Title of Thesis

Studies on Mechanisms of Visual and Auditory Attention in Temporal or Spatial Cueing Paradigm

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Abstract

In real life, a mass of information bombards us. Attention as a basic cognitive function can help us to select the useful information and filter out other useless. In this filtering process, two mechanisms are involved, i.e., endogenous and exogenous. Exogenous attention, which is also called involuntary or stimulus-driven attention, can be triggered reflexively by a salient sensory event from the external world. In contrast, endogenous attention is also called voluntary or goal-driven attention and involves a more purposeful and effort-intensive orienting process.

For the exogenous attention, there are two types of effects, i.e., facilitation and inhibition. Facilitation effect refers to faster responses to a target appearing at the previously attended location (also called the cued location) than to a target appearing at an unattended location (uncued location). Inhibition effect (also called inhibition of return) refers to slower a slower response to the target presented at the cued location than the target presented at the uncued location. The Chapter 2 of this thesis summarized previous studies to investigate the mechanisms of exogenous inhibition of return.

For the endogenous attention, a visual spatial cue, such as left or right arrow, can trigger a spatial orienting of attention and guide us to where a target might be presented. Similarly, a visual temporal cue, such as inner or outer circle, can trigger a temporal orienting of attention and predict when the target could appear. Previous neuroimaging studies found that the visually induced spatial or temporal orienting of attention were associated with common neural correlates, such as fronto-parietal network. Further the neural correlates of the spatial orienting of attention were specifically associated with right posterior parietal, while the temporal orienting of attention were specifically associated with left posterior parietal cortex.

This thesis aimed at investigating how a visual spatial or temporal cue modulates event-related potentials (ERPs) corresponding to auditory (Chapter 3) and visual (Chapter 4) processing. Utilizing the high temporal resolution of ERP, the real-time neuronal activity can be observed at a millisecond scale and thus determine which stage(s) of processing are modulated differently or similarly by the visual spatial or temporal cue. A classic cue-target paradigm was applied in three ERP studies. In this paradigm, a left or right arrow was served as a visual spatial cue to predict left or right lateralization of target stimuli, while an inner or outer circle was served as a visual temporal cue to predict short or long time interval prior to the target stimuli. Participants were instructed to respond to auditory and visual target. The ERP results of three studies showed that the visual spatial or temporal cue modulates the auditory and visual processing differently, but partially overlapping.

The present thesis investigated how a visual spatial or temporal modulate the unimodal auditory, unimodal visual and bimodal audiovisual processing. In daily life, vision and sound signals can be integrated in the human brain and provide a coherent cognition of the real world, which is called audiovisual integration. Therefore, future studies will focus on investigate whether spatial or temporal orienting of attention modulates audiovisual integration with ERP technique.

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Chapter 1 Introduction

Summary

This chapter introduces the concept of attention and audiovisual integration. The previous studies of attention, visual attention and auditory attention have also been summarized here. The technique of electroencephalogram (EEG) and event-related potential (ERP) have been introduced. At last, the purpose and contents of the thesis are briefly explained.

1.1 Attention

Human beings are almost always being bombarded with a mass of information in their daily lives. It is impossible for our brains to adequately process and make sense of every bit of these things. Instead, you and your brain tend to work together to decide which of these sensory experiences will be processed and what will be left out. Attention as a basic cognitive function can help us to select the useful information and filter out other useless. Attention is the behavioral and cognitive process of selectively concentrating on a discrete aspect of information, whether deemed subjective or objective, while ignoring other perceivable information [1].

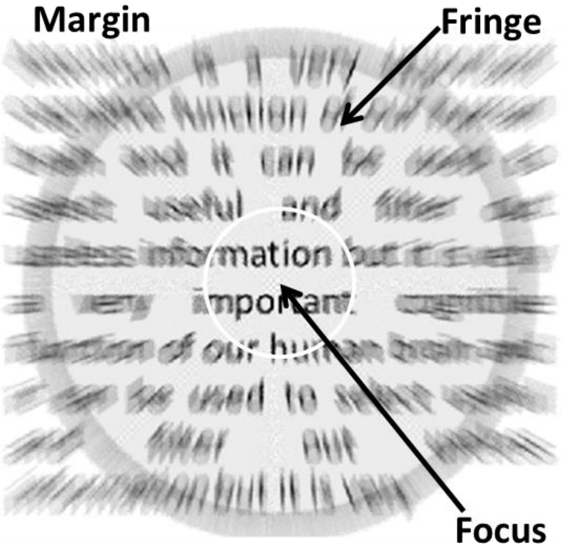

Figure 1.1 The spotlight model of attention

For the visual attention, there are at least two models which describe how visual information to be selected or filtered out. Visual attention is generally thought to operate as a two-stage process [2]. In the first stage, attention is distributed uniformly over the external visual scene and processing of information is performed in parallel. In the second stage, attention is concentrated to a specific area of the visual scene (i.e., it is focused), and processing is performed in a serial fashion. For example, the spotlight model [3] of visual attention described attention as having a focus, a margin, and a fringe (**Figure 1.1**). The focus is an area that extracts information from the visual scene with a high-resolution, the geometric center of which being where visual attention is directed. Surrounding the focus is the fringe of attention, which extracts information in a much more crude fashion (i.e., low-resolution). This fringe extends out to a specified area, and the cut-off is called the margin.

For auditory attention, in the daily life, selective auditory attention is often an unconscious process that takes over when you're trying to focus on a sound or a person's words. For example, the most famous cocktail party effect (**Figure 1.2a**), which is the phenomenon of being able to focus one's auditory attention on a particular stimulus while filtering out a range of other stimuli, much the same way that a partygoer can focus on a single conversation in a noisy room [4].

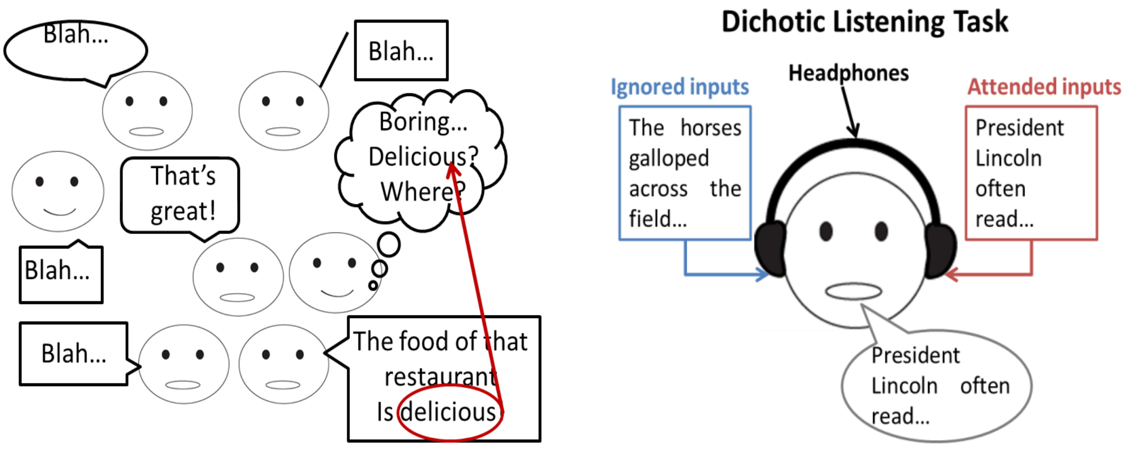

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Figure 1.2 a: the cocktail party effect; b: the dichotic listening task

The dichotic listening task is used as a behavioral test for hemispheric lateralization of speech sound perception [5], in which a participant is presented with two different auditory stimuli simultaneously (usually speech). The different stimuli are directed into different ears over headphones. Participants were instructed to repeat aloud the words they heard in one ear while a different message was presented to the other ear (**Figure 1.2b**). As a result of focusing to repeat the words, participants noticed little of the message to the other ear, often not even realizing that at some point it changed from English to German. At the same time, participants did notice when the voice in the unattended ear changed from a male's to a female's, suggesting that the selectivity of consciousness can work to tune in some information [6].

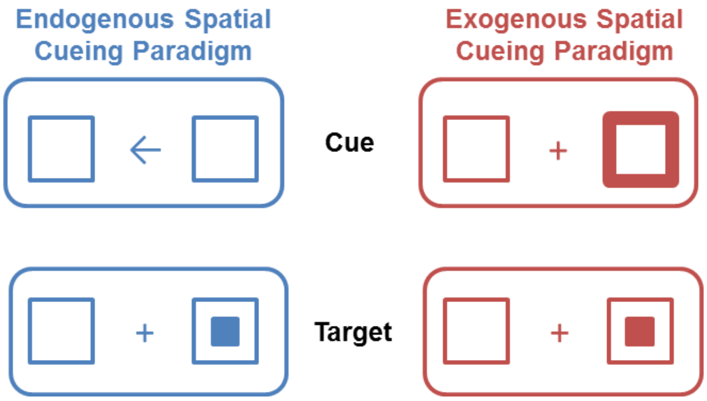

Figure 1.3 Spatial cueing paradigm of endogenous and exogenous attention. The endogenous paradigm is induced by the central arrow, while the exogenous one is induced by peripheral onset.

1.1.1 Exogenous Attention

Attention plays key roles in the selection of relevant and the ruling out of irrelevant modalities, spatial locations, or task-related objects. Two mechanisms, i.e., endogenous and exogenous, are involved in this filtering process. Exogenous attention, which is also called involuntary or ***stimulus-driven*** attention, can be triggered reflexively by a salient sensory event from the external world [7], e.g., the colorful clothing of your friend causing him/her to stand out. In contrast, endogenous attention is also called voluntary or goal-driven attention and involves a more purposeful and effort-intensive ***orienting*** process [8], e.g., orienting to a red table after someone tells you that your friend is at a red table.

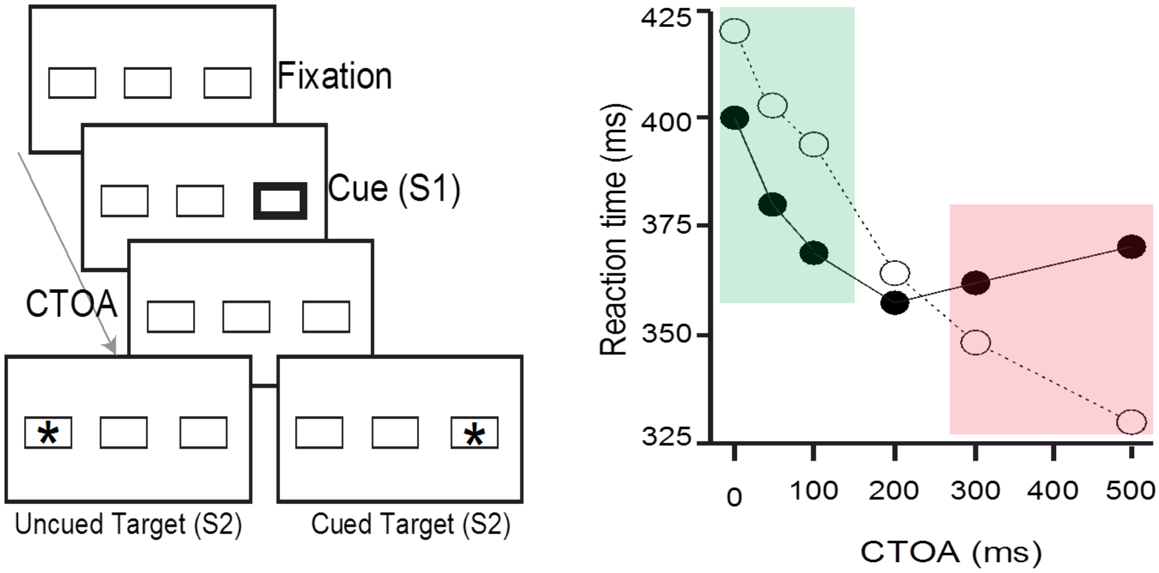

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Figure 1.4 Exogenous facilitation and inhibition of return. a: The sequence of events in a typical trial. A fixation display is followed by the first stimulus (S1, cue): the brightening of one of the two peripheral boxes. After varying intervals (cue–target onset asynchronies, CTOAs) from the onset of the cue, a target (S2), shown here as an asterisk, is presented at the cued (right) or uncued (left) location. The observer’s task is to make a speeded detection response as soon as the asterisk is detected. Catch trials with cues but no targets are included to discourage anticipatory responses and measure their frequency in the form of false alarms. b: The data from such an experiment, by Posner and Cohen [9]; responses to cued targets, filled circles; responses to uncued targets, open circles. Faster responding to cued targets at the shorter intervals (green) reflects the facilitatory effect of reflexive orienting of attention toward the cue. IOR is reflected in the slower responding to targets at the cued location at the longer intervals (red). (Picture from [10])

The spatial cueing paradigm is used to investigate the endogenous and exogenous attention [11,12]. In the exogenous spatial cueing paradigm, an uninformative peripheral cue appears at peripheral location to capture subjects’ attention. After a short or long stimulus onset asynchrony (SOA), the target is presented at the same location as the cue (cued location) or at a different location (uncued location). When the SOA was shorter than 200 ms, the reaction time (RT) of the target presented at the cued location was faster than that at the uncued location. Yet, when the SOA was longer than 250 ms, a slower response to the target presented at the cued location was found. This slowing of RT was termed the inhibition of return (IOR)[9,13,14](**Figure 1.4**).

1.1.2 Endogenous Attention

However, in the endogenous cueing paradigm, a central cue appears to direct attentional orienting to the direction of arrow, which is a visual spatial cue. The target is presented at the same or different direction of the central cue. The central cue (left or right arrow) can predict the location of the target stimuli [15]. With this paradigm, the consequence, which stimuli processing were speeded up at attended locations, was observed [15-17]. See examples in **Figure 1.3**.

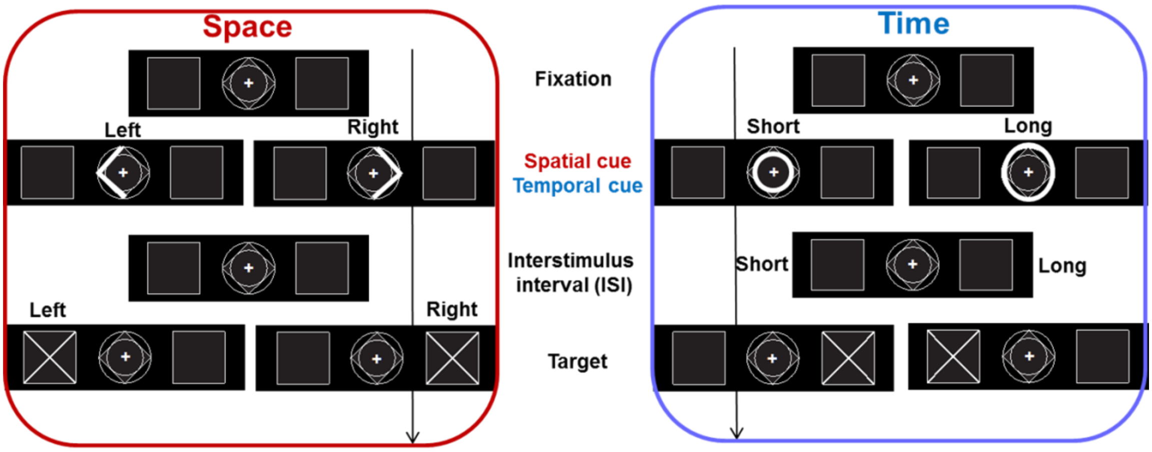

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Figure 1.5 Endogenous spatial or temporal cueing paradigm. A typical endogenous cueing paradigm was composed by an endogenous cue and target. a: The spatial cue will completely predict the target presented location. For example, if the spatial cue was left, then the target will be presented in the left box. b: The temporal cue will completely predict the time interval between the cue and target. For example, if the temporal cue was inner circle, then the target will be presented after the short time interval.

The cue-target paradigm is usually used to study endogenous attention (**Figure 1.5**), in which the central cue can provide the information for the following target stimuli [15]. On one hand, when the central cue is an arrow that direct left or right that can predict the location the target stimuli, the spatial orienting of attention (spatial attention) is elicited. With this paradigm, the consequence, which stimuli processing were speeded up at attended locations, was observed [15-17]. On the other hand, when the central is a big or small circle that can predict the time point of the following target stimuli, after a long or short time interval, the temporal orienting of attention (temporal attention) is triggered.

As showing in Figure 1.3, the exogenous cueing paradigm and the endogenous cueing paradigm were different. Previous studies have investigated differences between exogenous and endogenous orienting. For example, exogenous orienting is less affected by cognitive load than endogenous orienting. Observers are able to ignore endogenous cues but not exogenous cues. Exogenous cues have bigger effects than endogenous cues. And expectancies about cue validity and predictive value affects endogenous orienting more than exogenous orienting [18]. These differences between endogenous and exogenous attention might be caused by their different neural correlates, which will be discussed in detail below.

1.1.3 Neural Correlates with Exogenous and Endogenous Attention

It remains to be explored whether endogenous and exogenous attention stem from the same attention system. A common view states that the two processes are two modes of attentional system; they compete with each other for the control of attention [19-22]. The winner of the competition between the exogenous and endogenous orienting will take control of the attention and determine where or what is to be attended.

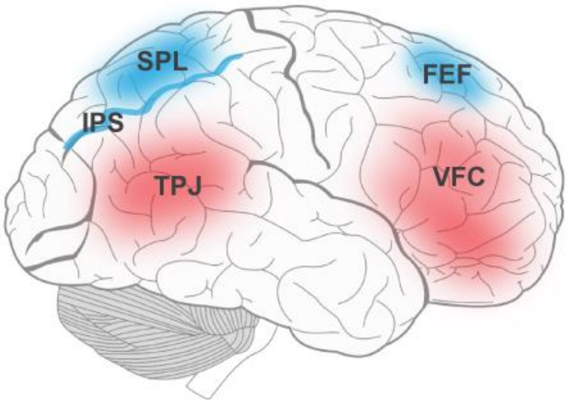

Figure 1.2 The different brain areas that are correlated with dorsal and ventral attention system. The dorsal attention system (blue) is bilateral and includes the superior parietal lobule (SPL), intraparietal sulcus (IPS), and the prefrontal cortex (e.g., frontal eye field, FEF). It is involved in voluntary (top-down) orienting and shows activity increases after the presentation of cues that indicate where, when, or to what subjects should direct their attention. The ventral attention (red) system is right lateralized and composed of the right temporal-parietal junction (TPJ) and the right ventral frontal cortex (VFC), including parts of the middle frontal gyrus (MFG) and the inferior frontal gyrus (IFG). It is involved in involuntary (stimulus-driven) orienting and shows activity increases after the presentation of salient targets, particularly when they appear in unexpected locations.

Another different view states that the endogenous and exogenous mechanisms are generally considered two distinct attention systems, though they largely share the same neural architecture [18,23,24]. Regarding visual system studies, unlike endogenous attention, exogenous attention demands no cognitive resources, is less susceptible to interference [25], and is more quickly oriented [26,27] behaviorally. Neuroimaging studies have revealed that although the two mechanisms are mediated by a largely common fronto-parietal network [23], endogenous attention is associated with the dorsal attention network and exogenous attention is associated with ventral attention network [28] (see **Figure 1.6**). Chica et al. (2013) put forward the hypothesis of "a dorsal frontoparietal network in the orienting of both endogenous and exogenous attention, a ventral frontoparietal counterpart in reorienting to task-relevant events"

[18,29]. Event-related potential (ERP) studies have shown that endogenous attention and exogenous attention modulate the different stages of stimulus processing. Specifically, endogenous attention exerts its effects on components of N1 [7] or P300 [25], whereas exogenous attention modulates the components of P1 [7,25]. A previous study, however, showed that the amplitude of P1 can be modulated by endogenous attention, but that N1 can be modulated by exogenous attention [30].

Regardless of whether the endogenous attention and exogenous attention are two distinct attentional system or two modes of the attention system, the majority of studies in the field have at least shown that the two mechanisms modulate the stimulus processing differently.

1.2 Event-related Potentials (ERPs)

1.2.1 Electroencephalogram (EEG)

A number of techniques are available to investigate the question of how and where in the brain particular perceptual and cognitive processes occur. Electroencephalography (EEG) is typically a non-invasive method to measure electrical activity of the brain along the scalp. The EEG signal reflects the summed postsynaptic activity in the underlying cortical regions. The key advantage of EEG is the high temporal resolution. For example, the sample resolution of our studies is 500Hz, i.e., 1 data point by each 2 millisecond (ms). **Figure 1.7** shows the recorded EEG data.

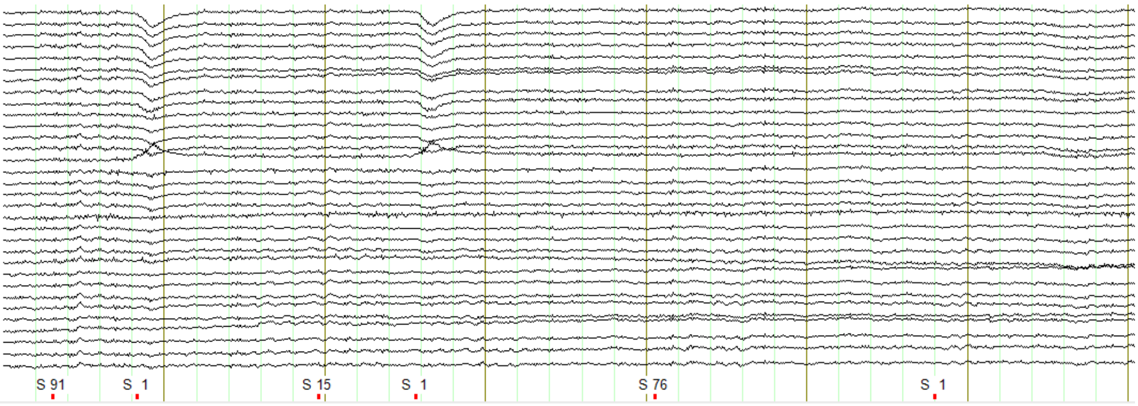

Figure 1.7 Raw data of EEG with triggers. If the stimulus is presented, the correspondence trigger will be presented.

Derivatives of the EEG technique include evoked potentials (EP), which involves averaging the EEG activity time-locked to the presentation of a stimulus of some sort (visual, somatosensory, or auditory). An event-related potential (ERP) is the measured brain response that is the direct result of a specific sensory, cognitive, or motor event [31]. More formally, it is any stereotyped electrophysiological response to a stimulus. The study of the brain in this way provides a noninvasive means of evaluating brain functioning in patients with cognitive diseases.

1.2.2 Event-related Potentials (ERPs)

Event-related potentials (ERPs) refer to averaged EEG responses that are time-locked to more complex processing of stimuli; this technique is used in cognitive science, cognitive psychology, and psychophysiological research. In the cognitive science studies, the ERPs components are typically investigate (**Figure 1.8**).

ERPs provide excellent temporal resolution—as the speed of ERP recording is only constrained by the sampling rate that the recording equipment can feasibly support, whereas hemodynamic measures (such as fMRI, PET, and fNIRS) are inherently limited by the slow speed of the BOLD response. The spatial resolution of an ERP, however, is much poorer than that of hemodynamic methods—in fact, the location of ERP sources is an inverse problem that cannot be exactly solved, only estimated. Thus, ERPs are well suited to research questions about the speed of neural activity, and are less well suited to research questions about the location of such activity [31].

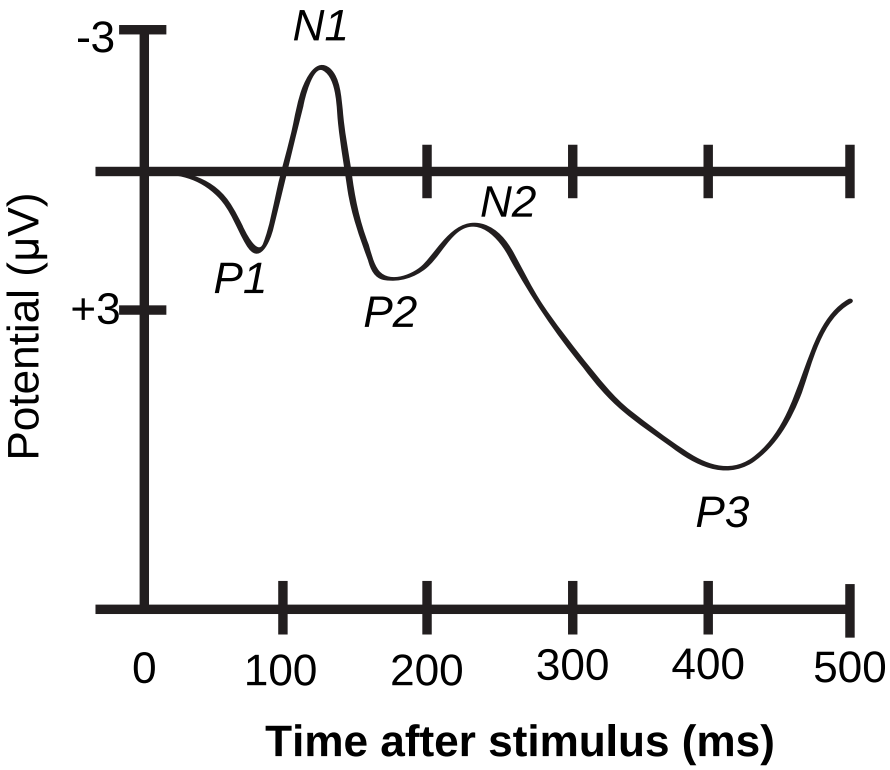

Figure 1.8 A waveform showing several ERP components, including the N100 and P300. Note that the ERP is plotted with negative voltages upward, a common, but not universal, practice in ERP research

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1.3 The purpose of the present thesis

The aim of this thesis studies was to investigate the mechanism of exogenous inhibition of return and how the visual spatial or temporal cue modulate the auditory and visual processing using behavioral and ERP with high temporal resolution. Now the content of each chapter will be summarized below.

Chapter 1 introduces the concept of attention, exogenous attention, inhibition of return, endogenous attention, and temporal or spatial cueing paradigm. Also, the electroencephalogram (EEG) and event-related potential (ERP) is introduced. The aim and contents of the thesis are also briefly described.

Chapter 2 describes the review study to summarize the previous studies on exogenous inhibition of return (IOR) and investigates the mechanism of IOR. The behavioral and neuroimaging results of previous studies are summarized. And some comments and prospective remarks on IOR are included.

Chapter 3 describes the second experiment study. Utilizing the high temporal resolution of event-related potentials (ERPs), how visual spatial or temporal cues modulated the auditory stimulus processing is examined. The visual spatial cue (VSC) induces orienting of attention to spatial locations; the visual temporal cue (VTC) induces orienting of attention to temporal intervals. Participants were instructed to respond to auditory targets. Behavioral and ERP responses to auditory stimuli following VSC were compared with those following VTC.

Chapter 4 describes the third experiment study. Combining the endogenous cue-target paradigm in which the central cue could completely predicts the target location or the appearance time point of target with go/no-go task, this study investigate whether the spatial attention and temporal attention could have difference effect on visual stimulus processing.

Chapter 5 gives a general conclusion based on the findings of the two experiments. And the future challenges are also given.

Chapter 2 Mechanisms of Exogenous Inhibition of Return: Evidence for Inhibitory Tagging

Summary

Inhibition of return (IOR) refers to a slower response to a target appearing at the previously attended location (also called the cued location) than to a target appearing at an unattended location (uncued location). Inhibitory tagging (IT) involving the attentional executive network is suggested to function by blocking or disconnecting the link between a stimulus representation and the corresponding response mapping at the cued location. Data from behavioral and neuroscience studies are integrated to discuss the IT theory. Behaviorally, the IT effect can be measured by the comparisons of the priming or conflict effects at the cued location versus effects at the uncued location. It has been suggested that IT can reduce or even eliminate the priming effect in semantic priming tasks and the conflict effect in the Stroop (either color-word or spatial Stroop) and the Flanker interference tasks at previously attended locations. Neural correlates of IT are also summarized. Specifically, the posterior parietal lobe, the anterior cingulate cortex (ACC), and the prefrontal cortex (PFC) are suggested to be involved in IT. Reduced event-related potentials (ERPs) components at the cued location provided evidences for IT; these included the N450 component, which is related to conflict resolution processing, and the N400 component, which is related to semantic priming processing, Finally, some comments and prospective remarks on IT are given.

2.1 Background

2.1.1 Inhibition of Return (IOR)

At any moment, there is a large amount of information bombarding us. Attention helps us select relevant stimuli and filter out irrelevant ones, and selection can be guided by either a top-down or a bottom-up approach [11,12]. The classic spatial cueing paradigm, (also called cue-target paradigm), in which an uninformative exogenous cue appears at a peripheral location (left or right) (see **Figure 2.1**), is frequently used to investigate how attention affects stimulus processing, in which an. After a short or long stimulus onset asynchrony (SOA), the target is presented at the same location as the cue (cued location) or at a different location (uncued location).

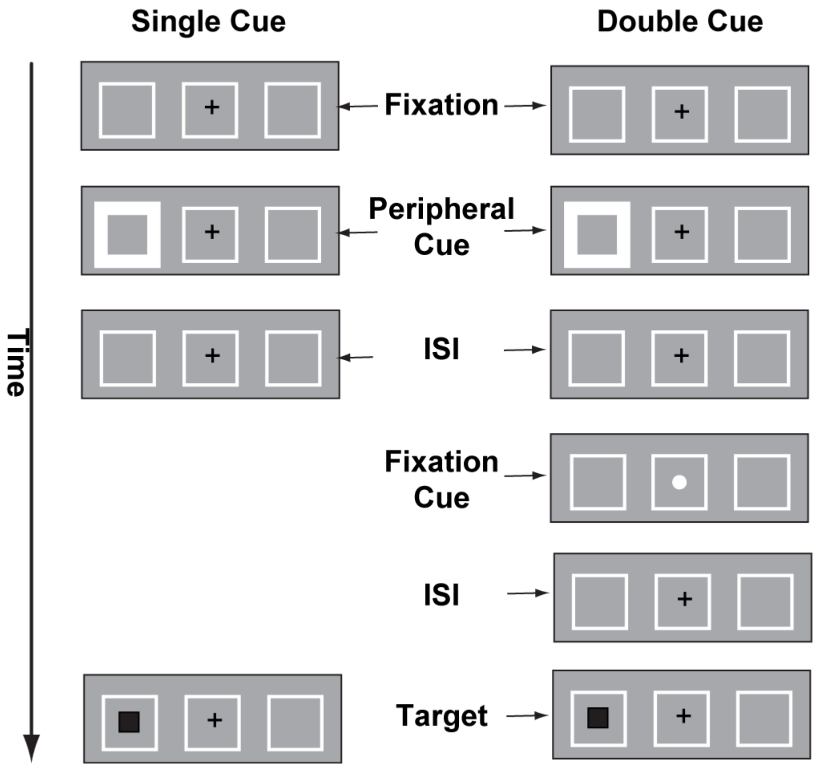


Figure 2.1 Illustration of the spatial cueing paradigm. The single-cue procedure is shown to the left of the dashed line, and the double-cue procedure is shown to the right of the dashed line. ISI is short for the interstimulus interval.

When the SOA was shorter than 200 ms, the reaction time (RT) of the target presented at the cued location was faster than that at the uncued location. Yet, when the SOA was longer than 250 ms, a slower response to the target presented at the cued location was found. This slowing of RT was termed the inhibition of return (IOR)[9,13]. Behaviorally, IOR is measured by the mean RT of the cued targets minus the mean RT of the uncued targets. The IOR effect can be found in both detection and the discrimination tasks [32]. Furthermore, it was demonstrated that the IOR effect can enhance visual search efficiency [10,33,34].

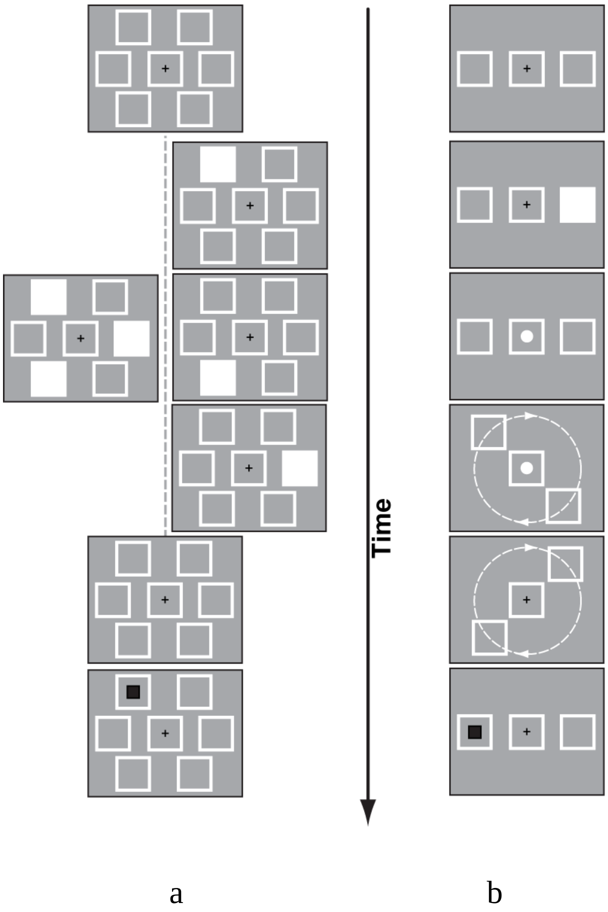


Figure 2.2 Illustration of different versions of the spatial cueing paradigm. (a) The synchronous cues are shown to the left of the dashed line; the successive cues are shown to the right of the dashed line. (b) Dynamic displays of the spatial cueing paradigm. In this condition, the target appears at the same location as the cue but within a different box.

In the classic spatial cueing paradigm, which is referred to as the single-cue procedure, only one peripheral cue was included. As IOR related research developed, additional versions of the cue-target paradigm were developed to accommodate specific experimental purposes (also see [35]). For example, (***a***) a central cue (also called a fixation cue) followed by a peripheral cue is used in the double-cue procedure (see Figure 1); this experimental design can enforce the attention coming back to the fixation location and thus enhance the IOR effect [36,37]. (***b***) In the multiple-cueing procedure (see Figure 2), multiple location cues are presented simultaneously or synchronously to ascertain that the inhibition effect can be associated with multiple locations [38-40]. (***c***) The dynamic display, in which moving boxes are involved to permit the dissociation of the attended object from its location when it was attended (see Figure 2), is assumed to have higher ecological validity. This procedure makes it possible to investigate whether the IOR effect is location-based or object-based [41-43]. In the classic cue-target design, the subjects are required not to respond to the first stimulus (cue) and to respond only to the second stimulus (target); this approach causes non-ocular response inhibition of the cue to contribute to the IOR effect. Thus, a target-target detection task, in which the subjects are instructed to respond to both the first stimulus and the second stimulus, is adopted to disassociate the response inhibition of the cue component from the IOR [44]. (See **Figure 2.2**)

2.1.2 Theories of IOR Mechanism

The early literature of IOR focused on identifying the actual factors that contribute to inhibitory phenomena. The focal issue at the beginning of IOR research was why IOR occurs and what has been inhibited in IOR. Generally, theories of the mechanism of IOR can be classified into two types, single component inhibition theories and double component inhibition theories. The theories of IOR concentrate on the debates which stages of the stimulus processing are affected. Stimulus processing contains two primary stages, an early stage associated with perceptual or attentional processing of the stimulus, and a late stage related to response preparation or decision-making.

The single component inhibition theories constantly debate whether the inhibition effect results from slowing of the early perceptual/attentional stages or the response-related stages of target stimulus processing. On one hand, the attentional/perceptual inhibition theory suggests that orienting of attention to sensory information in the previously attended (cued) location is inhibited [9,45]. Specifically, the peripheral cue first summons attention to the corresponding peripheral location (left or right); this attention heightens the responses to targets appearing at the attending location after shorter SOAs (e.g., shorter than 200 ms). However, with longer SOAs (e.g., longer than 350 ms), attention was shown to be capable of returning to the fixation location, although it was prevented from moving to the corresponding peripheral location again. In this case, targets presented at the cued location required more time for detection. Furthermore, studies of event-related potentials (ERPs) also found that the components related to attention and perception were attenuated or delayed at the cued location. More specifically, the mean amplitude of the early P1 and N1 ERP components elicited by the target stimulus was attenuated at the cued location [46,47], and the latency of the N2pc component, which is considered a marker of the deployment of spatial attention, was delayed when the target appeared at the cued location rather than at the uncued location [48].

In a challenge to the attentional/perceptual inhibition theory [49], the response inhibition theory holds that response-related processing is inhibited, consequently giving rise to the IOR effect. For example, eye movements (such as those directed by neurons in the superior colliculus, SC) to peripheral locations were automatically activated, while saccades to peripheral locations were forbidden. Thus, according the response inhibition theory, the inhibition of ocular responses can account for the IOR effect [50-52].

In contrast, double component inhibition theories indicate that both an attentional/perceptual component and a response-related component contribute to the IOR effect. A double dissociation of these two components was found by manipulating the task type. In the oculomotor response task, the subject was instructed to make the ocular movement as soon as the target appeared. In the manual response task, the subject was instructed to press a particular key corresponding to the location or type of the target. Hunt & Kingstone [53] found that the motor-based component contributed to the IOR effect in the oculomotor response task, while the attention-based component of IOR was present in the manual response task. Moreover, a speed-accuracy trade-off (SAT) procedure was used in which the subject’s sensitivity to the stimulus can be measured with the *d’* metric and the bias for responding in a particular direction can be determined with *c*, the decision criterion metric. The results supported the idea that effects on both response bias and perceptual processing contribute to the IOR effect [54]

2.2 INHIBITORY TAGGING

2.2.1 Background of Inhibitory Tagging

To examine the level at which IOR affects the detection of a target, researchers have adopted various methods, such as the semantic priming paradigm, the Flanker task, the Simon task, and the Stroop color-word task, together with the cue-target paradigm [55-58]. For example, when combining cue-target paradigms with other tasks, such as semantic priming tasks, semantic priming was affected at the cued location. In the semantic priming task, a prime word/picture was presented before the appearance of the target. The target could be taken from either the same or a different category as the prime item. The priming effect was measured by the mean RT of the related targets minus that of the unrelated targets; the former was normally faster than the latter. When the priming task was combined with the cue-target paradigm, the related or unrelated target was presented at a peripheral location (cued or uncued location). Thus, the priming effect in the valid condition (i.e., the target was presented at the same location as the cue), can be compared with the priming effect in the invalid condition (i.e., the target was presented at a different location than the cue). The results showed that the semantic priming effect was weakened in the valid condition. According to the single- or double- component IOR theories mentioned above, the target should be inhibited whatever it is related or unrelated to the prime item. However, it was experimentally found that the semantic effect in the valid condition was unequal to the semantic effect in the invalid condition, a finding that is inconsistent with the predictions of traditional IOR theories. Thus, a distinct mechanism, inhibitory tagging, was taken into consideration.

The observed decrease in the semantic priming effect is not easily explained by the previously proposed single- or double- component theories. According to those theories, if either the single or double components were inhibited, one would expect to find inhibition not only of the related target at the cued location but also of the unrelated target at the cued location. In that case, although both the related and unrelated targets were inhibited, the priming effect (related minus unrelated) at the cued location should be similar to that at the uncued location. However, the actual result, which is that the cue validity (cued/uncued) interacts with the prime-target relationship (related/unrelated), is inconsistent with this hypothesis. Therefore, a new mechanism must be proposed.

2.2.2 Inhibitory Tagging

The classic attentional networks proposed by Posner and his colleagues [59,60], are well known and widely accepted. First, the *alerting network*, which is associated with the brain stem and the right hemisphere, prepares for and sustains alertness with respect to the processing of high-priority signals during tasks. Second, the *orienting network*, which is associated with the parietal cortex, focuses on improving the efficiency of stimulus processing in the attended modality or location. The IOR effect is assumed to be controlled by this network. Finally, the *executive network*, which is associated with the middle frontal cortex and the anterior cingulated cortex (ACC), controls the responses to the target stimuli; for example, the resolving of conflicts in the Flanker interference task and the Stroop task. These three attentional networks work both independently and synergistically. For investigating the interaction between the orienting network and the executive network, for instance, the cue-target paradigm can be combined with the Stroop task.

The Stroop color-word task normally requires participants to report a word's printed color instead of its semantic meaning. In the Stroop task, three types of stimuli are used [61]. In a incongruent stimulus, the presented word (e.g., RED) literally means a color that differs from the print color; in a congruent stimulus, the word literally means the same color as the print color, and in a neutral stimulus, the meaning of the word stimulus is unrelated to its print color (e.g. XXX). The Stroop interference effect, or Stroop effect, refers to the slower response that is usually obtained to an incongruent stimulus than that to a congruent or neutral stimulus. However, Vivas, Fuentes and their colleagues [62,63] used the cue-target paradigm together with the Stroop color-word task and found that the Stroop interference effect was reduced or even eliminated when targets appeared at the cued locations compared to cases in which the targets were presented at the uncued locations. Furthermore, the IOR effect only occurred in the neutral condition. (See **Figure 2.3**)

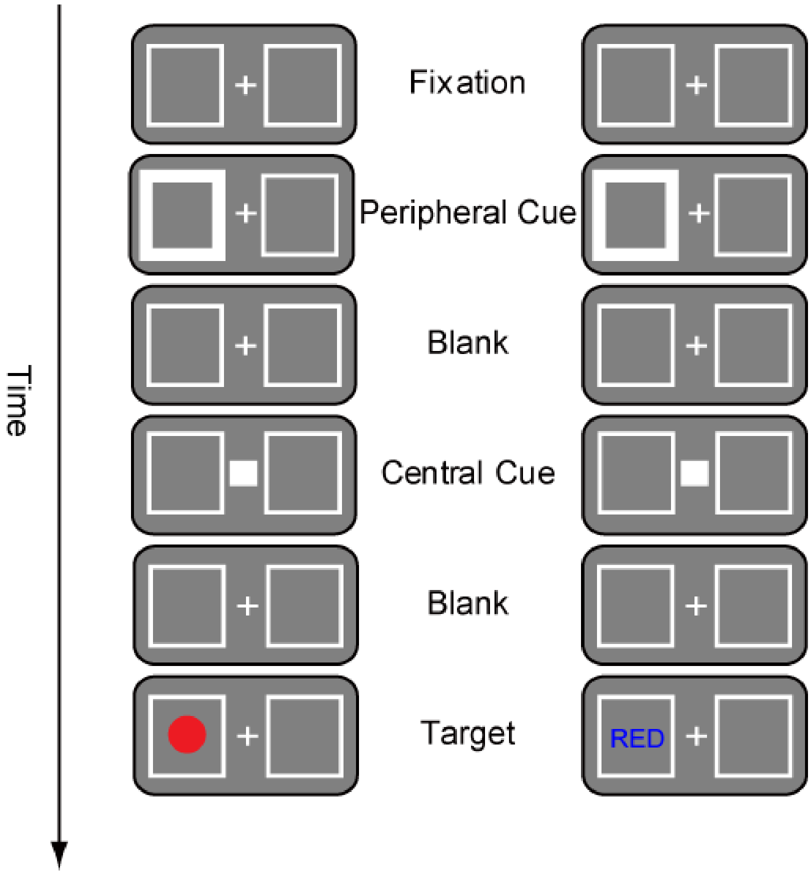


Figure 2.3 Illustration of the cue-target procedure. a: in the normal color ball detection task (left) or b: in the Stroop task (right). Here, an incongruent target (a blue "RED") was presented at the previously attended location (cued location).

To explain the above phenomenon, the inhibitory tagging (IT) mechanism was proposed [55,63]. IT, which is assumed to be associated with the executive network, functions by disconnecting or blocking the stimulus-response mapping/perception -response link at the cued locations [64]; this response is limited to the task-relevant features of the target [65]. In the task that combines spatial cueing procedure with the Stroop task, IT acts upon the Stroop color-word at the cued location by disconnecting the task-irrelevant word meaning from its potential response, consequently reducing its conflict with the activation of response code for the color of the incongruent word. IT was measured by the difference between the Stroop effect at cued locations and that at uncued locations (see **Table 2.1**) [62,63,66]. The mode of action of IT suggested that the executive network interacts with the orienting network to optimize the subject's reaction and permit completion of the related task [67,68] (see **Figure 2.4**).

Table 2.1: Measurement of Stroop effect, IOR, and IT.

		Stimulus Types		**Stroop Effect**	
		Incongruent	**Neutral/Congruent**		
Cue Validity	**Cued**	RT_1	RT_3	$RT_1 - RT_3$	
	Uncued	RT_2	RT_4	$RT_2 - RT_4$	
	IOR	$RT_1 - RT_2$	$RT_3 - RT_4$	**$(RT_1 - RT_3) - (RT_2 - RT_4)$**	**IT**

Note: RT indicates reaction time. **IOR** is short for inhibition of return; it is measured by the mean RT of target at the cued locations minus that at the uncued locations. The **Stroop effect** was measured by the mean RT of the incongruent targets minus that of the neutral or congruent targets. **IT** indicates inhibitory tagging; it is measured as the Stroop effect at the cued location minus that at the uncued location. **Cued** indicates a target presented at the same location as the cue. **Uncued** indicates a target presented at a different location from the cue. **Incongruent** means that the stimulus word's literal meaning was different from its print color, e.g., a blue "RED". **Congruent** means the stimulus word's literal meaning was consistent with the print color, e.g., a red "RED". **Neutral** means that the word meaning was unrelated to color, e.g., a blue "XXX".

Similarly, in the task that combined a cue-target paradigm with a priming task, the priming effect was weakened at the cue location [56,58], which can be accounted by IT. That is, the representation of the prime is activated, but the link to its response code is initially blocked or disconnected at the cued location; hence, the priming effect is attenuated.

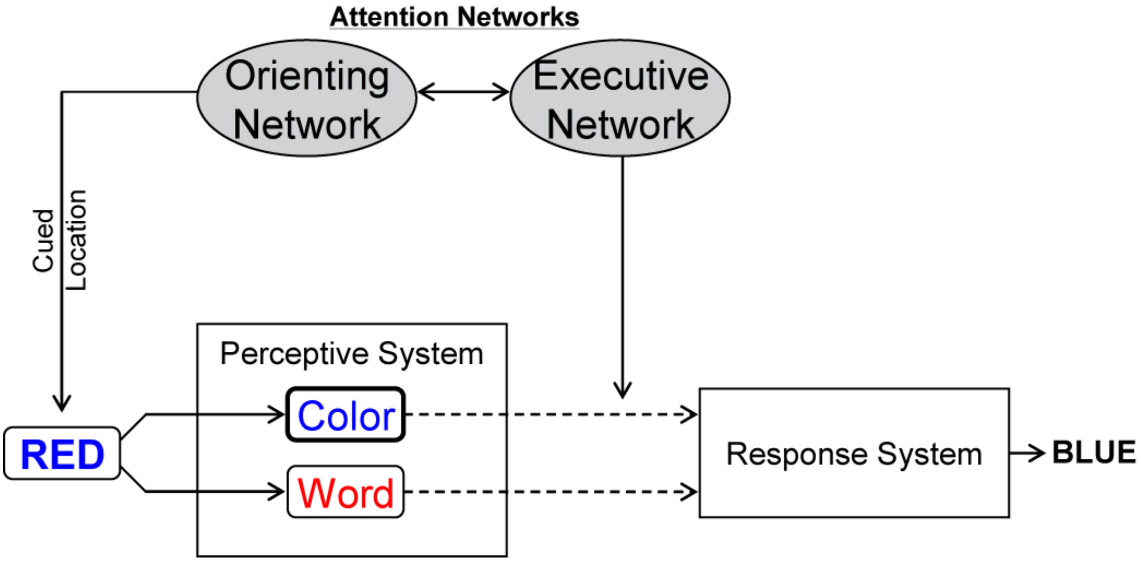


Figure 2.4 The inhibitory tagging (IT) theory of inhibition of return (IOR). The IT mode of the executive network acts on previously attended locations (cued locations) by blocking the link between stimulus and response, [64,67,68].

2.2.3 Inhibitory Tagging and Inhibition of Return

According to the above model, IOR and IT are inhibitory mechanisms that affect the processing of information appearing at previously attended locations. The former is assumed to be controlled by the orienting network, which is associated with the parietal cortex, while the latter is assumed to be controlled by the executive network, which is associated with the ACC. Studies involving elderly adults and patients also demonstrated the dissociation between IOR and IT. Specifically, it has been suggested that the time course of IOR changes as a function of age [69-72]; here, the time course of IOR refers to the SOA after which the processing of the target is slowed at the previously attended location. When older adults were test in the spatial cueing paradigm combined with the Stroop task, IOR was found, but no difference in the Stroop effect at the cued location and the uncued location was observed. But the control group of young adults showed normal IOR and IT effects; in this group, the Stroop effect was attenuated at the cued location [71].

The schizophrenia patients, who experience deficits in inhibitory processing controlled by attentional networks, revealed normal IOR effect, but no IT effect [62,73,74]. Furthermore, patients who had sustained damage to the posterior parietal lobe only showed IOR and IT on the contralesional side [75]. Although a dissociation between IT and IOR was demonstrated, IT requires intact IOR to act [67,68], that is, the inhibitory processing of the executive network (IT) might coexist with the inhibition in the orienting network (IOR).

It has been suggested that IT can only function with task-relevant features [65] that involve top-down goal controls. Thus, the IT effect supports the idea that the executive network is affected by the orienting network. In addition, Vivas & Fuentes [63] have found that coordination between the orienting and executive networks might lead the organism to explore new objects or locations. Fuentes & Campoy [76] found that by filtering out distracting flankers, visual cues could guide attention to a spatial location, consequently, leading to a decrease in the Flanker interference effect at the previously attended location. These results indicate that interaction of the orienting (IOR) and executive (IT) networks might depend on the primary goals imposed by tasks.

2.3 Evidences of Inhibitory Tagging

2.3.1 Behavioral Evidence for IT

Behaviorally, the IT effect has been found in tasks that combine spatial cueing procedure with other tasks, such as semantic priming and the Stroop task. Specifically, the priming effect (related minus unrelated) and the Stroop interference effect (incongruent minus congruent or neutral) were reduced or even eliminated at the previously attended location (cued location) (just as shown in **Table 2.1**). The IT effect has also been reproduced in other tasks. Like the Stroop task, the Flanker interference task is often used to test the ability to suppress responses that are inappropriate in a particular context. In this task, the target is flanked by non-target stimuli (distractors) that correspond either to the same response as the target (comparable/congruent flanker) or a response opposite to that of the target (incomparable/incongruent flanker) [77](see **Figure 2.5**).

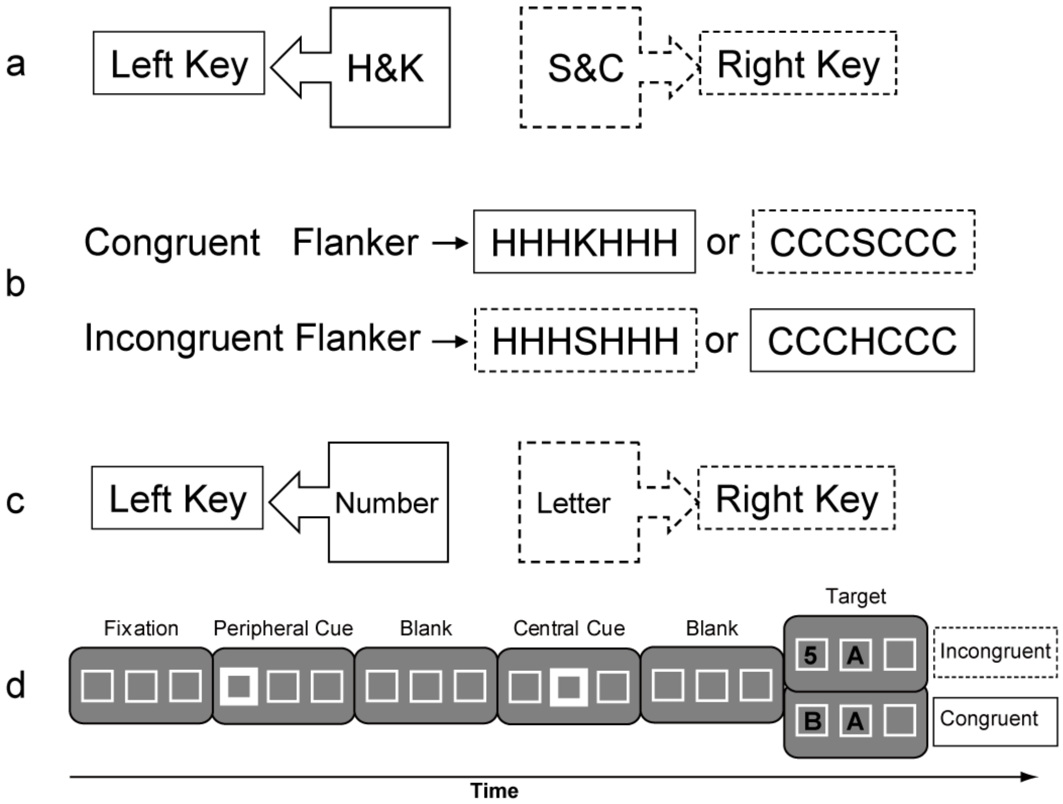


Figure 2.5 Illustration of the Flanker task. The target is the central letter. a: Letters H and K correspond to the left response key, while letters S and C correspond to the right response key. b: The congruent flanker and the incongruent flanker were composed. c: A Flanker task is combined with the cue-target paradigm. Here, ‘Letter’ corresponds to the right response key, while ‘Number’ corresponds to the left response key. d: A congruent or incongruent target was presented at the cued (or uncued) location.

The mean RT is found to be slower for the incongruent flanker than for the congruent flanker, a phenomenon that is termed the Flanker interference effect. The results of studies using the spatial cueing paradigm accompanied by the Flanker task suggest that the IT blocks connection between the perceptual representations of incongruent flankers and the motor representations of them at previously attended locations, resulting in reduction of the Flanker effect at those locations [55].

The IT effect is not restricted to the spatial cueing procedure in combination with object-related tasks such as semantic priming, the Stroop conflict task, and the Flanker interference task. It is also found in spatially based tasks accompanied by a spatial cueing procedure. In a spatial Stroop task, the stimuli are symbols of spatial locations, such as left or right arrows, i.e., "←" or "→". A left or right arrow is presented at a peripheral left or right location. In the congruent condition, the left arrow (←) is presented at the left side of the screen or a right arrow (→) is presented at the right side of the screen. When combined with a spatial cueing procedure (see **Figure 2.6**), the spatial Stroop effect (incongruent minus congruent) was found to be smaller at the cued location than at the uncued location [78-80].

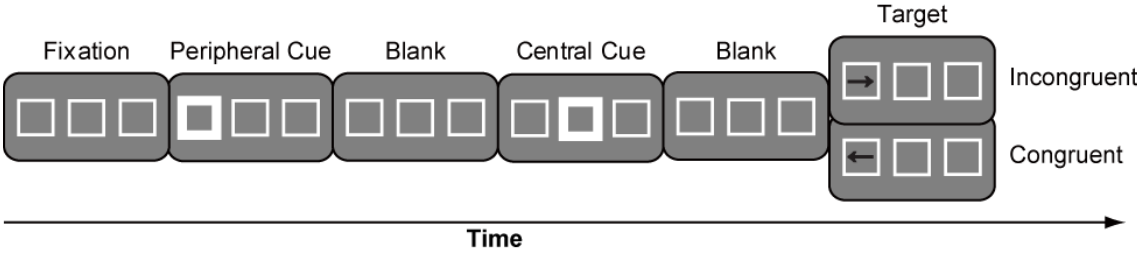


Figure 2.6 Illustration of the cue-target procedure together with a spatial Stroop task. Here, an incongruent target (→) or a congruent target (←) was presented at the previously attended location (cued location).

2.3.2 Neural Mechanisms of IT

Studies of pathological conditions were the first to reveal the neural systems related to the IT effect. Participants with damage to the posterior parietal lobe only showed IT and IOR effects to contralesional targets [75]. Thus, the posterior parietal lobe might directly or indirectly contribute to the mechanism of the IT effect at the cued location. This might be occur in one or more of the following ways: (***a***) The posterior parietal lobe directly affects IOR [81], which might be a carrier-like mechanism for IT. (***b***) Alternatively damage to the parietal lobe may lead patients to be insensitive to the relative salience of signals represented in a spatial map for directing attention [82], consequently indirectly affecting both orienting and executive networks (IOR & IT). In addition, studies of Alzheimer's disease (AD) [57,69,83], which is usually accompanied by degeneration in the temporal and parietal lobe and parts of the frontal cortex and the cingulate gyrus [84], failed to find any interaction between semantic priming and spatial cueing effects.

Related imaging studies have provided precise neurological evidence for IT and have led to new perspectives on what IT is. Functional magnetic resonance imaging (fMRI), which offers the advantage of high spatial resolution, has been used to locate the particular brain areas involved in IT and IOR. Chen et al.[85] used fMRI to investigate the neural correlates of the interaction between spatial attention and conflict processing. They combined the color-word Stroop task with the spatial cue-target paradigm and used two types of incongruent color-words, the incongruent response-eligible (IE) and incongruent response-ineligible (II). In this type of experiment, the participants are instructed to judge whether the color of a word is red or blue, which makes the meaning of the word task-irrelevant information. If the meaning of the word is ‘red’ or ‘blue’, it is an IE word and is associated with a potential response; or if the meaning of the word is ‘green’ and the print color of the word is ‘red’ or ‘blue’, it is an II word and its meaning is not in the response set. The IE word consisted of the incongruent pre-response representations and the incongruent response set output, while the II word only consisted of the incongruent pre-response representations. At the cued location, the left rostral ACC was involved in resolving the pre-response conflict [$\text{uncued}_{(\text{II-neutral})}$-$\text{cued}_{(\text{II-neutral})}$], and the left dorsal lateral prefrontal cortex (DLPFC) was associated with the response conflict [uncued$_{(IE\text{-}II)}$-cued$_{(IE\text{-}II)}$] [85].

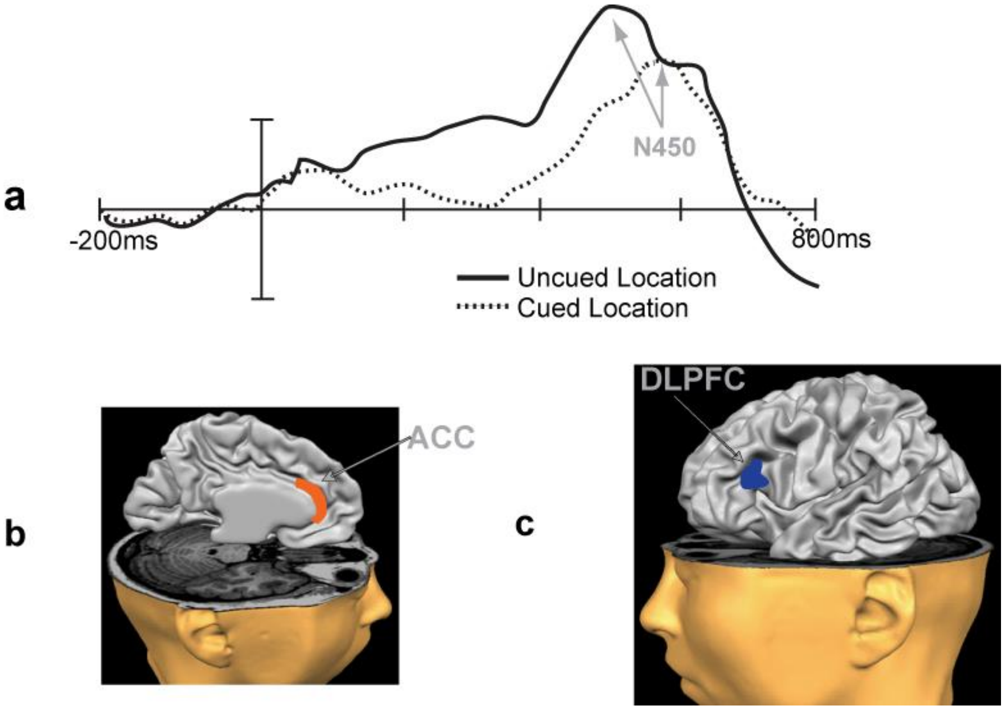


Figure 2.7 Illustration of IT-related neural correlates. a: ACC; b: DLPFC; and c:source waveforms of fitted dipoles of N450-related activation at cued and uncued locations [64,85].

Similar results have been found in event-related potentials (ERPs) studies. The so-called N450, a difference wave measured as ERPs of incongruent color-word minus ERPs of congruent/neutral color-word, has been suggested to be associated with conflict resolution [61,86]. Although the ERP technique is more rigorous due to its high temporal resolution, standardized low-resolution brain electromagnetic tomography analysis (sLORETA) can also be performed. The source analysis (a constrained dipole analysis) showed that the N450 originated from the ACC and the prefrontal cortex (PFC) [64]. Furthermore, not only was the amplitude of N450 at the cued location smaller than that at the uncued location, its latency was also delayed at the cued location (see **Figure 2.7**). These neural results are consistent with previous behavioral results that showed a reduction of the Stroop effect at the cued location. Moreover, the delayed latency of the N450 effect at the cued location demonstrated that inhibitory tagging acts temporally by disconnecting the links between activated representations of stimuli and their associated response codes at the previously attended location [64]. In addition, the so-called difference wave N400 has been suggested to be related to the semantic priming effect. Like N450, the amplitude of N400 showed a pattern related to the cue validity effect [58].

In addition to evidence supporting the existence of IT, there are also studies and opinions that do not support the IT theory. On one hand, IT was not reproduced in some studies [87,88]. On the other hand, although IT appears to function by blocking or disconnecting the link between representations of stimuli and the corresponding responses, the idea that inhibition of response to stimulus contributes to the IOR effect had been proposed prior to the IT theory. Thus, scholars who support more traditional theories of IOR have argued that the IT theory does not contribute a real innovation [10]. In addition, the IT discussed here is different from the inhibitory tagging described in visual search studies [33,89], which is associated with working memory.

2.4 Comments and Prospects on Inhibitory Tagging

The inhibitory tagging theory of inhibition of return is certain to be developed further. *Firstly*, IT provides explanations for many results that cannot be interpreted by other theories of IOR, such as the reducing of the Stroop effect, the priming effect, and the Flanker effect at previously attended locations. *Secondly*, the study of interactions between IOR and IT has revealed interactions between the orienting network and the executive network, suggesting that in addition to working independently, the various attentional networks can also cooperate with each other to achieve faster and more accurate stimuli processing. Moreover, the method that is used to investigate IT is an improvement or extension of the spatial cueing procedure that combines classic cue-target paradigm and other tasks.

In future studies, it is worth further investigating the prerequisites for the IT effect. The prerequisites for IT functioning, including its mechanism and its neural basis, have not been fully elucidated. For example, although it has been demonstrated that deaf persons possess enhanced peripheral attentional resources compared with the hearing, no IT effect was found in a group of deaf subjects [90], which might suggest the neural basis of IT related could damage in deaf persons. In addition, if IOR did not appear at short SOA, then whether IT worked or not [78,91]. On the other hand, the mechanisms by which the different attentional networks interact with each other also merit further study. It has been suggested that in carrying out the function of the attention system, the orienting and the executive networks work in coordination by biasing the organism to novelty [34]. The dissociations between attentional networks are also important in the diagnosis and rehabilitation of attention disorder diseases. In pharmacology, a double dissociation between the orienting network and the alerting network has been found: it is worth applying similar methodology to the double dissociation of other networks such as the orienting and the executive networks.

2.5 Concluding Remarks

The inhibitory tagging (IT) effect was demonstrated by blocking/disconnecting the link between the representation of a stimulus and the corresponding responses at the previously attended location. Specifically, IT was measured by comparison of conflict or priming effects at the cued location versus at the uncued location; the compared effects included the Stroop effect, the priming effect, and the Flanker effect. The interaction between inhibitory processing associated with the executive network (IT) and inhibitory processing associated with the orienting network (IOR) reveals the role of attention in biasing the organism for novelty. The IT effect was demonstrated not only by behavioral data but also by identification of its neural correlates. The posterior parietal lobe, the anterior cingulate cortex (ACC), and the prefrontal cortex (PFC) are involved in IT. In addition, the N450 component, a difference wave related to conflict resolution, and the N400 component, a difference wave related to the semantic priming effect, were less in evidence at previously attended locations. Current critical discussion of the IT theory should lead to its further development and refinement. Further studies could focus on how IT and IOR interact with each other and on more precisely identifying the brain areas that are related to IT.

Chapter 3 Modulation of Auditory Stimulus Processing by Visual Spatial or Temporal Cue: An Event-related Potentials Study

Summary

Utilizing the high temporal resolution of event-related potentials (ERPs), how visual spatial or temporal cues modulated the auditory stimulus processing is examined. The visual spatial cue (VSC) induces orienting of attention to spatial locations; the visual temporal cue (VTC) induces orienting of attention to temporal intervals. Participants were instructed to respond to auditory targets. Behavioral responses to auditory stimuli following VSC were faster and more accurate than those following VTC. VSC and VTC had the same effect on the auditory N1 (150-170ms after stimulus onset). The mean amplitude of the auditory P1 (90-110ms) in VSC condition was larger than that in VTC condition, and the mean amplitude of late positivity (300-420ms) in VTC condition was larger than that in VSC condition. These findings suggest that modulation of auditory stimulus processing by visually induced spatial or temporal orienting of attention were different, but partially overlapping.

3.1 Background

In the dynamic world, a mass of information bombards us. Spatial orienting of attention guides us to where a target might be presented [15]. Similarly, temporal orienting of attention directs us toward when the target could appear [92]. One procedure for studying these two types of orienting of attention is the cue-target paradigm in which a central visual spatial cue (VSC; left or right arrow) or visual temporal cue (VTC; inner or outer circle) predicts the location or time interval of an upcoming target stimulus. Studies using this paradigm have found that the target processing was speeded up at attended location or time interval [14,15,92].

A previous PET&fMRI study of electrophysiological effects of visual cues on target processing found that the neural correlates of visual target processing were similar in the fronto-parietal regions but differed in the parietal cortex. The neural correlates of modulation of visual target processing by spatial orienting of attention induced by VSC were associated with the right posterior parietal cortex, and those of temporal orienting of attention induced by VTC were associated with the left posterior parietal cortex [16]. Similarly, an ERP study found that VSC modulated early visual perceptual processing and VTC affected late stages of processing related to decisions and responses [17].

Sensory representations of attributes of visual stimuli are different from those of auditory stimuli [93]. For example, space is the basic organizing feature in the visual system, whereas sound frequency is the basic organizing feature of the auditory system. It can therefore be inferred that the neural correlates with modulations of visually induced spatial and temporal orienting of attention on auditory stimulus processing might differ from those on visual stimulus processing. Those possible differences in the effects of VSC and VTC on auditory stimulus processing were investigated.

A recent fMRI study indicated that neural correlates with modulations of auditory stimuli processing by VSC and VTC were partially overlapped in the dorsal lateral prefrontal cortex, but specific neural activations related to the two processes differed [12]. Specifically, neural activation of visually induced spatial orienting of attention was associated with the bilateral dorsal fronto-parietal network and the right ventrolateral prefrontal cortex, and neural activation of visually induced temporal orienting of attention was associated with the superior occipital gyrus. ERPs make it possible to observe real-time neuronal activity at a millisecond scale, and thus determine which stage(s) of processing are affected by a specific experimental manipulation [31]. However, it remains unclear how ERPs elicited by auditory stimuli are affected by visually induced spatial and temporal orienting of attention.

The aim of our study was to investigate how VSC and VTC modulate ERPs corresponding to auditory stimulus processing. VSC inducing spatial orienting of attention can predict left or right lateralization of auditory stimuli and VTC inducing temporal orienting of attention can predict short or long time interval prior to an auditory stimulus. Utilizing the high temporal resolution of ERPs, which stage(s) of auditory stimulus processing are affected by visually induced spatial or temporal orienting of attention similarly or differently can be observed.

3.2 Method

3.2.1 Participants

Twelve male undergraduate students (age range: 21-25; mean age: 22.9) were recruited as paid volunteers. All participants with normal or corrected-to-normal vision are right-handed. They had no neurological/psychiatric disorders and no hearing problems. The experimental protocol was approved by the Ethics Committee of

Okayama University.

3.2.2 Stimuli and Procedure

The experiment was conducted in a dimly lit, sound-attenuated room. Visual stimuli were presented centrally on a black background monitor 60cm from the subject. The fixation stimulus consisted of two concentric circles and one diamond (2°×2°). The VTC consisted of brightening of either the inner or outer circle’s border and gave no spatial information. If either the inner or outer border brightened, the interstimulus interval (ISI, the time interval between visual cue offset and auditory stimulus onset) was 600ms or 1800ms, respectively. The VSC consisted of brightening of either the left or right border of the diamond, with the brightened side corresponding to the lateralization of the upcoming auditory stimulus, and gave no ISI information. There were two types of auditory stimuli presented via earphones (Sennheiser, CX-300) monaurally to left/right. The standard stimulus, which comprised 77% of auditory stimuli, was a 1600Hz/65dB sinusoidal tone with linear rise/fall times of 5ms and required no response. The target stimulus was similar to the standard stimulus, but contained a transient dip of 20ms in intensity at the half way point in the stimulus presentation, which produced a subjective experience of the stimulus appearing to stutter. The target stimulus that comprised 23% of auditory stimuli was required response.

Each trial started with a fixation stimulus that appeared for 650ms. Subsequently, a VSC/VTC appeared for 100ms, which was followed by a 600/1800ms ISI. The auditory target/standard stimulus was then presented for 50ms. Finally, the fixation stimulus appeared for 800ms to allow participants to respond (see **Figure 3.1**).

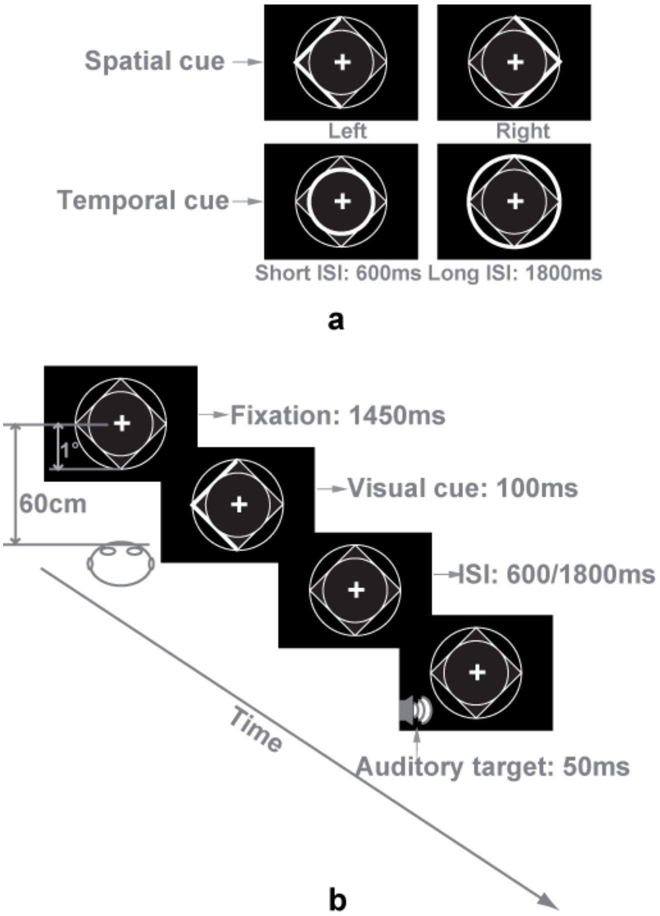


Figure 3.1 Illustration of experimental procedure. The visual spatial cues and visual temporal cue conditions are shown to the left or right of the dashed line.

3.2.3 Design and Task

The cue type (VSC/VTC) was blocked to evoke spatial or temporal orienting of attention independently, but the sequence was counterbalanced across participants. Participants maintained fixation on a center cross and took a 5-min break between blocks. There were 5 blocks per cue type. Each block consisted of 40 standard and 12 target trials, in which each ISI and lateralization occurred with equal probability. Participants were requested to predict the lateralization of target tone following VSC and to predict the moment of target onset following VTC. They press the left or right key of a mouse directly ahead of them with forefinger or middle finger of their right hand to predict left or right lateralized tone. The total experiment time was approximately 2 hours.

3.2.4 Data Recording and Analysis

Behavioral Measure

Presentation software (Neurobehavioral Systems, Inc.) was used to present stimuli and record responses. For each participant, the mean reaction time (RT) for each condition is calculated by taking the mean of all correct responses from 100 to 900ms. Hit rate (HR) was defined as the ratio of correct responses to the total of auditory target stimuli. Shapiro-Wilk test of normality showed that RT data were normally distributed (all $p>.3$), but HR data were not (all $p<.05$). Thus, the effect of cue type (VSC/VTC) on RT or HR was assessed via paired samples one-tailed t-test or Wilcoxon Signed-Ranks test respectively.

ERPs Measure

An EEG system (BrainAmp MR plus, Germany) was used to record EEG signals through 32 electrodes mounted on an electrode cap (Easy cap, Germany) as specified by the International 10-20 System. All signals were referenced to the combined signals from the bilateral earlobe. Horizontal eye movements were recorded from the outer canthus of left eye. Eye blinks and vertical eye movements were recorded from an electrode placed 1.5cm below the left eye. Impedance on all electrodes was below 5kΩ. The raw signals were digitized with a sample frequency of 500Hz with a 60Hz notch filter. The band pass of the amplifiers was DC to 250Hz.

The off-line analysis was carried out using Brain Vision Analyzer (version 1.05, Germany). To remove response movement, only ERPs elicited by standard auditory stimuli were analyzed. The continuous EEG signals were divided into epochs from -100 to 500ms. Baseline corrections were made against the data from -100 to 0ms. The artifact trials in which amplitude reached ±75μV from -100 to 500ms were rejected. And the data filtered with a band-pass filter retaining frequencies between 0.01 and 30Hz. The data from each electrode were then averaged and a grand average ERP was computed across all participants for each stimulus type. Because the cue type effect showed no significant differences between left and right lateralization or between short and long ISI (all $p>.05$), ERP data in each lateralization and ISI condition were combined to improve the signal-to-noise ratio of the ERPs [94].

The mean amplitude data were analyzed using ANOVA with the factors of cue type (VSC/VTC), time windows (50levels, 10ms/step during 0-500ms), and Electrodes (30levels). Based on analysis results and the mean latency of P1/N1/late positivity, three time windows (P1: 90-110ms; N1: 150-170ms; late positivity: 300-420ms) were selected. In those time windows, electrodes on which ERPs in VSC condition differed from those in VTC condition were selected (P1: FC5/6,T7/8,CP5/6; N1: Fz,Cz,F3/4, FC1/2,FC5/6; late positivity: Cz,Pz,C3/4,P3/4,CP1/2,CP5/6). And the mean amplitude of each selected electrode was calculated at the selected time windows. In each time window, the mean amplitude data were analyzed using repeated measures ANOVA with factors of cue type and electrode separately. The Greenhouse-Geisser epsilon or Bonferroni correction was used for non-sphericity or post hoc comparisons. Statistical level was set .05. Effect size of Cohen's d or partial eta-squared (η_p^2) was calculated for mean comparisons or ANOVA respectively.

3.3 Results

3.3.1 Behavioral Measure

Behavioral data from four of subjects were lost for technical reasons. Eight subjects' behavioral data were analyzed. The means and standard deviations of RT and HR for each cue type, ISI and lateralization are shown in **Table 3.1**. No significant effect of ISI and lateralization on RT and HR was found (all *p*>.05). Each lateralization/ISI was therefore combined into each cue type.

Table 3.1: Measures of average and variation of RT (ms) and HR for each Cue Type, ISI, and lateralization condition

		Visual Spatial Cue				VSC	Visual Temporal Cue				VTC
		Short_*L*	Short_*R*	Long_*L*	Long_*R*		Short_*L*	Short_*R*	Long_*L*	Long_*R*	
RT	***Mean***	456	450	450	440	**451**	471	476	473	467	**474**
	SD	(57)	(67)	(73)	(69)	**(65)**	(83)	(98)	(79)	(78)	**(87)**
HR	***Mean***	0.96	0.97	0.97	0.96	**0.99**	0.97	0.95	0.95	0.97	**0.97**
	SD	(0.06)	(0.04)	(0.08)	(0.04)	**(0.01)**	(0.05)	(0.05)	(0.08)	(0.08)	**(0.03)**
	Median	1	1	1	0.97	**0.99**	1	0.97	1	1	**0.97**
	IQR	(0.06)	(0.06)	(0.05)	(0.06)	**(0.03)**	(0.06)	(0.11)	(0.11)	(0)	**(0.06)**

For the normally distributed reaction time (RT) data, mean and standard deviation (SD) of RT in each Cue Type (visual spatial cue, VSC; visual temporal cue, VTC), ISI (short/long), and lateralization (left/right) are shown. For the non-normally distributed hit rate (HR) data, mean and SD in each condition are shown as well as medians and interquartile ranges (IQRs). Combined ISI and lateralization, measures of average and variation of RT and HR in VSC and VTC are also shown in the “VSC” and “VTC” columns.

RT in VSC condition was faster than that in VTC condition, [*t*(7)=-1.91,*p*<.05;*Cohen’s d* =0.35]. Additionally, HR in VSC condition was higher than that in VTC condition [*p*<.01; Wilcoxon Signed-Ranks test;*Cohen’s d* =1.76].

3.3.2 ERP Measure

As shown in **Figure 3.2**, ERPs of auditory standard stimuli in both cue type conditions were characterized by a P1 (peaking approximately 100ms post-stimulus) with a temporal scalp distribution, an N1 (peaking approximately 160ms) with a fronto-central distribution, and a late positivity (300-420ms) with a central-to-parietal scalp distribution. Although the latencies of measured P1/N1 components are long, the scalp distributions of P1/N1 are consistent with previous studies [95,96]. The latency of P1/N1 can be affected by such auditory stimulus parameters, as rise time, intensity, and frequency [97-99]. Further, the latency of P1/N1 observed here was similar to that of previous studies [100,101] that used stimulus parameters similar to ours.

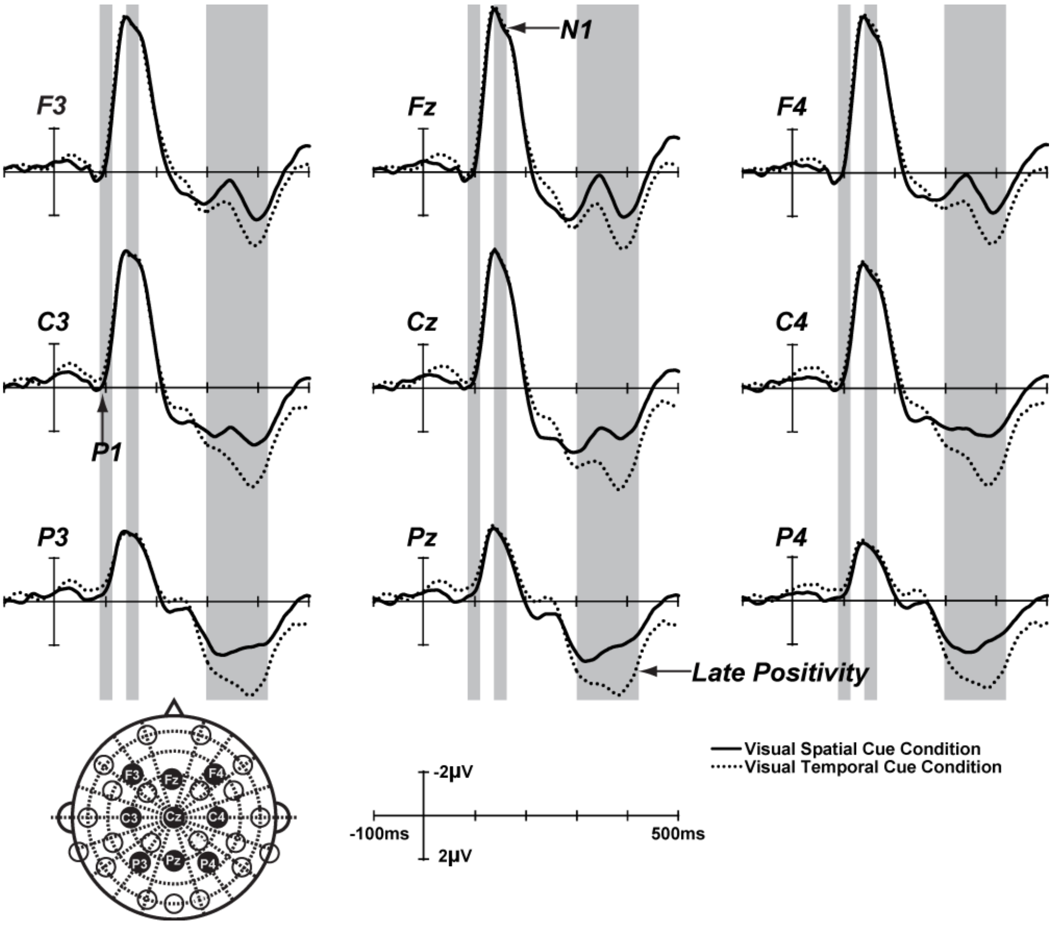


Figure 3.2 Grand average ERPs elicited by auditory stimuli in VSC (black solid line) and VTC (black dotted line) conditions. The time windows used for analyzing P1 (90-110ms), N1 (150-170ms) and late positivity (300-420ms) are shaded grey on the corresponding analyzed electrodes

Auditory P1 Component (90-110ms)

The main effect of electrode was significant in the ANOVA [F(2.43,26.74)=12.91,$p<.001$,$\eta_p^2=0.54$]. *Post hoc* comparisons showed that most activation occurred at T7/8 electrodes (all $p<.05$). Main effect of cue type approached statistical significance [F(1,11)=3.44,$p<.09$,$\eta_p^2=0.24$], and showed larger P1 amplitude in VSC than VTC condition. Cue type did not interact with electrode ($p>.05$). Additionally, the P1 amplitude was larger in VSC than in VTC in all analyzed electrodes ($T8_{S\text{-}T}=0.59\mu V$, $p<.05$; $T7_{S\text{-}T}=0.55\mu V$, $p<.08$; $FC5_{S\text{-}T}=0.55\mu V$, $p<.09$; $FC6_{S\text{-}T}=0.47\mu V$, $p<.1$; $CP5_{S\text{-}T}=0.51\mu V$, $p<.1$; $CP6_{S\text{-}T}=0.58\mu V$, $p<.09$). Furthermore, the maximum difference between VSC and VTC conditions was found in the T8 electrode ($p<.05$). Topographic differences in the P1 component were also observed for cue type (see **Figure 3.3a**).

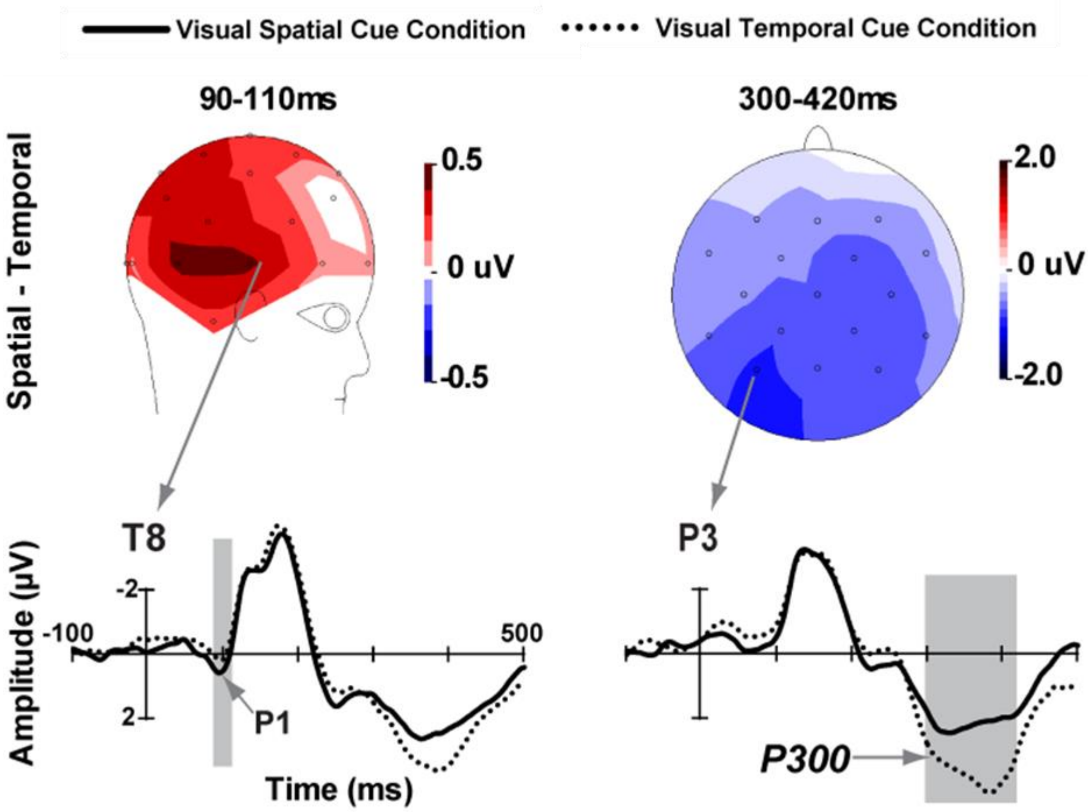
Auditory N1 Component (150-170ms)

ANOVA revealed that the main effect of electrode was significant [F(7,77)=4.24,$p<.05$,$\eta_p^2=0.28$]. Post hoc comparisons found the largest amplitudes at Fz, FC1/2 (all $p<.05$). There was no main effect of cue type and no interaction (all $p>.05$), and no topographic differences of cue type were observed.

Auditory Late Positivity Component (300-420ms)

The main effect of electrode was not significant ($p>.05$) but main effect of cue type was significant, [F(1,11)=14.56,$p<.01$,$\eta_p^2=0.61$], showing that the mean amplitude of late positivity in VTC condition was larger than in VSC condition. No interaction was found ($p>.05$). The cue type effect was found in all analyzed electrodes (all $p<.05$). As shown in **Figure 3.3b**, topographic differences between the VSC and VTC conditions were also observed at central-to-parietal scalp with the maximum difference (1.79μV) in

P3 electrode.



a b

Figure 3.3 The scalp topographies of VSC condition minus VTC condition are shown on the left. Grand average ERPs of maximum difference between VSC (black solid line) and VTC (black dotted line) conditions are shown on the right. a: The analysis time window for P1 (90-110ms) is shaded grey on T8 electrode. b: The analysis time window for late positivity (300-420ms) is shaded grey on P3 electrode.

Additionally, no effect of cue type was found in either vEOGs or hEOGs during summarized time windows (all *p*>.05), indicating that modulatory effects of cue type were not caused by small movements or blinking. Analysis of latencies of P1/N1/late positivity components found no significant cue type effect in any of the electrodes (all *p*>.05).

3.4 Discussion

3.4.1 Behavioral Data

The results showed that responses to auditory stimuli in VSC condition were faster and more accurate than those in VTC condition, which is consistent with the study of Li et al. [12]. This result is different from the previous study of Coull&Nobre [16] in which responses to visual targets in temporal orienting of attention were reported to be faster than in spatial orienting of attention. The task in this study is the same as Li et al., in which participants were asked to judge left or right lateralization of auditory targets. In contrast, Coull&Nobre's participants were instructed to detect the target wherever it appeared. The spatial relevance hypothesis (SRH) [102] suggests that the effect of spatial orienting of attention on auditory stimulus processing is stronger in a spatially related task than in a non-spatially task. The lateralization task might account for the faster response to auditory stimuli in VSC than in VTC condition. The behavioral results suggest that in a lateralization task, auditory stimulus processing with visually induced spatial orienting of attention is more efficient than that with temporal orienting of attention.

3.4.2 ERPs data

VSC and VTC showed similarities and differences in their modulation of ERPs elicited by auditory stimuli. The mean amplitude of P1 component (90-110ms) was larger in VSC condition than in VTC condition. The VSC and VTC had the same effect on N1 component (150-170ms). The mean amplitude of late positivity during 300-420ms was larger in VTC condition than in VSC condition.

Different modulation of auditory P1 by VSC or VTC

The greater auditory P1 component elicited by auditory stimuli in VSC condition than in VTC condition (Figure 3a) is observed. The temporal scalp distribution of P1 in both conditions corresponds to the position of the generators of the auditory P1 within Heschl’s gyrus (the transverse temporal gyrus) [95], and P1 has been suggested to be associated with early sensory processing of auditory stimuli [103]. The larger amplitude of P1 component is specifically associated with more efficient stimulus processing [104]. Previous studies [103,104] indicated that efficient stimulus processing is associated with superior processing in the early sensory stage reflected on the larger P1 component. Li et al. [12] found that the auditory stimulus processing following VSC was more efficient than that following VTC, which has been duplicated in our study. A larger P1 in visually induced spatial orienting of attention than in temporal orienting of attention is observed, which suggested the superiority of early auditory stimulus processing in visually induced spatial orienting of attention over that in temporal orienting of attention. But further studies are needed to confirm and elucidate relationships among more efficient stimulus processing, a larger P1, and superior early neurophysiological stimulus processing.

Same modulation of auditory N1 by VSC or VTC

The results found that N1 in VSC condition was the same as that in VTC condition. This and results of previous studies [96,105] suggest that spatial and temporal orienting of attention operate on similar processing in the time range of N1 [106]. This is direct evidence for overlapping modulation of auditory stimulus processing by visually induced spatial and temporal orienting of attention, at least on the auditory N1 component. A previous study [107] has shown functional dissociations of visual P1 (a facilitation of early sensory processing) and N1 (the orienting of attention to a task-relevant stimulus) components. The results showed that VSC and VTC modulations were reflected differently in auditory P1, but they were reflected similarly in auditory N1. This might indicate functional dissociation of auditory P1 and N1 components, which needs further studies.

Different modulation of late positivity component by VSC or VTC

The ERP results found that the mean amplitude of late positivity (300-420ms) was larger in VSC condition than it was in VTC condition. Late positivity in both conditions resembled a P3 component in its latency and scalp distribution [108,109], which can be interpreted as a reflection of the information content of the stimulus [110]. It has been suggested that the delivery of task-relevant information is accompanied with larger amplitude of P3 component [111]. The left or right lateralization information is task-relevant in the present lateralization task. In the visually spatial orienting of attention, the VSC provided sufficient lateralization information, making the same information delivered by the upcoming auditory stimulus unnecessary for completing the lateralization task. However, in the visually temporal orienting of attention, the VTC only provided time interval information, making the lateralization information delivered by the following auditory stimulus necessary for completing the lateralization task. The late positivity evoked by the auditory stimulus following VTC was therefore larger than that following VSC, indicating that the late stage of auditory stimulus processing was modulated differently by visually induced spatial or temporal orienting of attention.

3.5 Conclusion

The current study investigated modulation of auditory stimulus processing by VSC or VTC. Behavioral results indicate that auditory stimulus processing in VSC condition was more efficient than in VTC condition. The ERP results showed that VSC and VTC had the same effect on N1, and different effects on P1 and late positivity. These results and previous fMRI data [12] suggest the existence of a hybrid modulatory mechanism of auditory stimulus processing by visually induced spatial and temporal orienting of attention. The modulatory effects of the two processes are different, but partly overlapping.

Chapter 4 Modulation of Visual Stimulus Processing by Visual Spatial or Temporal Cue: An Event-related Potentials Study

Summary

Previous studies indicated that the spatial attention and temporal attention shared some common neural mechanisms, although they modulate the stimulus processing differently. Utilizing the high temporal resolution of event-related potentials (ERPs), combining the endogenous cue-target paradigm in which the central cue could completely predicts the target location or the appearance time point of target with go/no-go task, this study investigates whether the spatial attention and temporal attention could have difference effect on visual stimulus processing. The ERPs results showed that the spatial and temporal attention had the same effect on early ERPs component before 260ms post-stimulus. But the spatial and temporal attention had different effects on late ERPs data. Specifically, during the time window of 260-300ms, the spatial attention condition elicited larger negative amplitude than the temporal attention condition, while during the time window of 380-420ms, the temporal attention condition elicited larger positive amplitude than the spatial attention condition. The present ERPs results suggested that modulations of visual stimulus processing by spatial or temporal orienting of attention were different, but partially overlapping.

4.1 Background

Considering in a noisy crowd, you are finding a friend. If somebody tells you that your friend is sitting in a red table, it is much easier to find her/him. During this finding process, attention plays very important role in selectively concentrating on one aspect of the useful information in the environment while ignore others. There are two different mechanisms of attention: endogenous and exogenous. The first aspect is exogenous attention (bottom-up processing, stimulus-driven attention), which could be triggered reflexively by a salient sensory event making us have to attend it [112], e.g. your friend wearing a colorful coat that is easy to be found. The second aspect is endogenous attention (top-down processing, goal-driven attention). Endogenous attention involves a more purposeful orienting process which is under the control of the person who is attending [113], e.g. somebody telling you where your friend is. Some neurophysiologic studies suggested that the endogenous and exogenous attentional mechanisms were generally thought as two distinct attention systems even though they share largely the same neural architecture [23].

The cue-target paradigm is usually used to study endogenous attention, in which the central cue can provide the information for the following target stimuli [15]. On one hand, when the central cue is an arrow that direct left or right that can predict the location the target stimuli, the spatial orienting of attention (spatial attention) is elicited. With this paradigm, the consequence, which stimuli processing were speeded up at attended locations, was observed [15-17]. On the other hand, when the central is a big or small circle that can predict the time point of the following target stimuli, after a long or short time interval, the temporal orienting of attention (temporal attention) is triggered.

A study of us compared the modulation of auditory stimulus processing by spatial and temporal orienting of attention [114]. In this study, the behavioral responses to auditory stimuli following the visual spatial cue were faster and more accurate than those following the visual temporal cue. The event-related potentials (ERPs) data showed that the mean amplitude of the auditory P1 (90-110ms) in visual spatial attention condition was larger than that in visual temporal attention condition, and the mean amplitude of the late positivity (300-420ms) in the visual temporal attention condition was larger than that in the visual spatial attention condition. However, the spatial and temporal attention had the same effect on the auditory N1 (150-170ms) after stimulus onset. Using the same task, a study with functional magnetic resonance imaging (fMRI) has found that the neural correlates of auditory target processing were similar in the dorsal lateral prefrontal cortex, but specific neural activations related the two processes differed. Specifically, the bilateral dorsal fronto-parietal network and the right ventrolateral prefrontal cortex were involved in the spatial attention, while the superior occipital gyrus was correlated with the temporal attention [12].

In the visual cue-visual target condition, a previous positron emission tomography (PET) and fMRI study found that the fronto-parietal regions were shared by the spatial and temporal orienting of attention. The neural correlates of modulation of visual target processing by spatial attention was correlated with the right posterior parietal cortex, while the neural correlates of modulation of visual target processing by temporal attention was correlated with the left posterior parietal cortex [16].

The aim of the present study is to investigate whether different ERPs elicited by visual stimuli can be observed in the spatial or temporal attention. Using high temporal resolution of ERP technique, the general processing of visual stimuli can be observed, which are preceded by a central visual spatial cue predicting the location where the visual target appears or by a central visual temporal cue predicting the time point when the visual target appears. In the context of previous results mentioned above, The prediction can be proposed that the modulation of visual stimulus processing by spatial and temporal attention is different at some stage of processing and the same at some other stage of processing.

4.2 Method

4.2.1 Participants

Twelve undergraduate students (age range: 21-25 years; mean age: 22.9 years) were recruited in the experiment as paid volunteers. All participants, who were right-handed and had normal or corrected-to-normal vision, had no history of neurological or psychiatric disorders. They had not joined in similar experiments during the past year. The experimental protocol was approved by the Ethics Committee of Okayama University.

4.2.2 Stimuli and Procedure

The experiment was conducted in a dimly lit, sound-attenuated, electrically shielded room. Stimuli streams were randomly presented in black background. The subject seated 60cm before the center of the monitor (see Fig. 1). At the beginning of each trial, the normal stimuli, which was comprised of two peripheral left and right boxes (2°×2°; centers 7° from the center of the monitor) and fixation stimuli (2°×2°), was presented in the center of the monitor. The fixation stimuli consisted of two concentric circles and one diamond (2°×2°). The visual spatial cue consisted of brightening of either left or right border of the diamond (see **Figure 4.1**), which is corresponding the location of the following go/no-go stimulus, left or right. During this condition, that spatial cue predicts no time information for the following stimuli. The visual temporal cue consisted of brightening of either the inner or outer circle’s border (see **Figure 4.2**), which is corresponding the time interval of the following go/no-go stimulus, 600ms or 1800ms of interstimulus (ISI). During this condition, that temporal cue predicts no spatial information for the following stimuli. The go stimulus (×) frequency was 23%, to which subjects should press the left or right mouse key to locate it; the no-go stimulus (+) frequency was 77%, to which subjects need no response.

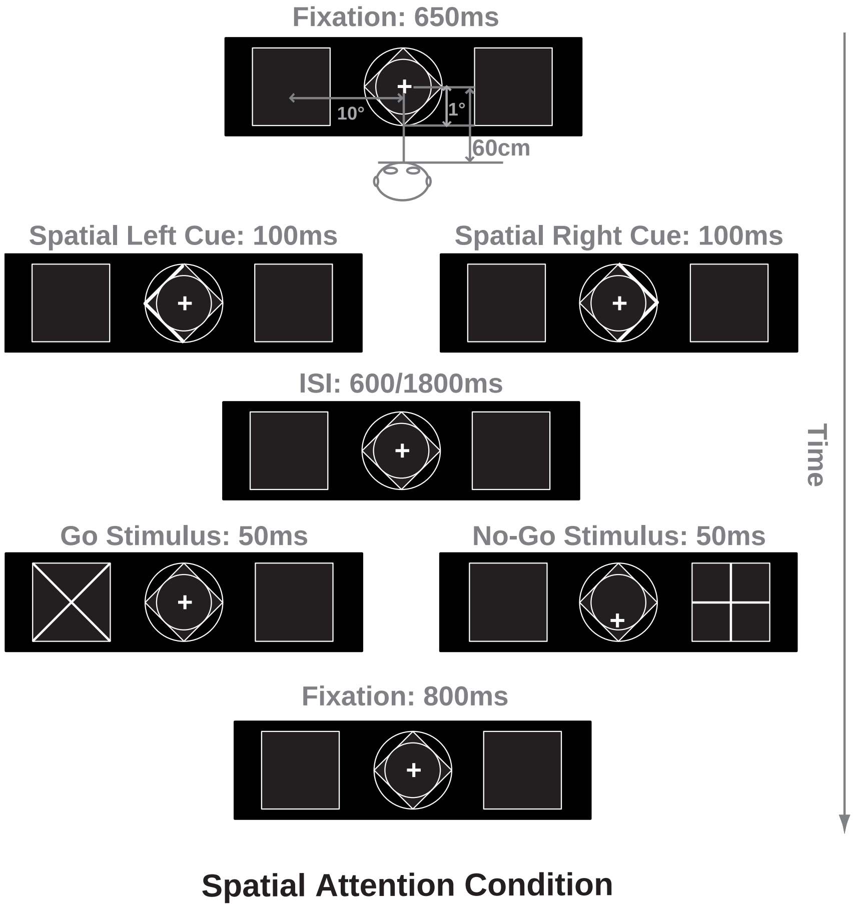


Figure 4.1 Illustration of the experiment stimuli and procedure of a trial in the spatial attention condition; the spatial cue will completely predict the go-stimuli or nogo-stimuli presented location. For the go target, subjects should response it. For the no-go target, subjects need no response.

At the beginning of each trial, the fixation was presented for 650ms to let the subject focus in the center of the display. The spatial or temporal cue appears for 100ms to provide the spatial or time information for the following go or no-go stimulus. Between the cue and the target stimulus, the normal stimuli will be presented for short or long interval of 600ms or 1800ms. After that, the go or no-go stimulus appeared for 50ms. At last, the normal stimuli will appear for 800ms to wait for the response of the subject. For each spatial cue trial, the ISI was set to either 600 ms or 1800 ms randomly; for the temporal cue trials, targets appeared in the left or right at random.

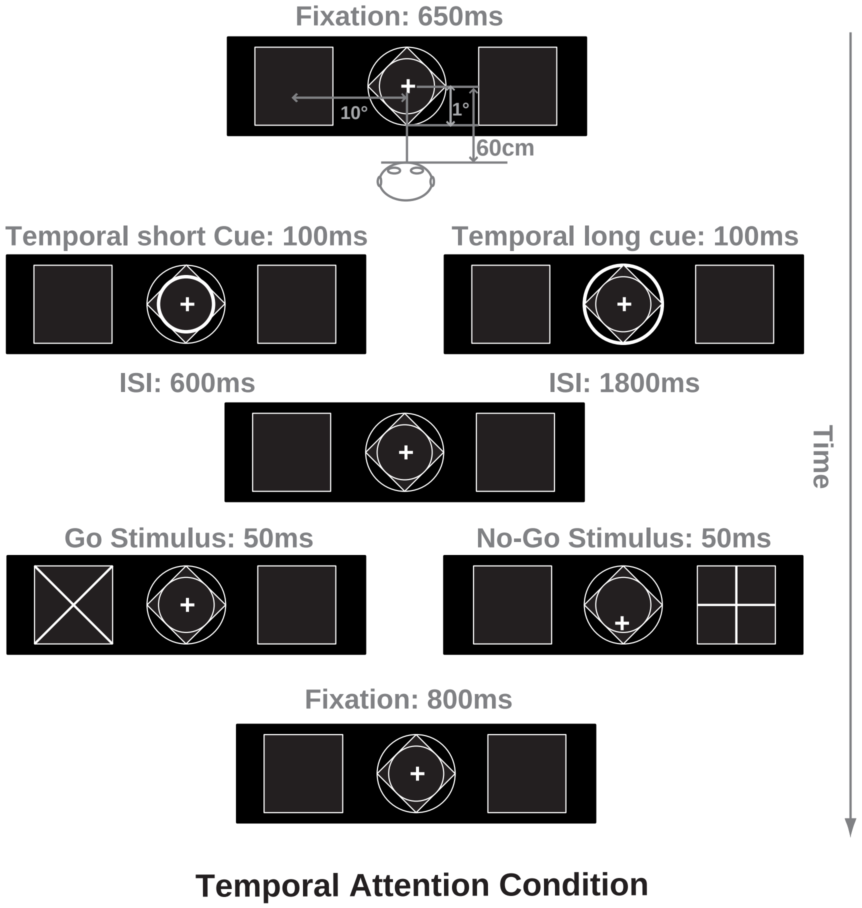


Figure 4.2 Illustration of the experiment stimuli and procedure of a trial in the temporal attention condition; the temporal cue will completely predict the go-stimuli or nogo-stimuli presented time interval. But the go or no-go stimuli appeared at left or right location randomly.

4.2.3 Apparatus and Software

An EEG system (BrainAmp MR plus, Gilching, Germany) was used to record EEG signals through 32 electrodes mounted on an electrode cap (Easy cap, Herrsching Breitbrunn, Germany) as specified by the International 10-20 System. All signals were referenced to the bilateral earlobe electrodes. Horizontal eye movements were recorded from the outer canthus of the right eye; eye blinks and vertical eye movements were recorded from vEOG electrode. The impedance of all the electrodes was kept below 5 kΩ. Raw signals were digitized with a sample frequency of 500Hz and stored continuously on a compatible computer for off-line analysis. The event-related potentials (ERPs) analysis was carried out using Brain Vision Analyzer software (version 1.05, Brain Products GmbH, Munich, Bavaria, Germany).

4.2.4 Design

The cue type (spatial or temporal cue) was blocked to evoke spatial or temporal orienting of attention independently, but the sequence was balanced by participants. Participants focused on the center cross and took a 5 minutes break between blocks. There were 5 blocks per cue type. Each block consisted of 40 no-go stimuli trials and 12 go stimuli trials, in which each ISI and lateralization occurred with equal probability. Participants were asked to maintain fixation on a cross at the center of the monitor in the experiment. At the beginning of the normal experiment, there was a practice block for participants to make them understand the experimental task. The total experiment time was approximately 2 hours.

4.2.5 Data Recording and Analysis

Only the ERPs elicited by the nogo-stimuli were analyzed to get rid of the response. Continuous EEG signals were divided into epochs from 100ms before the stimuli onset to 500ms after stimuli onset. Baseline corrections were made against -100ms-0ms, and an artifact criterion of ±75 uV is used to reject artifact trials. The data were then averaged for each stimuli type following digital filtering using a band-pass filter of 0.01-30Hz. The grand-averaged data were obtained across all participants for each stimuli type. Because the cue type effect showed no significant differences between left and right lateralization or between short and long ISI (all p<.05), ERP data in each lateralization and ISI condition were combined to improve the signal-to-noise ratio of the ERPs [94].

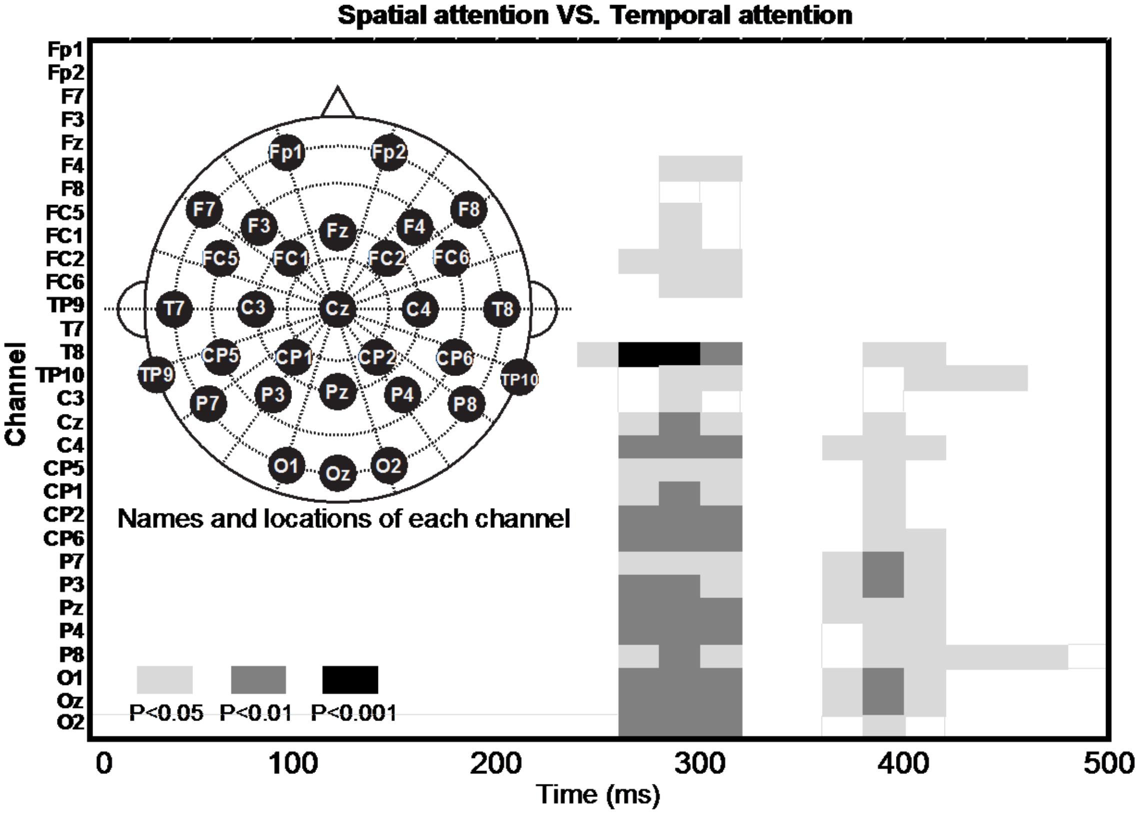


Figure 4.3 Statistical significance for AV stimuli in the short ISI condition comparing with those in the long ISI condition over all electrodes (30 channels) between 0 and 800ms post-stimulus. Electrode location with corresponding channel names.

From visual stimuli onset to 500ms, the spatial attention condition is compared with the temporal attention condition in each electrode (32 channels) by 20ms step, in which paired samples T test was adopted. The results have been illustrated in **Figure 4.3**. Based on inspection of the grand averages, we selected two late time windows

(260-300ms; 380-420ms), in which the mean amplitude of each time window is compared using repeated measures analysis of variance (ANOVA) with factors of the cue type (spatial vs. temporal), and Electrode (260-300ms: CP1, CP2, Pz, P3, P4, Oz, O1, O2; 380-420ms: Pz, P3, P4, Oz, O1, O2) separately. The Greenhouse-Geisser epsilon correction was used for non-sphericity when appropriate. Statistical level was set to .05. In addition, the Bonferroni correction to Post hoc comparisons is applied. The vEOGs and hEOGs electrodes for each condition in the two time windows with paired samples t-tests were also tested to remove differences between visual spatial and temporal cue conditions caused by micro-eye movements and slight blinks.

4.3 Results

ERPs to visual nogo-stimuli were characterized by a N2-like component, which was followed by a P3-like component (see **Figure 4.4**).

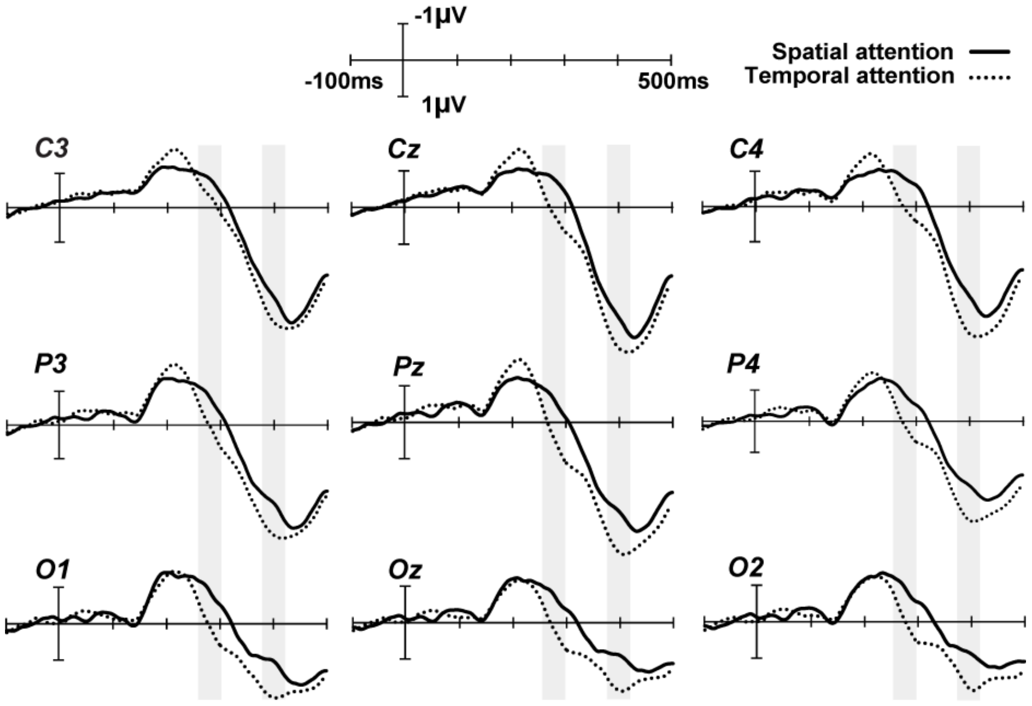


Figure 4.4 Grand average ERPs elicited by visual stimuli in spatial attention condition (black solid line) and temporal attention condition (black dotted line) conditions. The two analyzed

time windows were marked.

4.3.1 ERP Data post-stimulus from 260 ms – 300 ms

The mean amplitude of 260ms-300ms was submitted into ANOVA. The main effect of the cue type was significant, F (1, 11) = 16.514, p= 0.002. The results showed that the no-go stimuli cue elicited more negative amplitude following spatial cue than temporal cue (spatial condition: -1.361uV; temporal condition: 0.694uV). The main effect of the Electrode was not significant, F (7, 77) = 0.474, p= 0.851. The interaction between the Electrode and the cue type was not significant too, F (7, 77) = 0.721, p= 0.654, which suggest that the effect of cue type was shown at all selected electrodes. Further, topographic differences between the spatial cue condition and the temporal cue condition were observed over the central-parietal, parietal, and occipital sites, which is illustrated in **Figure 4.5** during the time window of 260-300ms. Paired-sample t-tests were not significantly different on the vEOG or the HEO during epoch of 260-300ms (p>0.05).

4.3.2 ERP Data post-stimulus from 380 ms – 420 ms

The mean amplitude during the time window of 380-420ms was submitted into ANOVA. The main effect of cue type was significant, F (1, 11) = 8.346, p= 0.015. The results showed that the no-go stimuli cue elicited more positive amplitude following temporal cue than spatial cue (spatial condition: -3.374uV; temporal condition: 5.127uV). The main effect of the Electrode was significant, F (5, 55) =29.853, p<0.001, which showed that the amplitude of parietal sites was larger than that of occipital areas. The interaction between the Electrode and the cue type was not significant too, F (5, 55) = 0.524, p= 0.757, which suggest that the effect of cue type was shown at all selected electrodes. Further, topographic differences between the spatial cue condition and the temporal cue condition were observed over the parietal and occipital sites, which are illustrated in **Figure 4.5** during the time window of 380-420ms. Paired-sample t-tests were not significantly different on the vEOG or the HEO during epoch of 380-420ms (p>0.05).

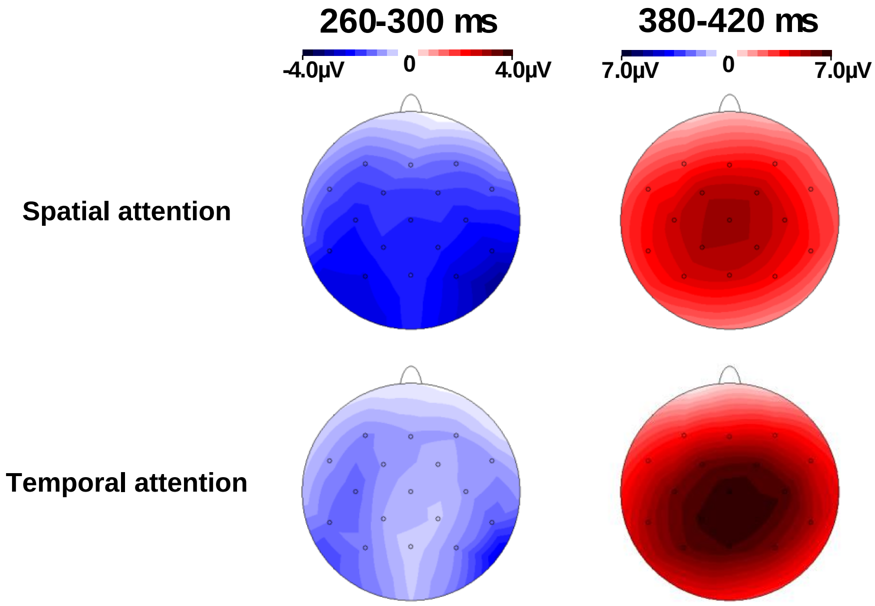


Figure 4.5 Two-dimensional (2D) parameter images of the spatial attention condition that is shown in the left and the temporal attention condition that is shown in the right during the two time windows: 260-300ms & 380-420ms after the onset of the visual no-go stimuli. During the time window of 260-300ms, the spatial attention condition elicited larger negative amplitude than the temporal attention condition, while during the time window of 380-420ms, the temporal attention condition elicited larger positive amplitude than the spatial attention condition.

4.4 Discussion

The present study aimed at investigating whether modulations of visual stimuli processing by spatial or temporal cue were different. The ERPs results showed that the spatial and temporal attention had the same effect on early ERPs component before 260ms post-stimulus (see **Figure 4.3**). But the spatial and temporal attention had different effects on late ERPs data. Specifically, during the time window of 260-300ms, the spatial attention condition elicited larger negative amplitude than the temporal attention condition, while during the time window of 380-420ms, the temporal attention condition elicited more positive amplitude than the spatial attention condition.

4.4.1 For the early components before 260 ms post-stimulus

The results found that the spatial attention and temporal attention had the same effect on visual stimulus processing during the early processing, before 260ms post-stimulus. This is consistent with previous studies [96,105,106,114], which has found that spatial and temporal orienting of attention operate on similar processing in the time range of N1 (150-170ms). This and results of previous results suggest that the spatial attention and temporal share common mechanisms.

4.4.2 For the early components from 260ms to 300ms post-stimulus

The ERP results showed that the spatial attention condition elicited more negative amplitude than the temporal attention condition during the time window of 260-300ms at central, parietal, occipital sites, which is a ERPs component of N2-like. Some previous study [115] have found that modulation by temporal attention or spatial attention was different. Previous studies found that the N2 enhancement has been interpreted as reflecting response inhibition, in which task require subjects to respond to go stimulus and inhibit responses to the no-go stimulus with enhanced N2 potentials being found to no-go stimuli [116,117]. Here, the N2 component elicited by no-go visual stimuli in spatial attention was larger than that in temporal attention is found, which can be attributed to the task that used here. Both in spatial and temporal attention condition, the current study asked participants to discriminate the location of go-stimulus: left or right. However, in spatial attention condition, the spatial cue can predict the location following go or no-go target stimulus completely (100%), while in temporal attention condition, the temporal cue cannot predict the spatial information for the following go or no-go stimuli. Thus, it is more difficult to inhibit the response to no-go stimuli during the spatial attention condition, that is, the no-go stimuli following the spatial cue elicit larger negative amplitude than those following the temporal cue during 260-300ms.

4.4.3 For the late components from 380ms to 420ms post-stimulus

The results found that the no-go stimuli in the temporal attention condition elicited larger negative amplitude than those in the spatial attention condition during the time window of 380-420ms at parietal and occipital sites, which is a ERPs component of P3-like. The P3 component is thought to reflect the information content of the stimulus [110,114]. In the present study, the location task was used, which makes the spatial information more important. During the spatial attention condition, the spatial cue has provided the spatial information for the go and no-go stimulus, which makes the spatial information carried by go/no-go stimuli not important for completing the location task. However, during the temporal attention, the temporal cue can only provide the temporal information for the go and no-go stimulus, which makes the spatial information carried by go/no-go stimuli more important for completing the location task. Further, it has been found that the delivery of task-relevant information is accompanied with larger amplitude of P3 component [111]. Thus, the no-go stimuli following the temporal cue elicit larger positive amplitude than those following the spatial cue.

4.5 Conclusion

In this study, the modulations on visual stimulus of spatial attention are compared with that of temporal attention. During the spatial attention condition, the spatial cue can predict the location of the following visual target stimuli (Go&No-go); while during the temporal attention condition, the temporal cue can predict the time point of the following visual target stimuli (go&no-go). The ERPs results showed that the spatial and temporal attention had the same effect on early ERPs component before 260ms post-stimulus. But the spatial and temporal attention had different effects on late ERPs data. Specifically, during the time window of 260-300ms, the spatial attention condition elicited larger negative amplitude than the temporal attention condition, while during the time window of 380-420ms, the temporal attention condition elicited larger positive amplitude than the spatial attention condition. The present ERPs results suggested that modulations of visual stimulus processing by spatial or temporal orienting of attention were different, but partially overlapping.

Chapter 5 General Conclusion and Future Projections

Summary

This thesis has investigated mechanisms exogenous inhibition of return, visual and auditory attention in spatial or temporal cueing paradigm. In this chapter, our findings are summarized below. Further, some future projections are included.

5.1 General Conclusions

The current thesis includes one review study and two experiment studies. The first review study aimed at summarizing previous literature to investigate the mechanisms of exogenous inhibition of return. The second and third experiment studies investigate how visual spatial or temporal cue modulate the auditory or visual stimulus by event-related potentials technique.

Chapter 2 introduces previous theories on mechanism of inhibition of return. This chapter focused on the theory of inhibitory tagging. IT provides explanations for many results that cannot be interpreted by other theories of IOR, such as the reducing of the Stroop effect, the priming effect, and the Flanker effect at previously attended locations. The study of interactions between IOR and IT has revealed interactions between the orienting network and the executive network, suggesting that in addition to working independently, the various attentional networks can also cooperate with each other to achieve faster and more accurate stimuli processing. Moreover, the method that is used to investigate IT is an improvement or extension of the spatial cueing procedure that combines classic cue-target paradigm and other tasks.

Chapter 3 describes the experiment study on auditory attention during spatial or temporal cueing paradigm by behavioral and event-related potentials measures. Utilizing the high temporal resolution of event-related potentials (ERPs), how visual spatial or temporal cues modulated the auditory stimulus processing is examined. The visual spatial cue (VSC) induces orienting of attention to spatial locations; the visual temporal cue (VTC) induces orienting of attention to temporal intervals. Participants were instructed to respond to auditory targets. Behavioral responses to auditory stimuli following VSC were faster and more accurate than those following VTC. VSC and VTC had the same effect on the auditory N1 (150-170ms after stimulus onset). The mean amplitude of the auditory P1 (90-110ms) in VSC condition was larger than that in VTC condition, and the mean amplitude of late positivity (300-420ms) in VTC condition was larger than that in VSC condition. These findings suggest that modulation of auditory stimulus processing by visually induced spatial or temporal orienting of attention were different, but partially overlapping.

Chapter 4 describes an experiment study on modulation of visual stimulus processing by spatial or temporal cue. Previous studies indicated that the spatial attention and temporal attention shared some common neural mechanisms, although they modulate the stimulus processing differently. Utilizing the high temporal resolution of event-related potentials (ERPs), the endogenous cue-target paradigm in which the central cue could completely predicts the target location or the appearance time point of target is combined with go/no-go task to investigate whether the spatial attention and temporal attention could have difference effect on visual stimulus processing. The ERPs results showed that the spatial and temporal attention had the same effect on early ERPs component before 260ms post-stimulus. But the spatial and temporal attention had different effects on late ERPs data. Specifically, during the time window of 260-300ms, the spatial attention condition elicited larger negative amplitude than the temporal attention condition, while during the time window of 380-420ms, the temporal attention condition elicited larger positive amplitude than the spatial attention condition. The present ERPs results suggested that modulations of visual stimulus processing by spatial or temporal orienting of attention were different, but partially overlapping.

5.2 Future Projections

The current thesis utilize the high temporal solution of event-related potentials to investigate whether the visual temporal or spatial cue modulates the unimodal auditory or visual processing in different ways. The results suggest that spatial or temporal attention modulates the unimodal visual and auditory processing differently, but partially overlapping. However, in daily life, humans are surrounded by information from multiple modalities, such as, visual, auditory, somatosensory, and so on. Information from visual and auditory is the most important for understanding the real world. Vision and sound signals can be integrated in the human brain and provide a coherent cognition of the real world, which is called ***audiovisual integration***. Therefore, future studies will focus on investigate whether spatial or temporal orienting of attention modulates audiovisual integration with ERP technique.

Another challenge is that the relationship between audiovisual integration and attention. By utilizing attention, it is possible to select stimuli from a multitude of sensory information to help the brain integrate useful and temporally coincident stimuli from various sensory modalities into coherent cognition. Conversely, because of its increased salience, an integrated multisensory stimulus can capture attention more efficiently in complex contexts. Recently, research associated with the interplay between multisensory integration and attention has blossomed in a spectacular fashion. To date, however, it is unclear under what circumstances and through what mechanisms multisensory integration and attention interact. Therefore, frameworks of the interactions between attention and audiovisual integration should have been proposed in the future.

Appendix

I. Simple Introduction of EEG Apparatus

The BrainAmp MR *plus* was manufactured by BrainProduct Inc., Germany. This amplifier is a compact solution for neurophysiology research that can be combined with other units within the same product family to cover a vast range of possible application areas. This fully portable solution can be used for standard EEG/ERP recordings and can also be placed inside of the MRI bore for simultaneous EEG/fMRI acquisitions.

Thanks to its 5 kHz sampling rate per channel, the BrainAmp can be used to record EEG, EOG, and EMG signals as well as evoked potentials with a frequency up to 1 kHz. The 16-bit TTL trigger input allows the detection of a large number of markers from visual, acoustic, electrical, magnetic or other stimulation modalities. The BrainAmps can be used both with passive and active electrodes offering a great degree of flexibility.

The 32 channel units can be stacked to expand the number of channels up to 256 and combined with the BrainAmp ExG to record EEG, EOG, EMG, ECG, GSR (Galvanic Skin Response) and many other types of bipolar and auxiliary signals.

BRAINVISION
professional BRAINAMP MR PLUS

Figure A1 EEG amplifier of BrainAmp MR *plus*

Table A1 Technical specifications of BrainAmp MR *plus*

Number of Channels per unit	32
Max. Number of channels	128
Reference Type	unipolar
MR-compatibility	Yes (for scanners up to 4 Tesla)
Bandwidth [Hz]	DC - 1000
High Pass Filter [Hz]	0.016 / 10 s AC or DC switchable
Low Pass Filter [Hz]	1000 / 250 switchable
Input Noise [µVpp]	≤ 1
Input Impedance [MΩ]	10 / 10000
Input Measurement Ground / Reference	Yes
A/D-C [bit]	16
A/D-Rate [Hz]	5000
Max. Sampling Frequency [Hz]	5000
Offset Compatibility [mV]	± 300
Operating Range [mV]	selectable: ±3.2768; ±16.384; ±327.68
Resolution [µV]	selectable: 0.1; 0.5; 10.0
CMRR [dB]	≥ 110
TTL Trigger Input [bit]	16
Synchronized Digital Trigger Input [bit]	up to 16
Max. Power Consumption [mA]	160
Power Supply	rechargeable Battery
Signal Transmission	optical
PC Interface	PCI, USB 2.0
Deblocking Function	Yes
Blocking of Unused Channels	Yes
Safety	Twin Fiber optical Transmission Protection Class II, Type BF IEC EN 60601 EMC tested, electrically safe
Classification to MDD 93/42/EEC	Class IIa
Dimensions H x W x D [mm]	68 x 160 x 187
Weight [kg]	1.1

The current thesis adapted 32 electrodes of this apparatus. The location and name of each channel is displayed in **Figure A2**.

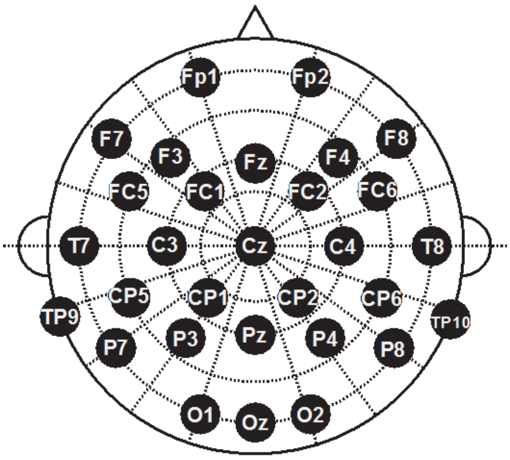


Figure A2 The locations and names of each electrode

II. Glossary

Orienting: The attentional orienting network is focused on the ability to prioritize sensory inputs by selecting a modality, location, feature, or object [59,60]. Orienting can occur overtly, that is, the act of directing sense organs towards a stimulus source (e.g., to detect where a noise originated by moving the ears to some possible location), or covertly, when attention shifts in the absence of the movement of a sensory organs (e.g., gazing at the fixation point while using peripheral vision to attend peripheral stimuli).

Stimulus-driven: A cognitive process in which people select some portions of sensory input for further processing that occurs when the features of stimuli/objects in the environment automatically capture attention irrespective of the goal of the person.

Bottom-up: A stimulus-processing mode that begins at the sensory/perceptual level and works up to the highest conceptual level.

Top-down: In contrast to “bottom-up”, this stimulus-processing mode begins at the highest conceptual/goal level and continues to the lower and primary processing levels, such as the sensory/perceptual level.

Publications

Journal Papers

1) **Xiaoyu Tang**, Chunlin Li, Qi Li, Yulin Gao, Weiping Yang, Jingjing Yang, Soushirou Ishikawa, Jinglong Wu: Modulation of auditory simulus processing by visual spatial or temporal cue: an event-related potentials study, *Neuroscience Letters*, 2013, 553, 40-45

2) Ming Zhang, **Xiaoyu Tang** and Jinglong Wu: Blocking the Link between Stimulus and Response at Previously Attended Locations: Evidence for Inhibitory Tagging Mechanism, *Neuroscience and Biomedical Engineering*, 2013, 1, 13-21

3) **Xiaoyu Tang**, Lingyun Wang, Ming Zhang: Effects of Masked Cue on Attentional Orienting – Facilitation and Inhibition, *Chinese Journal of Applied Psychology*, 2012, 18 (3), 204-212

4) Yulin Gao, Qi Li, Weiping Yang, Jingjing Yang, **Xiaoyu Tang** and Jinglong Wu: Effects of ipsilateral and bilateral auditory stimuli on audiovisual integration: a behavioral and event-related potential study, *NeuroReport*, 2014, 25 (9), 668–675

5) Yulin Gao, Chunlin Li, **Xiaoyu Tang**, Qi Li, Weiping Yang, Jingjing Yang, Ishikawa Soushirou and Jinglong Wu: Modulation of Response to Audiovisual Stimuli Presented Peripherally by Visually Cued Endogenous Temporal Attention: An Event-Related Potentials Study, *Neuroscience and Biomedical Engineering*, 2013, 1 (2), 125-132

6) Weiping Yang, Qi Li, Tatsuya Ochi, Jingjing Yang, Yulin Gao, **Xiaoyu Tang**, Satoshi Takahashi, Jinglong Wu: Effects of Auditory Stimuli in the Horizontal Plane on Audiovisual Integration: An Event-Related Potential Study, *PLoS One*, 2013, 8 (6), e66402

Book Chapter

Xiaoyu Tang, Yulin Gao, Weiping Yang, Ming Zhang, Jinglong Wu, Audiovisual Integration of Natural Auditory and Visual Stimuli in the Real-World Situation, *Biomedical Engineering and Cognitive Neuroscience for Healthcare: Interdisciplinary Applications*, IGI Global, 2012, ISBN 978-1-4666-2113-8, Chapter 35, pp. 337-344

International Conference Paper

1) **Xiaoyu Tang**, Chunlin Li, Qi Li, Yulin Gao, Weiping Yang, Jingjing Yang, Soushirou Ishikawa, Satoshi Takahashi, Jinglong Wu: Effect of spatial and temporal attention on audiovisual integration: an event-related potentials study, *IEEE/ICME International*

Conference on Complex Medical Engineering, 2015, 48-49

2) **Xiaoyu Tang**, Chunlin Li, Qi Li, Yulin Gao, Weiping Yang, Jingjing Yang, Soushirou Ishikawa, Satoshi Takahashi, Jinglong Wu: Effect of spatial and temporal attention on visual stimulus processing: an event-related potentials study, *ICME International Conference on Complex Medical Engineering*, 2014, 157-162
3) **Xiaoyu Tang**, Chunlin Li, Qi Li, Yulin Gao, Weiping Yang, Jingjing Yang, Soushirou Ishikawa, Satoshi Takahashi, Jinglong Wu: Effect of Cue-Target Interval on Audiovisual Stimuli Processing in Endogenous Spatial Attention: An Event-Related Potentials Study, *ICME International Conference on Complex Medical Engineering*, 2013, 656-661
4) Weiping Yang, Qi Li, Tatsuya Ochi, Jingjing Yang, Yulin Gao, **Xiaoyu Tang**, Satoshi Takahashi, Jinglong Wu: Influences of auditory stimuli in front and rear space on visual detection: an event-related potential study, *ICME International Conference on Complex Medical Engineering*, 2013, 7-12
5) Yulin Gao, **Xiaoyu Tang**, Chunlin Li Jingjing Yang, Weiping Yang, Satoshi Takahashi, Jinglong Wu: Effect of cue-target interval on temporally endogenous attention of No-Go target: Event-related potential evidence, *IEEE International Conference on Mechatronics and Automation*, 2012, 1405-1410
6) **Xiaoyu Tang**, Chunlin Li, Qi Li, Yulin Gao, Weiping Yang, Jingjing Yang, Soushirou Ishikawa, Ming Zhang, Jinglong Wu: Effect of cue-target interval on endogenous attention in Go/No-Go task: evidence from an event-related potentials study, *ICME International Conference on Complex Medical Engineering*, 2012, 669-672
7) Jingjing Yang, Tatsuya Ochi, Qi Li, Yulin Gao, Weiping Yang, **Xiaoyu Tang**, Satoshi Takahashi and Jinglong Wu: The Effect of Spatial Information of Auditory Stimuli on Audiovisual Interaction: Evidence from Event-related Potentials, *ICME International Conference on Complex Medical Engineering*, 2012, 699-704

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