study of attentional mechanisms in space and time and in the possible interaction between them.

The first experiment is the result of an international collaboration of our group at the Department of Neurological and Vision Sciences of the University of Verona with the Center of Neurology of the Hertie-Institute for Clinical Brain Research (University of Tübingen) and has been granted by the Italian CRUI and the German DAAD within the project “Vigoni”.

A TOJ paradigm has been employed to verify whether the manipulation of the temporal presentation of the stimuli plays a role in the modulation of the deficit of spatial selection of neglect patients. The neuropsychological syndrome of Spatial Neglect has been employed as a model to study the mechanisms of spatial cognition and selective attention. These patients present a severe impairment in detecting stimuli presented in the contralateral space and in initiating movements towards this part of the space. Many studies reported a severe deficit in selective spatial mechanisms. Longer manual or saccadic reaction times and a decrease in the

exploratory activity (both tactile and ocular) have been reported when the patients had to detect stimuli presented in the left hemispace, with performance dramatically improving when moving from the leftmost to more ipsilesional positions (Natale et al., 2005; Smania et al., 1998; Natale et al., 2007; Karnath & Fetter, 1995 and Karnath & Perenin, 1998). This evidence suggests the presence of an abnormal distribution of spatial attention with a rightwards bias favouring the ipsilesional space.

Recently, evidence has been provided that neglect patients may also manifest a deficit in the temporal selection of visual–spatial information (Rorden et al., 1997 and Baylis et al., 2002).

In the present experiment, we used a temporal order judgement task (TOJ) to verify whether a similar distortion of attentional mechanism can be found also for attention selection in time. The aim is to manipulate the spatial position of our stimuli within each visual hemifield. Thus it is possible to verify whether the deficit in temporal selection has the same rightwards biased distribution found using reaction time (RT) or spatial exploration. In previous TOJ studies this comparison was not possible because the stimuli were presented across the vertical meridian, one on each hemifield.

The last two experiments have been conducted in Anna Christina Nobre's Lab during the year that I spent as graduate visiting student at Oxford University.

In these two experiments I tested the influence of temporal expectation on attentional orienting using a naturalistic paradigm already shown in previous studies to be highly effective in mimicking the activity linked to the appearance of an attended upcoming event (Correa & Nobre, 2008; Doherty et al., 2005).

The task consists of a ball that moves along the diagonal of the screen from top or bottom left to the opposite corner. The movement of the ball could follow a regular or an irregular rhythm. In the last part of its trajectory it disappears for one step under an occluding band positioned on the right side of the screen. When the ball appears again after this occlusion period, the subject has to discriminate the presence of a cross or a plus in the last ball by pressing a key. Two experiments have been conducted using this paradigm.

The aim of the first experiment was to verify the presence of behavioural differences between endogenous and exogenous temporal expectations. Temporal expectations are built by the temporal predictability of a perceptual input. The use of timing to establish temporal expectation may be unintentional and unconscious (exogenous expectations) or conscious and deliberate (endogenous expectation) (Coull & Nobre, 2008). We want to verify if different kinds of expectation exert a different effect on behaviour.

In the second experiment event related potentials (ERPs) have been recorded for stimuli that appeared after the occlusion period. The validity of temporal expectancy has been manipulated and the effect of temporal orienting has been analyzed for the early components (P1 and N1) linked to perceptual mechanisms, and for the later component related to response selection and motor preparation (N2 and P3).

CHAPTER 2

Mapping spatial attention with a TOJ task in patients with spatial neglect

2.1 INTRODUCTION

2.1.1 Visual spatial neglect and extinction

Unilateral spatial neglect (otherwise known as hemispatial neglect, hemineglect, hemi-inattention, neglect) is a disorder characterized by a deficit in orienting, detecting, responding to stimuli presented in the contralateral portion of the space or to initiate movements towards this side. The impairment cannot be simply explained by a primary sensory loss or motor deficits.

Neglect is frequently observed after lesions of the right hemisphere caused by strokes of the right middle cerebral artery (Bowen et al. 1999) and less frequently observed after left hemisphere lesions. However, in the latter case symptoms are less severe and long-lasting than in the former (Beis et al., 2004). Brain lesion causing neglect was found to involve the right parietal lobe, in particular the angular gyrus in the inferior parietal lobule (Mort et al., 2003), the temporo-parietal junction (Vallar & Perani, 1986), the superior temporal cortex (Karnath et al., 2001), and subcortical structures (Karnath et al., 2002).

According to the definition proposed by Mesulam (1981), patients with severe neglect behave as if half of the world had ceased to exist. During the acute and sub-acute phase (first days after the lesion) caregivers can easily report the presence of neglect by simply observing the patient's behaviour. Often the patients show a spontaneous deviation of the head and eyes towards the ipsilateral side (Fruhmann Berger et al., 2008), ignore food on the left side of the plate, read only the rightmost page of a newspaper (Parton et al., 2004). Common clinical examination of neglect is based on tasks that require attention to be deployed over both sides of the space. For example, in paper-and-pencil tests known as cancellation tasks patients are asked to mark all the stimuli presented in the sheet (Albert, 1973) or all targets (stars, bells) presented among distracters (Gauthier et al., 1989; Halligan et al., 1989). Copying a figure or

drawing from memory are also used to assess the presence of neglect (Johannsen & Karnath, 2004; Halligan et al., 1989). The typical performance of neglect patients in cancellation tasks reveals an asymmetrical detection of stimuli in space, with a high hit rate in the ipsilesional side and an increasing omission rate for more contralesional stimuli. When requested to draw from memory or reproduce pictures, neglect patients often omit or misreport left-sided aspects of the figures or do not reproduce items presented in the left side of the sheet of paper. Thus, signs of neglect, as evident during spontaneous behaviour or assessed by formal clinical examination, indicate an asymmetrical distribution of performance in the left and right hemispace. This is taken as evidence of a distortion in the deployment of spatial attention, favouring stimuli in the ipsilesional portion of space.

Damage to the right hemisphere may also result in the phenomenon of extinction. Unlike neglect patients, extinction patients can easily detect contralesional stimuli presented alone, while failing to report them when presented simultaneously to stimuli in the ipsilesional space.

Extinction is usually assessed by the “confrontation” technique, where the examiner uses fingers of both hands to randomly deliver brief unilateral or bilateral stimulation. The task is to report the quantity (one, two) and the side (left, right, both left and right) of the stimulation. Whether extinction might be a mild form of neglect or, rather, it might represent a distinct syndrome is still matter of debate (Driver et al., 1997).

2.1.2 Space exploration in neglect

The clear asymmetrical distribution of performance shown by patients with neglect in copying and cancellation tasks can be also assessed in experimental setting where a larger portion of space than ever with paper-and-pencil tests can be examined. Several studies mapped the performance of neglect patients in space and analyzed the distribution of exploratory behaviour or the performance in detection tasks with stimuli presented at different eccentricities.

Behrmann and colleagues (1997) recorded eye movements while neglect patients were looking for a target in an array of letters extending 25° to the left and the right of fixation. The spatial distribution of eye movements of the patients was characterized by a steep gradient from left to right with a maximum at 18° to the right. A similar distribution of eye movements

was also found in a study where neglect patients were searching for a non-existent target in darkness (Hornack, 1992). Karnath and Fetter (1995) confirmed and extended these results by analysing a more extended portion of space (50° to the left and the right of fixation). A similar U-shaped distribution of exploratory movements was found in neglect patients as in control groups. However, while in normal subjects such a distribution was centred at 0° , in neglect patients was shifted towards an off-centred sector in the ipsilesional field (from about 10° to 20°). A similar rightwards bias in the distribution of responses has been also found in a study of tactile exploration of the peripersonal space (Karnath & Perenin, 1998). Kerkhoff and colleagues (1999) employed a sound localisation task and demonstrated that in neglect patients the subjective straight ahead, indexing the perceived orientation of the body along the horizontal plane (Ferber and Karnath, 1999), is significantly deviated toward the ipsilesional side as compared to control subjects.

The topography of the spatial deficit in neglect patients has been also examined by using speeded detection tasks with visual stimuli briefly present at different positions along the horizontal meridian (Natale et al., 2005; 2007; Smania et al., 1998).

Smania and colleagues (1998) analyzed the distribution of speed and accuracy of manual responses to brief stimuli presented along the horizontal meridian and spanning a wide portion of space (40° to the left and to the right). They found a strongly asymmetrical distribution of speed and accuracy of responses around the vertical midline. Both reaction times (RTs) and omission rate of neglect patients steeply decreased from the left-most position to an off-centred position in the right hemifield (around 20°), while they increased again from 20° up to 40° in the right field. Moreover, Natale and collaborators (2005) highlighted that the U-shaped rightwards centred distribution of RTs did not change when stimuli were presented in a blocked-point condition, that is when subjects knew in advance where the stimuli would appear. However, neglect patients were overall faster in the blocked-point than in the random condition. This indicated that the spared endogenous control of spatial attention cannot compensate for the spatially distorted distribution of exogenous attention favouring the ipsilesional space. Finally, evidence has been provided that a similar distribution of responses in neglect is found in a saccadic as in a manual RT task, suggesting that different types of motor responses are equally affected by abnormal mechanisms of spatial coding and attention selection (Natale et al., 2007).

In sum, the asymmetrical distribution of orienting and exploring behaviour in neglect patients can be taken as evidence of a spatial bias favouring an off-centred sector of space, where attention is abnormally deployed.

2.1.3 The temporal order judgement paradigm

The temporal order judgement task (TOJ) is a paradigm traditionally employed to study the effects of the deployment of attention on the speed of transmission of sensory information and the perception of temporal order of stimuli. In the past, this task has been extensively employed in studying the mechanisms of perception of order and successiveness (Exner, 1875), especially for stimuli presented in different sensory modalities (for example Hirsh & Sherrick, 1961). As reviewed by Stelmach and Knoll (1973), the procedure of a TOJ task involves the presentation of pairs of asynchronous stimuli and the manipulation of the interval between the onset of the two stimuli (SOA, stimulus onset asynchrony). In particular, the SOA varies on a trial-by-trial basis, so to have conditions where one (or the other) stimulus leads in time. However, conditions where the two stimuli are simultaneous are usually included. At the end of each trial, the subject has to judge which stimulus appeared first according to a two-forced-choice (“Right first” or “Left first”) or a three-forced-choice, including also the “simultaneous” response. The percentage of one type of response (for example “Right stimulus first then left stimulus”) is plotted as a function of the different SOAs and a psychometric function (sigmoid function) is fitted to the data. Two parameters of the sigmoid function are usually analysed: the Point of Subjective Simultaneity (PSS) and the Just Noticeable Difference (JND). The PSS is the SOA at which the observer judged the left (or right) stimulus as coming first on the 50% of the trials and reflects the point at which the observer is maximal uncertain about the order of two stimuli (Shore & Spence, 2005). The PSS has to be distinguished from the Point of Objective Simultaneity, that corresponds to the SOA equal to zero, that is the real simultaneity between the stimuli (Sternberg & Knoll, 1971). The JND is the value that refers to the slope of the sigmoid curve and is calculated as the half of the interval between the SOA values producing the 25 and 75% points on the psychometric function (Shore & Spence, 2005). Since the beginning of XX century, it has been recognized that the perception of the temporal order of two stimuli can be influenced by the direction of selective attention in the space. Titchener (1908) in his law of the prior entry stated that “*the stimulus to which we are predisposed requires less time than a like stimulus, for which we are unprepared, to produce its full conscious effect*”. The main idea conveyed by Titchener’s law is that sensory events occurring at a spatial location where spatial attention is focused are perceived prior to physically synchronous events at unattended locations, suggesting that attention speeds up the rate of information processing at attended relative to unattended positions. The TOJ task has been widely employed to study the effect of attention

on prior entry and, in particular, how the deployment of attention to a particular stimulus or spatial position influences the judgement of temporal order (for a review see Spence et al., 2001). The study by Stelmach and Herdman (1991) was one of the first to test the prior entry law in a TOJ task with visual stimuli and an explicit manipulation of visual attention. According to the traditional TOJ paradigm, these authors manipulated the SOA between two stimuli presented in two symmetrical positions, one in each hemifield. They found that attended stimuli were perceived to appear before unattended ones, even when the two stimuli were presented at the same time. Moreover, the unattended stimulus had to physically lead the attended one by at least 40 ms in order to be perceived as first. The prior entry effect has been replicated also in other studies with a TOJ task (Shore et al., 2001; Schneider & Bavelier, 2003) and reveals the profound impact that selective attention has on conscious perception of sensory events, speeding up the perceptual processing for attended as compared to unattended events. With respect to the two parameters of the psychometric function described above, the prior entry effect is evident in the magnitude of the difference between PSS and real simultaneity, corresponding to the temporal advantage needed by the unattended stimulus in order to be perceived as simultaneous to the attended stimulus (Shore & Spence, 2005). A general rule is that the more the attention focuses on one stimulus, the bigger the PSS. The JND, instead, is a measure of temporal resolution and refers to the precision of the temporal judgement. Specifically, it indicates how far apart in time the two stimuli have to be presented for the temporal asynchrony between them being reliably judged (Shore & Spence, 2005). It is still an open issue whether the direction of attention may influence both the parameters or whether it may affect more the PSS than the JND (Shore & Spence, 2005).

2.1.4 Performance of neglect and extinction patients in the TOJ task

The TOJ paradigm has been also employed to verify whether the rightwards bias in neglect may result in a prior entry effect favouring the selection in time of the ipsilesional over the contralesional stimulus.

Rorden and collaborators (1997) analysed the performance of two patients with visual extinction and mild signs of neglect. In their version of the TOJ task, two horizontal bars were presented, one in each visual hemifield, at various SOAs. The patients had simply to judge which bar appeared first. On average, the left-sided stimulus had to lead in time by about 200

ms for the two stimuli to be perceived as simultaneous. This result proved for the first time the presence of a prior entry phenomenon in extinction, leading to an earlier conscious detection of stimuli presented on the ipsilesional than the contralesional hemifield. Moreover, Rorden and colleagues (1997) highlighted that the temporal disadvantage for contralesional stimuli might provide a useful measure for the severity of the ipsilesional bias. The evidence shown by Rorden and colleagues (1997) has been confirmed by successive studies. Robertson and collaborators (1998) tested 8 patients with right-hemisphere lesions, showing neglect and/or visual extinction and found a substantially delayed time course of awareness for contralesional stimuli. On average, left stimuli needed an advantage of almost 500 ms in order to be perceived as simultaneous to right stimuli. A control group of patients with left-hemisphere lesions and comparable clinical and demographic characteristics were also tested. They did not show any prior-entry advantage for either side of the space. In their study, Baylis and colleagues (2002) exactly replicated these findings, supporting the existence of an ipsilesional bias associated to a delayed perception of stimuli presented to the contralesional visual field. Interestingly, these authors showed that the contralesional deficit was present both in patients with left and in those with right extinction. Evidence of a prior-entry bias favouring ipsilesional stimuli has been also reported in studies using auditory and tactile stimuli (Karnath et al, 2002; Guerrini et al., 2003; Guerrini & Aglioti, 2006) as well as a cross-modal presentation (Costantini et al., 2007; Eramudugolla et al., 2007; Sinnett et al, 2007).

2.1.5 Rationale and aim of the study

The aim of this study was to verify whether the rightwards bias in mechanisms of attention selection in space found in neglect and extinction patients by previous studies (Behrmann et al., 1997; Hornack, 1992; Karnath & Fetter, 1995; Karnath & Perenin, 1998; Kerkhoff et al., 1999; Natale et al, 2005; 2007; Smania et al., 1998) may also apply to mechanisms of attention selection in time. In particular, we analysed the performance of patients on a TOJ task in which both the temporal asynchrony in the presentation of the stimuli and the spatial position of stimuli was manipulated. Previous studies (Baylis et al, 2002; Bueti et al, 2007; Eramudugolla et al., 2007; Guerrini et al., 2003; 2006; Karnath et al., Robertson et al., 1998; Rorden et al., 1997; Sinnett et al, 2007) consistently demonstrated that the TOJ paradigm is

useful in revealing distortions in the distribution of spatial attention favouring particular sectors of the space at the expenses of others. Unlike previous studies, here pairs of asynchronous stimuli were randomly displayed at different spatial locations “within” each hemifield, rather than between hemifields (e.g. across the vertical meridian). We expected the PSS values to be modulated by the position of the stimuli, with higher values for stimuli presented in the left, contralesional than in the right, ipsilesional field. This prediction is based on the hypothesis that spatial and temporal disorders of conscious information processing in neglect may have a common functional basis. In particular, temporal and not only spatial deficits would relate to the same distorted distribution of attention as that assessed by mapping, for example, speeded reactions to visual stimuli (Natale et al., 2005; 2007; Smania et al., 1998). Thus, in neglect patients the steeper the attentional gradient between the spatial locations of two stimuli (as with pairs of stimuli presented in the left as compared to the right hemifield) the greater the impairment of the temporal selection of the left one. Clearly, the presentation of stimuli across the vertical meridian (between-hemifields condition) cannot be useful to test the above hypothesis. Indeed, it does not allow to compare a condition in which there might be a steep gradient between the spatial locations of two stimuli (within left hemifield presentation) with another one in which the same stimuli are presented in a spatial sector where attention might be more evenly deployed (within right hemifield presentation).

To our knowledge, this study would represent the first attempt to investigate in a suitable way the possible interaction between spatial and temporal aspects of the attentional impairment in neglect. So far, only two studies presented the stimuli in a within field condition (Snyder & Chatterjee, 2004; Cate and Behrmann, 2002). Cate and Behrmann (2002) asked neglect patients to report the temporal order of two asynchronous stimuli presented in different positions within each hemifield. Unfortunately, they introduced both a temporal and a spatial bias, by presenting stimuli only within the right hemifield and having an higher percentage of trials in which the right stimulus preceded the left one than vice versa. The unbalanced manipulation of both spatial and temporal variables makes it difficult to clear interpret their result. In another study, Snyder and Chatterjee (2004) presented one pair of vertically arranged stimuli within each hemifield. They found better temporal judgements for stimuli presented in the ipsilesional, than in the contralesional space. However, in this study only one spatial location per hemifield was tested, thereby, results could merely confirm the overall advantage of the right over the left hemifield in mechanisms of attention selection in time.

2.2 METHODS

2.2.1 Subjects

A total of 15 right-handed patients with right hemisphere lesions has been recruited for this study. Demographic and clinical information is reported in Table 1. The presence of neglect was assessed by cancellation tasks (two tasks selected among the following: Albert, 1973; Gauthier et al., 1989; Weintraub & Mesulam, 1985; Halligan et al., 1989) and figure copying (Johannsen & Karnath, 2004). In the cancellation tasks, subjects were required to mark all the stimuli presented in a horizontally oriented 21 x 29.7 cm sheet of paper (Albert, 1973), or to detect a target stimulus among distracters (Gauthier et al., 1989; Weintraub & Mesulam, 1985; Halligan et al., 1989). In the figures copying task, the subjects had to reproduce four pictures (a fence, a car, a tree, and an house), two presented in the left and two in the right side of the sheet of paper . Severe neglect was diagnosed following these criteria: at least five omissions of left-sided targets in cancellation tasks (Albert, 1973; Gauthier et al., 1989; Weintraub & Mesulam, 1985 and Halligan et al., 1989); a score higher than 1 in the copying task, where omissions of left-sided features were scored as 1 and omissions of a whole left-sided figure was scored as 2. The standard clinical confrontation technique was used to detect the presence of visual extinction. The experimenter kept his hands at the eye level of subject and rapidly flexed one or both the two index fingers, while the subject was fixating at the experimenter's nose. Extinction rate was the percentage of left misses in the bilateral condition corrected by the percentage of left misses in the unilateral condition. An extinction rate of 50% was the criterion to assess the presence of extinction.

The above criteria for a severe form of neglect were strictly fitted by six out of seven patients. However, also one patient with mild signs of neglect (case P13) was included in the study. Finally, nine right-damaged patients without neglect and visual extinction and ten right-handed subjects without neurological deficit served as control subjects. See Table 2.1.

Subject	Age	Sex	Time since lesion (days)	Lesion location in the right hemisphere	Cancellation (L/R omissions)	Figure coping score	Extinction rate
Right brain-damaged controls subjects (RBD)							
P1	38	F	3	Frontal cortex	Letters: 0/0 Bells: 0/0	0	0
P2	46	F	5	Putamen	Letters: 1/0 Bells: 0/0	0	0
P3	56	M	7	Basal ganglia	Letters: 6/4 Bells: 2/1	0	0
P4	75	F	8	Basal ganglia, insula, frontal cortex	Letters: 0/0 Bells: 0/0	0	10
P5	43	M	88	Fronto-temporo-parietal cortex, basal ganglia	Lines: 0/0 Bells: 1/1	0	0
P6	60	M	25	Thalamus, internal capsule	Letters: 0/1 Bells: 1/1	0	0
P7	68	F	35	Lenticular nucleus, internal capsule	Letters: 2/0 Bells: 2/0	1	0
P8	60	M	110	Internal capsule	Letters: 0/0 Bells: 0/0	0	0
P9	49	M	62	Fronto-parietal cortex	Lines: 0/1 Bells: 0/0	0	0
Mean	55		38				
Neglect/extinction patients							
P10	71	F	170	Fronto-parietal cortex	Lines: 18/0 Bells: 13/0	3	0
P11	49	M	203		Stars: 4/5 Bells: 8/8	0	100
P12	68	F	231	Frontal cortex, insula	Letters: 2/0 Bells: 15/0	3	100
P13	79	M	180	Temporo-parietal cortex	Letters: 0/1 Bells: 3/3	2	20
P14	79	F	11	Fronto-temporal cortex, insula	Lines: 21/2 Bells: 10/0	0	0
P15	43	F	12		Lines: 28/6 Bells: 15/1	1	0
P16	54	M	8	Basal ganglia, internal capsule	Letters: 15/9 Bells: 30/16	7	100
Mean	63		116				
Healthy control group							
HC (n=10)	Mean 61	Males (n=6)					

Table 2.1: Demographic and clinical data

2.2.2. Stimuli and apparatus

The experiment took place in a dimly illuminated room with patients sat in front of a computer screen at a distance of 57 cm. Stimulus presentation was controlled by a PC using the software MEL2 (Micro Experimental Laboratory, Schneider, 1995). A white fixation point was presented in the middle of the otherwise black screen throughout the whole experiment and subjects were instructed to fixate it. Stimuli were white squares subtending 1° of visual angle, presented in 5 different positions just above the horizontal meridian: there was one central position (0°) and two peripheral positions (6°, 12°) within each hemifield. The experimenter monitored the eye movements of the subjects and pressed a key to start the trial

only when subjects were keeping fixation. Stimuli appeared after a random delay between 1300 and 1800 milliseconds from the beginning of the trial.

2.2.3 Procedure

Preliminary visual detection task

In the simple visual detection task a white square was randomly presented for 100 ms in one of the 5 possible locations (see Figure 2.1). Subjects had to verbally detect both the presence and the spatial location of the stimulus on a trial-by-trials basis. Ten stimuli at least were presented at each spatial position. A detection rate equal or higher than 85% was the criterion to test subjects in the TOJ task.

Temporal order judgement task

In this task, a pair of squares (6° apart) was presented at four different positions: one near (0° - 6°) and one far (6° - 12°) within each hemifield. The stimulus onset asynchrony (SOA) between the two stimuli was manipulated. There were nine SOAs: 0, ± 100 , ± 200 , ± 300 , ± 400 ms (plus and minus signs indicate that the right- or left-sided stimulus of the pair, respectively, was leading in time by the SOA). The task was to indicate which square appeared first by a two-forced choice (“first left then right” or “first right then left”). Stimuli remained on the screen until subject’s verbal response. The experimenter collected the subject’s temporal judgment and started the new trial. At least 10 pairs per spatial position per SOA were presented in six blocks of trials.

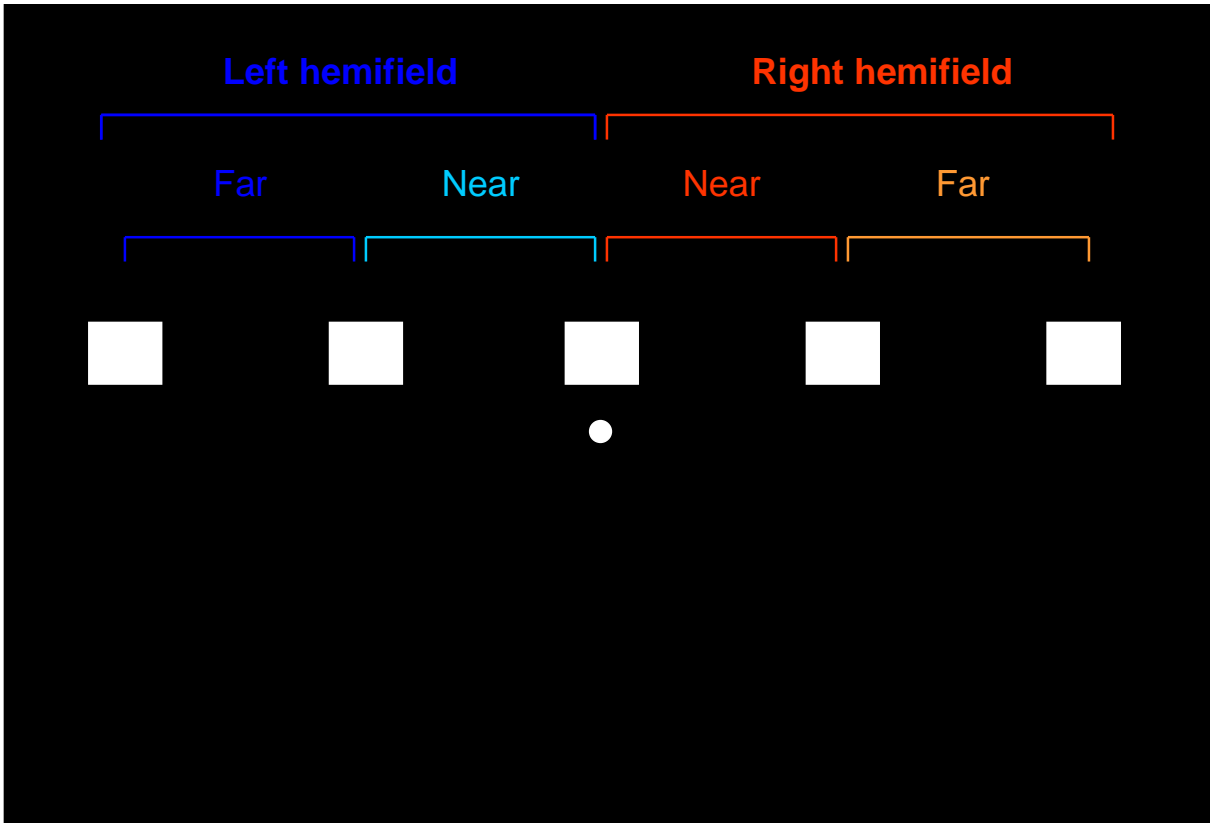


Figure 2.1: Spatial location examined in the detection task and in the TOJ task.

2.2.4 Data analysis

Percentage of “first right then left” responses was plotted as a function of the SOA, and fitted by a sigmoid curve for each spatial position. Specifically, data were fitted by the following function (Lewald & Karnath, 2001, Karnath et al., 2003):

$$f(\text{SOA}) = \frac{100}{(1 + e^{-k(\text{SOA} - \text{SOA}_{50\%})})}$$

where F is the percentage of the response “first right then left”, $\text{SOA}_{50\%}$ is the SOA where the frequency of “first right” judgement is 50%, k is the slope of the of the function at $\text{SOA}_{50\%}$ and e is the base of the natural logarithm. Two parameters of the sigmoid function were analysed to evaluate the performance of the subjects: the PSS, assessing possible differences in the efficiency of attention selection in time between the two stimuli; the JND, assessing the temporal resolution and precision of the temporal judgement. Moreover, the coefficient of

determination (R^2) was analysed to assess the presence of an “erratic” temporal judgement for any position. The R^2 value indexes the goodness of the fitting of the data by the sigmoid function. In a previous study by Zimmer and co-workers (2003), R^2 values smaller than 0.75 were regarded to as indicative of an “erratic” performance. This means that the subject is unable to perform the task. Zimmer and colleagues (2003) also argued that in case of erratic performance data cannot be properly fitted by the sigmoid function. Accordingly, in the present study PSS and JND were not analysed for those experimental conditions (spatial locations) where R^2 value was smaller than 0.75. PSS and JND were analysed as a function of two within-subject factors, stimulus side (left, right) and location (near, far), and one between-subjects factor, group (neglect/extinction patients, brain-damaged and healthy control subjects). The Kruskal-Wallis test and Mann-Whitney U-test were used to analyse between-subjects effects, whereas the Friedman test and Wilcoxon test to analyse within-subject effect.

2.3 RESULTS

Simple detection task

All normal and brain-damaged control subjects performed almost at ceiling. Also patients with neglect and/or extinction showed an high detection rate (overall above 85% for any location). See Table 2.2.

Group	LVF			RVF	
	Near	Far	Centre	Near	Far
Neglect (n=7)	97	100	100	98	100
rBDC	100	99	100	100	100
HC	100	100	100	100	100

Table 2.2: detection rate for the 5 spatial locations analyzed by the simple detection task

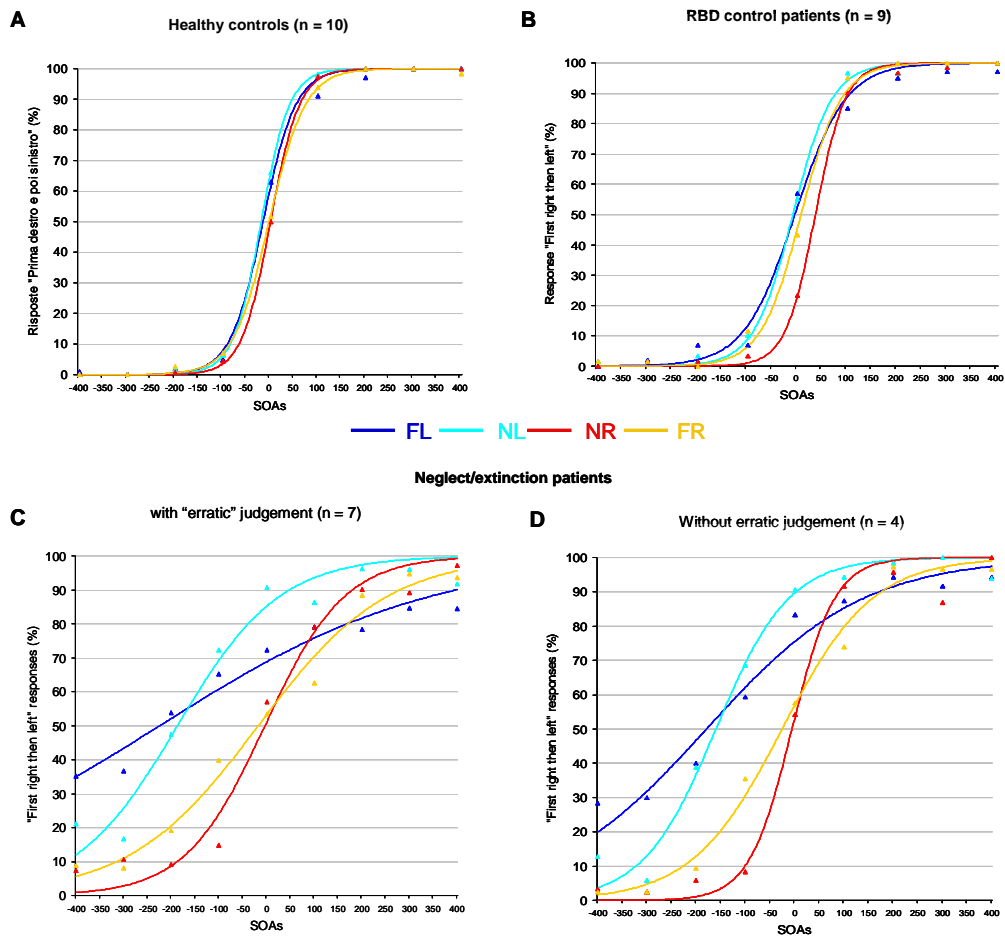


Figure 2.2: sigmoid functions reproducing the performance on TOJ task

Temporal order judgement task

Figure 2.2 shows sigmoid functions, fitting the distribution of the percentage of “first right then left” judgements as a function of the spatial location of stimuli and the SOA, for each group.

As can be seen by simply inspecting Figure 2.2A and B, both brain-damaged and healthy control subjects showed well-shaped curves that do not differ from each other. This indicates an overall good performance.

On the contrary, the performance of neglect/extinction patients was overall impaired as compared to control groups. This can be seen in Figure 2.2C, showing the overall performance of seven patients with neglect/extinction. The shape of the sigmoid functions is on average more “flatted” in neglect/extinction patients than in control groups, suggesting that patients had troubles in deciding the order of appearance of the two stimuli. This was

remarkably more evident for pairs presented in the left than in the right hemifield. In the former case, minimum and maximum points of the sigmoid function are far from the minimum and maximum value of the y-axis, as it would be expected, whereas this is not the case for the functions fitting responses to ipsilesional pairs. This indicates a more severely impaired performance for left, contralesional than ipsilesional pairs in neglect/extinction patients. In order to find out which factor might have specifically contributed to the performance of neglect/extinction patients, R^2 values were first analysed in all groups.

No evidence of erratic judgements was found in control groups. Erratic judgements were found in four out of seven patients, whose R^2 value was inferior to 0.75 for stimuli at the far right position and in the whole (near and far) left hemifield (P16), for stimuli at the far and near left positions (P14), for stimuli at the far left position (P10 and P12). Based on the results of this analyses, data of neglect/extinction patients were then plotted and fitted again, this time excluding cases P16 and P14, because of the presence of erratic judgments in most conditions, and responses to far left stimuli only of cases P10 and P12. As can be seen in Figure 2.2D, the performance of the group of four neglect/extinction patients without erratic responses improved as compared to the overall performance of the seven patients, especially for stimuli at near and far locations in the left hemifield. However, it remained overall impaired as compared to control groups, particularly for stimuli at the far left location.

As a second step, PSS and JND were analysed as a function of side, location and group.

Group	LVF		RVF	
	Near	Far	Near	Far
Neglect (n=4)	-160	-179	-5	-25
rBDC	-9	-4	21	12
HC	-11	-5	-4	0
Neglect (n=4)	73	158	43	91
rBDC	22	34	22	25
HC	18	27	23	27

Table 2.3: Mean PSS and JND values calculated for each spatial position

PSS

PSS values for the three groups are reported in Table 2.3.

In control groups, the position (near, far) of stimuli did not affect PSS values for pairs in the right and in the left hemifield (healthy subjects: right hemifield $\chi^2 = 0$, $P = 1$ and left hemifield $\chi^2 = 2.78$, $P = 0.096$; brain-damaged patients: right hemifield $\chi^2 = 1$, $P = 0.317$ and left hemifield $\chi^2 = 0.5$, $P = 0.48$). This was also true for neglect patients (right hemifield $\chi^2 = 0.2$, $P = 0.655$; but note the tendency toward a significant difference in the left hemifield $\chi^2 = 3$, $P = 0.083$). Data were then collapsed across position (near, far) in each hemifield to test for the effect of the side (left, right) within each group.

Side did not affect PSS in healthy controls ($\chi^2 = 0.111$, $P = 0.739$), whereas it did affect PSS both in RBD control patients ($\chi^2 = 5.444$, $P = 0.02$) and neglect/extinction patients ($\chi^2 = 5$, $P = 0.025$).

Finally, between-groups effects were analysed within each hemifield. A significant effect of the group was found for the left hemisphere ($\chi^2 = 10.526$, $P = 0.005$), but not for the right hemisphere ($\chi^2 = 5.556$, $P = 0.062$). Post-hoc comparisons revealed higher PSS values for neglect/extinction patients than healthy control ($Z = -2.939$, $P = 0.003$) and RBD control ($Z = -2.867$, $P = 0.002$) subjects in the left hemifield, whereas no difference between healthy and RBD control groups was found ($Z = -0.327$, $P = 0.78$).

JND

JND values for the three groups are reported in Table 2.3.

In control groups, the position (near, far) of stimuli did not affect JND values for pairs in the right and in the left hemifield (healthy subjects: right hemifield $\chi^2 = 0.4$, $P = 0.527$ and left hemifield $\chi^2 = 0.5$, $P = 0.739$; brain-damaged patients: right hemifield $\chi^2 = 0.111$, $P = 0.739$ and left hemifield $\chi^2 = 2.78$, $P = 0.48$). This was also true for neglect patients (right hemifield $\chi^2 = 1.8$, $P = 0.18$; but note the tendency toward a significant difference in the left hemifield $\chi^2 = 3$, $P = 0.083$). Data were then collapsed across position (near, far) in each hemifield to test for the effect of the side (left, right) within each group. Side did not affect JND in any group (healthy subjects: $\chi^2 = 0.111$, $P = 0.739$; RBD control patients: $\chi^2 = 2.778$, $P = 0.096$; neglect/extinction patients: $\chi^2 = 1.8$, $P = 0.18$).

As to the between-groups effects, only a marginally significant effect of the group was found for the left ($\chi^2 = 5.438$, $P = 0.066$) and the right ($\chi^2 = 5.536$, $P = 0.063$) hemifield.

2.4 DISCUSSION

In the simple detection task, neglect/extinction patients performed almost at ceiling similarly as control groups. This ensured that any between-groups difference in performance in the TOJ task cannot be simply accounted for by differences in detection rate at any spatial position as well as by differences in the level of vigilance and motivation to perform a visual detection task. Thereby, between-groups differences in performance found in the TOJ task, with neglect/extinction patients performing overall worst than control groups, can be reasonably taken as evidence of a specific impairment of neglect/extinction patients in performing a TOJ task.

We analysed three factors which might contribute to the impaired performance of neglect/extinction patients. First, we wanted to verify the possible contribution of erratic judgements to the performance. The presence of erratic responses, as assessed by the R^2 , is an index of inability to perform the TOJ task and results in a modification of the typical S-shape of the sigmoid curve fitting the distribution of temporal judgements as a function of the SOA (Zimmer et al., 2003). As can be seen in Figure 2, while the sigmoid curves fitting the performance of healthy and brain damaged control patients have the typical “S” shape of the psychometric function for temporal order judgements, those fitting the performance of neglect/extinction patients are overall more flattened than in control subjects, although this is more evident for the left than the right side. However, the shape of the curves did not significantly change when erratic responses from neglect/extinction patients were not plotted (compare Figure 2 C and D). This means that erratic judgements do not completely account for the performance of neglect/extinction patients, even if they are more frequent in those patients than in control subjects.

The shape of the sigmoid curve also depends on the JND. To our knowledge, only one study has analysed the JND value in neglect patients so far (Dove et al., 2007). While based on the R^2 one can evaluate the presence of erratic judgements and, therefore, the reliability of the performance, based on the JND one can evaluate the precision of a reliable temporal judgement. Between-subjects analyses indicated a tendency towards a difference as an effect of the group. This might be due to the fact that in neglect/extinction patients JND values are overall higher than in control subjects. Importantly, there was no difference in

neglect/extinction patients as an effect of the side, indicating that the temporal impairment as indexed by the JND is not spatially lateralised. All in all, these findings support evidence of non-spatially lateralised deficits in processing of temporal information in neglect and extinction (Husain et al., 1997; but see also Di Pellegrino et al., 1998; Hillstrom et al., 2004 for evidence favouring a lateralisation of the impairment).

For the purpose of the present study, the analysis of the PSS values was crucial. Unlike the JND, effecting the shape of the sigmoid function, changing in the PSS value results in shifts of the curve from zero. As can be seen in Figure 2, the curves of controls subjects are centred around SOA values very close to zero indicating that subjective simultaneity is really close to real simultaneity. The two sigmoid functions that refers to performance of neglect/extinction patients for right sided stimuli are really close to zero and were not different from the ones of controls subjects. The performance in the left visual field is characterized by a consistent shift of the curves towards negative SOA values. The shifted position of the two functions indicate a temporal disadvantage for the left sided stimulus of the pair. Statistical analysis confirmed that, while on the right visual field the performance of neglect/extinction patients was not different from the performance of both controls subject, on the left side the PSS values of neglect/extinction patients were significantly more negative with respect to the PSS reported by the controls groups. Neglect/extinction patients needed a temporal advantage for the left-sided stimulus of almost 180 ms in the far location and 160 ms in the near location in order to perceive the two stimuli as simultaneous. This indicates a consistent delay in the mechanisms of spatial selection in time and supports a strongly deteriorated deployment of attention on the left side. These findings are in line with predictions: the strong effect of the side confirmed a deteriorated performance only in the left visual field even with a within field presentation, while for stimuli presented on the right side, the performance was not different with respect to both healthy controls and RBD controls. Within left side, statistical analysis highlighted a tendency towards a difference for the two spatial locations, where the PSS values are more negative for far location than for near ones. This is suggestive of the existence of a steep gradient in the performance within the left side of space, and replicate findings of previous studies that employed different methods (Behrmann et al., 1997; Hornack, 1992; Karnath & Fetter, 1995; Karnath & Perenin, 1998; Kerkhoff et al., 1999; Natale et al., 2005; 2007; Smania et al., 1998).

A significant difference between PSS values for left and right side has been found also for RBD patients. These subjects reported negative PSS in the left and positive PSS in the right

side indicating a different deployment of attention in the two visual fields, probably caused by the lesion on the right cerebral hemisphere.

According to present data, the PSS seems to be the only parameter of the sigmoid curve reflecting a spatial bias in neglect/extinction patients and confirmed that PSS values are modulated by the side of presentation of the stimuli. In particular, it has been demonstrated that spatial and temporal disorder of conscious perception information processing share a common functional basis and that both temporal and spatial deficit are related to the same distorted distribution of attention.

2.5 CONCLUSIONS

We found evidence of spatio-temporal disorder of conscious information processing in neglect/extinction patients, thus supporting findings from previous studies (Baylis et al, 2002; Bueti et al, 2007; Eramudugolla et al., 2007; Guerrini et al., 2003; 2006; Karnath et al., Robertson et al., 1998; Rorden et al., 1997; Sinnott et al, 2007). Importantly, we also found that the PSS is the parameter of the sigmoid curve that reflects the spatial bias in neglect/extinction patients. It indicates that a consistent delayed perception of left sided stimuli, even with a within-field presentation. The tendency towards a significant difference between the two locations on the left side suggests that these disorders might be related to a similar gradient of spatial attention as that assessed by mapping speeded reactions to visual stimuli (Natale et al., 2005; 2007; Smania et al., 1998) as well as different responses across all sensory modalities (Behrmann et al., 1997; Hornack, 1992; Karnath & Fetter, 1995; Karnath & Perenin, 1998; Kerkhoff et al., 1999). Specifically, in neglect patients the steeper the attentional gradient between the spatial locations of two stimuli the greater seems to be the impairment in temporal selection of the left stimulus. In keeping with this possibility, neglect/extinction patients showed a comparable performance to that of control subjects when stimuli were presented in a sector of the ipsilesional field where attention is evenly deployed.

CHAPTER 3

Temporal expectation induced by regular rhythm

3.1 INTRODUCTION

We live in a complex environment that changes instant by instant and provides spatial and temporal information which needs to be decoded and interpreted in order to plan advantageous behaviour. Expectations are generated combining different sources of information and help us anticipate where and when an event will occur. Attention processes play a crucial role in detecting important information from the environment and preparing an effective response. Mechanisms of spatial orienting of attention have been widely investigated and it has been demonstrated that the preventive orientation of attention to a particular spatial position affects performance by improving detection and decreasing the time of response. These benefits of spatial orienting are well illustrated by the experimental paradigm developed by Posner and colleagues (1980). It consists of a central symbolic cue that informs in advance where a target stimulus will appear. When the information delivered by the cue is correct, subjects show shorter reaction times (RTs) and an improved stimulus detection, while when the cue is misleading, response is slowed down. Similar behavioural advantages have been found not only with spatial cueing, but also when attention can be focused in advance on objects (Yantis & Serences, 2003) or particular features (Maunsell & Treue, 2006).

Also temporal information plays an important role in generating expectations and improving behaviour, but the study of allocation of attention over time has been overlooked with respect to spatial attention. In the last years, the interest for temporal attention has greatly increased and many studies have tried to cast light on the neural mechanisms and cerebral areas involved in temporal expectation and attention to time intervals.

In the next paragraphs some of the main topics concerning attention to time and temporal expectations will be briefly considered in order to introduce the theoretical frame within which the two experiments subsequently described in this chapter have been devised.

3.1.1 The taxonomy of temporal expectations

In a recent review, Coull and Nobre (2008) underline as a complex construct as the one of time need to be analyzed considering the single parts that form the main structure. The studies on spatial attention revealed different mechanisms and brain structures involved, for example, in endogenous and exogenous orienting (Corbetta et al., 1993; Nobre et al., 1997). A similar taxonomy is possible also for attention in time. The main distinction proposed by Coull and Nobre (2008) is between explicit and implicit timing and it is based on the task instructions. Explicit timing mechanisms are recruited when subject is required to provide an overt estimate of duration, while implicit timing is engaged when sensory stimuli or motor responses adhere to a strict temporal framework even though the goal of the task is not temporal. Temporal expectations are a sub-category of implicit timing and refer to situations where expectations about some event are conveyed by the temporal predictability of a perceptual input. Timing may also emerge as a product of a temporal regularity of a motor output and in this case is defined “emergent timing”. The last important distinction is between exogenous and endogenous temporal expectations. When the subject explicitly uses a cue or a regular rhythm to predict temporal appearance we are in a situation of endogenous temporal expectations. Temporal expectations established unintentionally and not consciously as a result of a regular temporal structure are defined as exogenous. Recent electrophysiological studies in monkeys (Ghose & Maunsell, 2002; Janssen & Shadlen, 2005; Riehle et al., 1997) demonstrated a modulation of the firing pattern by exogenous temporal expectations. The neural discharge varies dynamically as a function of the conditional probability that a target will occur at a particular time, given that it has not yet occurred (the “hazard function”). A common finding in studies that tried to localize the brain areas involved in temporal expectations, is the activation of areas associated with action, like premotor or inferior parietal cortex, even in perceptual tasks (Assmus et al., 2005; Field & Wann, 2005; O’Reilly et al., 2008). The activation of motor-related areas by temporal expectations suggests that the primary scope of orienting in time is to optimise prospective motor behaviour (Coull & Nobre, 2008).

The functional taxonomy proposed by Coull and Nobre (2008) is not the only way to categorize the mechanisms involved in time perception. For example, Lewis and Miall (2003) proposed a distinction based primarily on the length of the time interval, distinguishing between automatic mechanisms for sub-seconds interval and cognitively controlled involved in supra-second intervals. Anyway, the distinction proposed by Coull and Nobre (2008) in

exogenous and endogenous temporal expectation is particularly useful with respect to the experiments presented in this chapter.

3.1.2 Temporal cueing paradigms

In the classical studies of orienting of spatial attention a warning signal (cue) is presented before the target stimulus and gives information about where the stimulus will appear (Posner et al., 1980). When the information given by the cue is correct (valid condition) subjects are faster and more accurate, while when the cue predicts the wrong location (invalid condition) performance decreases. Attention may also be oriented in time and temporal information about when a relevant event will appear optimizes behaviour. To study the mechanisms involved in temporal attention, Coull and Nobre (1998) developed a temporal analogue of the spatial orienting paradigm. In their task a centrally presented cue with high validity (75-85% probability) predicts the time interval at which the target stimulus would occur. Many different versions of this basic task have been developed to analyze the effect of different variables on temporal orienting (Coull & Nobre, 1998; Coull et al., 2000; Griffin et al., 2001, 2002; Miniussi et al., 1999). In particular different experiments manipulated the physical form of the stimuli, the duration of the temporal interval between cue and target and the kind of response required. Nobre (2001), Griffin and collaborators (2002) and Griffin and Nobre (2005) reviewed the main results of studies that investigated the effects of temporal orienting. Large RTs benefits were obtained when the target occurred at the correctly predicted time with respect to trials in which an invalid cue was presented. Moreover, comparing RTs of valid and neutral trials (when no temporal expectation was possible), it has been possible to highlight a facilitation of responses to stimuli that appeared at the predicted time with respect to trial in which there were any temporal expectation. These results demonstrated that symbolic cues were effective in generating temporal expectation that influenced some aspect of target processing and behavioural performance. The effects of temporal orienting were independent from the specific stimulus configuration or the shape of cue and target. A behavioural effect has been found for temporal intervals of different length (300/700, 600/1200, 600/1400 ms) demonstrating that temporal orienting is under a flexible control. Importantly, the behavioural benefits were more pronounced for short intervals with respect to long ones, possibly reflecting the effects of information inherent the passage of time itself (the

“hazard function”) (Elithorn & Lawrence, 1955) and the ability to re-orient towards a longer interval when the predicted short one failed to appear (Coull et al., 2002; Elithorn & Lawrence, 1955). The advantage of temporal orienting has been demonstrated also in experiments requiring difficult target discriminations and production of a choice response (Griffin et al., 2001). This demonstrates that the effects of temporal orienting are not only related to the preparation of a specific motor response. However, the effect of temporal cueing was smaller in discrimination with respect to detection tasks, suggesting that motor related mechanisms may contribute to temporal orienting.

3.1.3 Electrophysiology of attention to time

The temporal cueing paradigm was successfully employed also to investigate the online modulation of neural activity by temporal orienting. One of the first experiments designed to study temporal orienting was carried out by Miniussi and colleagues (1999). They recorded electroencephalographic (EEG) activity while subjects focused attention to short (500 ms) or long (1300 ms) temporal intervals signalled by cues. Both cue and target were presented foveally thus eliminating the influence of spatial attention. Evoked related potentials (ERPs) time locked to valid and invalid trials in the short condition were compared. The major finding was an enhancement of P3 amplitude and a decrease in the latency of P3 when the cue predicted correctly the time of appearance of the target. The authors suggested that temporal information may be used to prepare motor processes or improve processes related to decision and response preparation. Also N2 was modulated by temporal expectations with an increased negativity in invalid trials. This effect has been attributed to an inhibition of the response process (Kok, 1986), or to the detection of a deviation from an established stimulus-response association (Mantysälo, 1987). Primary visual components (P1 and N1) were not modulated by temporal orienting processes. Subsequent experiments (Griffin et al., 2001; 2002) confirmed this result for N2 and P3 components. A modulation of N1 amplitude was found in the attended condition, but these results not been replicated (experiment 2 in Griffin et al., 2002). A possible explanation for this effect of temporal orienting on N1 was related to the difficulty of the task that required a perceptual discrimination.

Correa and collaborators (2006) conducted an experiment in which they tried to replicate the modulation of components by temporal expectation by using a perceptual demanding task.

They found that targets appearing at attended moments elicited a larger P1 than unattended targets.

A completely different approach has been used by Lange and colleagues (2003) who investigated temporal orienting in the auditory modality. They adapted the sustained spatial attention paradigm developed by Hillyard and colleagues (1973). The subjects had to attend in different blocks to the offset of a short or a long empty interval, marked by bursts of white noise. Their task was to detect infrequent offset markers that differ from standard ones in frequency. The main comparison was between standard attended stimuli (for example, the short interval) and standard unattended stimuli (the long intervals). They found a larger N1 for attended standard stimuli with respect to the unattended ones. The authors speculated that, because of the superiority of auditory modality with respect to vision in temporal processing (Repp & Penel, 2002), temporal attention could affect earlier processes in auditor modality. Even though suggestive, this result may be due to differences in the characteristics of the task and in the manipulation of temporal expectations (Correa et al., 2006).

All together these studies demonstrate that temporal orienting modulates late components like N2 and P3, suggesting a role in response choice and motor preparation. Moreover, some evidence of a modulation of primary components has also been found for highly perceptual demanding tasks and for auditory stimuli.

3.1.4 Rhythm induced temporal expectations

The paradigm employing central symbolic cues has demonstrated efficacy in revealing the effects of temporal orienting. Anyway, this kind of task is quite far from the way in which temporal attention and expectation are built in everyday situations. In a natural context, temporal expectations are created by the properties of dynamic stimuli, like the pattern of movement. A more naturalistic paradigm has been developed by Doherty and collaborators (2005) based on previous works (for example Assad & Maunsell, 1995). In this task temporal expectation are created by the regular movement of a stimulus (a small ball) from the left to the right side of the screen. On the right side of the monitor an occluding band was present, under which the ball disappeared. Once the ball reappeared after the occlusion period the subject had to discriminate the presence of a small dot in the centre of the ball. Doherty and collaborators (2005) manipulated the pace of the movement to induce temporal expectation

(with a regular pace) or to create a situation in which no expectations were possible (irregular and unpredictable pace). Faster RTs were recorded for condition of temporal expectation. The analysis of ERPs time locked to the ball that reappeared after the occlusion period revealed an attenuation of N1 and N2 amplitudes by temporal attention. The conjunction of temporal and spatial expectations (conveyed when the ball moved following a linear trajectory) highlighted an enhancement of P1 amplitude. Finally, the modulation of P3 reported by previous studies has been replicated.

Correa and Nobre (2008) used the same paradigm and extended previous results to different speed of movement. Moreover, it also the duration of the occlusion foreperiod has been manipulated introducing a perturbation of the speed of the ball during the period in which it disappeared. According to the moment of reappearance, the temporal expectancy could be valid when the last ball reappeared at the expected time or invalid, if it appeared earlier or later than the expected moment. In valid trials a smaller N2 has been found. For the first time, temporal expectations modulated also the latency of N2 by anticipating it with respect to invalid conditions. As found in previous studies, P300 was significantly larger in valid condition.

Utilizing this paradigm, we developed two experiments to confirm and extend previous results. The first experiment is aimed to evidence behavioural differences between exogenous and endogenous temporal expectation. In the second experiment we analyzed the neural modulation induced by temporal expectation by recording ERPs.

3.2 EXPERIMENT 1

This experiment was designed to verify the impact of endogenous and exogenous temporal expectations on the performance of a perceptual discrimination task. In different blocks, participants were instructed to pay attention to the speed of a regularly moving circle (exogenous condition) or to the colour of the stimulus which was previously associated to foreperiods of different lengths (endogenous condition). We were interested in revealing differences in performance (RTs and accuracy) related to the different instructions.

METHODS

3.2.1 Participants

Twelve participants (8 females, mean age 30.8 years) gave informed consent to take part in the experiment. All reported being free of neurological disorders and had normal or corrected to normal visual acuity.

3.2.2 Stimuli and task

Participants were comfortably seated in a dimly illuminated room facing a computer monitor positioned 100 cm in front of them. They were required to fixate a small square (diameter : 0.2°) in the centre of the screen and to keep their eyes still during the trials.

The background of the screen was of a uniform light grey and a white bar was present during the whole experiment on the right side of the screen (12-14° eccentricity). The bar was vertically oriented, had a width of 2° and the same height of the screen. At the beginning of each trial a small square appeared in the middle of the screen and after 500 ms a white circle (diameter: 1°) appeared in the left top or bottom corner of the screen and moved towards the opposite corner in regular steps following a diagonal trajectory. The final position of the circle was the opposite corner of the screen with respect to the starting point. For example: when the

stimulus started to move from the upper left corner, its final position at the end of the trial was the bottom corner on the right. The sense of movement was conveyed by the appearing and disappearing of the circle from the screen in discrete steps. The stimulus stayed on the screen in each position for 200 ms then it disappeared for a variable time and reappeared in a new position, always with a diagonal movement. The circle reached the last spatial position before the white occluding band and then it “disappeared” for one step and reappeared again for the last time in the right top or bottom corner of the screen depending on the starting point. During the reappearance of the stimulus after the occlusion period, within the circle appeared an upright or a tilted cross (50% of trials). After 1000 ms the small square in the middle of the screen disappeared for 1000 ms signalling the end of the trial (see Figure 3.1).

Participants were instructed to discriminate as quickly and correctly as possible if in the last circle an upward or a tilted cross was present by pressing one of two keys. The response for “upward cross” always correspond to the “D” key of the keyboard and “tilted cross” to “K” key. Participants used the two index fingers to respond. Eye tracker recordings were used to monitor the eyes of the participants (IView X, SMI).

Participants completed 10 blocks of 48 trials each and the whole experiment took around 1 hour.

The circle could move across the screen according to two different kinds of movement: regular and irregular. In regular trials, the interval between the disappearance of the circle and the reappearance of the next one had always the same temporal length conveying an impression of a rhythmic movement. In irregular trials, all the SOAs between successive stimuli were randomly varied between 100 and 700 ms and it was not possible to predict when the next ball would appear. Moreover, in regular trials also the speed of the ball was manipulated and in the fast condition the SOA was of 200 ms while in the slow one it was of 600. The whole trial had different durations with respect to the speed of the circle. For fast moving balls one trial lasted 2600 ms, for slow ones 5500ms and in the irregular condition where each step had a different duration trials lasted from a minimum of 2100 to a maximum of 5000 ms.

The temporal expectation was manipulated in different blocks. In “endogenous expectations” trials the participant was instructed that the colour of the circle was indicative of the length of the occlusion period (foreperiod). Three different colours (green, blue and yellow approximately equated in luminance) have been used to indicate short, long, or neutral durations of the foreperiod. The coupling between colour and the different durations of occlusion was counterbalanced between subject. In the “exogenous expectations” condition

the participant was required to focus attention on the speed of the circle. In this condition the length of the foreperiod could be valid if it matched the speed of the ball during the first part of the trial, or neutral for trials with irregular speed.

The occlusion period preceding the appearance of the last ball containing the target was the real moment in which temporal expectations played their role. In the exogenous condition we expected that the regular movement on which subject focused during the trial could help in responding, while in the endogenous condition is the knowledge of the duration of foreperiod that is supposed to help the participant in preparing the response. We compared the performance in these two conditions to verify if different kind of temporal expectation have a different impact on performance.

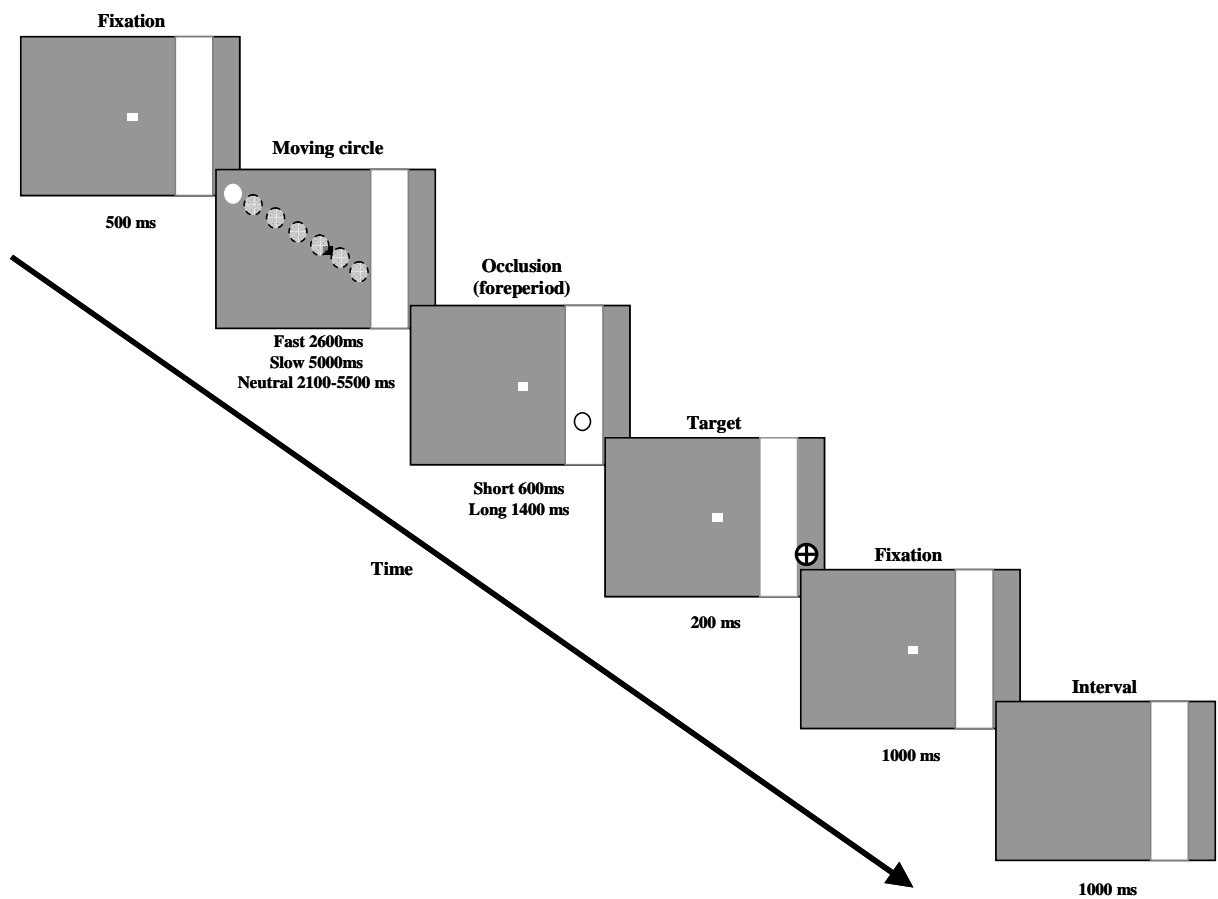


Figure 3.1: schematic representation of one trial. In experiment 1 the circles were coloured (blue, green or yellow) according to the different duration of the occlusion foreperiod.

3.2.3 Data analysis

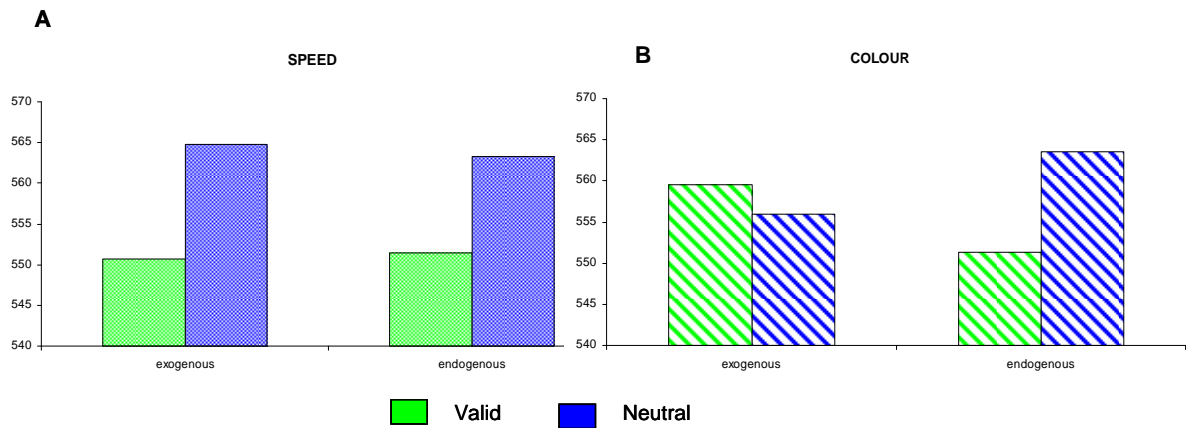
Mean RTs were analyzed using a repeated-measure ANOVA with the following factors: speed of movement (fast and slow), temporal expectations (endogenous and exogenous), speed (regular and neutral) and colour (predictive and neutral).

Paired samples t test were used for post-hoc comparison and p values were corrected according to Bonferroni.

3.3 RESULTS

The statistical analysis of RT yielded a the main effect of speed of movement ($F_{(1,11)} = 13.134$, $p = 0.004$) and speed ($F_{(1,11)} = 11.452$, $p = 0.006$), while no significant effect was found for the factor temporal expectations ($F_{(1,11)} = 0.005$, $p = 0.944$) and colour ($F_{(1,11)} = 1.676$, $p = 0.222$). Post-hoc t test revealed that in trials in which the movement of the circle was fast, RTs were significantly faster than slow trials ($t_{(11)} = -3.624$, $p = 0.004$). Moreover, a decrease of RTs was found also for conditions where the speed of the circle was regular with respect to neutral conditions in which the stimulus moved with steps of different length ($t_{(11)} = -3.384$, $p = 0.006$). See Graph 3.1.

Interaction between instructions and colour ($F_{(1,11)} = 5.298$, $p = 0.042$) and speed and colour ($F_{(1,11)} = 5.356$, $p = 0.041$) were found to be significant, while a tendency towards significance was found for the interaction between speed of movement and speed condition ($F_{(1,11)} = 3.525$, $p = 0.087$). The significant interaction between temporal expectations and colour did not survive post-hoc comparisons and all p values were higher than 0.05. Post-hoc t test for the interaction between speed and colour revealed that condition where both speed and colour were informative (regular and predictive, respectively), RTs were faster with respect to trials in which none of cues was informative (both colour and speed were neutral) ($t_{(11)} = -3.590$, $p = 0.004$) or when only the colour was informative ($t_{(11)} = -3.850$, $p = 0.003$).



Graph 3.1: mean RTs averaged over 12 subjects divided for valid and neutral speed trials (A) and valid and neutral colour trials (B). Data are divided according to the temporal expectation (exogenous and endogenous).

3.4 DISCUSSION

The main result of this experiment was that the instruction to pay attention to a particular temporal cue with respect to another one has no influence on performance. It seems that this lack of effectiveness could be ascribed to the powerfulness of the exogenous cue that has a greater impact on speed of response with respect to the knowledge of foreperiod length. Temporal expectancy is more effective when it is built up by the regular speed of the circle. This seems to confirm the superiority of exogenous temporal cues compared to endogenous ones, irrespectively of instruction. Participants anecdotally reported that even if their attention was focused on the colour of the ball and this information was used to expect the reappearance of the ball after the occlusion foreperiod, it was impossible not to be not influenced by the rhythmic movement of the ball. Anyway, endogenous and exogenous expectation interact significantly indicating that participants have some advantage on focusing on both kinds of information.

Also an effect of the speed of movement was found, with faster RTs for trials in which the circle moved fast with respect to trials in which the movement was slow. This result confirms again the pervasive effect of the exogenous cue and of temporal expectancy provided by the rhythm of the stimulus. The frequency of the rhythm that conveys the sense of movement clearly affects the preparation of the motor response: when the rhythm is more frequent RTs are faster.

3.5 EXPERIMENT 2

The aim of this experiment was to replicate and extend previous findings on the neural mechanisms of the effects of temporal expectations. The task was similar to previous ones (Correa & Nobre, 2008; Doherty et al., 2005) in which temporal expectation is generated by the regular rhythm of a moving stimulus. With respect to previous studies, we kept a regular trajectory of the stimuli without introducing uncertainty about spatial variables and manipulated the regularity of the rhythm. In particular, we were interested on the effect of exogenous expectancy elicited incidentally by the regular movement of the stimulus on the different components of the ERPs.

METHODS

3.5.1 Participants

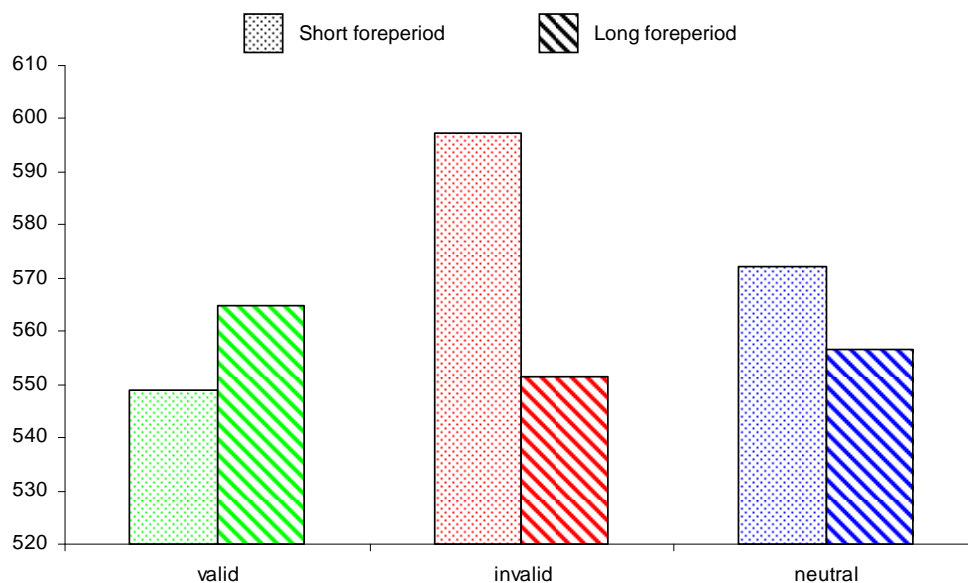
Thirty-one students (mean age 24.8) of Oxford University took part as paid volunteers and gave informed consent to participate. All were free from neurological disorders and had normal or correct to normal visual acuity. Eleven participants were eliminated from the analysis because of high percentage of errors or misses or unsatisfactory ERP recording (eye movements or noise caused by muscle activity). Therefore, behavioural and electrophysiological data analyzed in this experiment refer to 20 subjects (13 females).

3.5.2 Stimuli and task

All the experimental conditions (size of the stimuli and their timing of presentation) were the same as in the previous experiment except for the white colour of the circle in all the conditions (see Figure 3.1). Also the task was the same: participants were required to discriminate as fast and correctly as possible the shape contained in the last circle after the occlusion foreperiod (an upward or a tilted cross) by pressing two keys of the keyboard (“D” and “K”).

The circle moved across the screen with regular steps (with two speeds, fast and slow) or irregular steps of different temporal duration. The specific characteristic of this experiment was the implicit construction of temporal expectations and their breakdown on some trials. On a trial by trial basis, the movement of the circle conveyed specific temporal predictions about when the circle would re-appear after the occluding bar, except in the condition of irregular movement. Across trials, the time at which the circle appeared after the occlusion period could confirm (valid trial) or violate (invalid trials) the temporal expectation generated by the movement of the circle. In the “irregular” movement, no temporal expectation was possible (neutral trials). In fast invalid trials, the last circle reappeared with a delay of 800 ms with respect to the expected time, while in invalid slow the circle reappeared in advance after only 600 ms instead of the expected 1400 ms.

Participants were seated in a dimly illuminated room, facing a computer monitor positioned 100 cm in front of them. They were required to fixate the small square in the centre of the screen and to keep fixation steady. The whole experiment took 1 hour and 15 minutes and participants completed 14 blocks of 36 trials each.



Graph 3.2: mean RTs of 20 subjects divided with respect to the length of the foreperiod (short and long) and with respect to validity of temporal expectations generated by the movement (valid, invalid, neutral).

3.5.3 EEG recording

The EEG was recorded using Ag/AgCl electrodes mounted on an elastic cap according to the 10-20 International system. The montage included 6 midline electrodes (Fz, FCz, Cz, Pz, and Oz), and 14 sites over each hemisphere (Fp1/Fp2, F7/F8, F3/F4, FT7/FT8, FC3/FC4, T7/T8, C3/C4, TP7/TP8, CP3/CP4, P7/P8, P3/P4, PO7/PO8, PO3/PO4 and O1/O2). Additional electrodes were used to record the vertical and horizontal eye movements and as ground and reference sites. Electrodes placed at the ocular canthi were used to record horizontal eye movements while vertical eye movements and blinking were detected by an electrode placed under the right eye. Eye movements were also monitored using an infrared eye tracker (IView X, SMI). All the electrode were referenced to the right mastoid during the recording and re-reference off-line to the average of left and right mastoids. Data were acquired at a sampling rate of 1000 Hz. using a NuAmp amplifiers (Neuroscan, El Paso, TX). Recording was done with a low pass filter at 200 Hz and with no high pass filter (DC).

3.5.4 Data analysis

Behaviour

Mean RTs were analyzed using a repeated-measures ANOVA with the following factors: occlusion period (long and short), temporal expectation (valid, invalid and neutral), position of the last circle (top and bottom) and response type (upward cross or tilted cross). Paired samples t test were used for post-hoc comparisons and p values were corrected for repeated measures (Bonferroni).

ERPs

The continuous EEG was filtered off-line with a 40 Hz low pass filter and segmented into epochs starting 200 ms before and ending 600 ms time-locked onto the onset of the last circle reappeared after the occlusion foreperiod. As in previous studies, a strict baseline from 0 to 50 ms has been used to minimize the misalignment of the waveforms caused by the anticipatory neural activity (CNV) (Correa et al., 2006; Correa & Nobre, 2008; Griffin et al., 2002). Epochs with large (50 μ V) deflections on the eye channels or excessive noise or drifts in the other channels (100 μ V) were rejected.

Trials were averaged according to temporal expectations (valid, invalid and neutral) and only the trials with correct responses have been included in the average. A minimum criteria of 20

trials for condition has been set in order to ensure a sufficient signal-to-noise ratio. Participants with less than 20 trials in any condition have been eliminated from the analysis. A repeated-measure ANOVA assessed the effects of temporal expectation (valid, invalid and neutral), electrode position (different for each component) and electrode side (left, midline and right, substituted by the factor hemisphere in the analysis of P1 and N1). When necessary, Greenhouse-Geisser ϵ correction for nonsphericity was applied (Jennings & Wood, 1976). T tests were employed for post-hoc comparisons and Bonferroni correction was used to correct p values.

Time windows and electrodes were chosen by visual inspection of the grand average waveforms and according to previous studies (Doherty et al., 2005; Correa & Nobre, 2008).

The P1 was analyzed over occipital and parietal electrode (O1/2, PO3/4 and PO7/8). Because of callosal transmission time two different time windows were employed for this component: an interval between 105 and 125 ms for contralateral electrodes, with respect to the position of the last circle, and 115 and 135 for ipsilateral ones. N1 was recorded between 160 and 200 ms on the same electrodes as P1. N2 was analyzed between 250 and 300 ms over centro-parietal and parietal electrodes (CP3/Z/4 and P3/Z/4). P3 was evident between 400 and 500 ms over frontal, fronto-central, central and parieto-central position (F3/Z/4, FC3/Z/4, C3/Z/4 and CP3/Z/4).

3.6 RESULTS

3.6.1 Behavioural results

A mean error rate of 7% was found in this task. This relatively high percentage of errors could be caused by an objective difficulty in discriminating the two targets presented within the last circle given the peripheral position of the visual field where the target appeared.

Statistical analysis of RTs revealed a main effect of occlusion foreperiod ($F_{(1,19)} = 10.24$, $p = 0.005$), temporal expectation ($F_{(2,38)} = 21.521$, $p = 0.001$) and of response type ($F_{(1,19)} = 26.342$, $p = 0.001$), where RTs for the tilted were faster than that for the upward cross. Post-hoc comparisons revealed that valid trials were significantly faster than both invalid ($t_{(22)} = -5.812$, $p = 0.001$) and neutral ($t_{(22)} = -3.483$, $p = 0.002$) trials which were faster than invalid ($t_{(22)} = -4.74$, $p = 0.001$) trials. The only significant interaction was between occlusion

foreperiod and temporal expectations ($F_{(2,38)} = 32.461$, $p = 0.001$). Paired t test revealed that for short foreperiod valid trials were faster than invalid ($t_{(22)} = -8.43$, $p = 0.001$) and neutral ($t_{(22)} = -6.621$, $p = 0.001$) trials and that neutral were faster than invalid ($t_{(22)} = -5.62$, $p = 0.001$) trials. For the long foreperiod, the only significant difference was that RTs for valid trials were longer than neutral ($t_{(22)} = 3.008$, $p = 0.006$) trials.

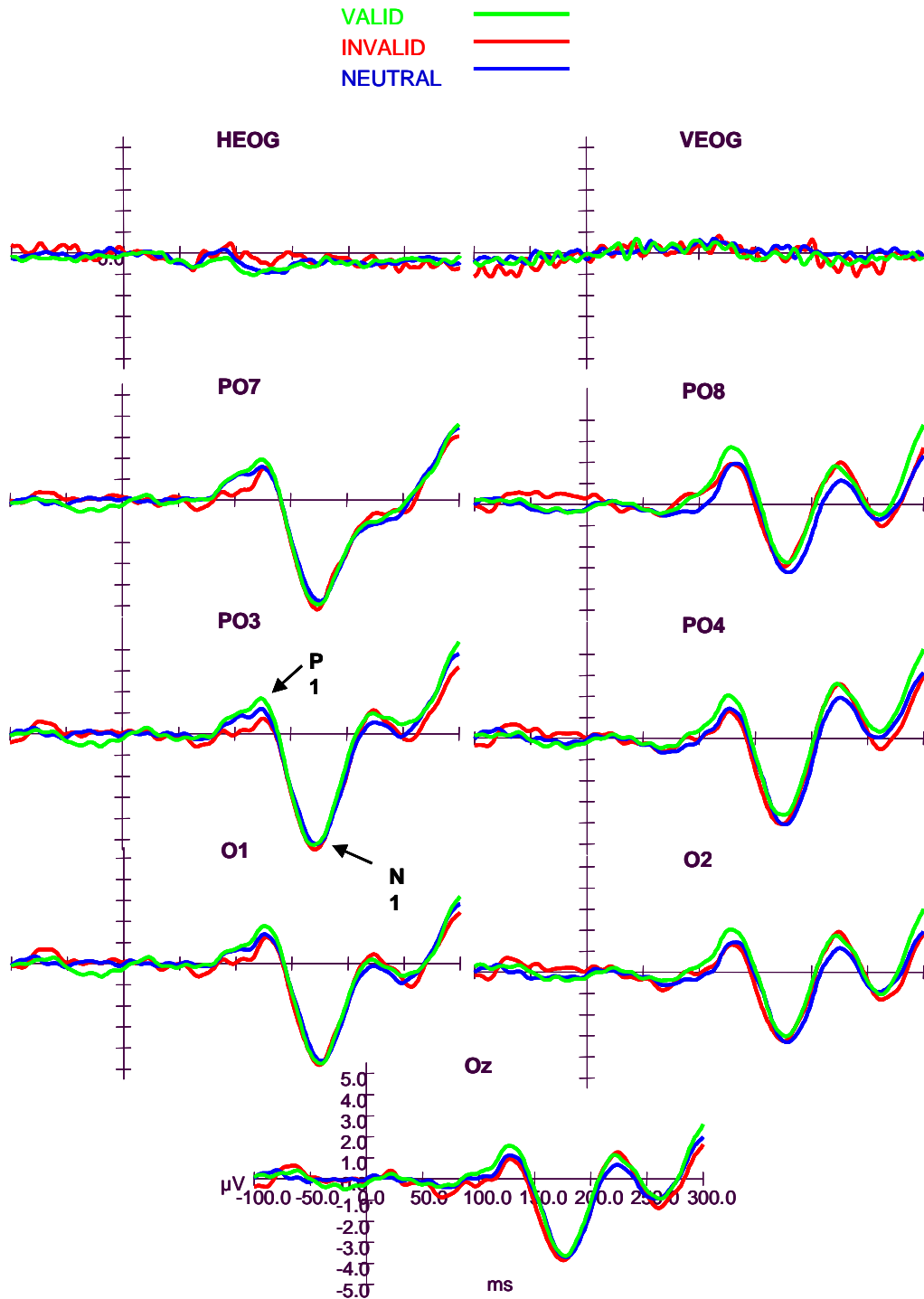


Figure 3.2: Waveforms for posterior electrodes. Average of ERPs time locked to the last circle for 20 participants for valid, invalid and neutral conditions after short occlusion foreperiod.

3.6.2 Electrophysiological results

Electrophysiological analysis was conducted only for trials of the short occlusion foreperiod condition.

The mean amplitude of P1 showed a marginally significant main effect of temporal expectations ($F_{(2,38)} = 3.884$, $p = 0.052$) and post-hoc t test revealed a significant difference between valid and neutral trials ($t_{(19)} = 3.625$, $p = 0.002$). Moreover, the main effect of electrode position ($F_{(2,38)} = 8.166$, $p = 0.004$) and hemisphere ($F_{(1,19)} = 4.521$, $p = 0.047$) also resulted significant indicating higher amplitude for PO7/8 with respect to O1/2 ($t_{(19)} = -5.484$, $p = 0.001$) and also to PO3/4 ($t_{(19)} = -2.804$, $p = 0.011$) and on the right hemisphere ($t_{(19)} = -2.126$, $p = 0.047$) with respect to the left hemisphere.

N1 was not modulated by temporal expectations ($F_{(2,38)} = 0.25$, $p = 0.78$), but the main effect of electrode position ($F_{(2,38)} = 4.254$, $p = 0.022$) and hemisphere ($F_{(2,19)} = 17.477$, $p = 0.001$) were found to be significant and also the interaction between these two factors ($F_{(2,38)} = 4.637$, $p = 0.016$). N1 was more negative on the PO3/4 electrodes and over the left hemisphere. Post-hoc comparisons revealed that N1 was more negative over the left hemisphere for electrode O1 ($t_{(22)} = -4.285$, $p = 0.001$), PO3 ($t_{(22)} = -3.355$, $p = 0.003$) and PO7 ($t_{(22)} = -4.143$, $p = 0.001$) with respect to =2, PO4 and PO8, respectively (Figure 3.2).

The amplitude of N2 was marginally affected by temporal expectation ($F_{(2,38)} = 3.625$, $p = 0.057$) and post-hoc comparisons revealed a significant difference between valid and neutral condition ($t_{(19)} = 2.622$, $p = 0.017$) and a marginally significant difference between valid and neutral ($t_{(19)} = -3.355$, $p = 0.003$) trials. N2 was more positive (and less wide) in valid temporal expectations. The main effect of electrode position was also significant ($F_{(2,38)} = 4.565$, $p = 0.042$) and post-hoc tests revealed a significantly more negative N2 for central electrodes with respect to central-parietal ones ($t_{(19)} = -2.901$, $p = 0.017$).

P3 amplitude was affected by temporal expectation ($F_{(2,38)} = 8.948$, $p = 0.001$) and valid trials were more positive than invalid ($t_{(19)} = 3.710$, $p = 0.001$). Also electrode position ($F_{(4,76)} = 5.481$, $p = 0.001$) and electrode side ($F_{(2,38)} = 3.822$, $p = 0.031$) were found to be significant. Over more frontal electrodes P3 amplitude was less pronounced and increased moving towards more posterior electrodes (F vs. FC: $t_{(19)} = -9.006$, $p = 0.001$; FC vs. C: $t_{(19)} = -6.850$, $p = 0.001$; C vs. CP: $t_{(19)} = -5.146$, $p = 0.001$). P3 amplitude was higher over midline electrodes with respect to electrodes over the right hemisphere ($t_{(19)} = 2.925$, $p = 0.009$). Interactions between temporal expectation and electrode side ($F_{(4,76)} = 4.605$, $p = 0.007$) and electrode position and electrode side ($F_{(6,114)} = 10.437$, $p = 0.001$) were found to be

significant. Paired T tests revealed that in valid condition P3 was more positive over middle electrodes than left electrodes ($t_{(19)} = -3.864$, $p = 0.001$) or right ones ($t_{(19)} = 3.8$, $p = 0.001$), while in invalid condition the amplitude of P3 over left hemisphere was lower than on right ones ($t_{(19)} = -4.626$, $p = 0.001$). The post-hoc analysis of the interaction between electrode position and electrode side revealed that the amplitude of P3 increased significantly moving from the more frontal electrodes towards more posterior sites for electrodes on the left and right hemisphere and for electrode on the midline (F3 vs. FC3: $t_{(19)} = -6.439$, $p = 0.001$; FC3 vs. C3: $t_{(19)} = -6.323$, $p = 0.001$; C3 vs. CP3: $t_{(19)} = -3.44$, $p = 0.003$; Fz vs. FCz: $t_{(19)} = -7.924$, $p = 0.001$; FCz vs. Cz: $t_{(19)} = -6.585$, $p = 0.001$; Cz vs. CPz: $t_{(19)} = -5.336$, $p = 0.001$; F4 vs. FC4: $t_{(19)} = -7.701$, $p = 0.001$; FC4 vs. C4: $t_{(19)} = -5.006$, $p = 0.001$; C4 vs. CP4: $t_{(19)} = -5.864$, $p = 0.001$) (Figure 3.3).

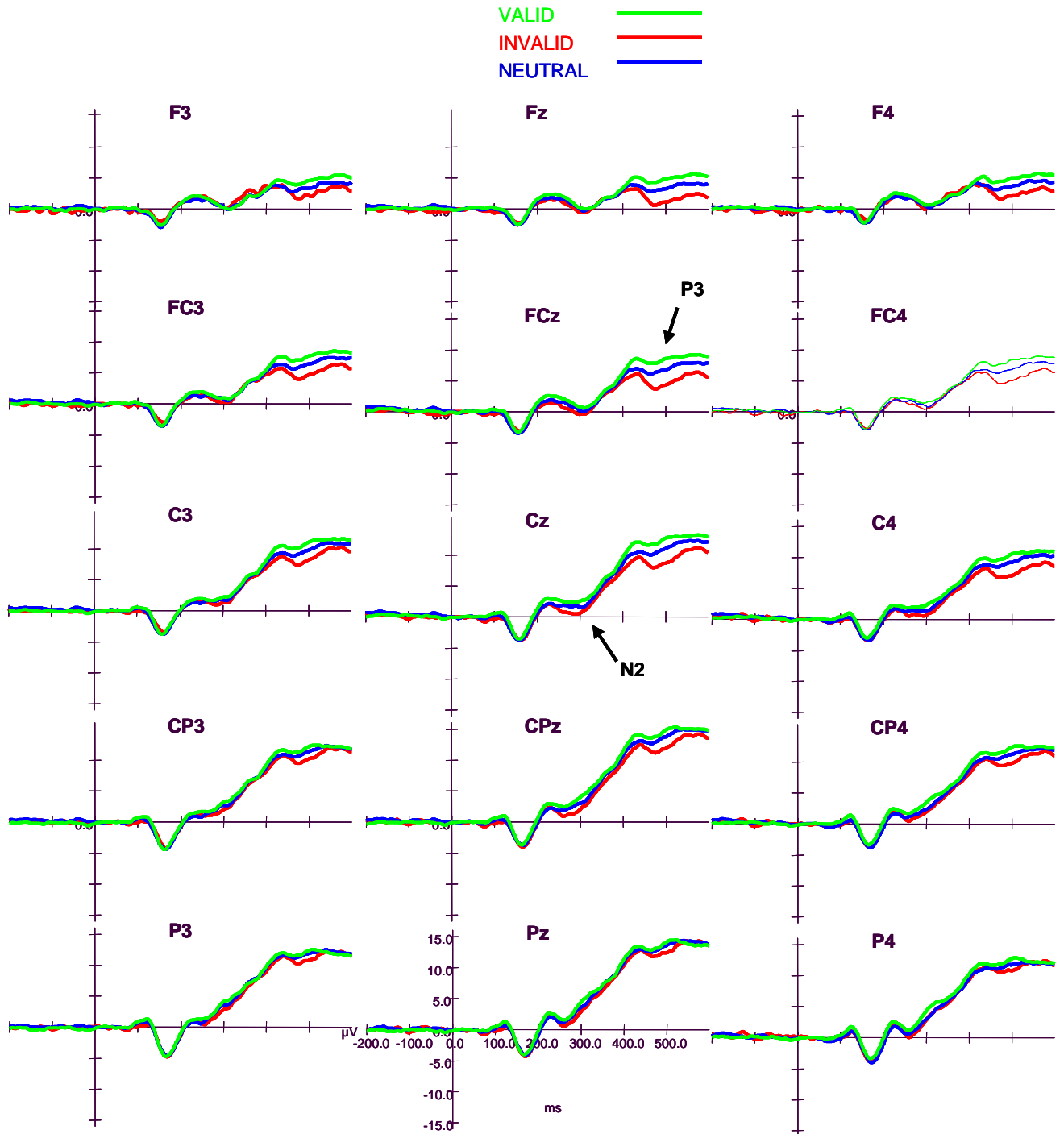


Figure 3.3: Waveforms for parietal central and frontal electrodes. Average of ERPs time locked to the last circle for 20 participants for valid, invalid and neutral conditions after short occlusion foreperiod.

3.7 DISCUSSION

The aim of this experiment was to verify the effect of exogenous temporal expectations on behaviour and in particular on neurophysiological responses. Exogenous temporal expectations are generated incidentally by a regular temporal structure (Coull & Nobre, 2008). In this specific case, the regular appearing and disappearing of a small circle in the

screen conveyed a sense of regular movement and established a rhythm. Participants did not receive any particular instruction about the movement of the circle but the behavioural results confirmed that they used it to improve performance. The effect of temporal expectations generated by the rhythm of the circle was evident in a decrease of RTs in the valid condition, that is, when the movement was not perturbed during the occlusion foreperiod, with respect to the invalid condition, but also to the neutral one. The difference between neutral and valid expectations of attention in time confirmed the power of the temporal information conveyed by the regularity of the rhythm in enhancing behavioural performance. This enhancement of performance agrees with the classical findings of studies that used explicit symbolic cues (Nobre, 2001). Moreover, the benefit obtained by the rhythmic movement was present both in fast and slow conditions confirming the flexibility of temporal expectations already highlighted by a previous study (Correa & Nobre, 2008)

The shortening of RTs for longer occlusion foreperiods has been already described in the past (Elithorn & Lawrence, 1955): with long foreperiods, the variability produced by the foreperiod is reduced by using the information provided by the flow of time itself. In terms of “hazard function“ this means that the probability that an event occurs increases if it is not yet occurred. In our task, with long occlusion foreperiods the probability of target appearance increases with time and the participant is more and more prepared to respond.

The effect of temporal expectations on the ERPs components has been investigated by previous studies and it is quite well established. Orienting attention in time affects later components related to decision processes and response preparation like N2 and P3 (Miniussi et al., 1999; Nobre, 2001; Griffin et al., 2001 and 2002). One study (Griffin et al., 2002) revealed an enhancement of N1 when participants attended to stimuli occurring after a short temporal interval with respect to a long one. Unfortunately, this result has not been replicated by the authors (Griffin et al., 2002) and still needs to be explained. In a paradigm similar to the one employed in this experiment, Doherty and collaborators (2005) found an increased amplitude of P1 in conditions when spatial and temporal expectations interact. It is well known that P1 amplitude is modulated by spatial attention (Eimer, 1998; Mangum, 1995). Interestingly, the enhancement of P1 by Doherty and colleagues (2005) was greater in the condition that combines the two kinds of expectations, spatial and temporal, with respect to a condition of spatial expectation alone. In our experiment we found that P1 amplitude was modulated by temporal expectancy. The task did not overtly manipulated spatial expectancy and the last position of the target was inferred by the regular diagonal trajectory followed by the circle. This result corroborates previous finding adding new evidence that temporal

information can influence perceptual analysis as is the case with spatial information. N1 amplitude was not modulated by temporal orienting thus confirming previous findings (Correa & Nobre, 2008).

We found a modulation of N2 by temporal expectation over central and parietal electrodes. With respect to previous studies (Correa et al., 2008; Doherty et al., 2005), the modulation of N2 was present only on midline electrodes and over the right hemisphere and no modulation was evident for electrodes on the left hemisphere. The N2 component reflects temporal orienting and several studies reported that temporal expectation attenuated it (Correa et al., 2006; Doherty et al., 2005; Griffin et al., 2002). The meaning of this modulation it is still not clear. N2 has been associated to temporally deviant stimuli in oddball paradigms (Loveless, 1986) and response inhibition (Kok, 1986). Correa and Nobre (2008) hypothesized that N2 reflects a mechanism of response inhibition that prevents response in the wrong moment. This explanation is consistent with the increased negativity of this component for invalid trials where the target appeared later than the expected moment.

As in previous studies (Griffing et al., 2002; Miniussi et al., 1999), P3 was strongly modulated by temporal expectation and this effect was connected to response-related processing. This component is more positive for valid trials and is related to motor response preparation (Mangun, 1995).

The electrophysiological analysis of this experiment are still in progress. We are also interested in analyzing the frequency activity in the alpha (α) and mu (μ) band generated by the rhythm and to highlight how the oscillatory activity is modified by the breakdown of temporal expectations.

3.8 CONCLUSIONS

These two experiments shed light on some aspects of the mechanisms involved in temporal expectations. They have highlighted the pervasive cueing effect exerted by the rhythmic movement that cannot be deleted by the use of endogenous temporal expectations. These results suggest a superiority of exogenous mechanisms in driving temporal expectation with respect to more cognitively-controlled instructions. Moreover, they confirmed the synergistic effect of the combination of spatial and temporal expectation. To know how and when a stimulus will appear has a strong impact on the neural activity linked to primary steps of

visual analysis indicating an influence of both kind of mechanisms on sensory processing stages.

CHAPTER 4

General conclusions

The three experiments reported in this thesis are quite different among each other. They cover different topics within the main field of attentional selective mechanisms in space and time and different techniques (TOJ paradigm, RTs and ERPs) have been employed to highlight the multifaceted mechanisms involved in these processes.

The first experiment used a TOJ paradigm to map the deficit in selective spatial attention of patients with signs of neglect or visual extinction. This paradigm allows to obtain an index of the temporal advantage for unattended stimuli with respect to attended ones. Previous studies (Bueti et al., 2007; Eramudugolla et al., 2007; Guerrini et al., 2003; 2006; Karnath et al., 2002; Robertson et al., 1998; Rorden et al., 1997; Sinnett et al., 2007) used TOJ tasks to evaluate the performance of neglect patients in different sensory modalities. The common finding is a consistent temporal delay in the perception of the stimulus presented in the left hemispace with respect to the one presented in the right portion of space. We extended the previous findings by manipulating both the temporal delay and the spatial position of the stimuli and analyzing the performance of patients at different eccentricities within each visual field. The results confirmed a strong temporal disadvantage for stimuli presented within the left visual field, while in the ipsilesional visual field the performance of neglect patients did not differ from control subjects. Moreover, it has been found a tendency towards a significantly different performance within left visual field. The left-sided stimulus of the pair presented in far left position needs a greater temporal advantage with respect to the left-sided stimulus presented in near position. The modulation of performance according to eccentricity adds new evidence to the existence of a gradient in the deficit of attentional selection reported by previous studies (Behrmann et al., 1997; Hornack, 1992; Karnath & Fetter, 1995; Karnath & Perenin, 1998; Kerkhoff et al., 1999; Natale et al., 2005; Natale et al., 2007; Smania et al., 1998). Interestingly, the present results provide evidence for the existence of a modulation of the temporal selection within a deficit in spatial selection. In the left visual field, where the spatial selective mechanisms of neglect patients are impaired there is also an impairment of temporal mechanisms and both deficits decrease together moving towards more ipsilesional positions. This interaction between spatial and temporal aspects of the stimulation suggests a possible common basis for these mechanisms.

The two experiments that investigated temporal expectations built by regularly moving stimuli have a different theoretical background with respect to the TOJ task but are still useful in demonstrating an interaction between attention to space and time. In particular, the ERPs experiment corroborated previous findings (Doherty et al., 2005), proving that the combination of spatial and temporal expectations influences the amplitude of the early visual component P1 thus reflecting an improvement in the first stages of visual analysis. Doherty and colleagues (2005) demonstrated that this effect is not simply caused by spatial focusing. It is well known that spatial attention enhances the amplitude of P1 (Eimer, 1998; Mangun, 1995), but in Doherty's experiment the increased amplitude in the condition of both temporal and spatial focusing was significantly greater than in the condition of spatial expectations alone. The synergistic effect obtained by combining spatial and temporal information demonstrates that spatial and temporal information can be used simultaneously to improve attentional selection over the benefit obtained by the use of either information alone. The same results have been obtained also with different paradigms. Kristiásson and Nakayama (2002) added a spatial component to an AB task, while Coull & Nobre (1998) and Milliken and colleagues (2003) used cues with both temporal and spatial properties. Trying to cast more light on the specificity of the mechanisms of spatial and temporal attention, neuroimaging studies compared the anatomical areas involved in temporal and spatial orienting. Coull and Nobre (1998) employed both positron-emission tomography and functional magnetic resonance imaging in a task requiring to attend to spatial locations or temporal intervals according to a symbolic central cue. A strong hemispheric asymmetry was found between regions activated by spatial with respect to temporal orienting. While spatial attention preferentially activated right posterior parietal areas, temporal orienting was associated with activation of left inferior parietal cortex and left inferior lateral premotor cortex. The pattern of cerebral areas activated by temporal orienting of attention has been confirmed also in a successive study (Coull et al., 2000). This evidence suggests that a parietal-frontal sensorimotor circuit may contribute to general mechanisms involved in attentional orienting, while differently lateralized sub-system are activated by specific type of expectations (Nobre, 2001).

The scenario reproducing the relationship between attentional mechanisms in space and time is complex and articulated. Recent findings (and also studies reported in this thesis) suggest the existence of strong interactions between these two mechanisms but still many aspects need to be clarified. It is still unclear if spatial and temporal attention depend on the same general

mechanisms, or the way in which information about space and time interact successfully increasing performance.

In the last years the interest in studying the mechanisms of temporal orienting is greatly increased and hopefully always more and more energy will be devoted to the investigation of this emergent topic in neuroscience.

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