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AGING EFFECT ON AUDIOVISUAL INTEGRATIVE
PROCESSING IN SPATIAL DISCRIMINATION TASK

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Aging Effect on Audiovisual Integrative Processing in
Spatial Discrimination Task

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A thesis submitted in partial fulfilment of the
requirements for the Degree of Doctor of Philosophy

February, 2018

CERTIFICATE OF ORIGINALITY

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_____ (Sign)

ZOU Zhi _____ (Name)

DEDICATION

I would like to dedicate this thesis to my beloved daughter, Winnie.

ABSTRACT

Delivery of information from multiple sensory modalities is useful for enhancing perceptual discrimination and subsequently behavioral performance. Older adults have been reported having greater enhancement in the behavioral performance. The mechanism underlying how the multisensory modulation occurs among older adults remains unclear. The aim of this thesis was to investigate how aging impacts on the multisensory integration process which in turn influences the sensory, response selection and generation, and motor execution processes. There are two studies in this thesis.

The first study (Study 1, Chapter Four) was to validate the audiovisual discrimination task used in this study for generating the multisensory integration process among a group of younger participants. In this study, adults performed in a spatial discrimination task based on visual or auditory information or a combination of both, while electroencephalogram (EEG) as well as electromyography (EMG) data was captured. The behavioral measures were accuracy rate and reaction time on the audiovisual discrimination task. The neurophysiology measures included event-related potentials (ERP), lateralized response potentials (LRP), and muscle activities based on EMG. The results obtained were compared with those reported in previous studies on audiovisual integration. Behavioral results demonstrated higher accuracy rate in the audiovisual (AV) condition compared with both auditory (A) and visual (V) conditions. The results were consistent with the previous findings. Moreover, ERP results also showed a sub-additive pattern of fronto-central P2 in the AV condition which was also consistent with those reported in previous findings. The results of first study indicated that the audiovisual discrimination task used in this thesis was valid for generating the multisensory integration process. The

measurements used were capable to generating meaningful data for the next study.

The second study recruited older participants of who completed the same audiovisual discrimination task and same parameters of measurements in Study 1. The aim was to investigate the impact of aging on the audiovisual integration process affecting the subsequent sensory, response selection and generation, and motor execution processes. Due to the observations of obvious speed-accuracy trade-off existed in the older group, inverse effectiveness score (IES) was used to normalized the task-related behavioral measures. Results of Study 2 demonstrated that older participants could benefit more from the audiovisual integration process than their younger counterparts in terms of lower IES in the AV condition. The super-additive patterns of the fronto-central P2 were significantly and negatively correlated with the IES scores. These suggested that the enhanced task performance is likely to be due to the modulated audiovisual integration influencing perceptual and feedback processes. Furthermore, the fronto-central P2 was also positively correlated with participants' MoCA attention sub-score. These findings indicated that audiovisual integration may play a role in compensating the deteriorated attention function among the older participants. For the post-audiovisual integration motor responses, between-group differences were only revealed in the response generation process. Older participants showed less negative-going r-LRP in audiovisual condition while no significant differences in the r-LRP were observed among the younger participants. The r-LRP amplitudes were further revealed to be negatively correlated with the IES score. These results suggested that the audiovisual integration could have modulated the response generation process, which enhanced older participants' performances on the task. These observations were not found among the younger participants.

In summary, the results of the two studies indicated that the enhanced performances on audiovisual discrimination task observed among the older participants would have contributed by the super-additive audiovisual integration processes, which modulated the perceptual and feedback stages as well as response generation process. The super-additive audiovisual integration may serve a functional role to compensate the deterioration of attention function as well as the response generation due to aging.

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**PRESENTATIONS AT CONFERENCE ARISING FROM THE
THESIS**

Zou Zhi, Bolton Chau, Chetwyn Chan

Effects of multisensory integration on enhancing motor preparation and execution processes, *Movement, brain, body, cognition, Oxford*, Jul 2017

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LIST OF ABBREVIATIONS

| | |
|-------|---------------------------------------|
| A | auditory condition |
| AG | angular gyrus |
| ANOVA | analysis of variance |
| AV | audiovisual condition |
| C | control condition |
| dPMC | dorsal premotor cortex |
| EEG | electroencephalograph |
| EMG | electromyogram |
| EOG | electro-oculograms |
| ERP | event related potential |
| fMRI | functional magnetic resonance imaging |
| GCS | general cognitive slowing |
| IES | inverse efficiency score |
| IPL | inferior parietal lobe |
| LECR | left extensor carpi radius |
| LFCR | left flexor carpi radius |
| LRP | lateralized readiness potential |
| MEG | magnetoencephalography |
| mIPS | mid-posterior intraparietal sulcus |
| MoCA | Montreal cognitive assessment |
| PPC | posterior parietal cortex |
| pSTG | posterior superior temporal gyrus |
| pSTS | posterior superior temporal sulcus |
| PT | planum temporale |
| RECR | right extensor carpi radius |
| RFCR | right flexor carpi radius |

| | |
|-------|---|
| r-LRP | response-locked lateralized readiness potential |
| RSVP | rapid serial visual presentation |
| SC | superior colliculus |
| SD | standard deviation |
| s-LRP | stimulus-locked lateralized readiness potential |
| SPOC | superior parieto-occipital cortex |
| STG | superior temporal gyrus |
| STS | superior temporal sulcus |
| TMS | transcranial magnetic stimulation |
| TPJ | temporo-parietal junction |
| V | visual condition |

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CHAPTER ONE

GENERAL INTRODUCTION

In real life, people seldom face sensory input from only one modality. Take crossing a busy street as an example: the traffic information can be received by both visual and auditory modalities and people make use of information from different modalities to decide where and how to move. This chapter focuses on the background knowledge of multisensory integration, including the definition and principles of multisensory integration. The effect of multisensory integration on behavioral performance in both younger and older adults is also introduced. Most of the previous multisensory studies focused on the mechanism of the enhanced behavioral performance in younger participants in the sensory process, but the influence of the modulation in the sensory process on the consequent process, such as the response selection and generation is not widely studied. Although behavioral evidence demonstrates that older people can benefit more in behavioral performance from multisensory integration compared to their younger counterparts, the mechanism of this phenomenon still remains unclear.

1.1 Multisensory integration definition

Multisensory integration, that is, how and when the information from various modalities is processed in the brain, has been studied for decades. Multisensory integration can be defined in two levels: the neural process level and the cellular level. At the neural process level, multisensory integration can be defined as the process of synthesizing information from different modalities (Stein et al., 2008), while at the cellular level, the multisensory process is

defined more operationally, that is “a statistically difference between the number of impulses evoked by a cross-modal combination of stimuli and the number evoked by the most effective of these stimuli individually” (Stein et al., 2008). The multisensory process can be reflected by the different neural response magnitude (super-additive or sub-additive) between the uni-sensory and multisensory condition.

When multisensory information is received, different magnitudes of multisensory integration can occur, for example, the magnitude of multisensory integration at the single neuron level can be defined in three levels: super-additivity, additivity and sub-additivity. When multisensory information is received by a single neuron, if the level of response is larger than the sum of inputs, the magnitude of multisensory integration is defined as super-additivity. On the contrary, if the level of response in a single neuron is only larger than the most vigorous component but still does not exceed the sum of all the input components, the magnitude of the multisensory process is defined as sub-additivity (Stein et al., 2008). Similarly, the additive pattern is defined as the sum of uni-sensory responses being the same as the multisensory response. Although this definition is derived from single neuron studies, this kind of magnitude classification can also be used at the sensory process level and has been employed by a large number of electroencephalograph (EEG) and functional magnetic resonance imaging (fMRI) multisensory studies (Cappe et al., 2010; Saldern & Noppeney, 2013; Stephen et al., 2010). In EEG and fMRI studies which measured the response of a group of neurons, the super-additive and sub-additive pattern could be used to compare the amplitude of the multisensory condition and the amplitude of the sum of uni-sensory conditions to find out the time window and brain regions involved in multisensory integration. For example, an event-related potential (ERP) study compared the amplitude of ERP waveform at each time point between the sum of auditory and

visual conditions and the auditory-visual condition to find a time window of 60-95 ms after the stimulus, and the posterior superior temporal region is involved in multisensory integration (Cappe et al., 2010). This thesis also employs these patterns to find the time window and regions involved in multisensory integration.

Although different multisensory magnitudes can be observed when receiving sensory input from various modalities, the relationship between the magnitude and behavioral response is still not very clear yet. However, consistent evidence has demonstrated that the congruency of the information provided by various modalities could modulate the behavioral response. Prior evidence showed that when information from different modalities carries congruent content, which means the information provided by each modality is consistent, such as the same direction or speech content, the information can integrate with each other and enhance the behavioral response, for example, increasing the accuracy rate and response speed (Bockler et al., 2011; Fischer et al., 2007, 2010; Kiesel & Miller, 2007; Van Wanrooij et al., 2009). However, when the information from different modalities is incongruent, for example, the spatial information is inconsistent between the information provided by each modality, the information interacts with each other and an illusion can be induced by the more vigorous modality (Bonath et al., 2007; Dhamala et al., 2007; Mishra et al., 2007; Naghavi et al., 2007) and decrease the accuracy. For example, when the participants were required to locate a sound source, and at the same time a visual stimulus was provided simultaneously from another location, the perceived location of the sound was shifted to the visual source resulting in low accuracy in regard to locating the sound, which is also called spatial ventriloquism (Chen et al., 2013). Therefore, the congruency of the information, including content and spatial information could result in multisensory integration or interaction. The reason for this phenomenon could be because the brain integrates information from the

same source and the congruent information as well as congruent spatial location would be more probable to be regarded as being from the same source. Also researchers concluded three principles of multisensory integration which are spatial, temporal as well as inverse effectiveness principles (Stein & Meredith, 1993; Stein et al., 2008 for review).

1.2 Principles of multisensory integration

Three principles of multisensory integration have been demonstrated, that are, spatial rule, temporal rule and inverse effectiveness (Stein & Meredith, 1993; Stein et al., 2008 for review). Both the spatial rule and temporal rule demonstrate that if the spatial or temporal parameter of the information from different modalities is congruent, the information from different modalities is much more likely to be regarded as from the same source so the probability of integration would be high and vice versa. The principle of inverse effectiveness demonstrates that when the effectiveness of the stimulus from different modalities is low, the magnitude of multisensory integration can be enhanced (Meredith & Stein, 1986; Stanford et al., 2005; Stanford & Stein, 2007; Perrault et al., 2005). For example, Meredith and Stein (1986) firstly reported that when a single neuron in a cat's superior colliculus (SC) received stimulus with minimal intensity, the multisensory response increased more than 50% compared to the condition of receiving optimal stimulus. Additionally, evidence in human studies has demonstrated that the enhanced multisensory integration further causes a higher level of facilitation in the behavioral response in terms of reaction time and accuracy rate (Bell et al., 2005; Diederich et al., 2004; Saldern & Noppeney, 2013). For example, a recent study showed that in a motion discrimination task, when the stimuli were intact, which means clear and reliable, the accuracy rate and response speed in the audiovisual condition were only higher than those of the auditory condition, but lower than the visual condition

(Saldern & Noppeney, 2013). However, when the stimuli were degraded and blurred, increased accuracy rate and response speed could be observed in the audiovisual condition compared to both the visual and auditory condition (Saldern & Noppeney, 2013).

As multisensory integration follows these three principles, the inverse effectiveness may confound the results of aging effect in multisensory integration studies. Specifically, because of the deteriorated peripheral sensory organs in older adults, when the same intensity of auditory and visual stimuli are provided to both younger and older people, the older adults may take them as weaker ones compared to the younger people. This thesis investigates the aging effect in multisensory integration. As inverse effectiveness may confound the results in the older group, the intensity of the stimuli was calibrated in both studies reported in this thesis to control the inverse effectiveness, which will be described in detail in Chapter 3. Up to now, very few studies have controlled the inverse effectiveness which may be the reason of inconsistent behavioral findings in older adults. The behavioral response in both younger and older participants is introduced in the next two sections.

1.3 Congruent multisensory integration in younger participants

A lot of evidence has supported that congruent multisensory information can facilitate behavioral performance (Besle et al., 2004; Calvert et al., 2001; Frassinetti et al., 2002a; Klucharev et al., 2003; Liu et al., 2007; Saldern & Noppeney, 2013; Stephen et al., 2010; Teder-Salejarvi et al., 2002; Van Wassenhove et al., 2005). The enhanced behavioral performance due to multisensory integration can be observed in different tasks, such as speech recognition, object detection and discrimination tasks (Frassinetti et al., 2002a; Saldern & Noppeney, 2013; Stephen et al., 2010). Evidence showed that when

the speech messages were provided by both auditory and visual information, improved speech discrimination can be observed (Besle et al., 2004; Calvert et al., 2001; Klucharev et al., 2003; Van Wassenhove et al., 2005). Also in stimulus detection tasks, when an auditory stimulus is presented simultaneously with a visual stimulus, the perceptual sensitivity can be increased (Frassinetti et al., 2002a). Similarly, in motion discrimination and spatial discrimination tasks, enhanced behavioral performance in the multisensory condition compared to uni-sensory conditions could be observed (Saldern and Noppeney, 2013; Stephen et al., 2010). Specifically, Saldern and Noppeney (2013) demonstrated that when congruent visual and auditory motion was provided simultaneously, especially when the reliability of information from both modalities was low, the reaction time decreased significantly compared to the conditions in which only auditory or visual information was provided.

The mechanism of multisensory integration enhancing behavioral performance has been studied a lot and is discussed in Chapter 2. Studies using ERP have revealed components associated with multisensory integration in the early process (P1 and C1) (Cappe et al., 2010; Santangelo et al., 2008) to late process (P2) (Stekelenburg & Vroomen et al., 2013; Vidal et al., 2008). The P2 component elicited in the fronto-central region, which is an important marker for multisensory integration, has been reported becoming sub-additive when receiving multisensory information (Stekelenburg and Vroomen, 2007). However, most of the previous multisensory studies focused on the sensory process, but whether the sub-additive pattern of P2 can influence the subsequent process, such as response selection and generation, is not well studied yet. Previous evidence showed multisensory stimuli can facilitate the response selection and generation process (Hackley et al., 1999; Jepma et al., 2009; Kiesel & Miller, 2007). Specifically, the latency of response selection was decreased and the response force increased when receiving accessory sound

simultaneously with a visual stimulus (Hackley et al., 1999; Jepma et al., 2009; Kiesel & Miller, 2007). However, this accessory sound contained no task-related information, which may only serve as a cue that prepares the sensory and motor system for the coming stimuli (Los & Burg, 2013). As such, the visual and auditory information may not be integrated in this kind of experimental design (Los & Burg, 2013). Taking all these findings together, evidence of the modulation of auditory-visual integration in the response selection and generation is still insufficient.

1.4 Congruent multisensory integration in older participants

The modulation of multisensory integration in both sensory and motor processes also remains unclear. Behavioral evidence focusing on multisensory integration in older adults produced inconsistent results. Specifically, some of the studies demonstrated that older adults can benefit more from audiovisual integration compared to younger adults (Diederich et al., 2008; Hugenschmidt et al., 2009; Laurienti et al., 2006; Mahoney et al., 2014; Peiffer et al., 2007) while others showed the opposite (Mahoney et al., 2011; Stephen et al., 2010). A study used a color discrimination task to investigate the audiovisual integration in older participants and three conditions were involved in this study (Laurienti et al., 2006). Specifically, in the visual condition, a red or blue circle was shown on the screen and in the auditory condition, a speech word of red or blue was presented via an earphone; in the combined condition, visual and auditory stimulus which conveyed congruent color information was simultaneously presented (Laurienti et al., 2006). The results showed that both groups could benefit from the audiovisual integration in terms of reaction time, but the older adults could benefit more compared to the younger participants. As older adults suffered general cognitive slowing (GCS) which may confound the results, a study conducted by the same lab-controlled GCS by employing a simple

reaction task (Peiffer et al., 2007). In this study, the same stimuli as in Laurienti's (2006) study were used and the participants were instructed to respond as soon as possible when they detected either or both of the stimuli. The results still demonstrated that older adults can benefit more from multisensory integration compared to their younger counterparts, indicating that the enhanced behavioral performance when receiving multisensory information in older adults could be related to the different multisensory process compared to younger adults rather than GCS (Peiffer et al., 2007). However, opposite evidence was also provided by two studies. Specifically, Stephen and colleagues (2010) showed that when performing a spatial discrimination task, although both younger and older participants showed decreased reaction time in the audiovisual condition, no extra beneficial effect was found in the older group. Similar results were also found in another study which adopted a simple reaction task showing that older adults could not benefit more in the audiovisual integration condition compared to the younger participants (Mahoney et al., 2011). These two studies found no increased benefit from multisensory integration in older adults.

Although behavioral studies have demonstrated conflicting results, most multisensory studies showed different behavioral performance between younger and older participants when receiving multisensory information, indicating a different multisensory process between the two groups. However, very few studies have investigated the neural process of the changed behavioral performance in older adults when receiving multisensory information. Stephen et al. (2010) by employing magnetoencephalography (MEG) measurement reported a sub-additive pattern in the audiovisual (multisensory) condition at the superior temporal gyrus (STG) around 200 ms after the stimulus compared to the auditory condition. Also, the sub-additive pattern was significantly correlated with less benefit of behavioral performance in terms of reaction time in the older

group. The inconsistent findings on the aging effect in behavioral results as well as the insufficient evidence of the neural process of multisensory integration in older adults motivated us to investigate the aging effect in multisensory integration. Furthermore, previous evidence showed the main reason for the prolonged process in older adults was related to the generation of motor response (Falkenstein et al., 2006; Roggeveen et al., 2007; Yordanova et al., 2004), which also motivated us to investigate whether multisensory integration can modulate the response selection and generation in older groups.

1.5 Overview of the thesis

As no prior studies have provided evidence of aging effect in response selection and generation when receiving congruent audiovisual information, the aim of the thesis is to investigate the aging effect in audiovisual integration in both sensory and motor processes in spatial discrimination task. Most of the previous studies focused on object discrimination, while spatial discrimination or orientation is important in daily life. Hence, the task used in this thesis was spatial discrimination in which the arrow direction (visual stimulus) and/or the direction of “Bat-ears” sound (auditory stimulus) should be discriminated by the participants. As the task and the stimuli were not used in previous multisensory studies, a model of audiovisual integration in healthy younger participants was built in the first study (Study 1, Chapter 4) to validate the task. If the results were similar to the results reported in previous multisensory studies in younger participants, this task would be valid. In this study, the influence of multisensory integration in the sensory process and the consequent influence on response selection and generation processes were investigated by employing ERP and EMG measurement. Similar results as previous studies reported, the modulation in early sensory process (<100 ms after the stimulus) as well as the modulation in perception and feedback processes were expected. In the second study (Study

2, Chapter 5), the aging effect on multisensory integration was investigated by comparing the different neural process between healthy older and younger participants in both sensory and motor processes by employing EEG and EMG measurement. The modulation of multisensory integration in the perceptual and feedback processes as well as response selection and generation processes was investigated.

The results of this thesis will provide knowledge of the aging effect in auditory-visual integration from sensory process to motor process. This thesis can fill the gap of the relationship between the enhanced behavioral performance and the neural process in both younger and older adults. The extended knowledge provided by this thesis can also serve as the basis of further study of other situations in the multisensory process, such as post-stroke patients.

CHAPTER TWO

LITERATURE REVEIW

Before multisensory integration was introduced in the literature in the last two decades, the sensorimotor process was studied within each sensory modality, for example, visual or auditory modality. As when and where multisensory integration takes place has always been the focus of multisensory integration, the neural substrate responsible for the uni-sensory process serves as the basis of multisensory process studies. In the first part of this chapter, the uni-sensory process in both visual and auditory modalities is reviewed and the multisensory integration is reviewed in the second part. As the aim of the thesis is to investigate the aging effect in multisensory integration, the response generation process which causes the delayed sensorimotor process in older adults is also reviewed. In the last part, the neurophysiology methods used in this thesis as well as the rationale of this thesis are introduced.

2.1 Uni-sensory-motor process

2.1.1 Visual-motor process

The visual system can provide quite reliable and detailed spatial information in a retinotopic pattern by processing the information gathered from the visual environment (Larry et al., 2012). As one of the important goals of visual information input is to guide motor output, the two pathways involved in the visual information process as well as the motor planning process is reviewed in this section.

2.1.1.1 Two pathways in the visual information process

The information from both eyes travels to the lateral geniculate nucleus of the thalamus projected to the primary visual cortex by the optic nerve (Larry et al., 2012). After the information travels to the primary visual cortex from the thalamus, the process of visual information in the cortex may consist of both hierarchical and parallel processing. Specifically, the visual shape and pattern information and the visuospatial information are processed by two pathways which travel parallel to each other. However, the information in each pathway is processed hierarchically from the primary visual cortex to temporal or parietal cortex. Two pathways have been demonstrated in the visual system in the processing of different information—the ventral pathway as well as the dorsal pathway. The ventral pathway, also called “what” pathway, runs from the occipital lobe to the inferior temporal lobe (V1→V2→V3→V4→inferotemporal cortex) and extends to the ventrolateral prefrontal cortex (Milner et al., 2008). The ventral pathway conveys the information about shape and pattern (Milner et al., 2008). Stimulus discrimination and orientation tasks were employed to investigate the function of the two pathways. For example, in a fMRI study, the participants were required to watch object manipulation video clips, such as object grasping and focus on different aspects, such as object identity (Shmuelof & Zohary, 2005). The results showed that the fusiform gyrus, which is a neural substrate in the ventral pathway was activated when participants focused on object identity (Shmuelof & Zohary, 2005). The dorsal pathway, which is also called the “where” pathway, runs from the occipital lobe to the parietal lobe (V1→V2→medial temporal cortex →medial superior temporal cortex →parietal cortex) and extends to the dorsolateral prefrontal cortex. The dorsal pathway is involved in spatial information process as well as using spatial information to guide motor output (Milner et al., 2008). Similar as investigating the function of the ventral pathway, a task involving visuospatial stimuli discrimination was used when investigating the function of the dorsal pathway. For example, a

fMRI study demonstrated that during grasping, the neural substrates, such as anterior intraparietal cortex and lateral occipital complex, in the dorsal pathway were activated (Culham et al., 2003; Zachariou et al., 2014). In summary, the visual information is processed by two parallel pathways which run dorsally and ventrally, with dorsal pathway processing spatial information and ventral pathway processing shape and pattern information.

2.1.1.2 Visuospatial information process

Visuospatial information provides the location of objects in space, which is processed by the dorsal pathway. As this thesis used visuospatial information as the visual stimuli, the structure of the dorsal pathway, that is the “where” pathway is reviewed further in this section. Some brain structures in the dorsal pathway have been shown to be responsible for the visuospatial information process. For example, the superior temporal gyrus (STG)(Ellison et al, 2004; Karnath et al., 2004; Malherbe et al., 2017), temporo-parietal junction (TPJ)(Wang et al., 2016; Vallar, 2001; Verdon et al., 2010), posterior parietal cortex (PPC) and frontal middle gyrus (MFG)(De Graaf et al., 2009; Gillebert et al., 2011; Vandenberghe et al., 2012).

Among the research studies on the visuospatial process, both lesion studies and neuroimaging studies with younger participants were involved (De Graaf et al., 2009; Ellison et al., 2004; Waberski et al., 2008). Specifically, a lesion study by comparing spatial neglect patients and normal participants demonstrated that the right STG and insular damage contribute to the spatial neglect (Ellison et al., 2004). Regarding the studies investigating normal participants, a combined fMRI and TMS study showed when conducting a visuospatial landmark task, the information can flow from medial frontal gyrus to PPC (De Graaf et al., 2009). Neurophysiology studies, such as electroencephalograph (EEG) and transcranial

magnetic stimulation (TMS) can provide more temporal information for the visuospatial information process which also provided evidence of the route of information traveling along neural substrates in the visuospatial pathways. For example, an EEG study demonstrated that when conducting a visuospatial localization task, the right middle occipital gyrus, right superior posterior parietal, bilateral inferior occipital and right inferior posterior parietal cortex activated sequentially, indicating the visuospatial information travels from the right middle occipital gyrus to right inferior posterior parietal cortex (Waberski et al., 2008). EEG evidence also demonstrated that the visual feature detection may start around 200 ms after the stimulus indexed by visual P2 (Pernet et al., 2003). Furthermore, the visuospatial information process is more dominated in the right hemisphere which was proved by both neuroimaging studies (Büchel et al., 2004; Corballis et al., 2002, 2003; Herve et al., 2013; Shulman et al., 2010) and neurophysiology studies (Fierro et al., 2001; Longo et al., 2015). For example, a TMS study (Fierro et al., 2001) demonstrated that a single pulse of TMS over the right parietal cortex can induce contralateral neglect suggesting that the right parietal cortex contributes to visuospatial processing. Another ERP study also demonstrated similar results that the right hemisphere dominates in spatial attention (Longo et al., 2015). In this study, the participants were required to conduct landmark discrimination and color discrimination task. The results showed the component related to spatial attention was observed in the right occipito-parietal site indicating the right hemisphere is specialized in visuospatial attention. These results indicated that the right hemisphere dominates the visuospatial process. Combining the evidence provided by studies with various methods showed the visuospatial information may travel from the primary visual cortex to the temporal and parietal cortex and the right hemisphere is specialized in this process.

2.1.1.3 Motor planning

One of the goals of visuospatial information processing is to guide motor output. For example, when crossing a busy street, the localization of vehicles and pedestrians can be used to guide motor output. Hence, this section reviews the neural substrates responsible for motor planning when visual information is received.

Some regions located in the parieto-occipital cortex play important roles in motor planning (Filimon et al., 2009; Vesia et al., 2010). For example, a TMS study demonstrated the role of the superior parieto-occipital cortex (SPOC), mid-posterior intraparietal sulcus (mIPS) as well as angular gyrus (AG) in reaching and saccade (Vesia, et al., 2010). In Vesia et al (2010) study, repetitive TMS was used to stimulate either SPOC, mIPS or AG when conducting the task. Healthy younger participants were required to conduct a saccade with both eyes or reaching with the left or right hand during the task. When conducting the task, a cue represented on the screen to inform the participants to conduct saccade or reaching and after which, the target appeared in peripheral visual site. The results demonstrated a higher variability of the reaching and a lower accuracy rate in saccade when either mIPS or AG was stimulated which indicated that these two regions play a role of planning a reach and saccade vector (Vesia, et al., 2010). However, when the SPOC was stimulated, only the reach direction moved close to fixation and no effect on saccade was observed suggesting the SPOC is selective in the reaching process in the peripheral visual area (Vesia, et al., 2010). Another study demonstrated similar results that the SPOC involved in visual-motor process when the participants conducting reaching movement (Filimon et al., 2009). Therefore, the neural substrates responsible for motor planning when receiving visual information are located in the parietal as well as parieto-occipital cortex.

2.1.2 Auditory-motor process

The auditory system, which is the system responsible for hearing, can provide spatial information to some extent by comparing the difference in level and time between the sounds in two ears. Unlike the visual information process, before arriving at the auditory cortex, the auditory information has already been encoded in the subcortical regions, such as cochlear nuclei (Larry et al., 2012). However, the process of auditory information in the cortex also involves two pathways similar to the visual system. Although auditory information can provide spatial information, the spatial information provided is less detailed than visuospatial information but the auditory-spatial information can still guide motor output, such as saccade.

2.1.2.1 Two pathways in the auditory information process

Similar to the visual system, evidence has demonstrated that the auditory cortical processing pathways are also organized dually: one pathway is responsible for the processing of object information, and the other is for processing of space and motion (Petrides, 2005; Rauschecker, 2007; Rauschecker & Tian, 2000; Tian et al., 2001). Evidence from animal studies demonstrates that the ventral pathway, also known as the “what” pathway runs from the rostral field, through rostral belt and parabelt into the ventral lateral prefrontal cortex (Yale et al., 2013). The dorsal pathway, also known as the “where” pathway, runs from the primary auditory cortex through caudal belt and parabelt into the dorsal lateral prefrontal cortex (Yale et al., 2013). The “what” pathway is responsible for processing verbal and musical stimuli while the “where” pathway is responsible for processing spatial information. Similar to investigating the function of dual pathways in the visual system, a task of location and pitch discrimination was used to investigate the function of dual pathways in the auditory system. For example, in a fMRI study (Alain et al.,

2001), the participants were required to conduct a delayed match location comparison task and pitch comparison task. A silent task was used as the control task. In the location comparison task, the participants were required to discriminate if the target location was the same as the location provided previously. In the pitch discrimination task, the participants were required to discriminate if the pitch was the same as the pitch provided previously. The results demonstrated that when processing auditory spatial information, activation of the posterior temporal cortex and parietal cortex was observed; when the pitch information was processed, the inferior frontal gyrus was activated. The results demonstrated that when processing pitch information, the brain regions in the ventral pathway are activated while when processing auditory-spatial information, the brain regions in the dorsal pathway are activated. Therefore, the results indicated a similar dual pathway in auditory information processing (Alain et al., 2001). In summary, the auditory system involves two pathways for processing auditory information which is similar to the visual system.

2.1.2.2 Auditory-spatial information process

As reviewed in the previous section, the auditory information process involves two pathways which are similar to the visual system. So this section follows the same structure of the previous “visuospatial information process” section to review the dorsal pathway which is responsible for auditory spatial information processing. The posterior superior temporal gyrus (pSTG), which is also reported to be a neural substrate in the visual dorsal pathway, including the planum temporale (PT) is an important region in the auditory dorsal pathway. The pSTG is part of the dorsal pathway of auditory information processing which processes sound localization information more than non-spatial information (Degerman et al., 2006). The PT is a region that serves as a

computational hub, which can analyze complex auditory information before segregating it to different higher cortical regions (Griffithsa et al., 2002). Moreover, PT is also quite sensitive to spatial information (Deouell et al., 2007). Deouell et al. (2007) demonstrated that when participants were required to focus on a visual target, the PT could still be activated when the background auditory spatial information changed. Therefore, auditory spatial information may be decoded in the PT, before running to the parietal lobe for further analysis. A magnetoencephalography (MEG) study with high temporal resolution demonstrated the peak latency difference in three critical auditory-spatial information process areas: Heschl's gyrus 139 ms, pSTG 156 ms and inferior parietal lobe (IPL) 162 ms, suggesting information of auditory localization may travel from Heschl's gyrus to IPL via the STG (Brunetti et al., 2005). Another combined fMRI and MEG study demonstrated similar results that the pSTG and PT can be activated 70-150 ms after receiving auditory spatial information (Ahveninen et al., 2006).

Similar to the visuospatial information process, the parietal lobe, especially the right parietal lobe also plays an important role in processing auditory spatial information (Bushara et al., 1999). A number of the regions responsible for auditory-spatial information process overlap the visuospatial information process. For example, the inferior parietal lobe (Alain et al., 2001; Arnott et al., 2004; Brunetti et al., 2005; Zatorre et al., 2002); superior parietal lobe (Griffiths et al., 1998) and TPJ (Tata et al., 2005). However, not all the regions of visual and auditory spatial information processing overlap with each other. For instance, a fMRI study demonstrated that visual and auditory spatial information processing may activate different regions in the parietal lobe (Salmi et al., 2007). For example, the inferior parietal lobe can be activated by auditory spatial tasks and the superior parietal lobule can be activated by visuospatial tasks, indicating that different regions in the parietal cortex are involved in auditory and visual

spatial information processing (Salmi et al., 2007). In summary, similar to the dorsal visual pathway, the auditory dorsal pathway is responsible for auditory spatial information processing and some of the neural substrates in visual and auditory dorsal pathways are in common.

2.1.2.3 Motor planning

Similar to visuospatial information, auditory spatial information can also guide motor output, such as saccade, reaching or navigation. The dorsal auditory pathway may transform auditory signals to the premotor cortex and prefrontal cortex to generate a motor program before commanding the motor cortex to give a certain movement response (Warren et al., 2005). For example, neuroimaging studies show that posterior prefrontal and precentral cortical regions can be activated when conducting sound localization tasks with certain movement, for example, key pressing (Zatorre et al., 2002). However, different from visuospatial information processing, auditory spatial information may travel to the motor cortex directly via the pSTG. Evidence shows that the pSTG and dorsal premotor cortex (dPMC) connect with each other directly by white matter (Frey et al., 2008). Furthermore, neuroimaging studies demonstrate that even when passively hearing auditory spatial information, the premotor cortex can be activated (Warren et al., 2002). Since the dPMC is responsible for movement planning, spatial-movement guiding and motor preparation (Churchland et al., 2006; Cisik & Kalaska, 2005; Connolly et al., 2007), these results indicate that sound embedded with a spatial or motor component computed in the pSTG may give motor commands to the premotor cortex directly (Warren et al., 2005; Zatorre et al., 2007 for review).

As auditory-spatial information cannot provide detailed and reliable information compared to visuospatial information, auditory information is

seldom used to guide reaching or navigation in real life. Researchers also argued that auditory-spatial information may just play an attention orientation role to direct saccade (Arnott & Alain, 2011). The neural mechanism of auditory spatial information in guiding motor output (including motor planning, preparation and execution) such as reaching or pointing in healthy participants has not been studied well yet.

2.2 Audiovisual integration process from the sensory process to response generation process

As reviewed above, the studies focusing on the auditory or visual pathways used stimuli from only one modality, but in the real world people always receive information from more than one modality. Take crossing a busy street as an example. Both visual information and auditory spatial information is needed to localize vehicles before moving. Therefore, investigating where and when the information from different modalities integrates with each other is important. In the next few sections, “when” and “where” multisensory integration exists in humans is reviewed.

2.2.1 Audiovisual integration in perceptual and feedback processes

Multisensory integration can be observed at quite an early stage (<100 ms after the stimulus, Figure 2.1) (Cappe et al., 2010; Molholm et al., 2002; Musacchia et al., 2006; Talsma et al., 2007). Specifically, Cappe et al. (2010) employed a task in which the participants were required to focus on both visual (a disc) and auditory (a 1000 Hz complex tone) stimuli without giving a response, and the results found the C1 wave (~60-95 ms) showed sub-additive pattern, which means the amplitude of C1 is less positive going in the audiovisual condition compared with the sum of both auditory and visual

conditions, at the parieto-occipital region. The results indicated that the early perceptual process could be modulated by audiovisual integration. This kind of early multisensory integration can also be modulated by attention (Talsma et al., 2007). In Talsma's (2007) ERP study, the participants were required to detect visual, auditory or audiovisual targets which appeared below the fixation when a rapid serial visual presentation (RSVP) letter stream was presented above the fixation. The results showed that the P50 component became super-additive in the fronto-central region when the participants attended to audiovisual stimuli. However, a reversed integration pattern, that is, a sub-additive pattern of the P50 component appeared when the RSVP was attended (Talsma et al., 2007). As the P50 component was observed 50 ms after the stimulus, the results supported that multisensory integration occurs at the early stage of processing. Furthermore, when the target of attention changed (RSVP or audiovisual stimuli), the pattern of audiovisual integration changed accordingly (sub-additive or super-additive) indicating the early multisensory integration could be modulated by attention and this early audiovisual integration reflects a sensory gating process that inhibits unrelated information.

Audiovisual integration can also occur in the later processing stage, which is 100-300 ms after the stimulus (Fig. 2.1). Specifically, Teder-saljarvi et al. (2002) demonstrated that the auditory input may modulate the visual information process in the inferior occipital cortex at 130-170 ms after the stimulus. Similar empirical evidence provided by ERP studies showed decreased amplitude in the audiovisual condition compared to the sum of uni-sensory conditions in the extrastriate cortex in the time window of 155-200 ms after the stimulus, which suggested that the auditory information saves the energy for vision in the stimulus discrimination task (Besle et al., 2004). Additionally, the sub-additive pattern can also be observed in the fronto-central region. Specifically, the onset latency of fronto-central N1 and P2 decreased when

visual information from both auditory and visual modalities was provided simultaneously (Giard et al., 1999; Molholm et al., 2002; Stekelenburg et al., 2007; Vidal et al., 2008). Fronto-central P2 is an important marker in the multisensory process. Specifically, a study demonstrated that the amplitude of P2 component became more positive-going in the audiovisual condition compared to the sum of uni-sensory conditions at the fronto-central region when conducting a shape discrimination task, in which the participants were required to discriminate the shape of stimulus (Giard et al., 1999). Similar results were also reported by Molholm et al. (2002) by employing a stimulus detection task, in which the participants were required to press a key as soon as they detected the stimulus. Even in a task without involving motor responses, enhanced amplitude of fronto-central P2 can still be observed in the multisensory condition (Vidal et al., 2008). Another study using a similar task showed the sub-additive pattern of P2 amplitude that is less positive-going P2 in the multisensory condition compared to the sum of uni-sensory conditions (Stekelenburg & Vroomen, 2007). All these studies with different tasks demonstrated P2 modulation when processing audiovisual information, suggesting fronto-central P2 may reflect the genuine auditory-visual integration (Giard et al., 1999; Molholm et al., 2002; Vidal et al., 2008). The reason for the different modulation, that is, some of the studies demonstrated the super-additive pattern of P2 while others showed sub-additive pattern of P2, could be because of the different tasks employed in different studies or the subtraction model that is $(AV+C)-(A+V)$ model. The $(AV+C)-(A+V)$ model was used in Stekelenburg & Vroomen's study (2007) while other studies used the $AV-(A+V)$ model. These two models were used to find the multisensory process and the details of the models as well as the difference between the two models are reviewed later in the "ERP method" section of this chapter.

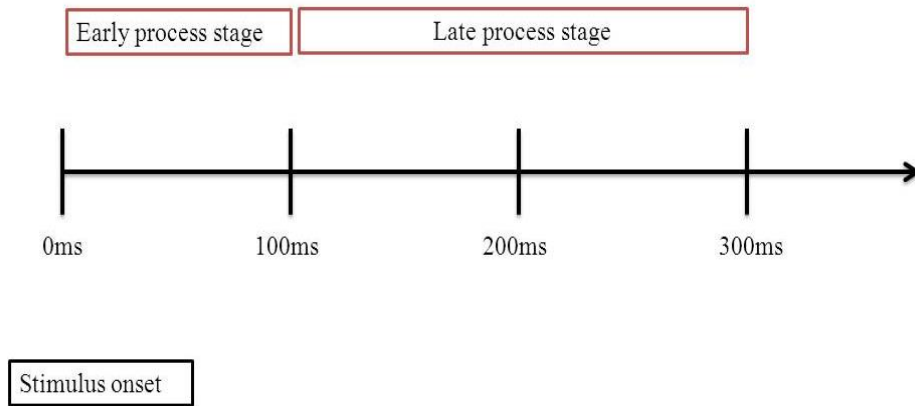


Figure 2.1 Time window of early and late process stages. The figure shows that the early sensory process time window was earlier than 100 ms after the stimulus while the late sensory process time window was from 100 to 300 ms after the stimulus.

The fronto-central P2 could also serve as a marker for the aging effect in audiovisual integration. A MEG study showed the MEG amplitude was different between younger and older groups around 200 ms after stimulus at the STG (Stephen et al., 2010). Specifically, the older group showed super-additive pattern when comparing the amplitude of audiovisual condition and auditory condition ($AV < A$). However, the younger group demonstrated super-additive pattern ($AV > A$). Moreover, the less benefit of behavioral performance in terms of reaction time in the multisensory (audiovisual) condition in older group was correlated with the sub-additive pattern of P2, suggesting the fronto-central P2 acts as a marker of the aging effect in the auditory-visual integration.

In summary, audiovisual integration could be observed from a very early sensory process (<100 ms after the stimulus) to a late process stage (100-300 ms after the stimulus) and the fronto-central P2 serves as an important marker for audiovisual integration. However, most of the studies focused on the multisensory integration effect in younger adults, and seldom evidence has demonstrated the modulation of multisensory integration in older adults.

2.2.2 Audiovisual integration in the response selection process

In the response selection process of audiovisual integration, in which the identified stimulus is mapped to a certain response (Keus et al., 2005; Woodward et al., 2014), insufficient evidence has been provided (Bockler et al., 2011; Fischer et al., 2007; Hackley et al., 1999; Saldern & Noppeney, 2013). Lots of behavioral studies with the aim of investigating the effect of providing sound simultaneously with visual stimuli demonstrated that when accessory sound which contains no task-related information provided prior to or simultaneously with visual stimuli, the response time decreased (Bockler et al., 2011; Fischer et al., 2007; Kiesel & Miller, 2007). Specifically, Kiesel and

Miller (2007) measured simple reaction time using a go-no go task with an accessory auditory signal presented. The task manipulated the contingency between accessory sound and response or stimulus conditions. The results showed that accessory sound can decrease the response time to a larger degree when the contingency in the response changes, suggesting the accessory sound provided simultaneously with visual stimulus can facilitate the response selection process (Kiesel and Miller, 2007). Neurophysiology evidence demonstrated that the onset latency of stimulus-locked LRP (s-LRP) becomes earlier when accessory sound is provided simultaneously with or prior to visual stimuli compared to the visual only condition, suggesting accessory sound can facilitate the early phase of response selection (Jepma et al., 2009). Also, the activation of both the contralateral and ipsilateral motor cortex increased when accessory sound is provided indicating the accessory sound activates both motor cortices but cannot activate the motor cortex contralateral to the response hand selectively (Jepma et al., 2009). However, the sound without task-related information may only serve as a cue that prepares the sensory and motor system for the coming stimuli so the studies with accessory sound as auditory stimulus may not be able to investigate the audiovisual integration (Los & Burg, 2013). To the author's best knowledge, no ERP evidence demonstrates the effect of congruent audiovisual integration in the response selection process. However, a neuroimaging study provided indirect evidence suggesting the audiovisual integration modulates the motor preparation process (Saldern & Noppeney, 2013). In Saldern and Noppeney's (2013) study, a disc moving from one side to the other (left or right) was used as the visual stimulus, and moving sound contained congruent direction with the motion of the disc was employed as the auditory stimulus. During the experiment, the participants were required to discriminate the direction of stimuli-moving based on visual, auditory or audiovisual information. The results demonstrated that the putamen with the function of mapping sensory inputs onto an overlearned response (Lehe'ricy et

al., 2004) can be activated when auditory and visual information is received simultaneously (Saldern & Noppeney, 2013). Whether congruent auditory visual information provided simultaneously can influence the response selection phase still remains unanswered and this thesis will address this literature gap.

2.2.3 Audiovisual integration in the response generation process

Few studies have demonstrated the multisensory integration in the response generation process in which the motor response is produced. Evidence showed when receiving both accessory sound and visual stimulus simultaneously, the response force increased compared to the uni-sensory condition (Kiesel & Miller, 2007; Stahl & Rammsayer, 2005). For instance, Kiesel and Miller (2007) measured the simple reaction time using a go-no go task with an accessory auditory signal presented. In this study, the participants were required to press a force-sensitive key when the visual stimuli were presented and the force of response was recorded. The results demonstrate that the response force increased in the multisensory condition compared to the uni-sensory condition. However, as mentioned above, the accessory sound may only play a role to increase the attention level (Los & Burg, 2013). Hence, whether congruent auditory and visual information provided simultaneously can influence the response generation process still remains unanswered and this thesis will address this literature gap.

2.2.4 Brain regions involved in the audiovisual integration process

The previous section reviews the audiovisual integration in different process stages and this section focused on the brain regions involved in audiovisual integration, including the primary cortex, heteromodal cortex which receives and processes information from various modalities as well as sub-cortical regions.

2.2.4.1 The role of the primary cortex in the audiovisual process

By comparing the multisensory condition (e.g. audiovisual) and the sum of uni-sensory conditions (e.g. auditory + visual), neuroimaging studies demonstrated that the primary visual and auditory cortex can be activated during multisensory integration (Ciaramitaro et al., 2007; Saldern et al., 2013). For example, when conducting a stimulus discrimination task, the visual cortex V5+ (Ciaramitaro et al., 2007; Saldern & Noppeney, 2013) and primary auditory cortex (Lewis et al., 2000) can be activated (Klemen et al., 2009, 2010). Specifically, in Saldern and Noppeney's (2013) study, the participants were required to discriminate the moving direction of a disk or a sound or both. The results demonstrated that when compared with the sum of uni-sensory conditions, visual motion areas hMT+/V5+ were activated when receiving audiovisual information simultaneously, suggesting the participation of the primary visual cortex in the audiovisual integration.

2.2.4.2 The role of the heteromodal cortex in the audiovisual process

Most of the association cortices, such as the STG, IPL and PPC which were previously believed to process uni-sensory information serve as a convergence and integration region for the audiovisual information (Atteveldt et al., 2004; Beauchamp et al., 2004). Some regions in the temporal cortex serve as heteromodal cortex, involved in integrating information from various modalities. For example, a fMRI study employed a task which used pictures of objects in different categories as visual stimuli (e.g. a cat) and the sound of that object (e.g. "meow") as auditory stimuli (Beauchamp et al., 2004). The results showed an increased activation level in the posterior superior temporal sulcus (pSTS) when receiving both visual and auditory information simultaneously compared to the

condition of receiving information from only one modality, suggesting that the STS can process information from both auditory and visual modalities as well as integrating the information across modalities (Beauchamp et al., 2004). Similarly, the STG has also been reported to be a heteromodal region responsible for multisensory information computation (Wassenhove et al., 2005).

In addition to the temporal cortex, the parietal cortex is involved in the temporal and shape information process when receiving audiovisual information. Two regions play an important role in audiovisual integration, which are the IPL (Baumann et al., 2007; Dhalama et al., 2007; Saito et al., 2005) and PPC (Amedi et al., 2007; Saito et al., 2005). Specifically, the IPL is involved in the audiovisual temporal information process. A fMRI study demonstrated that the IPL is activated when asynchronous audiovisual information is provided suggesting the role of processing asynchronous audiovisual signals in this region (Dhalama et al., 2007). The PPC is regarded as a region related to shape information processing when receiving multisensory information (Amedi et al., 2007). In a fMRI study, the participants were required to decide if the vowels presented by a human face (visual stimuli) and the vowels they heard (auditory stimuli) were congruent. The task involved three conditions, which were auditory-auditory, visual-visual and auditory-visual condition (Saito et al., 2005). The results showed the bilateral posterior parietal cortex could be activated more in the auditory-visual condition compared with auditory-auditory and visual-visual condition indicating that the PPC serves as a region discriminating the shape when receiving visual and auditory information (Saito et al., 2005).

In summary, the association areas such as the STG, IPL and PPC serve as a heteromodal cortex involved in multisensory integration and each of them is responsible for different functions.

2.2.4.3 The role of the subcortical regions in audiovisual processing

Besides the cortical regions reviewed previously, a number of subcortical regions have also been demonstrated to be involved in audiovisual integration. Evidence showed both the superior colliculus (Dhamala et al., 2007) and putamen (Olson et al., 2002) can process temporal information in multisensory integration. Specifically, the superior colliculus has been reported to contain neurons receiving both auditory and visual information input (Stein & Meredith, 1993). Dhamala et al. (2007) used fMRI further demonstrated that the superior colliculus could be activated when the participants perceived physically synchronized auditory and visual stimuli, suggesting superior colliculus is involved in processing temporal information in audiovisual integration. Similarly, Olson et al. (2002) demonstrated that when receiving synchronized visual and auditory information the putamen can be activated indicating the putamen serves as a timer to signal synchronized visual and auditory information. The thalamus is another important structure for multimodal processing, which acts as a gatekeeper to expel irrelevant information or distractors (Baier et al., 2006).

The enhanced behavioral performance observed in multisensory integration could also be related to the contribution of the sub-cortical regions. Specifically, both the superior colliculus and thalamus can contribute to the decreased reaction time in multisensory integration (Cappe et al., 2009) and the increased accuracy rate was reported to be related to the contribution of the putamen (Gonzalo et al., 2000; Mayer et al., 2009). For example, Cappe et al. (2009) argued that the decreased reaction time is related to the thalamic-cortical loop. As the thalamus is a relay station for numerous cortical areas (Gutierrez et al., 2000), the rapid multisensory response may be related to the thalamic-cortical

loop which conveys the multisensory information rapidly to the premotor cortex which is responsible for motor preparation (Cappe et al., 2009). In summary, rather than synthesizing multisensory information which is the responsibility of the cortical areas, the most important function of the subcortical regions is to play the role of relay stations to increase the sensory-motor process speed and accuracy rate in multisensory integration.

2.3 Aging effect in the attention and central motor process

Studies showed older adults suffer attention degeneration (Jennings et al., 2007; Mahoney et al., 2011). Furthermore, studies demonstrated that P2 can serve as a marker of attention deficit (Barry et al., 2009; Ceponiené et al., 2005; Lijffijt et al., 2009; Treder & Blankertz, 2010; Wild-Wall & Falkenstein, 2010). For example, Barry et al. (2009) demonstrated that when conducting a cross auditory-visual odd-ball task, the participants with attention deficit demonstrated an increase of P2 amplitude compared to normal controls. According to the decreased attention function in older adults, the enhanced behavioral performance when receiving multisensory information in older adults could be the consequence of the declined selective attention compared with younger adults which makes them integrate everything they get from the environment. However, empirical evidence showed this was not the case (Hugenschmidt et al., 2009). Hugenschmidt et al. (2009) demonstrated that in a stimuli discrimination task with cues, the older participants demonstrated enhanced behavioral performance compared to their younger counterparts in both selective attention and divided attention conditions. However, the older participants still showed reduced integration in the select attention condition similar to their younger counterparts indicating that the increased benefit from multisensory integration in older adults is not related to attention deficit (Hugenschmidt et al., 2009). Although the enhanced behavioral performance was not related to the decreased

top-down suppression, which means integrating everything together, whether the attention function can modulate multisensory integration within an older group still remains unclear and this thesis will address this literature gap.

Besides attention function deficit, older adults demonstrate deterioration in visual and auditory organs as well as decreased ability of visuospatial and auditory localization (Dobrevá et al., 2011; Drag et al., 2016; Lorenzo-Lopez et al., 2008; Otte et al., 2013; Pesce et al., 2005). However, evidence showed that when conducting choice reaction tasks, the main reason for the prolonged sensorimotor process in older adults was related to the generation of motor response (Roggeveen et al., 2007; Falkenstein et al., 2006; Yordanova et al., 2004). Furthermore, an ERP study (Kolev et al., 2006) showed no significant difference between younger and older adults in s-LRP onset latency which reflects the response selection process, while a significant difference of r-LRP onset latency was found. These findings suggest that the motor generation process contributes to the increased reaction time in older adults. The more negative-going r-LRP amplitude in the older group when compared to their younger counterparts has also been reported in previous studies (Amenedo et al., 2014; Wiegand et al., 2013). Specifically, a study which used a visual search task demonstrated that the r-LRP was significantly delayed and pronounced in the older group (Wiegand et al., 2013). The more negative-going r-LRP in older adults could be related to the increased activation in the contralateral motor cortex (Kolev et al., 2006; Yordanova et al., 2004). Specifically, the excitability of the contralateral motor cortex in older adults is decreased (Peinemann et al., 2001), so a higher level of activation is needed in the primary motor cortex which is the generator of the LRP (Kolev et al., 2006; Yordanova et al., 2004). Taken together, these results implicate that the decreased excitability level in the motor cortex contralateral to the response hand contributed to the more negative-going r-LRP amplitude and further increased the reaction time. A

previous fMRI study also demonstrated that when performing a simple motor task, additional motor-related areas are recruited in older adults indicating less effective activation of the primary motor cortex (Mattay et al., 2002). The structural change in the brain of older adults could contribute to this kind of functional deficit, such as gray matter and white matter volume decrease (Courchesne et al., 2000) and cerebrospinal fluid volume increase (Dekaban, 1978). A recent fMRI study also demonstrated that both functional and structural change in older brains contributes to the declined motor performance in older adults (Stewart et al., 2014). Specifically, increased activation in the dorsal premotor cortex and declined white matter tracts in connection with the sensorimotor was observed in older adults when performing an action selection task in which the participants were required to move a joystick to the left or right according to the shape or size of the cue. These structural changes could cause functional changes and further increase the reaction time and decrease the accuracy rate of older adults.

2.4 Neurophysiology methods employed in this thesis to investigate the multisensory integration effect as well as aging effect

2.4.1 EEG method

Electroencephalography (EEG) is a noninvasive neurophysiology method which can record electrical activity in the brain by placing electrodes on the scalp to measure the voltage fluctuation caused by ionic flow in neuron activation (Niedermeyer & Silva, 2004). The event-related potential (ERP) which includes the marker of some critical time points, for example, the onset of stimuli and response, can separate different neural processes by averaging and other sophisticated techniques (Luck, 2014). The $[(AV+C)-(A+V)]$ model has been widely used in multisensory studies and this thesis also employed this model so the $[(AV+C)-(A+V)]$ model is reviewed in the next section. This thesis

also employed a test of significant potential difference which is widely used in multisensory studies, so this kind of significance test is also reviewed. Furthermore, to test the aging effect in motor process, lateralized readiness potential was employed as the marker for response selection (s-LRP) and response generation (r-LRP). Therefore, the following three sections review 1) the ERP analysis method commonly used in multisensory study in the sensory process stage; 2) the significant testing of potential difference; and 3) the component used to analyze the motor process stage that is the LRP.

2.4.2 [AV-(A+V)] and [(AV+C)-(A+V)] model in multisensory ERP study

The [AV-(A+V)] model was firstly used by Barth et al. (1995) in animal studies. Barth et al. (1995) used this method to find a region which exclusively responds to a multisensory stimulus. In this model, AV represents the neural response in the multisensory condition, for example, audiovisual condition; A and V represent the neural response in the uni-sensory condition, for example, A for auditory only and V for visual only. Hence, the assumption of this model is: “if subpopulations of cells that respond separately to auditory and visual stimulation do not respond uniquely to multisensory stimuli, their contribution to the multisensory signal will be the linear sum of their contributions to the auditory and visual signal respectively”. After subtracting the sum (A+V) from multisensory condition (AV), the model [AV-(A+V)] can be obtained. The [AV-(A+V)] model can be used to distinguish brain regions that are uniquely activated by multisensory stimulation (Barth et al., 1995).

The AV-(A+V) model has been widely used in ERP, MEG and fMRI studies to analyze data related to multisensory integration (Klucharev et al., 2003; Laurienti et al., 2005; Möttönen et al., 2004; Senkowski et al., 2005). However, this model has received some criticisms because of the biases in the

computation (Calvert & Thesen, 2004; Teder-Salejarvi et al., 2002). These biases can be limited by a number of manipulations (Besle et al., 2004). The first bias caused by this model is that the common activity has been added twice in (A+V) but only subtracted once in the formula. The common activity includes different types, such as target processing, response selection or motor process (Hillyard et al., 1998). Therefore, adding a no-stimulation condition can limit this bias, which was employed by a lot of ERP studies to subtract the common activity (Gondan et al., 2006; Mishra et al., 2007; Talsma et al., 2005). In other words, the adjusted formula became $[(AV+No-stim)-(A+V)]$. By adding this no-stimulation condition, some of the common activities, for example target processing could be canceled out. However, the motor process-related activity cannot be canceled out because the no-stimulus condition requires no motor response. A recent fMRI study added a control condition which only contained auditory and visual noise and changed the formula into $(AV+C)-(A+V)$ which can remove most of the common activity effectively (Saldern & Noppeney, 2013). Different from the no-stimulaton condition, the control condition requires a motor response. Specifically, the participants are required to provide a random response in the control condition. Therefore, this model may cancel out the motor process-related activity. As this research adopted a similar study design as in Saldern and Noppeney's study (2013), the $[(AV+C)-(A+V)]$ model was employed.

2.4.3 Significance testing of potential difference

As reviewed in the previous section, the $[(AV+C)-(A+V)]$ model has been widely used in multisensory studies to find the time window and region for the multisensory process. This model compares the difference between two ERP waveforms, which are (A + V) and (AV + C), with paired t-test. However, the comparison at each time point cannot be generalized to other adjacent points.

Therefore, the paired t-test was performed at each electrode and each time point resulting in hundreds of paired t-tests being performed. If Bonferroni correction is conducted to correct the significance level, the statistical power can be decreased. Hence, Guthrie and Buchwald (1991) provided a method to compromise this deficit, which tested whether there is some interval of statistical significance of the potential pairwise difference that may have arisen by chance alone.

In this method (Guthrie & Buchwald, 1991), each point in the ERP waveform is regarded as correlated with the adjacent points and the correlation is regarded as autocorrelation. By taking the autocorrelation, sample size as well as the length of series into consideration, the authors calculated the significant length. To achieve a higher statistical power, the authors also suggested cutting down the epoch to a shorter length, for example, 300-500 ms (Guthrie & Buchwald, 1991). This method has been widely used in multisensory studies (Stekelenburg & Vroomen, 2007; Vidal et al., 2008). Therefore, the thesis used this consecutive time-point method to analyze the ERP data to reduce Type I errors (Guthrie & Buchwald, 1991).

2.4.4 Lateralized readiness potential (LRP)

As the LRP is a component that reflects the response selection and generation process which are the process investigated in this thesis, the LRP is reviewed in this section. The LRP is a negative-going potential which can be observed over the motor cortex. It is widely used to measure the time point at which the brain starts to prepare the motor output (Frame et al., 2014; Jepma et al., 2009; Masaki et al., 2004; Van Vugt et al., 2014). The LRP can be calculated by double subtraction with the formula: $\{[C4' (t) - C3' (t)] \text{ left hand} + [C3' (t) - C4' (t)] \text{ right hand}\} / 2$ (Coles, 1989). Evidence showed the generator of the LRP

can be the primary motor cortex (Coles, 1989; Leuthold et al., 2002) or premotor cortex (Sterr & Dean, 2008). As the onset of the LRP can reflect the completion of hand selection and the start of motor programming (Masaki et al., 2004), the LRP can be used to assess the motor process. According to the different zero time point selection, the LRP can be categorized into the stimulus-locked LRP (s-LRP) in which the equation can be calculated for time points relative to the stimulus onset (Luck & Kappenman, 2012). The latency between the stimulus and the s-LRP onset reflects the duration of stimulus processing before the response activation which includes the whole sensory process and part of the motor process (Luck & Kappenman, 2012). Similarly, the response-locked LRP (r-LRP) in which the equation can be calculated for time points relative to the response onset (Luck & Kappenman, 2012). The latency between the r-LRP onset and response onset can represent the response activation and peripheral motor process (Luck & Kappenman, 2012). As the LRP amplitude is computed as the difference of activity between the contralateral and ipsilateral motor cortex to the responding hand, it can reflect the evidence accumulation in the motor cortex until one of the response options outweighs the other (Jepma et al., 2009; Van Vugt et al., 2014). Therefore, a more negative-going LRP amplitude can indicate a higher level of competition between the two options at the motor cortex level (Frame et al., 2014).

2.5 Rationale and hypothesis of this thesis

As reviewed above, although older adults can benefit more from receiving multisensory information simultaneously, empirical evidence for the underlying mechanism is still not well investigated. Based on previous findings, we assume that older adults may benefit from multisensory integration in perceptual and feedback processes as well as at the response generation process. In order to address the literature gap, the aim of this thesis is to explore the aging effect of

audiovisual integration in both sensory and motor processes when receiving congruent multisensory information simultaneously. Two studies are reported in this thesis. The aim of the first study was to validate the task and investigate if audiovisual integration can influence response selection and generation processes as a consequence of modulation in the perceptual and feedback processes. In this study, only younger adults with the mean age of 24.9 were recruited to replicate the results of previous multisensory studies. It was hypothesized that 1) enhanced behavioral performance can be observed in multisensory condition indexed by increased accuracy rate compared to the uni-sensory conditions; 2) in the perceptual and feedback processes, a sub-additive pattern of P2 could be observed in the fronto-central region; 3) the response selection process can be modulated by multisensory integration indexed by decreased onset latency of the s-LRP, but the response generation stage cannot be modulated by multisensory integration. To test these hypotheses, both of the younger and older participants should indicate the direction of the visual and/or auditory stimuli by wrist extension or flexion. The EEG and EMG data were recorded during the whole task. The aim of the second study was to investigate the impact of aging on multisensory integration from perceptual and feedback processes to response selection and generation processes. It was hypothesized that 1) older participants can benefit more in behavioral performance from multisensory integration compared to their younger counterparts indexed by increased accuracy rate and reaction speed; 2) the multisensory integration can modulate the perceptual and feedback processes indexed by fronto-central P2 and response generation process indexed by r-LRP differently between younger and older groups; 3) the increased gain in behavioral performance in older group is related to the fronto-central P2 modulation in perceptual and feedback processes as well as r-LRP modulation in response generation process. To test these hypotheses, older adults were recruited in the second study with the mean age of 67.7 years. The task that is

the same as the task in the first study was employed in the second study and EEG as well as EMG data were collected during the whole task.

CHAPTER THREE

GENERAL METHODS

As this thesis reports two studies with similar methods, such as the EEG and EMG measurement, the methods used in both of the studies are presented in this chapter. To provide an overview of the thesis, the overall study design is firstly introduced followed by the characteristics of the participants, pre-experiment and main experiment tasks as well as the procedures of both studies. EEG and EMG data acquisition and analysis used in both studies are discussed at the end of this chapter.

3.1 Overall study design

Two studies are reported in this thesis. The first study (Study 1, Chapter 4) recruited healthy younger participants and the aim of this study was to build a neural mechanism model of audiovisual integration for healthy younger adults and validate the task used in this thesis. The second study (Study 2, Chapter 5) recruited healthy older participants and compared the different neural processes of audiovisual integration between the healthy younger participants recruited in the first study with the aim of investigating the impact of aging in audiovisual integration. Both studies investigated the effect of multisensory integration on perceptual and feedback processes as well as the consequent influence on the response selection and generation processes. The paradigm used for both groups was the same and the intensity of stimuli was calibrated at the individual level.

3.2 Participants

Twenty-nine healthy younger adults (16 males (55%), aged 19 - 30 years old with the mean age of 24.9 years) and thirty-four healthy older adults (12 males (35%), aged 60-78 years old with the mean age of 67.7 years) were recruited. The younger participants were recruited from local universities and the older adults were recruited from the local community. All of the participants had intact visuospatial and auditory-spatial ability tested by auditory and visual calibration as outlined below (see “Pre-experimental task” section). The visual acuity or corrected visual acuity was tested by a standard logarithmic visual acuity chart test (> 0.8). The exclusion criteria were: 1) suffering from severe major chronic diseases, including stroke or other neurological deficits; and 2) had long-term or professional training in playing musical instruments which may strengthen the connection between the auditory and motor cortex (Zatorre et al., 2007). The cognitive ability of the older participants was tested by Montreal cognitive assessment (MoCA) Hong Kong version and older participants with a score lower than 22 were excluded ($n=2$ participants). One older adult was also excluded from Study 2 because the accuracy rate in the auditory condition in the experimental task was close to chance level, that is 0.25 (accuracy rate = 0.26). Hence, the data of 29 younger adults and 31 older adults in the two studies were analyzed. Both studies passed the human subjects ethics approval from the Human Subjects Ethics Application Review System of the Departmental Research Committee (HSEARS20140627001).

3.3 Pre-experimental task

In this pre-experimental task section, both auditory and visual stimuli were included.

3.3.1 Auditory stimuli

The auditory stimuli used in the study were generated from the electronic “Bat-ears” device developed by He and Chan of The Hong Kong Polytechnic University (Chan et al., 2012). The device cued the position of a target in left-right and near-far directions in terms of the intensity and pitch of the stereo tone (a “da da da” sound), which was emitted in the audible frequency range by a pair of earphones. In particular, the “Bat-ears” device involved an emitter component for emitting ultrasound, a receiver component for detecting ultrasound bounced back from the objects in the environment and a transformer that converted the detected ultrasound into an audible cue. The spatial information embedded in the “Bat-ears” sounds are distances (far or near) and directions (right or left). The sounds used in the experiment were recorded from echoes reflected from obstacles located at near (1 m) and far (4 m) distances with the azimuth of 45° and 135°. These gave a total of four different categories of sounds: left-far (azimuth 135°, 4 m), right-far (azimuth 45°, 4 m), left-near (azimuth 135°, 1 m), and right-near (azimuth 45°, 1 m). All the auditory signals were presented by an earphone. The “Bat-ears” sound with no lateralized spatial information (azimuth 0°, 1 m) was used as the control sound. The pitch of “Bat-ears” sound fell in the range of 2600-4900 Hz and the range of intensity was 30-55 dB (Tao, 2015; Tao et al., 2015).

All participants were involved in a pre-experiment session to ensure that they could discriminate the auditory stimuli as well as to calibrate the difficulty level to 0.75, which means the accuracy rate reached 0.75. Participants in the younger and older groups had different level of performance in the experimental tasks. In particular, the declined visual and auditory perceptual sensitivity of the older participants may have resulted in inverse effectiveness (Bell et al., 2005; Stanford & Stein, 2007; Stein & Stanford, 2008), which could bias the results (Laurienti et al., 2006; Stephen et al., 2010). To tackle the potential

between-group differences, the difficulty levels of perceiving the auditory and visual stimuli were set at 75% (or 0.75) for both the younger and older groups. The setting of this difficulty level could also encourage the participants to concentrate on the task which further increased the signal to noise ratio of the EEG signals. Two sessions were conducted in the pre-experiment task and in the first session of auditory pre-experiment task, the participants were required to discriminate the “Bat-ears” sound which presented 1000 ms via earphone. The response should be provided by pressing a designated response pad on the response device with wrist extension or flexion. Only when the accuracy rate achieved 75% or above could the participants begin the next auditory pre-experiment session. This was based on participants taking a total of 40 trials with 10 trials for each of the four directions. The only difference between the first session and the second session was the duration of sound presentation. Specifically, the duration of sound presentation was cut down to 500 ms in the second session. The whole auditory pre-experiment session ended when the accuracy rate reached 0.75 in the second session. Based on the data in the pilot study, the participants who failed to pass the auditory pre-experiment within one hour were excluded from the study.

3.3.2 Visual stimuli

A Gaussian visual noise board was placed at the background to build 3D space. An arrow was placed in the 3D space within the foveal region with the internal edge of 0.7° , external edge of 1.7° and the center point of 1.2° in the visual field to facilitate the participant to have a clear view of the visual stimuli as well as to control their eye movement (Bargh & Chartrand, 2000). The arrow head was oriented in four directions: left-far (135°), right-far (45°), left-near (225°), and right-near (315°). To be comparable with the auditory difficulty level, the arrow was blurred to the difficulty level of 0.75 which means the accuracy

rate reached 0.75 (see below). The blurriness level of the visual stimuli (arrows) was fabricated by Photoshop software (version CS3 10.0; Adobe Systems) so as to increase the difficulty in perceiving the direction to be indicated by the visual image of the arrow: 0 represents totally blurred, while 100 represents totally clear. As the pilot study showed that the blurriness level was in the range of 25 to 90 to achieve the difficulty level of 0.75, this range was used in the visual pre-experimental task in both studies in this thesis.

In the visual pre-experimental task, the participants were also required to discriminate the direction of the arrow head which was presented for 500 ms. The visual pre-experimental task ended when the participants' accuracy rate on perceiving the visual images of the arrow reached 0.75. Similarly, there were 40 trials. The levels of blurriness of the visual stimuli ranged from 30 to 60 (mean = 35) for the younger group and 40 to 90 (mean = 75) for the older group.

3.4 Main experimental task used in both Study 1 and Study 2

Four conditions were involved in the audiovisual spatial discrimination task: auditory condition (A, uni-sensory), visual condition (V, uni-sensory), audiovisual (AV, multisensory) as well as the control condition (C) (Figure 3.1C). In the A condition, the auditory stimuli ("Bat-ears" sound) were presented simultaneously with the visual noise board and the participants were required to give a response only based on the spatial information provided by the "Bat-ears" sound, while in the V condition, the visual stimuli (arrows) were presented simultaneously with the control sound and the participants were required to give a response only based on the spatial information provided by the arrow. In the AV condition, the visual stimuli and auditory stimuli were presented simultaneously, and the participants had to attend to both "Bat-ears" sound and arrows. As the stimuli from both modalities always contained congruent spatial information in the experimental task, the participants had to give a response after

perceiving the spatial information embedded in both visual and auditory stimuli. In the C condition, the visual noise board and the control sound were presented simultaneously, and the participants were required to touch any of the response pads as quickly as possible.

In each trial, the uni-sensory or multisensory stimuli were presented for 500 ms after a white cross served as a fixation for 2,000 ms (ranging from 1,440 ms to 2,560 ms). After encoding the spatial information embedded in the uni-sensory or multisensory stimuli, the direction of both auditory and visual stimuli should be indicated by the stimuli by 30° wrist extension or flexion within 4000 ms (Figure 3.1B). Extension indicated far distance and flexion indicated near distance while the left and right hand indicated the left and right direction. For example, right wrist flexion meant right-near and left wrist extension indicated left-far. In this study, the method used for registering the participants' responses in the task was by means of movements in the wrists (extension and flexion) rather than pressing keys on a keyboard. The main reason was that responses by movements in the left and right wrists, and extension and flexion, would be more direct for representing the left or right direction of the stimuli, as well as their far or near orientation. In here, the "far" was represented by an "extension" movement in the wrist, while the "near" was represented by a "flexion" movement in the wrist. If the pressing the key method had been adopted, the participants would have been required to couple each of the four keys with the specific direction and orientation of the stimuli. In the pilot study, participants with similar demographic characteristics with those in the main study were asked to use the keyboard or joystick methods. The experiences gained from the pilot study were that the both methods required more intense and lengthy training and resulted in lower accuracy rates when compared with the wrist movement method. The joystick method was found to produce excessive interferences to the EEG signals because of the associative

shoulder movements involved. Another reason for choosing the wrist movement method was that it would have been consistent with the focus of the study, which is on response selection and generation. The main experimental task involved eight blocks with four conditions, which were the A, V, AV and C conditions, randomly presented in each block. The total number of trials was 896 and each condition contained 224 trials. The participants needed approximately 2.5 hours to complete the whole experiment.

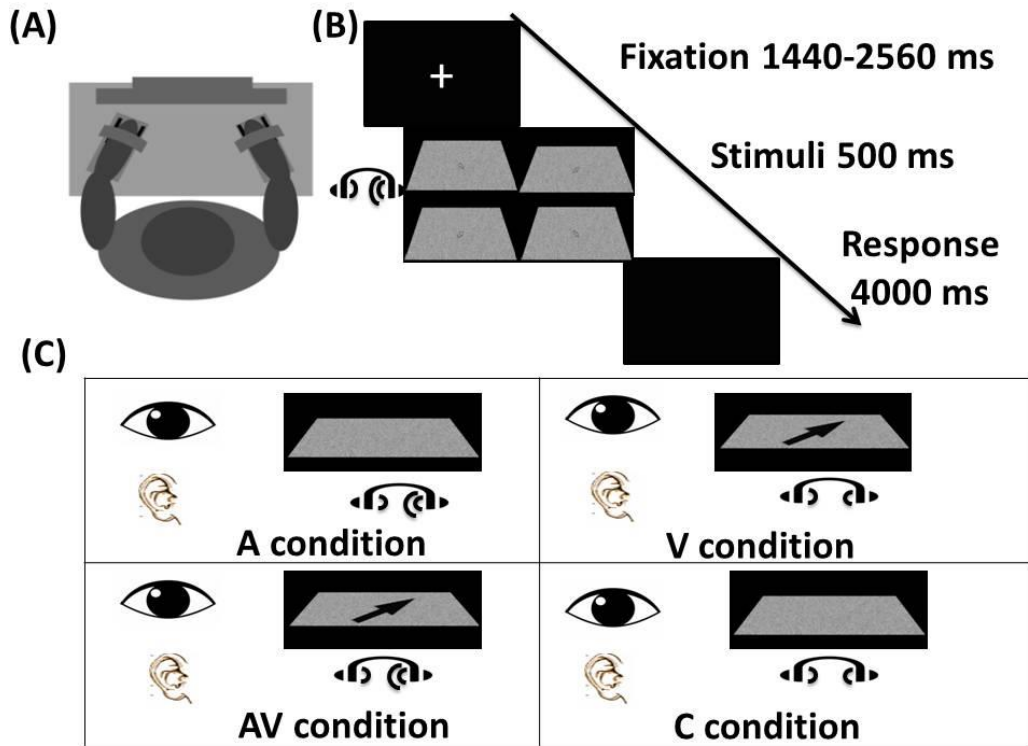


Figure 3.1 Experimental procedure and conditions for both Study 1 and 2. (A) The participant sat comfortably in front of a screen with both of his/her forearms on the response device placed on the desk which was adjusted to elbow height. Both hands were placed between the two plastic keys which were used to give responses. The distance between the eyes and the screen was adjusted to 80 cm. **(B)** The procedure of the experiment. The arrows used in the experiment as the visual stimuli showed the direction of left-far, left-near, right-far and right-near. **(C)** Four conditions of the main experimental task. The arrows were clear and enlarged for the sake of reading.

3.5 Procedures in both Study 1 and Study 2

The participants sat comfortably in a dim and soundproof room with the monitor placed 80 cm from their eyes. The participants were required to put both of their forearms on the response device which was placed on a height-adjustable table. Their forearms were required to be in a neutral position with elbow flexion of 90° and shoulder internal rotation. As excessive movement would produce potential artifacts in both EEG and EMG data, both of the participants' forearms were stabilized on the response device with straps to reduce redundant movements. The response device was made of two wooden boards on which the participants could place both of their forearms. Two plastic keys with the size of 5 cm × 3 cm were placed on one end of each wooden board serving as response pads which were connected to the computer to record response time as well as response type. The response pads were parallel to each other and perpendicular to the wooden board. The two response pads were approximately 2 cm apart and the distance was adjustable to fit the thickness of the palms of participants (Figure 3.1A & Figure 3.2). As the response device was connected to the computer, when the response pad moved 10°, the response time and response type (right-near, right-far, left-near or left-far) which related to the accuracy rate could be recorded by the computer. Before the commencement of each block, the participants were provided the specific instructions of the task. They were required to give responses based on the spatial information embedded in the stimuli as accurately and as quickly as possible. After providing a response, the participants had to move their wrist back to the neutral position immediately before the next trial started.

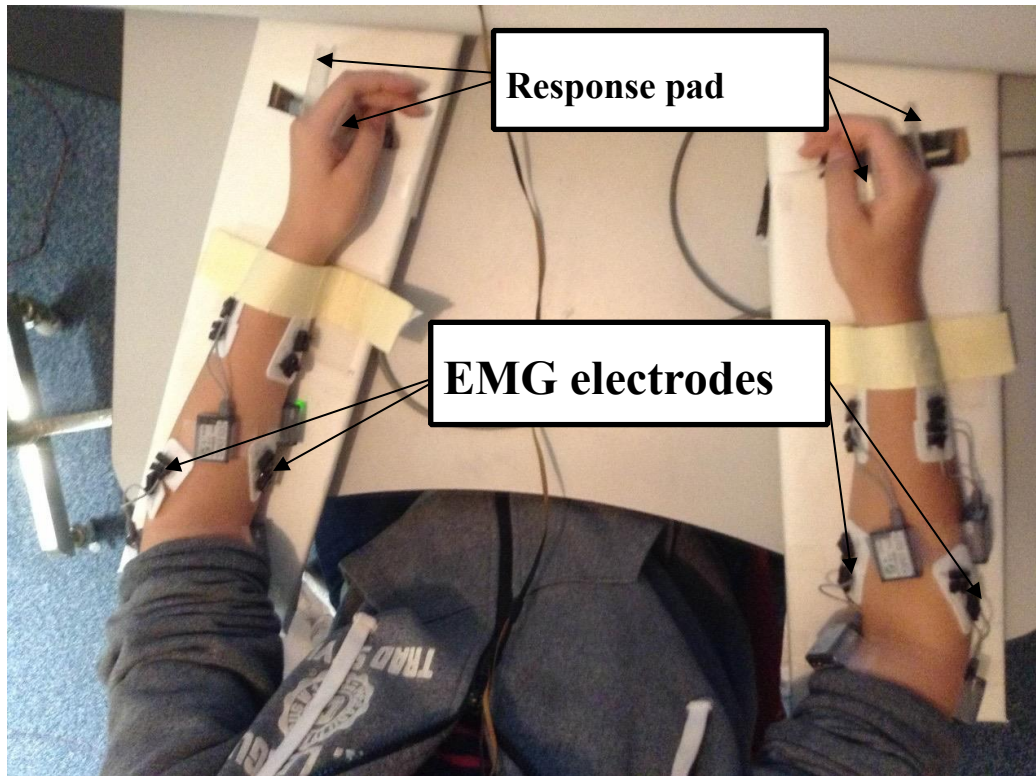


Figure 3.2 Setup of the experiment for both Study 1 and Study 2: The response device and the placement of EMG electrodes. The straps were used to eliminate the forearm movements. Two response pads were placed at both sides of the hands and the participants had to respond by pressing the associated response pad with wrist flexion or extension.

3.6 Data acquisition and pre-processing

Both Study 1 and Study 2 employed EEG and EMG measurement and the same pre-processing procedure was also employed for both studies. Therefore, the following were applicable to both Study 1 and Study 2.

3.6.1 EEG data acquisition and pre-processing

Event-related potential (ERP) data were captured by NuAmps Digital DC EEG Amplifier with 64 channels using Curry 7 software (CURRY 7 EEG Acquisition and Analysis Software, Compumedics Neuroscan USA Ltd) in a sound-proof chamber. EEG signals were amplified and digitized at a sampling rate of 1024 Hz. The montage was referenced to the right ear lobe electrode. A ground electrode was placed on the forehead. Reference impedances were set below 5 K Ω . All inter-electrode impedances were maintained below 5 k Ω . Vertical and horizontal electro-oculograms (EOGs) were recorded by two pairs of electrodes to monitor eye movements.

Only trials with correct response were analyzed. The EEG data preprocessing was conducted using Curry 7, including re-referencing the data to half of the M2 electrode, baseline correction of the data using a time window between -200 ms and 0 ms before stimulus presentation. Digital band-pass filter was used with the range of 0.1-30 Hz. The criterion of eye movements was set as ± 100 μ V in both of the horizontal and ventral EOG channels and the EEG data was corrected with a regression algorithm when an eye movement is detected. Epochs were cut from -200 ms to 1000 ms from the onset of each stimulus and those with amplitude larger than 100 μ V were discarded from the analysis. The epoched ERP data which were time-locked to the stimulus were averaged in each condition for each electrode.

3.6.2 LRP data pre-processing

For the pre-processing of the EEG data for motor-related process analysis, that is the LRP component analysis, similar pre-processing methods used for the EEG data of the sensory process were employed, such as baseline correction, filtering and eye movement correction. The s-LRP was calculated with the stimulus onset as reference and the r-LRP was calculated with the response onset as reference (Luck & Kappenman, 2012). Therefore, the epochs for the s-LRP were cut from -200 ms to 2000 ms from the onset of stimulus and the epochs for the r-LRP were cut from -1000 ms to 200 ms from the onset of a response. All the epochs with amplitude larger than 100 μ V were discarded. The epoched data were averaged in each condition for C3 and C4 electrodes. After averaging the ERP data, the LRP was calculated with the formula $\{[C4'(t)-C3'(t)]_{\text{left hand}} + [C3'(t) - C4'(t)]_{\text{right hand}}\}/2$ (Coles, 1989).

3.6.3 EMG data acquisition and pre-processing

The EMG signals were collected from four forearm muscles which control the hand and wrist movements: right/left extensor carpi radials (ECR) and right/left flexor carpi radials (FCR) (Figure 3.2). The EMG signals were collected by the Noraxon Telemetry 2400T G2 System (Noraxon, USA Inc. USA) with the sampling rate of 1500 Hz. Bipolar Ag/AgCl surface electrodes (White Sensor, Ambu WS, India) with the diameter of 36 mm were put on each muscle to be measured. The inter-electrode distance was standardized at 2 cm. The hair in the electrode placed area was removed to improve the electrodes' adhesion. To decrease the skin impedance, dead skin cells were also removed by conductive cleansing gel. An alcohol pad was used to further decrease the skin impedance before collecting EMG data. The electrodes were placed on the muscle bulk along the muscle fibers based on Criswell (2010), Perotto et al. (2004) and Gustafsson et al. (2008).

The EMG data were pre-processed with the Noraxon Telemetry 2400T G2 System (Noraxon, USA Inc. USA). All the data were visually examined before filtering with a FIR band-pass filter with a high pass of 20 Hz and low pass of 250 Hz. This was followed by full-wave rectification and smoothing with a window of 100 ms.

3.7 Data analysis for both Study 1 and Study 2

3.7.1 Data analysis for Study 1

As only one group of participants was recruited in Study 1, only within-group comparison was employed in this study.

3.7.1.1 Behavioral data analysis

IBM SPSS Statistics 23.0 for Windows was used to analyze the behavioral data. One-way repeated measures analysis of variance (1-way repeated measures ANOVA) was used to measure the condition effect (A, V and AV) on reaction time and accuracy rate. Significance was set as $P < 0.05$. In the case of a significant condition effect, post-hoc comparison was used to test the differences between pairs of conditions and Bonferroni correction was employed to correct the significant p-value to 0.017.

3.7.1.2 ERP waveform analysis

For the ERP data, the audiovisual integration was calculated by conducting a two-tailed t-test to compare between (AV+C) and (A+V) in each electrode and each time point. As the ERP data from 50 - 350 ms (300 time points) were

analyzed, at least 24 consecutive points showing significant difference from zero ($P < 0.05$) were regarded as audiovisual integration with the purpose of minimizing Type I errors (Guthrie & Buchwald, 1991; Stekelenburg & Vroomen, 2007; Vidal et al., 2008).

3.7.1.3 LRP waveform analysis

The criterion of the LRP onset latency was set as when the amplitude exceeded 50% of peak amplitude (Ulrich & Miller, 2001; Miller et al., 1998). As the variation between subjects was large, the onset latency of the LRP was hard to detect. Therefore, jackknife method was used to compare the differences in onset latency between conditions (Cespón et al., 2013; Falkenstein et al., 2006; Roggeveen et al., 2007; Wide-Wall et al., 2008). This method used grand-average ERP data to estimate the LRP onset latency and estimate the standard deviation (Miller et al., 1998, 2009; Ulrich & Miller, 2001). The uni-sensory and multisensory conditions were compared in terms of the mean amplitudes for both the s-LRP and r-LRP. The time window of 700 - 1500 ms after the stimulus was used to calculate the mean amplitude for the s-LRP in both Study 1 and Study 2. For the r-LRP mean amplitude, the time window of -200 to 200 ms which was used in previous studies (Frame, 2014; Kolev et al., 2006) was employed in both Study 1 and Study 2. One-way repeated ANOVA was used to measure the within-group difference, that is, the condition effect of the mean amplitude.

3.7.1.4 EMG waveform analysis

The baseline of EMG was set as 1000 ms before the onset of stimulus. When the EMG amplitude reached the mean + 3 standard deviation (SD) of the baseline amplitude, the time point was regarded as the EMG onset time (Fabio,

1987; Hodges & Bui,1996; Silva et al., 2013). The peak amplitude was defined as the amplitude of the most positive point of the EMG waveform. One-way repeated ANOVA was used to measure the within-group difference, that is, the condition effect of the EMG onset latency and peak amplitude.

3.7.2 Data analysis for Study 2

Older adults were recruited in Study 2 to compare the different neural process and behavioral performance with the data obtained in the younger participants in Study 1. Hence, the analysis focused on between-group comparisons.

3.7.2.1 Behavioral data analysis

IBM SPSS Statistics 23.0 for Windows was used to analyze the behavioral data. Preliminary review of the data showed a strong correlation between the accuracy rate and reaction time in the older group (A condition: $r = -0.23$, $P = 0.108$; V condition: $r = -0.34$; $P = 0.016$; AV condition: $r = -0.32$, $P = 0.023$), which indicated the existence of a speed-accuracy trade-off. In such a way, neither the reaction time nor accuracy rate was ideal as an index for assessing performance. As analyzing accuracy rate and response speed separately would confound the results, the inverse efficiency score (IES) proposed by Townsend and Ashby (1978) was computed (reaction time divided by accuracy rate) to assess the behavioral performance. Better performances were indexed by smaller values of the IES. Behavioral data in the control condition were not analyzed as it did not involve accuracy rate.

The IES between-group difference was analyzed by two repeated ANOVA among the A, V and AV conditions. The first repeated ANOVA compared the IES

in each condition (A, V or AV). The first repeated ANOVA was used to measure 1) between-participant effect (age), 2) within-participant effect (condition), and 3) their interactions (age \times condition) on IES. The second model employed the IES in AV condition as a baseline to test the benefit from audiovisual integration. Specifically, the potential difference in sensitivity of visual or auditory senses between younger and older participants was controlled by employing the IES in the AV condition as the baseline. Specifically, we defined the A modulation as the difference of IES between AV and V conditions, i.e.(AV-V) and the V modulation as the difference of IES between AV and A conditions, i.e.(AV-A). Therefore, the second repeated ANOVA measured the between-participant effect (age), within-participant effect (modulation, that is [AV-V], [AV-A]) and their interactions (age \times modulation) on IES. Significance was set as $P < 0.05$. For significant main and interaction effects, post-hoc comparison was used to test the differences between pair(s) of groups or conditions.

3.7.2.2 ERP waveform analysis

Only the data in correct trials were included in the data analysis. Similar to the analysis in the younger group in Study 1, the AV interaction was calculated by conducting a two-tailed t-test to compare between (AV+C) and (A+V) at each electrode and each time point for the within-group comparison. The same as the analysis in younger participants in Study 1, at least 24 consecutive points exhibiting significant difference from zero were regarded as AV integration or interaction (Guthrie & Buchwald, 1991; Stekelenburg & Vroomen, 2007; Vidal et al., 2008). The fronto-central P2 was compared between groups and due to the delay of the P2 component in the older group, different time windows were selected for the two groups. Specifically, 150 - 230 ms after the stimulus were selected for the P2 component in the younger group (Liu et al., 2014; Marsic et al., 2015), while 190 - 270 ms (40 ms delay) was selected for the P2 component

in the older group (Martin et al., 2005; Ozmeral et al., 2016; Ross et al., 2007). The P2 mean amplitude of [(AV+C)-(A+V)] was used to calculate between-group differences with a t-test at each electrode site. To investigate whether there was a relationship between the neural and behavioral results, we employed multiple regression analysis to test if this neural signature P2 amplitude of [(AV+C)-(A+V)] could predict the behavioral benefit. Furthermore, in the next step of multiple regression analysis, whether age could modulate the relationship between neural and behavioral findings was tested. In the first step of multiple regression analysis, the regressors were the amplitude of (AV+C)-(A+V) in the P2 component as well as age. In the second step of multiple regression analysis, we added an interaction term (the product of the centered age and P2 amplitude) into the model (Aiken & West, 1991). Furthermore, with the aim of exploring impact of the age, the correlations between the neural signature P2 amplitude of [(AV+C)-(A+V)] and the MoCA sub-scores and total scores were computed in the older group.

3.7.2.3 LRP waveform analysis

The same pre-processing procedure of the LRP as the pre-processing employed in Study 1 was employed in the data for older participants and jackknife method was employed to analyze the onset latency of the LRP. The amplitude difference between uni-sensory and multisensory conditions in both the s-LRP and r-LRP were compared in terms of the mean amplitude. Besides, as the waveforms of both younger and older participants were similar, the same time window as that used in the younger group was employed for the older group. Two-way repeated ANOVA was employed to measure the within-group difference (condition), between-group difference (age) and interaction effect (condition \times age) of the mean amplitude of the s-LRP and r-LRP respectively.

3.7.2.4 EMG waveform analysis

The baseline of EMG was set as 1000 ms before the onset of stimulus. When the EMG amplitude reached mean + 3 SD of the baseline amplitude, the time point was regarded as the EMG onset latency (Hodges and Bui, 1996; Fabio, 1987; Rose, 2012; Silva et al., 2013). Two-way repeated ANOVA was employed to measure the within-group difference (condition), between-group difference (age) and interaction effect (condition \times age) of the EMG onset latency and peak amplitude.

CHAPTER FOUR

STUDY 1 RESULTS AND DISCUSSION – AUDIOVISUAL INTEGRATION AUGMENTED MOTOR FUNCTION (FORMULATING THE MODEL BASED ON YOUNGER SUBJECTS)

This chapter covers the results of Study 1 which include behavioral results, ERP results as well as LRP results and EMG results.

4.1 Results

4.1.1 Demographic results

As revealed in Table 4.1, 29 healthy younger participants were recruited in the first study with the mean age of 24.9 ± 3.4 years (from 18 to 30 years old). The participants had received education for 16.7 ± 1.7 years. The mean accuracy rate of auditory calibration was 0.84 ± 0.04 and the mean accuracy rate of visual calibration was 0.83 ± 0.05 . No significant difference was found in the accuracy rate of calibration between the visual and auditory modalities ($t(28) = 1.38$, $P = 0.177$).

Table 4.1 Demographic results

| Subject No. | Education | Gender | Age | Accuracy rate of auditory calibration | Accuracy rate of visual calibration |
|-------------|-----------|--------|-----|---------------------------------------|-------------------------------------|
| 1 | 19 | F | 28 | 0.86 | 0.81 |
| 2 | 16 | F | 24 | 0.88 | 0.82 |
| 3 | 20 | M | 30 | 0.88 | 0.78 |
| 4 | 19 | M | 28 | 0.88 | 0.87 |
| 5 | 19 | M | 27 | 0.88 | 0.78 |
| 6 | 16 | M | 24 | 0.88 | 0.76 |
| 7 | 16 | M | 27 | 0.81 | 0.88 |
| 8 | 16 | F | 23 | 0.84 | 0.85 |
| 9 | 19 | M | 27 | 0.84 | 0.76 |
| 10 | 16 | F | 24 | 0.85 | 0.87 |
| 11 | 16 | F | 23 | 0.86 | 0.88 |
| 12 | 17 | F | 26 | 0.89 | 0.89 |
| 13 | 16 | F | 25 | 0.86 | 0.76 |
| 14 | 16 | M | 29 | 0.85 | 0.89 |
| 15 | 16 | F | 24 | 0.80 | 0.88 |
| 16 | 19 | M | 30 | 0.88 | 0.87 |
| 17 | 16 | M | 24 | 0.84 | 0.87 |
| 18 | 14 | M | 20 | 0.82 | 0.85 |
| 19 | 16 | F | 25 | 0.83 | 0.86 |
| 20 | 19 | M | 28 | 0.87 | 0.88 |
| 21 | 19 | M | 30 | 0.77 | 0.85 |
| 22 | 13 | F | 18 | 0.77 | 0.76 |
| 23 | 17 | F | 24 | 0.86 | 0.77 |

| | | | | | |
|------|------|----------|------|------|------|
| 24 | 15 | F | 20 | 0.89 | 0.85 |
| 25 | 15 | F | 21 | 0.86 | 0.80 |
| 26 | 16 | M | 20 | 0.76 | 0.75 |
| 27 | 16 | M | 20 | 0.78 | 0.77 |
| 28 | 15 | F | 25 | 0.85 | 0.88 |
| 29 | 17 | M | 27 | 0.85 | 0.83 |
| Mean | 16.7 | 55% male | 24.9 | 0.84 | 0.83 |

4.1.2 Behavioral results

4.1.2.1 Accuracy rate comparison of multisensory and uni-sensory conditions

The main effect (condition effect) of accuracy rate was significant ($F(2,56) = 70.71, P < 0.001$) and post-hoc analysis with paired t-tests showed the accuracy rate in the audiovisual (AV) condition was significantly higher than that in the auditory (A) condition ($t(28) = -11.75, P < 0.001$) as well as the visual (V) condition ($t(28) = -12.13, P < 0.001$). Figure 4.1A reveals the accuracy rate comparison between the AV, A and V conditions.

4.1.2.2 Reaction time comparison of multisensory and uni-sensory conditions

The main effect (condition effect) of reaction time was significant ($F(2,56) = 72.18, P < 0.001$) and post-hoc analysis with the paired t-test showed the reaction time in the AV condition was significantly faster than that in the A condition ($t(28) = 9.59, P < 0.001$), but no significant difference was observed when compared to the V condition ($t(28) = -1.21, P = 0.235$). Figure 4.1B reveals the comparison of reaction time among these three conditions.

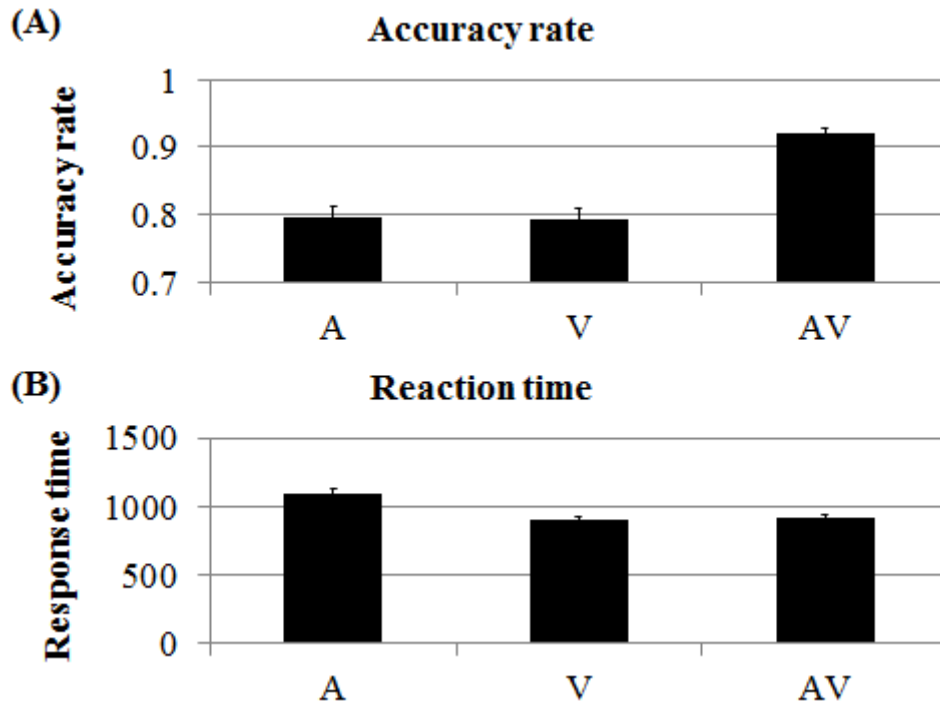


Figure 4.1 (A) The figure shows the behavioral results in terms of accuracy rate in the auditory, visual and audiovisual conditions. **(B)** The figure shows the behavioral results in terms of reaction time in the auditory, visual and audiovisual conditions. The x-axis shows different types of conditions and the y-axis shows the accuracy rate or reaction time (ms).

4.1.3 ERP results

The audiovisual integration was calculated by $[(AV+C)-(A+V)]$ (Saldern & Noppeney, 2013). When the t-value in more than 24 consecutive time points passed the criterion ($P < 0.05$), the time window consisting of these consecutive time points can be regarded as significant different time windows between the (A+V) and (AV+C). Two time windows exhibited significant differences between the amplitude of $[(AV+C)-(A+V)]$ and zero: the first time period was from ~145 - 175 ms after stimulus onset; and the second time period was from ~170 - 220 ms after stimulus onset (Figure 4.2 & Figure 4.3).

4.1.3.1 First time window (~145 - 175 ms time window)

In this time window, the amplitude of $[(AV+C)-(A+V)]$ was significantly different from zero in the electrodes in the frontal (FPz), frontotemporal (F6 and F8), and fronto-central (FC4 and FC6) regions (Figure 4.2). The waveform shapes of the three conditions were similar. The difference of $[(AV+C)-(A+V)]$ amplitude was because of the less positive-going waveform of (AV+C) compared to (A+V). This sub-additive pattern appeared continuously in the whole time window. According to the topography and time window, the waveform in this time window could correspond to the ascending limb of fronto-central P2 till just before its peak. The pattern of the ERP waveforms in this time window indicates the sub-additivity in the multisensory condition compared to the uni-sensory condition.

4.1.3.2 Second time window (~175 - 220 ms time window)

In this time window, the amplitude of $[(AV+C)-(A+V)]$ was significantly different from zero in the fronto-central (FC2, FC4 and FC6), central (C2 and

C4) and temporo-parietal (TP8) regions (Figure 4.2). The waveform shapes of the three conditions were similar. The difference of $[(AV+C)-(A+V)]$ amplitude was because of the less positive-going waveform of (AV+C) compared to (A+V). This sub-additive pattern appeared continuously during the whole time window. According to the topography and time window, the waveform in this time window may correspond to the waveform around the peak of fronto-central P2.

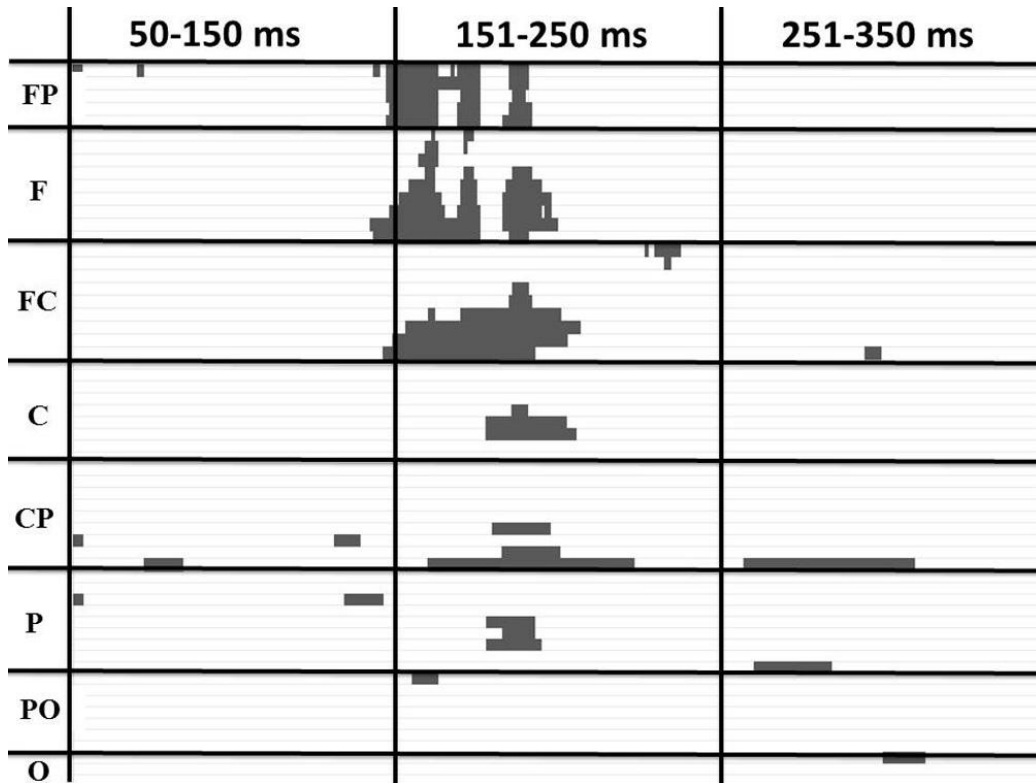


Figure 4.2 The figure shows the p-value of paired t-test between (AV+C) and (A+V). The x- and y-axes show the timeline and electrodes respectively. The figure only shows the point for which the p-value is less than 0.05.

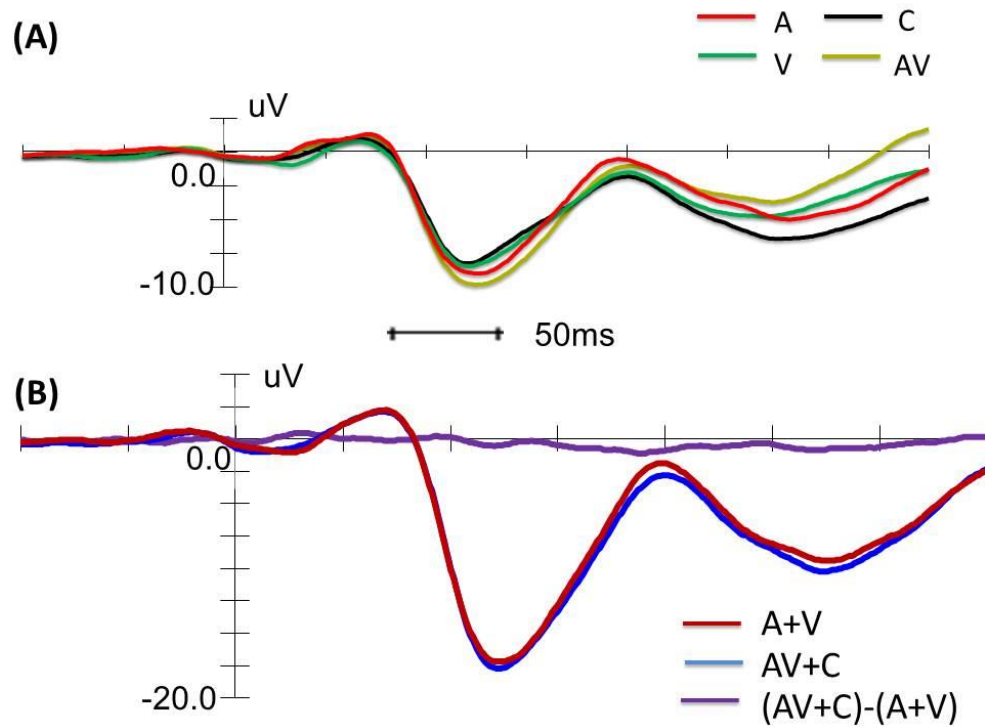


Figure 4.3 The figure shows the ERP waveform in auditory (A), visual (V) and cross audiovisual (AV) conditions. The x-axis shows the timeline (ms) from 100 ms before the onset of stimulus to 350 ms after the onset of stimulus and the y-axis shows amplitude (uV). (A) The ERP waveform in A, V, AV and control conditions. (B) The sum waveform of uni-sensory conditions (A+V) and the sum waveform of audiovisual and control conditions (AV+C) as well as the subtraction waveform of both summed waveforms [(AV+C) - (A+V)].

4.1.4 LRP results

4.1.4.1 LRP mean amplitude comparison across the A, V and AV conditions

The main effect (condition effect) of the s-LRP mean amplitude was significant ($F(2,56) = 4.25$, $P = 0.034$) and post-hoc comparison showed that the mean amplitude of the AV condition was significantly less negative-going than that of the A condition (mean difference: $0.88 \mu\text{V}$, $t(28) = -2.84$, $P = 0.008$), while no significant difference was observed between the AV and V conditions (mean difference: $0.11 \mu\text{V}$ less negative-going in the AV condition, $t(28) = -0.48$, $P = 0.633$)(Figure 4.5 & Figure 4.6).

The main effect (condition effect) of the r-LRP mean amplitude was significant ($F(2,56) = 7.69$, $P = 0.001$) and post-hoc comparison showed no significant difference between the AV and A conditions (mean difference: $0.45 \mu\text{V}$, less negative-going in the AV condition, $t(28) = -2.04$, $P = 0.051$) or between the AV and V conditions (mean difference: $0.34 \mu\text{V}$, more negative-going in the AV condition, $t(28) = 1.84$, $P = 0.077$).

4.1.4.2 LRP onset latency comparison across the A, V and AV conditions

The onset latency of the s-LRP was significantly faster in the AV condition compared with the A condition (mean difference: 231 ms , $t(28) = 4.08$, $P < 0.001$) while the difference between the AV and V conditions was marginally different (64 ms faster in the AV condition, $t(28) = 1.92$, $P = 0.066$)(Figure 4.4 & Figure 4.6).

Unlike the onset latency of the s-LRP, no significant difference was observed between the AV and A conditions (27 ms faster in the AV condition, $t(28) = 1.71$, $P = 0.499$), as well as between the AV and V conditions (43 ms

faster in the V condition, $t(28) = 1.57$, $P = 0.127$)(Figure 4.4 & Figure 4.7).

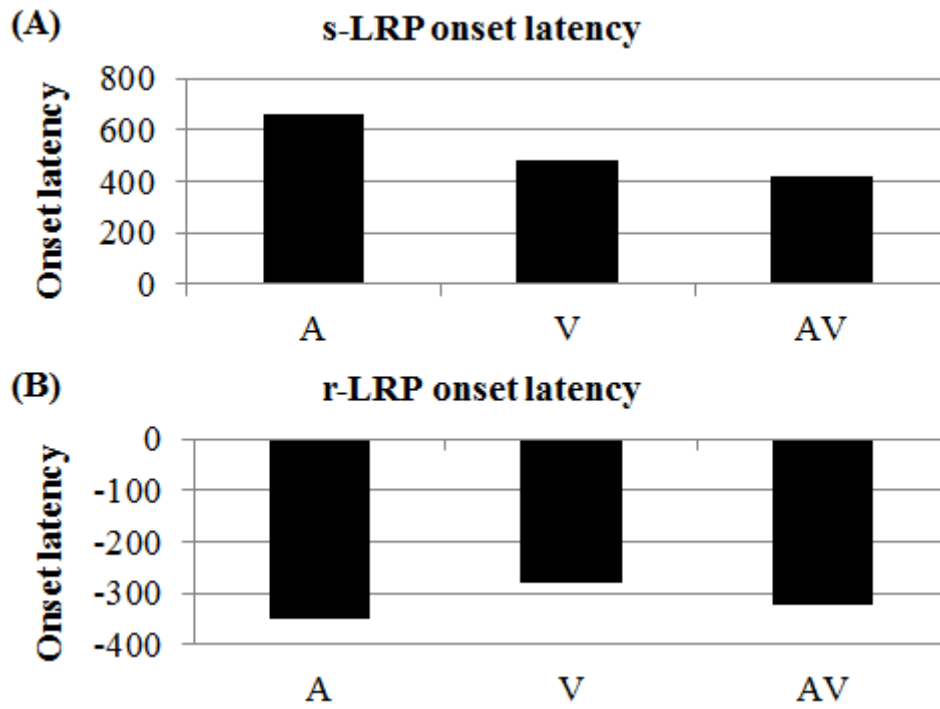


Figure 4.4 (A) This figure shows the onset latency of the s-LRP in the A, V and AV conditions; (B) This figure shows the onset latency of the r-LRP in the A, V and AV conditions. The x-axis shows different conditions and the y-axis shows the onset latency (ms).

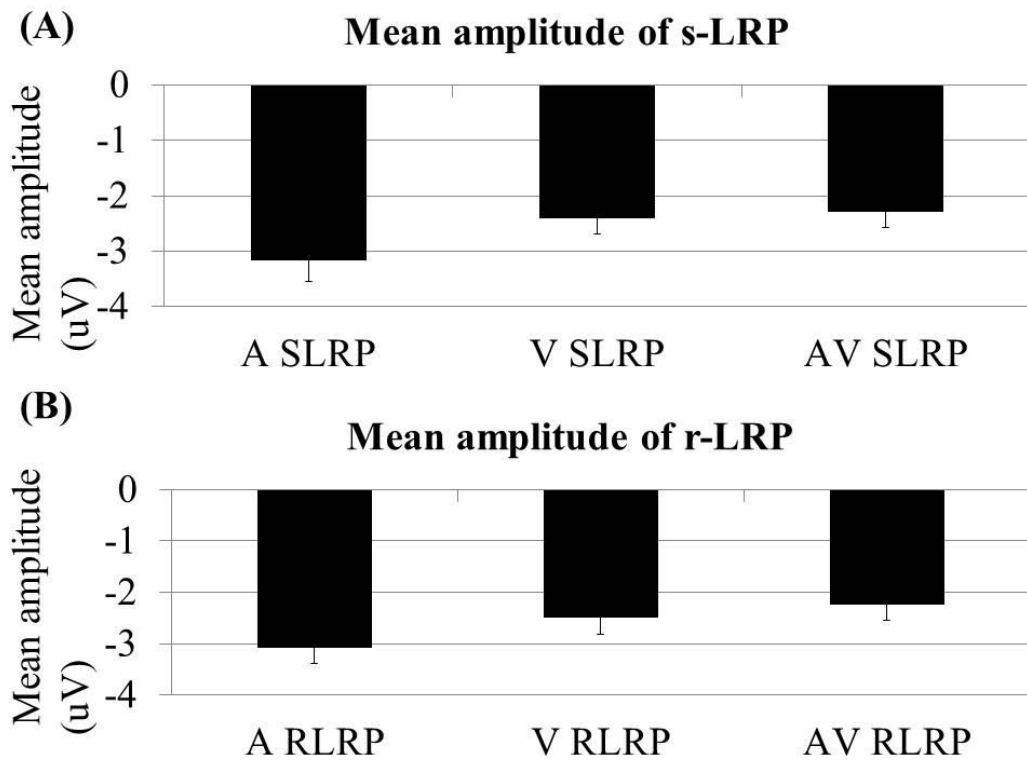


Figure 4.5 (A) This figure shows the mean amplitude of the s-LRP in the A, V and AV conditions; (B) This figure shows the mean amplitude of the r-LRP in the A, V and AV conditions. The x-axis shows different conditions and the y-axis shows the mean amplitude (uV).

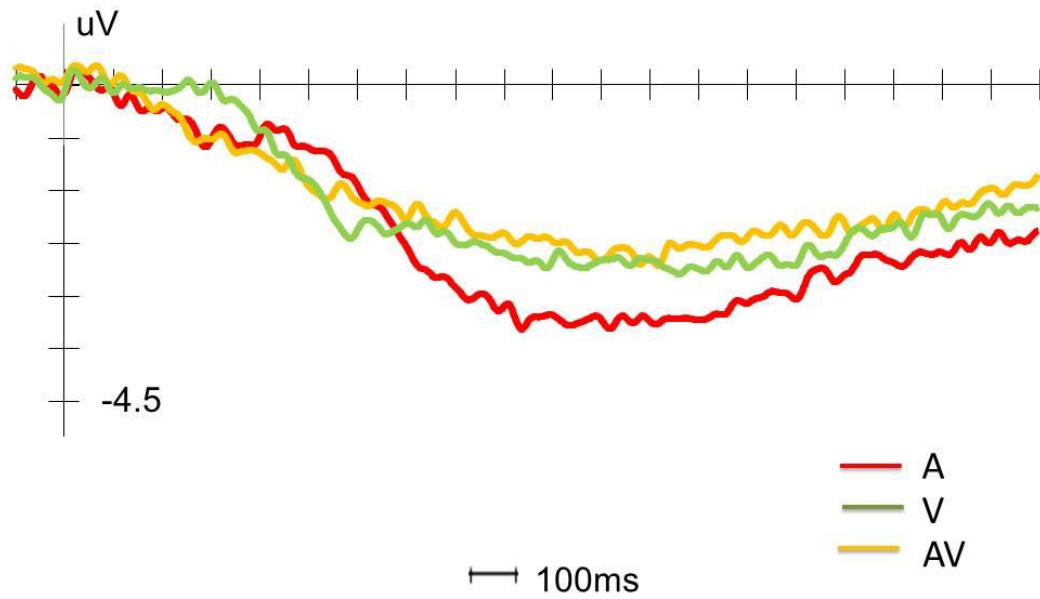


Figure 4.6 This figure shows the waveform of the s-LRP in the A, V and AV conditions. The x-axis shows the time line (ms) and the y-axis shows the amplitude (uV).

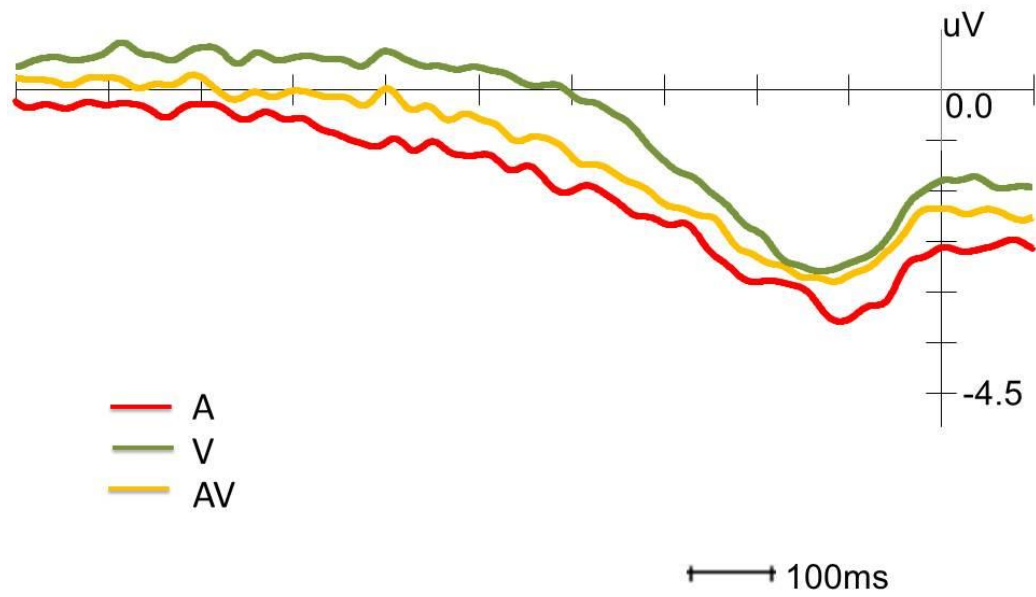


Figure 4.7 Waveform of r-LRP in the A, V and AV conditions. The x-axis shows the time line (ms) and the y-axis shows the amplitude (uV).

4.1.5 EMG results comparison across the A, V and AV conditions

4.1.5.1 Onset latency

No significant main effect (condition effect) difference was observed between the AV condition and A or V condition in the EMG onset latency of the left extensor carpi radius (LECR) which is the muscle responsible for left wrist extension ($F(2,56) = 0.98, P = 0.366$)(Figure 8A & Figure 10A). The main effect (condition effect) of the EMG onset latency of the right extensor carpi radius (RECR) which is the muscle responsible for right wrist extension was significant ($F(2,56) = 4.55, P = 0.015$). Post-hoc comparison with paired t-test showed the onset latency of the AV condition was significantly earlier than that of the A condition ($t(28) = 2.71, P = 0.011$), but no significant difference was observed between the V and AV conditions ($t(28) = -0.77, P = 0.451$)(Figure 8B & Figure 10B).

The main effect (condition effect) of the EMG onset latency of the left flexor carpi radius (LFCR), which is responsible for left wrist flexion, was significant ($F(2,56) = 18.19, P < 0.001$). Post-hoc comparison with paired t-test showed the onset latency of the AV condition was significantly earlier than that of the A condition ($t(28) = 4.82, P < 0.001$), but no significant difference was observed between the V and AV conditions ($t(28) = 0.05, P = 0.958$)(Figure 8C & Figure 10C). No significant main effect (condition effect) of the EMG onset latency of the right flexor carpi radius (RFCR), which is responsible for right wrist flexion, was observed ($F(2,56) = 1.84, P = 0.168$)(Figure 8D & Figure 10D).

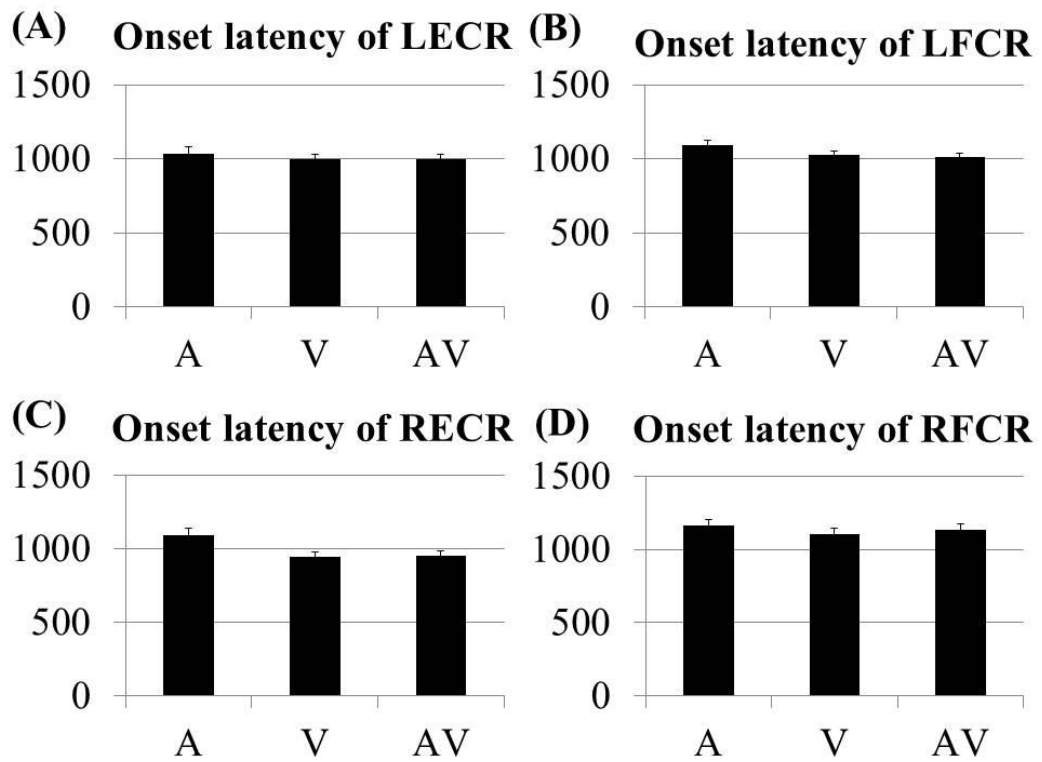


Figure 4.8 (A) This figure shows the EMG onset latency of the LECR measured in the A, V and AV conditions; **(B)** This figure shows the EMG onset latency of the LFCR measured in the A, V and AV conditions; **(C)** This figure shows the EMG onset latency of the RECR measured in the A, V and AV conditions; **(D)** This figure shows the EMG onset latency of the RFCR measured in the A, V and AV conditions. The x-axis shows different conditions and the y-axis shows the onset latency (ms).

4.1.5.2 Peak EMG amplitude comparison across the A, V and AV conditions

The main effect (condition effect) of the LECR EMG peak amplitude was significant ($F(2,56) = 20.17, P < 0.001$). Post-hoc comparison showed that the peak amplitude was significantly higher in the AV condition compared to the A condition ($t(28) = -4.89, P < 0.001$), but no significant difference was demonstrated between the AV condition and V condition ($t(28) = -0.83, P = 0.412$)(Figure 9A & Figure 10A). The main effect (condition effect) of the LFCR EMG peak amplitude was significant ($F(2,56) = 3.28, P = 0.045$). Post-hoc comparison showed that the peak amplitude was significantly higher in the AV condition compared to the A condition ($t(28) = -2.19, P = 0.037$), but no significant difference was demonstrated between the AV condition and V condition ($t(28) = -0.16, P = 0.872$)(Figure 9B & Figure 10B).

The main effect (condition effect) of the RECR EMG peak amplitude was significant ($F(2,56) = 15.21, P < 0.001$). Post-hoc comparison showed that the peak amplitude was significantly higher in the AV condition compared to the A condition ($t(28) = -3.65, P = 0.001$), but no significant difference was demonstrated between the AV and V conditions ($t(28) = -0.12, P = 0.904$)(Figure 9C & Figure 10C). No significant main effect (condition effect) was observed for the RFCR EMG peak amplitude ($F(2,56) = 1.39, P = 0.257$)(Figure 9D & Figure 10D).

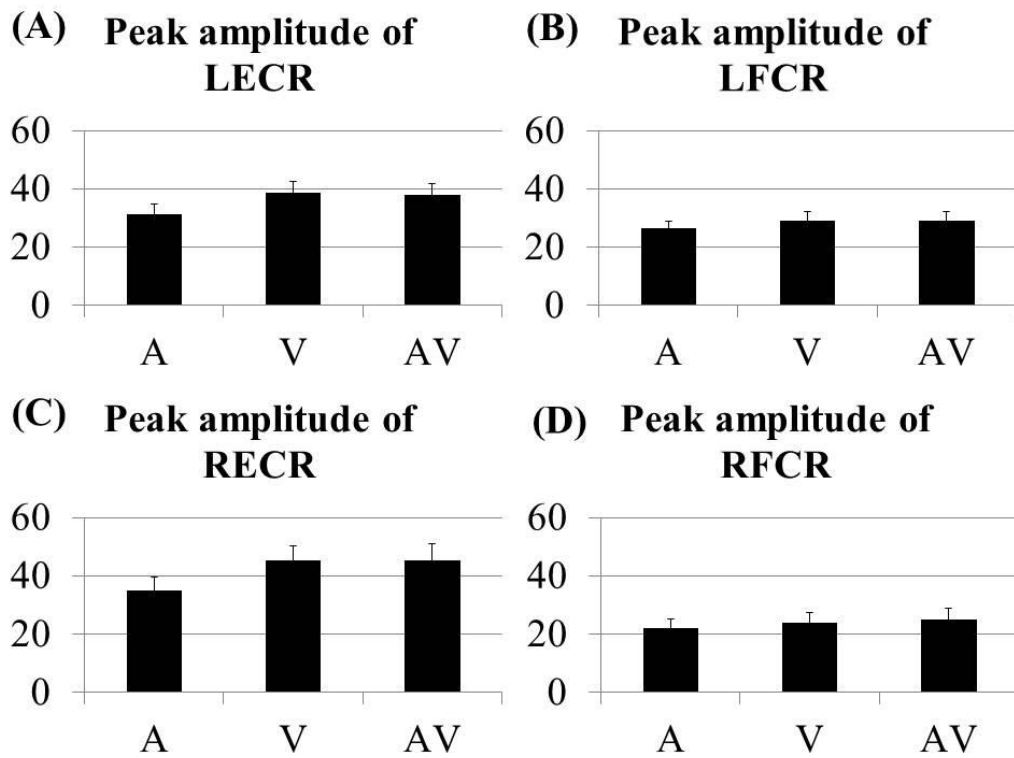


Figure 4.9 (A) This figure shows the EMG peak amplitude of the LECR measured in the A, V and AV conditions; **(B)** This figure shows the EMG peak amplitude of the LFCR measured in the A, V and AV conditions; **(C)** This figure shows the EMG peak amplitude of the RECR measured in the A, V and AV conditions; **(D)** This figure shows the EMG peak amplitude of the RFCR measured in the A, V and AV conditions. The x-axis shows different conditions and the y-axis shows the peak amplitude (uV).

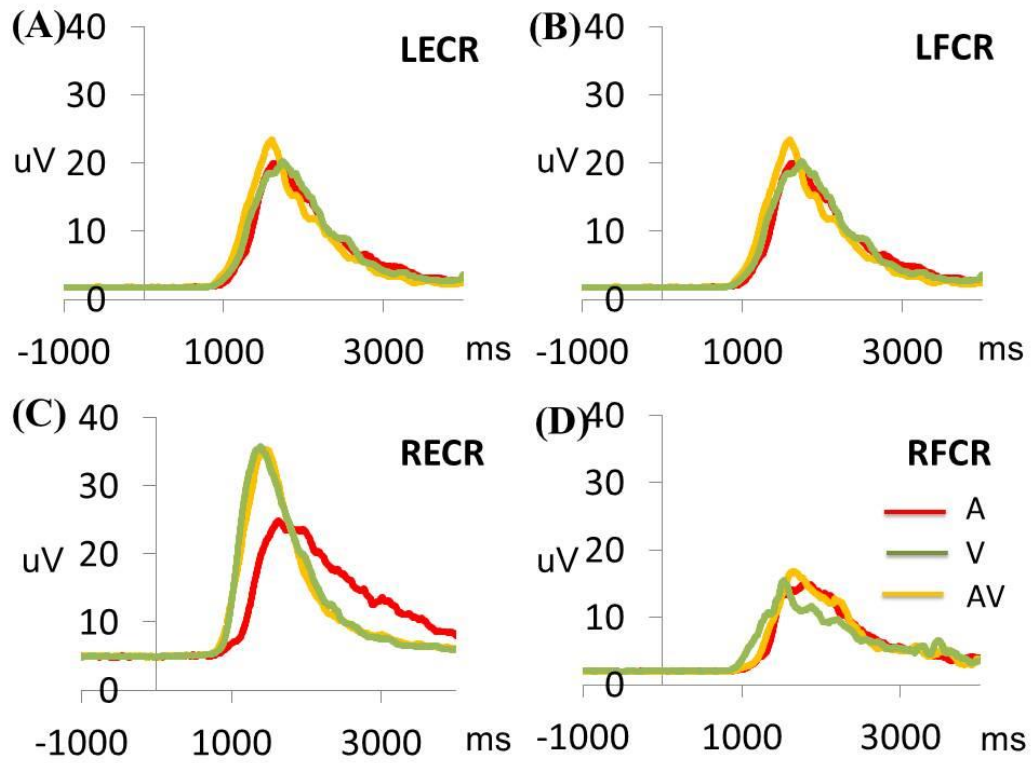


Figure 4.10 (A) This figure shows the EMG waveform of the LECR measured in the A, V and AV conditions; **(B)** This figure shows the EMG waveform of the LFCR measured in the A, V and AV conditions; **(C)** This figure shows the EMG waveform of the RECR measured in the A, V and AV conditions; **(D)** This figure shows the EMG waveform of the RFCR measured in the A, V and AV conditions. The x-axis shows the time line (ms) and the y axis shows the amplitude (uV).

4.2 Discussion

The aim of this study was to validate the audiovisual integration task used in both Study 1 and Study 2. The results of this study demonstrated enhanced behavioral performance in terms of accuracy rate in the multisensory condition (AV), which was consistent with the previous findings (Liu et al., 2007). Furthermore, the ERP data demonstrated the sub-additive pattern in the frontal and fronto-central region around 200 ms when receiving multisensory information which also replicated the results of a previous study (Stekelenburg & Vroomen, 2013). These results indicated that the audiovisual integration task used in Study 1 is valid to investigate multisensory integration as both the behavioral and neurophysiological results in this study were consistent with previous studies. Moreover, this study also demonstrated that multisensory integration might modulate the response selection process indexed by the marginally decreased s-LRP onset latency in the multisensory condition. However, the response generation process could not be modulated because both the r-LRP onset latency as well as the amplitude demonstrated no significant difference between multisensory and uni-sensory conditions.

4.2.1 Audiovisual integration in perceptual and feedback stages

Two time windows of multisensory integration were observed in the frontal and fronto-central regions. Furthermore, these two time windows could be the ascending and descending limbs of fronto-central P2. In multisensory studies, fronto-central P2 served as a marker for multisensory integration in different stimuli and study designs (Giard & Peronnet, 1999; Molholm et al., 2002; Stekelenburg & Vroomen, 2013; Vidal et al., 2008). As the stimulus process involved discrimination of multisensory stimuli in the audiovisual spatial discrimination task, the fronto-central P2 observed in this paradigm could reflect the evaluation of the multisensory stimuli. This proposition was supported by

the previous finding that the fronto-central P2 can reflect the location of sound source in the azimuthal plane in the sound localization task (Tiitinen et al., 2006). Also, a study demonstrated that the generator of fronto-central P2 may be the planum temporale (PT) which is a region responsible for the auditory spatial process and also a heteromodal cortex which can process both visual and auditory information. This result is also congruent with previous studies which showed the audiovisual integration benefits the early sensory process (bottom-up) rather than the later higher-order cognitive process (Mahoney et al., 2011; Peiffer et al., 2007). Putting them together, the results of Study 1 showed multisensory integration modulates the perceptual and feedback stages indexed by fronto-central P2 which is consistent with previous findings.

The results of this study are inconsistent with previous findings that no significant results were revealed for the early components, such as C1 and P1 (around 100 ms post stimulus) (Cappe et al., 2010). The plausible reason could be because of the noise added to the auditory and visual stimuli. Similar to the results reported in this study, an fMRI study which embedded noise in both auditory and visual stimuli also demonstrated that no activation was observed in the both primary visual and auditory cortices which are responsible for perceptual processes (Saldern & Noppeney, 2013). When noise is added to the stimulus, the process of multisensory information and uni-sensory information becomes similar in the primary sensory cortices. As the early components such as C1 and P1 represent the processes in the primary sensory cortices (Cappe et al., 2010), no significant difference was observed in these two components.

4.2.2 Audiovisual integration in the response selection and generation processes

In the response selection process, the onset latency of the s-LRP in the AV

condition was significantly earlier than the A condition and marginally earlier than the V condition ($P = 0.066$). The results were similar to those in a previous study (Jepma et al., 2009) which demonstrated earlier onset of the s-LRP in the AV condition. As the interval between stimuli and s-LRP onset involves both sensory and motor processes, the decreased onset latency of the s-LRP can be related to faster sensory or motor processes or both. However, the ERP results demonstrated no significant difference between multisensory and uni-sensory conditions in the onset latency of fronto-central P2 which is the marker of multisensory integration in the perceptual and feedback stages. Hence, the results suggest that the decreased s-LRP onset latency could be related to the faster response selection process. No significant difference was observed between multisensory and uni-sensory conditions in r-LRP onset latency which indicates that the multisensory process may not be able to increase the speed of the response generation process. In summary, the results of LRP onset latency indicate that audiovisual integration modulates the response selection process in younger adults. However, the response generation process cannot be modulated by audiovisual integration in younger participants.

No significant difference of LRP amplitude between multisensory and uni-sensory conditions was observed. The LRP amplitude can reflect motor inhibitory control (Cid-Fernández et al., 2014; DeJong et al., 1990; Roggeveen et al., 2007; Vallesi & Stuss, 2010). Therefore, no significant difference in LRP amplitude indicates that multisensory integration is not able to influence motor inhibition. However, the alternative explanation is that normal younger adults present no deficit of motor inhibitory control. Hence, the activation may already reach the ceiling in the uni-sensory process which causes non-significant modulation of multisensory integration. People may also argue that the audiovisual integration task used in Study 1 was too easy for the younger participants resulting in non-significant results in the LRP amplitude. However,

the accuracy rate was significantly lower than 0.95 in each condition (A condition: $t(28) = 10.17$, $P < 0.001$; V condition: $t(28) = 11.34$, $P < 0.001$; AV condition: $t(28) = 3.10$, $P = 0.04$) which indicates that the task was not easy for the younger participants. All in all, the non-significant results of LRP amplitude were not due to the difficulty level of the task. Hence, multisensory integration cannot modulate the response generation process in younger adults.

The EMG data showed non-significant results between multisensory and uni-sensory conditions in performing the audiovisual integration task with wrist extension and flexion, indicating multisensory integration cannot modulate the peripheral motor process, such as the response force. The results are inconsistent with previous findings that when presenting accessory sound prior to or simultaneously with visual information, the response force can be enhanced (Kiesel & Miller, 2007; Stahl & Rammsayer, 2005). The accessory sound was just a simple tone and conveyed no task-related information. Therefore, the accessory sound may only serve as a cue that increases the attention level and further prepares the sensory and motor system for the coming stimuli. Hence, visual and auditory information may not be integrated (Los & Burg, 2013). As the motor system was prepared by the accessory sound, more motor units could be recruited to further increase the response force. However, noise was provided with the target information in this study, which could not increase the attention level or prepare the motor system. Therefore, no significant difference was observed between uni-sensory and multisensory conditions.

4.2.3 Conclusion of Study 1 and the implication for Study 2

This study (Study 1) provided similar results to the previous findings that multisensory integration can enhance behavioral performance in terms of accuracy rate of completing audiovisual discrimination tasks. Furthermore, the

audiovisual modulation of perceptual and feedback stages indexed by fronto-central P2 was also consistent with previous findings indicating the audiovisual discrimination task used in the study is valid to investigate multisensory integration. Additionally, this study also showed that multisensory integration can modulate the response selection process indicated by the decreased s-LRP onset latency. No r-LRP amplitude or onset latency modulation could be observed which may be because no motor inhibition deficits were present in younger participants which caused the ceiling effect in the uni-sensory process. However, prior evidence has demonstrated that older adults suffer from motor inhibition deficits (Cid-Fernández et al., 2014; Roggeveen et al., 2007; Vallesi & Stuss, 2010) or motor cortex dysregulation (Cespón et al., 2013; Hutchinson et al., 2002; Kolev et al., 2006; Mattay et al., 2002; Sailer et al., 2000; Wild-Wall et al., 2008; Yordanova et al., 2004). Furthermore, this kind of dysregulation indexed by a more negative-going r-LRP amplitude could significantly delay the speed of the sensorimotor process in older participants. This evidence prompted us to investigate whether audiovisual integration can modulate the response generation process in older groups differently from younger groups. Moreover, we were also interested in if the modulation in motor generation process of older groups is the consequent effect of the modulation on the sensory process. Hence, we attempted to investigate how the audiovisual integration modulates the perceptual and feedback process as well as the response selection and generation processes in older adults and compare their multisensory integration modulation with the younger adults in the second study (Study 2).

CHAPTER FIVE

RESULTS AND DISCUSSION - AGING EFFECT ON AUDIOVISUAL INTEGRATIVE PROCESSING IN A SPATIAL DISCRIMINATION TASK

This chapter covers the results of Study 2 which include behavioral results, ERP results as well as LRP results and EMG results of older adults and the comparison between older and younger groups.

5.1 Results

5.1.1 Demographic results

As revealed in Table 5.1, 31 healthy older participants were recruited in this study with the mean age of 67.3 ± 4.4 years (from 60 to 78 years old). The participants in this study (Study 2) received education for 9.9 ± 0.7 years. The mean score of MoCA was 27.3 ± 2.1 (ranging from 23 to 30). The mean accuracy rate for auditory calibration (A) was 0.84 ± 0.04 and the mean accuracy rate for visual calibration (V) was 0.83 ± 0.04 . No significant difference was found between the accuracy rate of calibration for visual and auditory modality ($t(30) = 0.96, P = 0.343$).

Between-group comparison showed that the education level in the younger participants was significantly higher than that in the older group ($t(58) = 9.20, P < 0.001$). No significant difference of the accuracy rate was observed in both visual ($t(58) = -0.40, P = 0.692$) and auditory ($t(58) = 0.32, P = 0.749$) calibration.

Table 5.1 Demographic results of older participants

| Subject No. | Education | Gender | Age | MoCA | Accuracy rate of auditory calibration | Accuracy rate of visual calibration |
|-------------|-----------|--------|-----|------|---------------------------------------|-------------------------------------|
| 1 | 6 | F | 63 | 24 | 0.76 | 0.78 |
| 2 | 11 | M | 66 | 27 | 0.83 | 0.85 |
| 3 | 11 | M | 71 | 25 | 0.85 | 0.80 |
| 4 | 12 | M | 67 | 28 | 0.90 | 0.84 |
| 5 | 11 | F | 65 | 23 | 0.81 | 0.80 |
| 6 | 6 | F | 65 | 24 | 0.88 | 0.86 |
| 7 | 4 | F | 66 | 27 | 0.87 | 0.80 |
| 8 | 8 | F | 65 | 29 | 0.88 | 0.80 |
| 9 | 11 | F | 65 | 27 | 0.84 | 0.83 |
| 10 | 11 | F | 68 | 28 | 0.86 | 0.78 |
| 11 | 8 | M | 73 | 28 | 0.81 | 0.81 |
| 12 | 9 | F | 68 | 30 | 0.89 | 0.90 |
| 13 | 10 | F | 68 | 28 | 0.83 | 0.86 |
| 14 | 6 | F | 62 | 30 | 0.87 | 0.81 |
| 15 | 16 | M | 67 | 28 | 0.88 | 0.90 |
| 16 | 20 | F | 78 | 25 | 0.84 | 0.85 |

| | | | | | | |
|------|-----|----------|------|------|------|------|
| 17 | 16 | M | 64 | 27 | 0.80 | 0.76 |
| 18 | 11 | F | 72 | 30 | 0.87 | 0.83 |
| 19 | 11 | M | 65 | 23 | 0.79 | 0.82 |
| 20 | 9 | M | 70 | 27 | 0.89 | 0.89 |
| 21 | 8 | M | 78 | 27 | 0.84 | 0.87 |
| 22 | 6 | M | 62 | 25 | 0.85 | 0.83 |
| 23 | 9 | F | 61 | 27 | 0.87 | 0.82 |
| 24 | 7 | F | 66 | 30 | 0.84 | 0.88 |
| 25 | 6 | F | 65 | 29 | 0.81 | 0.82 |
| 26 | 9 | F | 66 | 29 | 0.75 | 0.81 |
| 27 | 9 | F | 68 | 27 | 0.85 | 0.89 |
| 28 | 16 | M | 60 | 30 | 0.84 | 0.85 |
| 29 | 12 | M | 70 | 29 | 0.77 | 0.81 |
| 30 | 5 | M | 70 | 28 | 0.88 | 0.90 |
| 31 | 12 | F | 73 | 26 | 0.83 | 0.82 |
| Mean | 9.9 | 35% male | 67.3 | 27.3 | 0.84 | 0.83 |

5.1.2 Behavioral results: Comparison of the audiovisual integration task performance between younger and older participants

As the significant correlation between accuracy rate and reaction time was observed in the older group which indicated a speed-accuracy trade-off, the inverse effective score (IES) was compared between conditions and groups in this study. The first ANOVA model with the factors of condition (A, V and AV) and age (older and younger) compared the performance of the three conditions between the younger and older group. The main effect consisted of condition effect and age effect and the interaction tested the interaction between condition and age. The results revealed significant main effects of condition ($F(2,114) = 101.68, P < 0.001$; Figure 5.1A) and age ($F(1,57) = 21.80, P < 0.001$). The interaction effect between condition and age was also significant ($F(2,114) = 6.33, P = 0.007$). Post-hoc analysis demonstrated that in all three conditions significantly lower IES was observed in younger participants compared with their older counterparts (AV: $t(58) = -3.65, P = 0.001$; V: $t(58) = -3.60, P = 0.001$; A: $t(58) = -4.65, P < 0.001$). As the control condition did not include the accuracy rate parameter to calculate IES, no results were presented for this condition.

The second ANOVA model tested the modulation effect (V modulation: AV-A; A modulation: AV-V), the age effect as well as the interaction effect between age and modulation. The results showed a significant main effect of age ($F(1,57) = 21.75, P < 0.001$; Figure 5.1B) as well as modulation ($F(1,57) = 40.82, P < 0.001$). No significant interaction effect was demonstrated between modulation and age ($F(1,57) = 2.65, P = 0.109$). Post-hoc analysis demonstrated a higher modulation level in the older group compared with the younger in both visual and auditory modulation (AV-V: $t(58) = -2.10, P = 0.042$; AV-A: $t(58) = -3.22, P = 0.002$). As the control condition did not include the accuracy rate parameter to calculate IES, no results were presented for this condition.

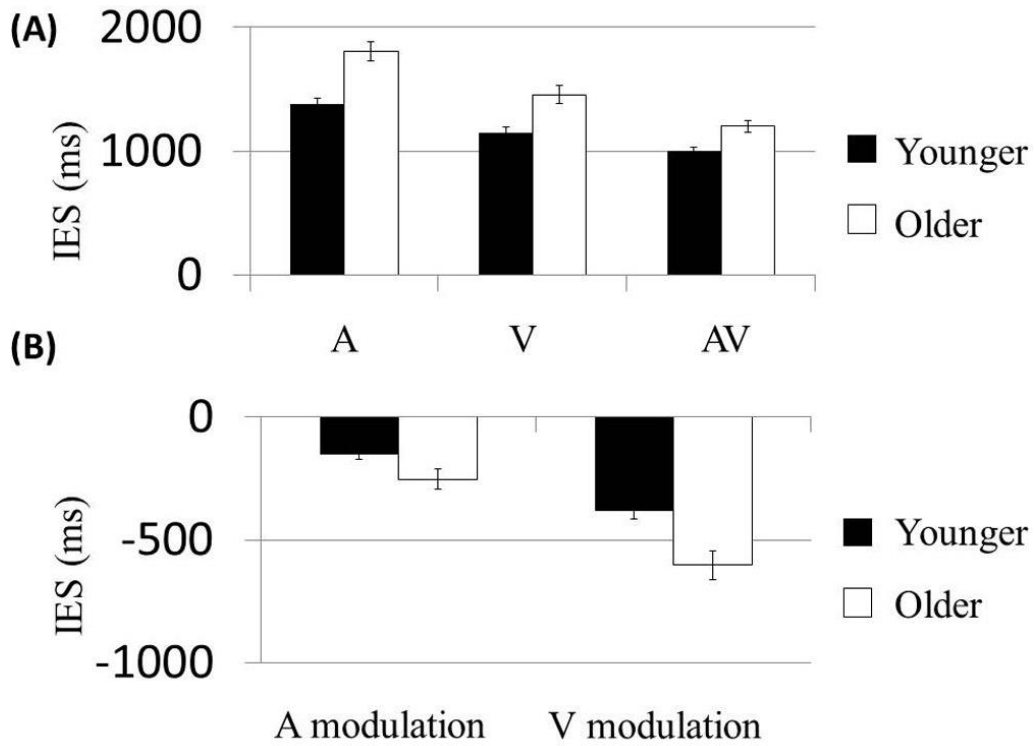


Figure 5.1 The figure shows the behavioral results comparison between the younger and older group. The younger participants were from Study 1 and the older participants were from Study 2. (A) The figure shows the mean IES in three conditions (A, V & AV) of the younger and older participants. (B) “Modulation” scores were computed as the difference in IES between multisensory (AV) and uni-sensory (either A or V) conditions. Specifically, the A modulation was computed as AV-V, and the V modulation was computed as AV-A. The error bars represent standard errors.

5.1.3 ERP results

5.1.3.1 Time window and sites of audiovisual integration in the older group

Unlike the younger participants, only one time window showed the amplitude of the [(AV+C)-(A+V)] significantly different from zero: ~194 - 222 ms after stimulus onset (Figure 5.2). In this time period, the amplitude of [(AV+C)-(A+V)] was significantly different from zero in the frontal (Fz), fronto-central (FC1 and FC), and central (C1) regions. The waveforms of uni-sensory and multisensory were similar (Figure 5.3B). The difference of [(AV+C)-(A+V)] amplitude in all the regions was related to the more positive-going waveform of (AV+C) compared to (A+V). This pattern appeared continuously during the whole time period. According to the topography and time window, the waveform in this time period corresponded to the waveform of ascending limb and the peak of P2. The pattern of the ERP waveforms in this time window indicated the super-additivity in the multisensory condition compared to the sum of uni-sensory conditions.

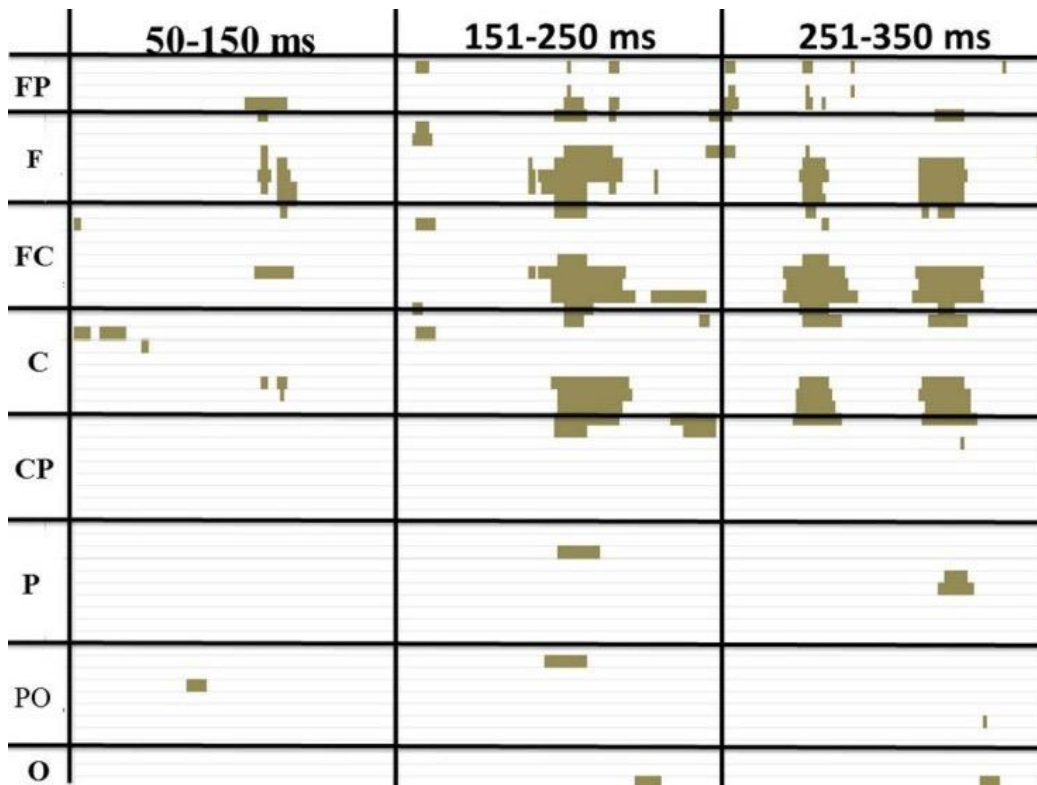


Figure 5.2 The figure shows the p-value of the paired t-test between (AV+C) and (A+V) in the older group. The columns show the timeline and the rows show the electrodes respectively. The figure only shows the point at which the p-value is less than 0.05.

5.1.3.2 *The comparison of P2 amplitude between younger and older groups*

The P2 component was found to be distributed in the fronto-central region. Older participants demonstrated significantly delayed peak latency of P2 in the three conditions compared with the younger group (A condition: $t(58) = -8.08$, $P < 0.001$; V condition: $t(58) = -6.10$, $P < 0.001$; AV condition: $t(58) = -9.32$, $P < 0.001$)(Figure 5.3 A&B). The older group also showed more positive-going P2 mean amplitude compared to the younger group in the AV and V conditions (AV condition: $t(58) = -3.67$, $P < 0.001$; V condition: $t(58) = -4.61$, $P < 0.001$) but not in the A condition ($t(58) = 1.61$, $P = 0.113$)(Table 5.2). The mean amplitude of [(AV+C)-(A+V)] was significantly larger than zero in older adults ($t(30) = 2.63$, $P = 0.013$), while the mean amplitude of [(AV+C)-(A+V)] was significantly smaller than zero in younger adults ($t(29) = -2.15$, $P = 0.040$)(Figure 5.3C). Also, the P2 mean amplitude of [(AV+C)-(A+V)] at FC2 was significantly more positive-going in the older group than the younger group ($t(58) = -3.31$, $P = 0.002$)(Figure 5.3D). These results demonstrate that older adults mainly exhibit super-additive multisensory integration while the younger group mainly showed sub-additive multisensory integration in the P2 component in the frontal-central region.

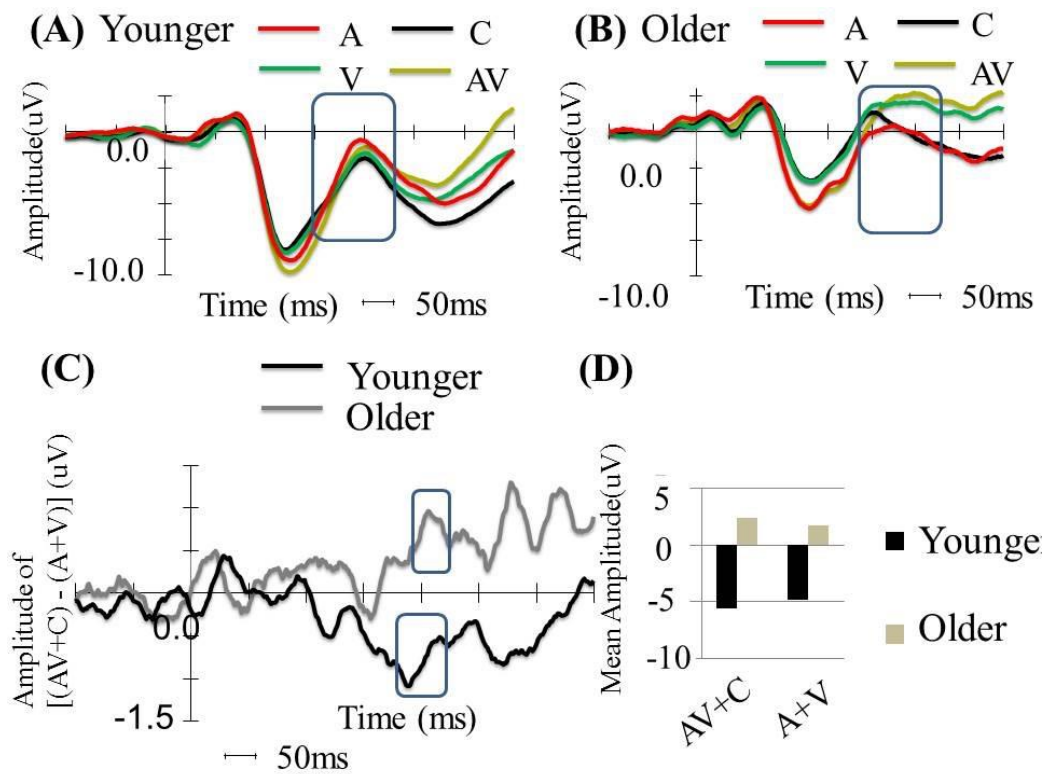


Figure 5.3 The figure shows the comparison of the ERP waveform between two groups for the FC2 electrode. (A) ERP waveform of younger participants with four conditions: auditory (A), visual (V), audiovisual (AV) and control (C) conditions. The waveform shows auditory P1, N1 and P2. (B) ERP waveform of older participants with four conditions: A, V, AV and C. The waveform shows auditory P1, N1 and P2. (C) Difference in amplitudes between (AV+C) and (A+V) in younger and older participants. (D) P2 mean amplitude of (AV+C) and (A+V) comparison between two groups.

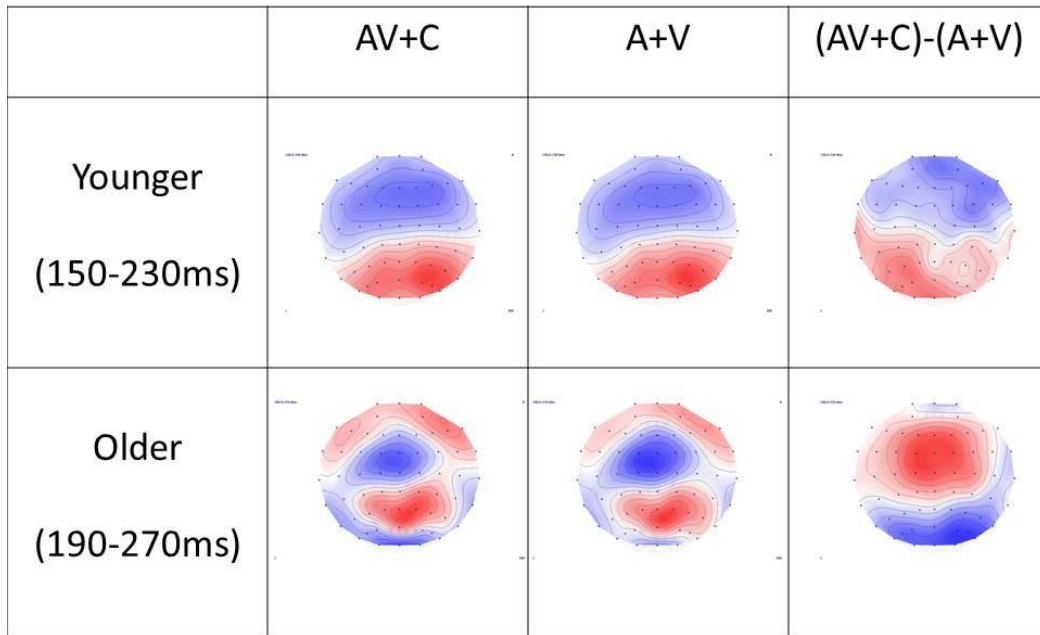


Figure 5.4 The figure shows the topography of (A+V), (AV+C) and [(AV+C)-(A+V)] in younger and older groups. In the younger group, the time window of P2 was chosen as 150-230 ms after the stimulus. The topography is mainly negative in the frontal-central region and positive in the parietal-occipital region in all three conditions. In the older group, the time window of P2 was chosen as 190-270 ms after the stimulus. A similar topography was observed in the (AV+C) and (A+V) conditions and reversed topography in the (AV+C)-(A+V) condition. Specifically, the positive result was in the frontal-central region while the negative result was in the parietal-occipital region, indicating a super-additive pattern in the frontal-central region.

Table 5.2 Mean amplitude (uV) of the P2 component in four conditions (A, V, AV and C) for younger and older participants. The figures are mean \pm SD.

| Mean amplitude / Condition | A | V | AV | C |
|-------------------------------|------------------|------------------|------------------|------------------|
| Younger | -2.06 \pm 4.59 | -2.76 \pm 3.53 | -2.50 \pm 4.66 | -3.06 \pm 3.66 |
| Older | -0.21 \pm 4.34 | 1.98 \pm 4.36 | 2.00 \pm 4.83 | 0.41 \pm 3.51 |

5.1.3.3 Moderation analysis between behavioral data and ERP data

We demonstrated in the behavioral analysis that multisensory information was more beneficial to older adults than younger adults in conducting audiovisual spatial discrimination tasks. Furthermore, in our ERP analysis we found super-additive integration of auditory-visual information in older adults, while we found sub-additive integration in younger adults. Next, we investigated whether there was a relationship between the neural and behavioral findings. For the neural index, the P2 amplitude of [(AV+C)-(A+V)] was regarded as a neural signature for audiovisual (super-additive or sub-additive) integration. For the behavioral index, we calculated the V modulation (IES (AV-A)) and A modulation (IES (AV-V)) as an indicator of the behavioral benefit from multisensory information. Hence, we employed stepwise multiple regression analysis to test if this neural signature P2 amplitude of [(AV+C)-(A+V)] could predict the behavioral benefit and if age was a moderator of this relationship. In the first step, age and P2 amplitude of [(AV+C)-(A+V)] were involved as regressors. In the second step, we added an interaction term (the product of the centered age and P2 amplitude) into the regression model (Aiken & West, 1991).

In the first step of the regression analysis, there was a significant effect of age ($\beta = -0.33$, $P = 0.014$) but not P2 amplitude of [(AV+C)-(A+V)] ($\beta = -0.17$, $P = 0.188$) on the multisensory modulation of the IES score. These regressors accounted for a significant amount of variance ($R^2 = 0.16$, $F(2,59) = 6.45$, $P = 0.003$). Interestingly, the second step regression showed that the addition of the interaction term accounted for a significant proportion of the variance of the change of IES score ($\Delta R^2 = 0.16$, $\Delta F(1,59) = 9.94$, $P < 0.001$). Then, we performed post-hoc analysis to examine the interaction effect by running correlation analysis in each group. The correlation analysis demonstrated that in the younger group, the correlation between IES score of the behavioral benefit and the P2 amplitude of [(AV+C)-(A+V)] was non-significant ($r = 0.35$, $P =$

0.060; Figure 5.5, diamonds). However, a significant correlation was observed between the IES score of behavioral benefit and the P2 amplitude of [(AV+C)-(A+V)] in older group ($r = -0.42$, $P = 0.018$; Figure 5.5, squares).

5.1.3.4 Correlation analysis between MoCA and P2 amplitude of [(AV+C)-(A+V)]

The scores in four subscales were lower, which were visuospatial/executive (mean = 4.7 out of 5), attention (mean = 4.6 out of 5), memory (mean = 3.4 out of 5) and abstraction (mean = 1.7 out of 2). The correlation analysis was conducted between the EEG amplitudes at the FC2 electrode and the total score as well as the four subscales. Significant correlation was observed between the attention subscale and the V condition ($r = -0.42$, $P = 0.020$), as well as the P2 amplitude of [(AV+C)-(A+V)] ($r = 0.37$, $P = 0.043$). No other correlations were statistically significant for [(AV+C)-(A+V)] ($P > 0.050$)(Figure 5.6).

No significant correlations were observed between the mean amplitude of P2 in the AV, A, and V conditions or [(AV+C)-(A+V)] ($P > 0.050$) and the mean total score of MoCA.

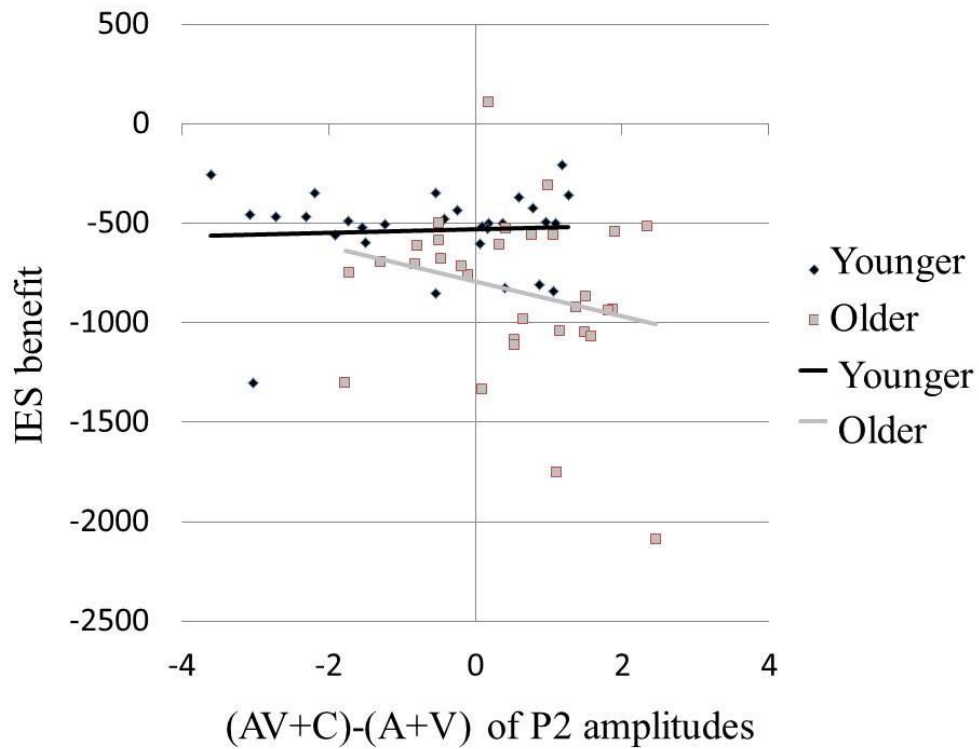


Figure 5.5 The figure shows the correlation between behavioral performance (IES) and neural integration ($[(AV+C)-(A+V)]$ of the P2 amplitude). Larger behavioral benefits were related to larger neural integration in multisensory information (indexed by $[(AV+C)-(A+V)]$ of the P2 amplitude in FC2) in older participants. Behavioral benefit in multisensory integration was indexed by the average between V modulation ($IES(AV-A)$) and A modulation ($IES(AV-V)$). Older participants with larger behavioral benefits (more negative values) also showed larger super-additive neural integration (more positive values; squares \blacksquare). However, in younger participants, the degree of behavioral benefit was marginally related to the degree of neural integration (diamonds \blacklozenge).

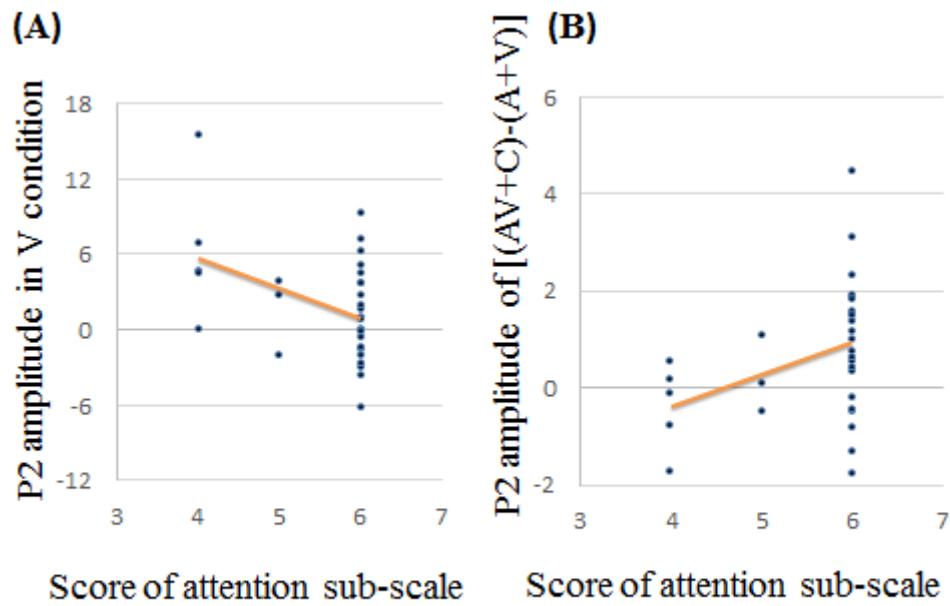


Figure 5.6 The figure shows the correlations between the attention sub-scale score of MoCA and the P2 amplitude in V condition as well as the P2 amplitude of [(AV+C)-(A+V)] at FC2 electrode in the older group. Figure A shows that the P2 amplitude in V condition was negatively correlated with the score of attention sub-scale. Figure B shows the P2 amplitude of [(AV+C)-(A+V)] was positively correlated with the attention sub-scale score.

5.1.4 LRP results

5.1.4.1 Mean amplitude of the LRP

A two-way ANOVA was performed to test the effects of condition (AV, A or V) and age (older or younger) on the mean amplitude of the s-LRP with the time window at 700 - 1500 ms. The results showed a significant condition effect ($F(2,116) = 7.90, P = 0.003$), but no significant age effect ($F(1,58) = 0.21, P = 0.465$) or condition \times age effect was observed ($F(2,116) = 0.66, P = 0.458$). Post-hoc analysis which tested the main effect of the conditions showed that the s-LRP mean amplitude in the AV condition was significantly less negative-going than that in both the A ($t(59) = -3.65, P=0.001$) and V conditions ($t(59) = -2.77, P = 0.008$)(Figure 5.7).

Next, we tested the effects of condition (AV, A or V) and age (older or younger) on the mean amplitude of the r-LRP. The results showed a significant condition effect ($F(2,116) = 8.73, P = 0.001$) and age effect ($F(1,58) = 4.39, P = 0.041$). The interaction effect between condition and age was also significant ($F(2,116) = 4.30, P = 0.025$). Post-hoc comparisons showed that the mean amplitude of the r-LRP in the younger group was significantly less negative-going than that in the older group in both uni-sensory conditions, i.e. A ($t(58) = 2.27, P = 0.025$) and V conditions ($t(58) = 3.92, P < 0.001$). However, there was no significant difference between the younger and older participants in AV condition ($t(58) = 1.53, P = 0.131$). In the younger group, no difference between the A and AV conditions ($t(28) = -2.04, P = 0.051$) or between the V and AV conditions ($t(28) = 1.84, P = 0.077$) was observed. However, in the older group, the amplitude in the AV condition was significantly less negative-going than in the A condition ($t(30) = -2.88, P = 0.007$) and V condition ($t(30) = -4.82, P < 0.001$)(Figure 5.8).

5.1.4.2 Correlation between LRP amplitude and behavioral data

To test the neural process that is responsible for the behavioral enhancement, a correlational analysis was conducted to explore the correlation between the mean amplitude of both s-LRP and r-LRP and the behavioral performance indexed by the IES in each condition (AV, A and V). To explore if the modulation in s-LRP is correlated with the modulation of P2, the correlation analysis was also conducted between the P2 amplitude and LRP amplitude in each condition (A, AV and V). As the recruitment of contralateral brain cortex increased for non-dominant hand side movement in older group compared to their younger counterparts (Wang, 2016), the LRP which calculated with both hand movements may contaminate the results. In other words, as all the participants of the present study were right handed and there was no lateralization in P2 process, the LRP calculated by $\{[C4' (t) - C3' (t)] \text{ left hand} + [C3' (t) - C4' (t)] \text{ right hand}\} / 2$ could be larger in the older adults as the lateralization increased. Hence, the correlation analysis of the P2 amplitude with the LRP (calculated with C3-C4) for right hand response and left hand response (calculated with C4-C3) was also conducted respectively for each condition. The results demonstrated a non-significant correlation between the mean amplitude of the r-LRP and IES in the AV condition in the younger group ($r = -0.23$, $P = 0.232$) but the older group demonstrated a significant correlation ($r = -0.43$, $P = 0.016$) (Figure 5.8). No significant correlation between the IES and r-LRP amplitude in uni-sensory conditions (A and V conditions) was observed. Only the correlation between the P2 amplitude and the s-LRP calculated with (C3-C4) for right-hand response was significant in each condition (A: $r = 0.46$, $P = 0.010$; V: $r = 0.37$, $P = 0.038$; AV: $r = 0.41$, $P = 0.023$) and no other significant correlation was observed between the P2 amplitude and both the s-LRP and r-LRP amplitude.

5.1.4.3 LRP onset latency

In terms of the s-LRP onset latency comparison, significant condition \times age effect was observed ($F(2,116) = 4.45, P = 0.014$). The results also showed a significant main effect of condition ($F(2,116) = 17.80, P < 0.001$) and non-significant age effect ($F(1,58) = 0.34, P = 0.715$). Post-hoc analysis demonstrated that the onset latency in the AV condition was significantly earlier than the A condition in both groups (younger group: 231 ms, $t(28) = 4.08, P < 0.001$; older group: 76 ms, A & AV: $t(30) = 3.24, P = 0.003$). The onset latency in the AV condition was marginally earlier than in the V condition in the younger group (64 ms, $t(28) = 1.92, P = 0.066$), but no significant difference was found in the older group (22 ms, $t(30) = 1.16, P = 0.254$).

In terms of the r-LRP onset latency, the results showed a significant main effect of condition ($F(2,116) = 6.06, P = 0.031$) and age ($F(1,58) = 9.88, P = 0.003$), but no significant condition \times age effect ($F(2,116) = 1.44, P = 0.241$). In order to examine the modulation of the multisensory process on response generation, the post-hoc comparison compared the onset latency of the r-LRP with the entire sample (both younger group from Study 1 and older group from Study 2). The results showed no significant onset latency between the AV and V conditions (21 ms faster in V; $t(59) = 0.56, P = 0.581$) as well as between the AV and A conditions (130 ms faster in AV; $t(59) = -2.18, P = 0.037$, with the significant threshold of $P = 0.017$).

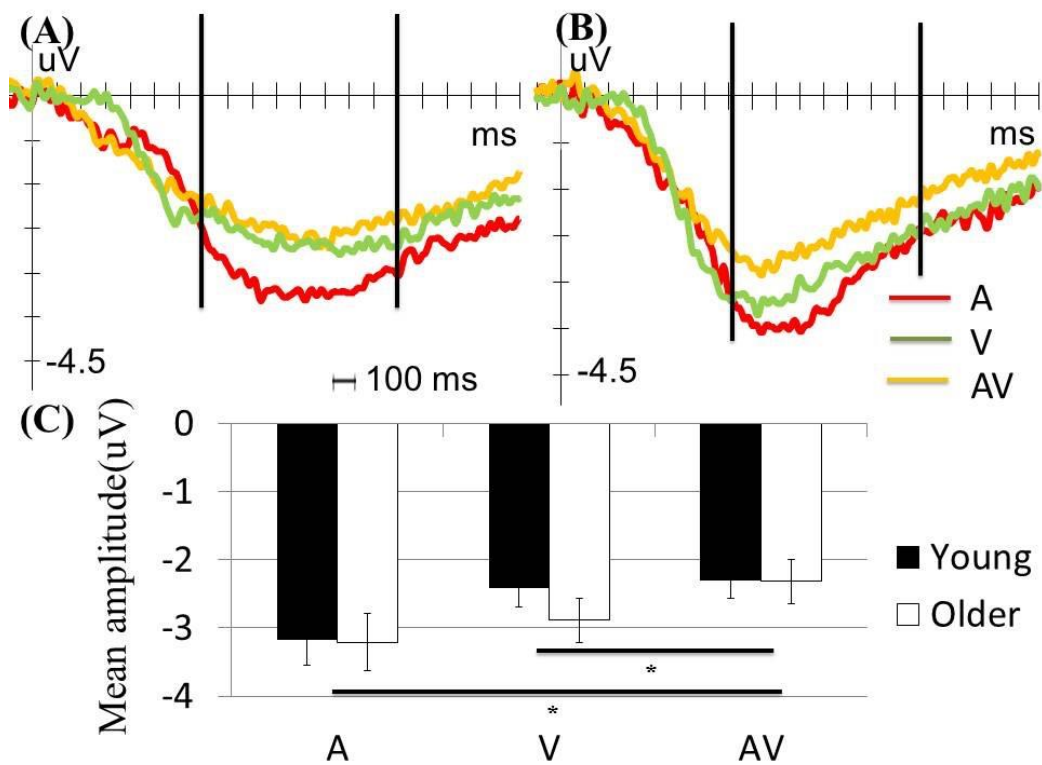


Figure 5.7 The figure shows the waveform of the s-LRP as well as the comparison of mean amplitude of the s-LRP between the younger and older groups. (A) The figure shows the s-LRP waveform of the younger participants in Study 1. (B) The figure shows the s-LRP waveform of the older participants in Study 2. (C) The figure shows the comparison in the A, V and AV conditions of the s-LRP amplitude between the younger and older participants. The x-axis shows different conditions and the y-axis shows the mean amplitude (uV). The bars show the time window of the mean amplitude calculation. The error bars show the standard error.

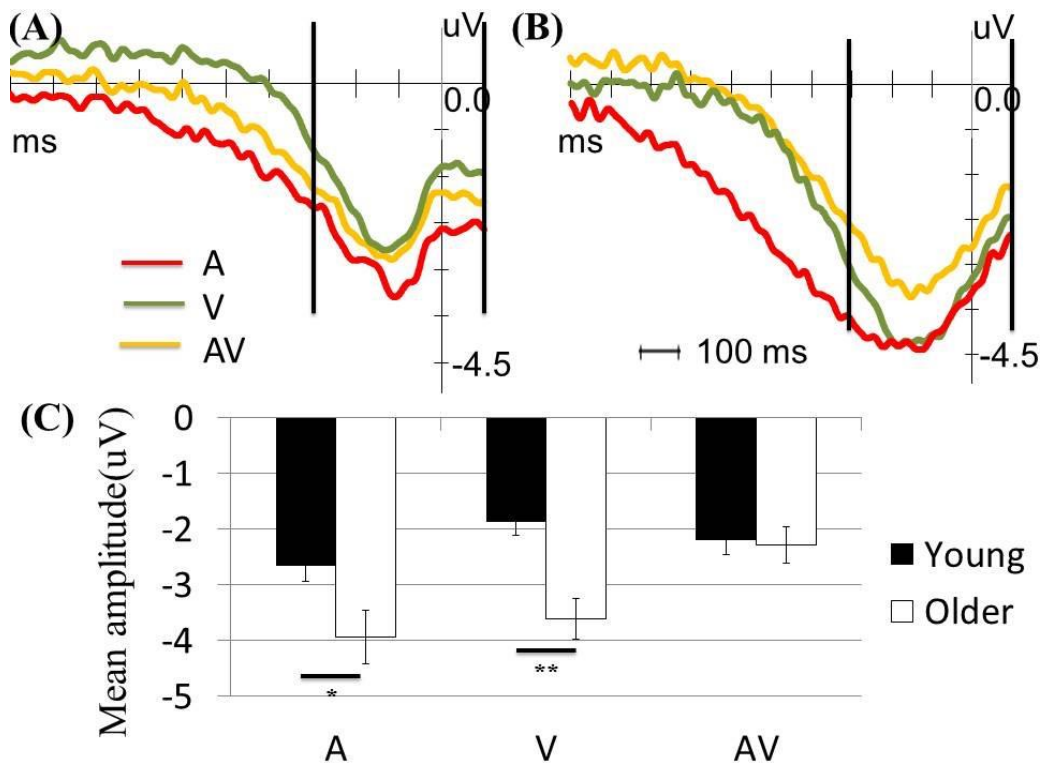


Figure 5.8 The figure shows the waveform of the r-LRP as well as the comparison of mean amplitude of the r-LRP between the younger and older groups. (A) The figure shows the r-LRP waveform of the younger participants in Study 1. (B) The figure shows the r-LRP waveform of the older participants in Study 2. (C) The figure shows the comparison in the A, V and AV conditions of the r-LRP mean amplitude between the younger and older participants. The x-axis shows different conditions and the y-axis shows the mean amplitude (uV). The bars show the time window of the mean amplitude calculation. The error bars show the standard error.

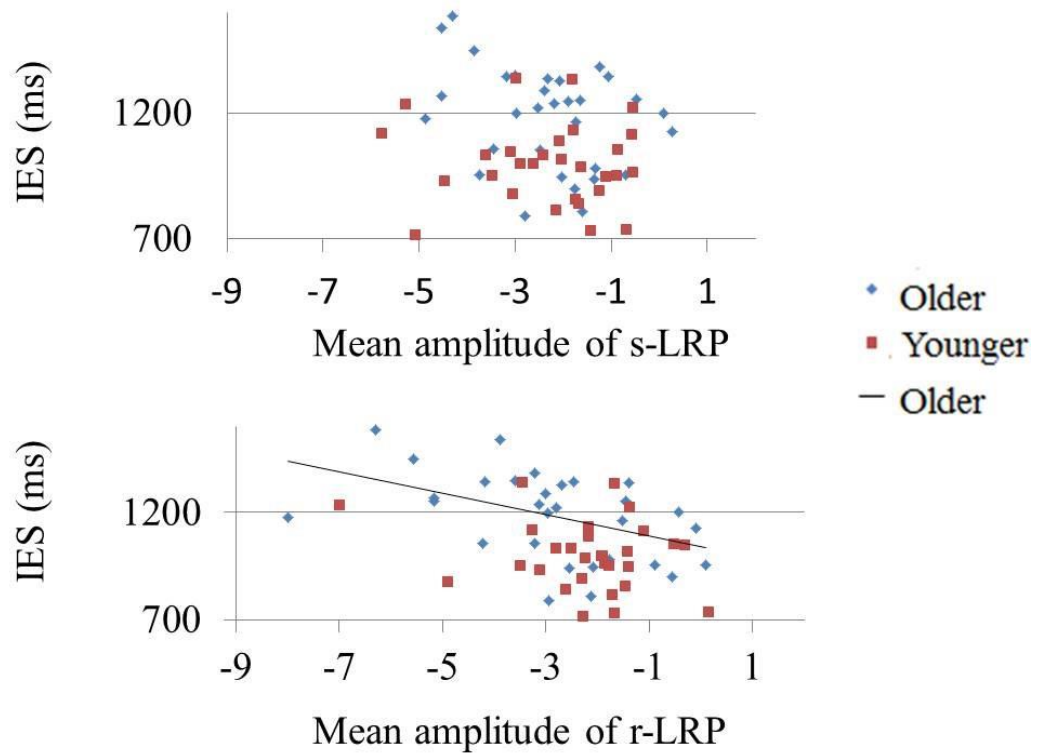


Figure 5.9 (A) The figure shows the IES score and s-LRP mean amplitude in both younger and older groups. No significant correlation was revealed between the behavioral performance in the AV condition and s-LRP mean amplitude. **(B)** The figure shows the IES score and r-LRP mean amplitude in both younger and older groups. Enhanced behavioral performance in the AV condition was related to less negative-going r-LRP amplitude in older participants. Older participants with enhanced behavioral performance in the AV condition (smaller IES) also exhibited less negative-going r-LRP amplitude (squares ■). However, in younger participants, the behavioral performance in the AV condition was not correlated with the r-LRP amplitude (diamonds ♦).

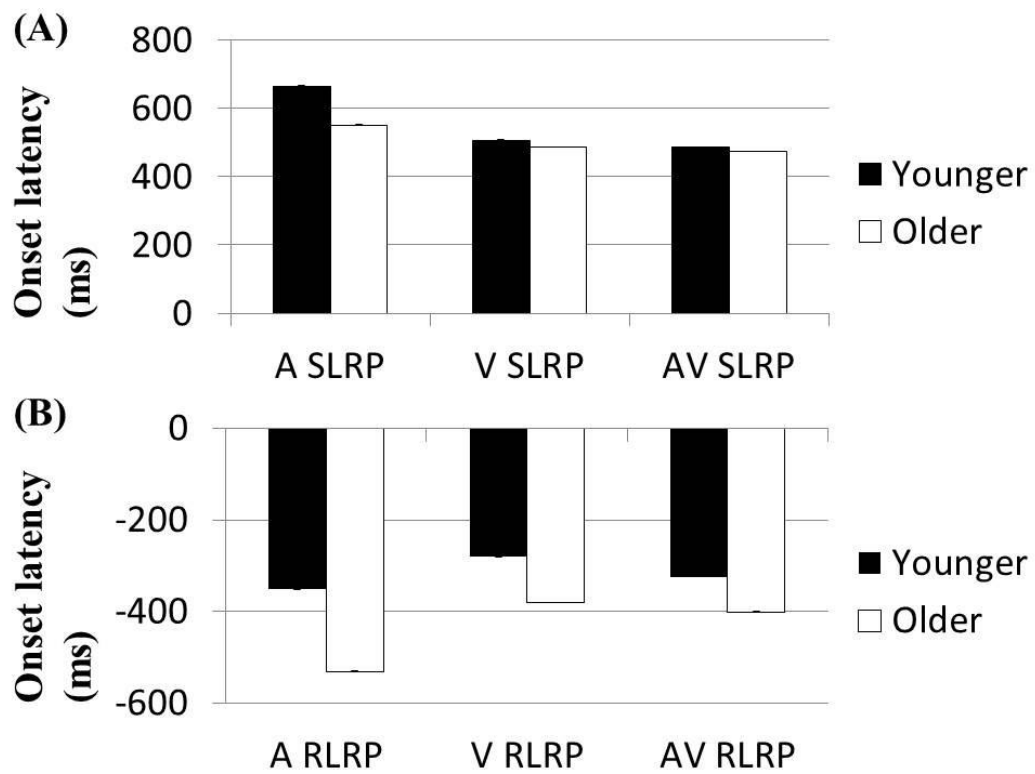


Figure 5.10 The figure shows the onset latency of both the s-LRP(A) and r-LRP(B) in the A, V and AV conditions compared between younger and older participants. The x-axis shows different conditions (A,V and AV) and the y-axis shows the onset latency (ms).

5.1.5 EMG results

5.1.5.1 Onset latency of EMG

The condition effect of the left extensor carpi radius (LECR) which is the muscle responsible for left wrist extension onset latency was significant ($F(2,116) = 5.98, P = 0.003$) while no significant interaction effect ($F(2,116) = 1.54, P = 0.223$) or age effect ($F(1,58) = 1.22, P = 0.274$) was observed (Fig. 5.11A). Similar results were also observed for the left flexor carpi radius (LFCR) which is the muscle responsible for left wrist flexion which demonstrated a significant condition effect ($F(2,116) = 4.54, P = 0.019$) while no significant interaction effect ($F(2,116) = 0.25, P = 0.738$) or age effect ($F(1,58) = 1.00, P = 0.321$) was observed (Fig. 5.11B).

A significant condition effect ($F(2,116) = 35.17, P < 0.001$) as well as age effect ($F(1,58) = 4.69, P = 0.035$) of the onset latency of the right extensor carpi radius (RECR) which is the muscle responsible for right wrist extension was observed, while the interaction effect was non-significant ($F(2,116) = 0.21, P = 0.752$)(Fig. 5.11C).

The condition effect of the right flexor carpi radius (RFCR) which is the muscle responsible for right wrist flexion onset latency was significant ($F(2,116) = 11.75, P < 0.001$), but not the age effect ($F(1,58) = 1.49, P = 0.228$). Significant interaction effect was observed ($F(2,116) = 3.47, P = 0.035$)(Fig. 5.11D). Post-hoc comparison with the paired t-test showed that in the younger group, no significant difference was observed between the AV and A conditions ($t(28) = -0.05, P = 0.960$) or V condition ($t(28) = -1.61, P = 0.118$), while in the older group, the onset latency of the AV condition was significantly earlier than that of the A condition ($t(30) = 3.16, P = 0.004$), but the onset latency of the V condition was significantly faster than that of the AV condition ($t(30) = -2.46, P$

= 0.020).

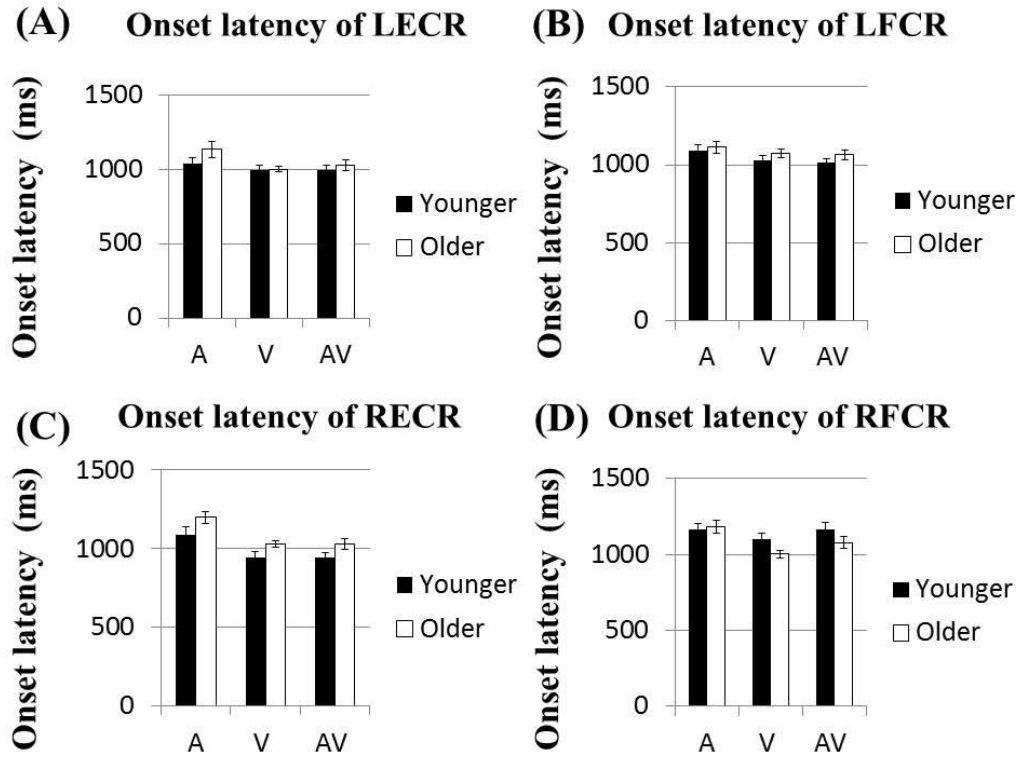


Figure 5.11 The figure shows the onset latency of the four muscles measured (LECR, LFCR, RECR, RFCR) in the A, V and AV conditions compared between younger and older participants. The x-axis shows different conditions and the y-axis shows the onset time (ms). The error bars show the standard error.

5.1.5.2 Peak amplitude of EMG

The main effect of condition of the LECR peak amplitude was significant ($F(2,116) = 19.19, P < 0.001$), but no significant age effect ($F(1,58) = 0.73, P = 0.398$) or interaction effect was observed ($F(2,116) = 0.50, P = 0.610$)(Fig. 5.12A). Similarly in the RECR, the main effect of condition was significant ($F(2,116) = 15.07, P < 0.001$), but no significant age effect ($F(1,58) = 0.11, P = 0.743$) or interaction effect was observed ($F(2,116) = 1.49, P = 0.229$)(Fig. 5.12C).

The condition effect of the LFCR peak amplitude was significant ($F(2,116) = 5.41, P = 0.006$), but no significant interaction effect ($F(2,116) = 0.003, P = 0.958$) or age effect ($F(1,58) = 0.39, P = 0.537$) was observed (Fig. 5.12B). Similarly, the main effect of condition of the RFCR peak amplitude was significant ($F(2,116) = 4.93, P = 0.011$), but no significant interaction effect ($F(2,116) = 0.003, P = 0.958$) or age effect ($F(1,58) = 0.92, P = 0.342$) was observed (Fig. 5.12D).

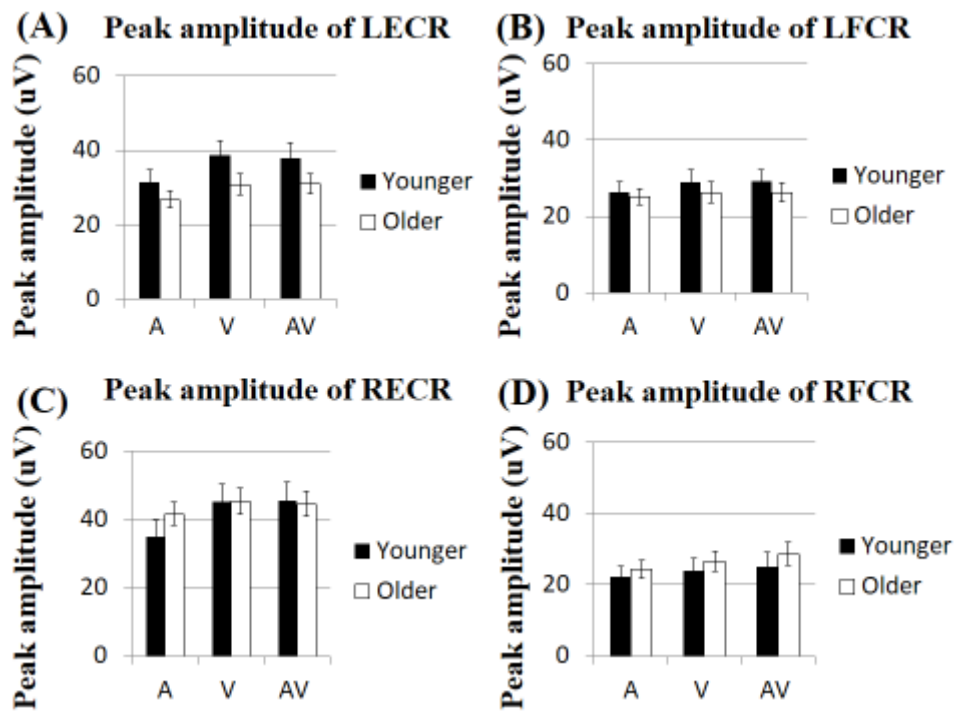


Figure 5.12 The figure shows the peak amplitude of the four muscles measured (LECR, LFCR, RECR, RFCR) in the A, V and AV conditions compared between younger and older participants. The x-axis shows different conditions and the y-axis shows the peak amplitude (uV). The error bars show the standard error.

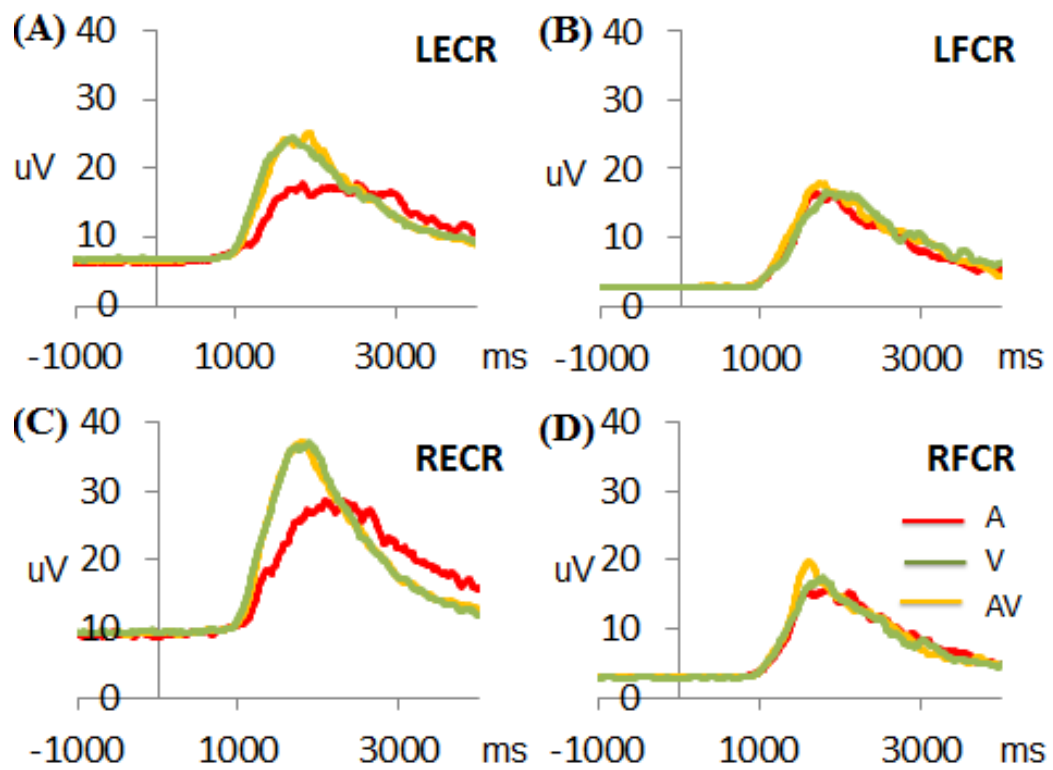


Figure 5.13 EMG waveform of the four muscles measured in the experiment (LECR, LFCR, RECR, and RFCR) in the older group. The x-axis shows the time line (ms) from -1000 ms before the onset of stimulus to 3000 ms after the onset of stimulus and the y axis shows the amplitude (uV).

5.2 Discussion

This study (Study 2) aimed to explore the aging effect on the neural processes of audiovisual integration from the early sensory process to the response selection and generation processes. The results show that in the perceptual and feedback processes, age modulated the audiovisual integration at around 200 ms after the stimulus. Specifically, older adults mainly exhibited super-additive pattern while the younger participants mainly exhibited sub-additive pattern in the fronto-central region, indicating the aging effect modulates the perceptual and feedback stages in audiovisual integration. The behavioral results demonstrated more behavioral improvements (larger degrees of decrease in the IES score) when older participants received multisensory (audiovisual) stimuli, compared to younger participants. Also, the moderation analysis showed a higher $[(AV+C)-(A+V)]$ of the P2 amplitude which could predict a lower IES score. These results demonstrate that multisensory information is particularly beneficial for improving the perceptual and feedback processes in older adults and this is related to the super-additive multisensory integration in the P2 component at the FC2 region. This kind of P2 component modulation could be a compensation of the declined attention in older group. In the motor process stage, the multisensory integration modulates response selection in a similar fashion in younger and older adults while the multisensory integration modulates the motor generation differently between younger and older people. Specifically, the s-LRP amplitude in the multisensory condition (AV) was less negative-going compared to both uni-sensory conditions (A or V) in both groups. Furthermore, in the older group, the P2 amplitude was significantly correlated with the s-LRP amplitude suggesting the modulation in the response selection process is a consequence of the perceptual and feedback stage modulation. Although the r-LRP amplitude was less negative-going in the AV condition compared to either uni-sensory conditions, such modulation effect was different between the younger and older groups. That is, the older

participants showed a significantly less negative going r-LRP in the multisensory condition compared to the visual and auditory conditions. However, no such difference was observed in the younger group. This suggests that the enhanced behavioral performance in older adults when receiving congruent multisensory information could be related to the enhanced effectiveness of the motor response generation process.

No significant results were observed at the occipital site in the older group in the perceptual and feedback processes suggests that the modulation could have more influence on auditory rather than visual functions. Similarly, no significant results were observed in the EMG data. As the EMG signal is composed of motor unit action potential, the more motor units are recruited in the movement the higher the EMG amplitude is. No significant differences were revealed in the EMG amplitudes between the multisensory and uni-sensory conditions suggesting that multisensory integration does not have significant effects on modulating the peripheral motor execution.

5.2.1 Aging effect in the perceptual and feedback processes

The results in this study demonstrate that the fronto-central P2 is modulated by aging when conducting audiovisual integration tasks, indicating that multisensory integration is modulated by the aging effect in the perceptual and feedback processes. The results in perceptual and feedback processes in younger participants were consistent with previous findings that the P2 component in the fronto-central region exhibited a sub-additive pattern in younger adults (Stekelenburg & Vroomen, 2013). Stekelenburg and Vroomen (2013) demonstrated that younger healthy participants exhibited a decreased P2 amplitude in the audiovisual condition compared to the sum of auditory and visual conditions (A+V), indicating the sub-additive pattern. The fronto-central

P2 could also serve as a marker of aging effect in various tasks. Specifically, in attentional tasks which require attention allocation (Moreno et al., 2011; Staub et al., 2014; Tallus et al., 2015; Wild-Wall et al., 2012) as well as response-conflict tasks which require stimulus evaluation (Gajewski et al., 2008 ; Potts et al., 2004), older adults demonstrated a significant delayed and increased P2 component compared to their younger counterparts. The delayed P2 peak latency indicated that the older adults suffered a greater delay in discriminating auditory information compared to younger adults (Lister et al., 2011). On the other hand, previous study demonstrated that the P2 amplitude could represent the stimulus evaluation process (Gajewski et al., 2008). Hence, the increased P2 amplitude found in this study suggests the aging effect modulates the stimulus evaluation process when discriminating stimuli from visual and auditory modalities.

In the audiovisual integration task used in this study, the participants were required to discriminate the four locations conveyed by visual or auditory or both modalities, which involved the encoding and discrimination of the stimuli. The super-additive pattern of P2 component at the fronto-central site in the older group compared to their younger counterparts in AV condition represented that it could be very important for the older participants to integrate audiovisual spatial information to provide correct response. The significant correlation between the P2 amplitude of $[(AV+C)-(A+V)]$ and behavioral benefit could further support this hypothesis. The evidence provided by another study also supported this hypothesis (Getzmann et al. 2013). Specifically, they demonstrated that after training the older participants to discriminate pitch from the background noise, their behavioral performance in terms of accuracy rate could be enhanced and the P2 amplitude could be increased after training, indicating the increased behavioral performance was positively correlated with the P2 amplitude (Getzmann et al., 2013). Prior evidence also showed that the fronto-central P2

could reflect the judgment of auditory frequency process indicating the fronto-central P2 could represent the process of auditory information (Noguchi et al., 2015). Taking all these results together, the increased P2 amplitude that is the super-additive pattern of the P2 amplitude in the older group indicated that audiovisual integration enhances the deteriorated encoding and evaluation of auditory information in older adults.

The alternative explanation to the super-additive pattern of the P2 component is that it could be related to the deteriorated attention function in older adults. It has been reported that cognitive functions especially attention, working memory as well as executive function decline in community-dwelling older adults (Chan et al., 2017; Hsu et al., 2015). The fronto-central P2 was also reported to be a marker of attention, especially for the physical properties of sound (Tiitinen et al., 2006). In this study, the results also demonstrated a significant positive correlation between the P2 amplitude of $[(AV+C)-(A+V)]$ with the score of attention subscale in MoCA, which indicated that the modulation for older participants who had higher attention function could be enhanced more while the older participants with decreased attention function gained less from audiovisual integration. The findings in this study are also consistent with the previous evidence that older adults demonstrate declined attention ability in both unimodal (Andrés et al., 2006; Yang & Hasher, 2007) as well as multimodal conditions (Alain & Woods, 1999; Poliakoff et al., 2006).

The results of this study were inconsistent from a previous study which used MEG as the neurophysiology measurement (Stephen et al., 2010). Stephen (2010) and her colleagues reported that the difference between younger and older group was in the STG around 200 ms after stimulus. Specifically, a sub-additive pattern of P2 in the fronto-central region was observed in the older group and a super-additive pattern of P2 was reported in the younger group.

The reason of the inconsistent results may be related to the control condition involved in this study and a different formula used to compute the audiovisual integration. In this study, $[(AV+C)-(A+V)]$ was used while $(AV-A)$ was employed in the previous study (Stephen et al., 2010). Specifically, the modulation effect that is the comparison of $(AV-A)$ and $(AV-V)$ could adjust the potential baseline difference in the uni-sensory conditions (A and V) between younger and older groups. However, as reviewed in the second chapter, involving the control condition and adopting the formula of $[(AV+C)-(A+V)]$ could cancel out most of the common activities (Gondan et al., 2006; Mishra et al., 2007; Talsma et al., 2005).

Another inconsistent result was that no significant differences were demonstrated in this study for the early components for the perceptual process, such as C1 and P1 (around 100 ms post stimulus)(Cappe et al., 2010). This inconsistent finding could also be related to the noise added in the stimuli. A fMRI study which embedded noise in both auditory and visual stimuli also provided similar results as the results in this study (Saldern & Noppeney, 2013). Specifically, Saldern and Noppeney (2013) demonstrated that no activation was observed in the both primary visual and auditory cortices which are responsible for perceptual processes.

In this study, the difference in multisensory integration between the two groups was only observed in the frontal-central region, which is related to auditory processes. However, the difference was not found in the occipital region, which is related to visual processes. One of the reasons could be related to the dominance modality in the spatial localization task. Previous studies demonstrated that visual messages could provide more reliable and detailed spatial information (Beierholm et al., 2009; Callan et al., 2015). Hence, both younger and older participants provided their response based on visual

information more than auditory information when they receive audiovisual stimuli at the same time. However, this proposition is less convincing in that in the pre-experiment session. The participants in both groups had been trained to calibrate the difficulty of stimuli to the same level for both visual and auditory stimuli. Furthermore, no significant difference of accuracy rate was found between visual and auditory conditions after calibration. The alternative explanation of non-significant occipital-parietal modulation is that the older participants would rely more on the visual information compared to their counterparts as there had been a steeper deterioration in their auditory rather than visual functions. This hypothesis was consistent with previous evidence which demonstrated that older participants relied more on visual than auditory information during speech perception while the younger relied more on auditory than visual information (Cienkowski & Carney, 2002). The declined sensitivity of the auditory system in aged people could contribute to this different reliance between younger and older group (Freigang et al., 2014). Recent evidence also demonstrates that the effective multisensory integration could be related to learning from experience (Bauer et al., 2015; Hecht & Gepperth, 2015). The results in this study also showed increased accuracy rate in auditory condition compared with visual condition in older adults ($P = 0.005$) which supported the older adults learned to rely more on visual information. However, no significant difference was observed in younger group of the accuracy rate between visual and auditory conditions ($P = 0.834$). Hence, in the older group, the information evaluation process in auditory modality could be helped by visual modality and the behavioral performance could also be enhanced.

5.2.2 Aging effect in response selection and generation processes

The results in this study demonstrate that the multisensory integration in the response generation process is modulated by aging effect, but no modulation of

aging effect could be observed in the response selection process. As the LRP component measures the difference of activation level between two premotor cortices in the left and right hemispheres (Sterr & Dean, 2008), the less negative-going r-LRP amplitude in the older group could represent more effective activation in the motor cortices. Previous studies demonstrated that the more negative-going LRP amplitude could represent dysregulation of the motor cortex (Falkenstein et al., 2006; Wang, 2016; Yordanova et al., 2004). Furthermore, Wang (2016) employed different difficulty levels of a sensorimotor task in older and younger participants. Their results showed that when the participants performed a stimulus discrimination task with a lower difficulty level, the r-LRP amplitude became significantly less negative-going in the older group but not in the younger group, indicating that the more negative-going LRP amplitude in complex stimulus discrimination tasks could be related to the increased dysregulation of the motor cortex in older adults. Therefore, the less negative-going r-LRP in the multisensory condition compared to the uni-sensory condition could be caused by the decreased complexity of the task in the multisensory condition and further induce more effective activation in the motor cortex for motor response generation. The modulation in the response generation stage could be contributed by the “cortico-thalamo-cortico” route (Cappe et al., 2012). This route involves the connection between the cortex and thalamus (Sherman, 2007). Prior evidence showed that the thalamus, which relays information between sensory and motor areas, is involved in multisensory integration (Cappe et al., 2009a, 2009b). Specifically, a study of macaque monkeys as subjects demonstrated that the thalamus can receive sensory information from various modalities and project the information to the motor cortex (Cappe et al., 2009b). This result indicates that the thalamus could integrate different sensory modalities with motor attributes. These authors also argued that rapid perceptual discrimination with multisensory stimuli, relative to uni-sensory stimuli, is also related to more rapid relay of information from the

thalamus to the motor cortex (Cappe et al., 2009b, 2012). Therefore, the thalamus may integrate the information from heteromodal cortices and further relay the integrated information to the motor cortex (cortico-thalamo-cortico route) and further enhance the behavioral performance.

People may also argue that the task was too easy for the younger participants resulting in no further improvements being observed in the younger group. As shown in Table 5.3, the accuracy rate in the younger group did not reach the ceiling (100% correct) in each condition. Statistical analysis also demonstrated that the accuracy rate in the younger group was significantly lower than 0.95 in each condition. These results indicate that the task was not easy for the younger participants. Therefore, the non-significant finding in the r-LRP amplitude between multisensory condition and uni-sensory condition observed in the younger participants was not related to the ceiling effect.

Table 5.3 Accuracy rate in the three conditions (A, V, and AV) in both the younger group in Study 1 and the older group in Study 2. The figures are mean \pm SD.

| Accuracy rate | A condition | V condition | AV condition |
|---------------|-----------------|-----------------|-----------------|
| Younger | 0.80 \pm 0.07 | 0.79 \pm 0.07 | 0.92 \pm 0.05 |
| Older | 0.66 \pm 0.11 | 0.73 \pm 0.12 | 0.85 \pm 0.10 |

The results of this study are inconsistent with previous study which demonstrated that accessory sound cannot modulate the r-LRP amplitude (Jepma et al., 2009). The authors argued that the reason for the non-significant change in the r-LRP could be that the LRP measures the activation difference between the relevant and irrelevant motor cortex, while accessory sound increases the activation of both motor cortices (Jepma et al., 2009). Los and Burg (2013) also demonstrated that accessory sound may not necessarily integrate with the visual stimuli, so accessory sound could have only increased the attention level of the participants. However, the auditory stimuli used in Studies 1 and 2 reported in this thesis contained task-related information which could be integrated with visual stimuli. Therefore, the audiovisual integration might modulate the motor cortex specifically and further increase the r-LRP amplitude and the less negative-going r-LRP in the multisensory condition could be related to the effect of multisensory integration which modulated the response generation process.

The more negative-going r-LRP mean amplitude in the uni-sensory condition in the older group in comparison with the younger is consistent with the findings of previous studies (Amenedo et al., 2014; Wiegand et al., 2013). A study which used a visual search task demonstrated that the r-LRP was significantly delayed and pronounced in the older group (Wiegand et al., 2013). The more negative-going LRP associated with uni-sensory information in older adults was related to the functional dysregulation in the older motor cortex (Kolev et al., 2006; Yordanova et al., 2004). Specifically, the pre-activation of cortical motor areas could become insufficient in older adults, so a higher activation in the motor cortex contralateral to the response hand is needed (Kolev et al., 2006; Yordanova et al., 2004). Previous functional magnetic resonance imaging (fMRI) studies also demonstrated that when performing a simple motor task, additional areas, such as frontal region are recruited in older adults suggesting that the motor cortex is less effective in generating the motor

responses in older adults (Heuninckx et al., 2008; Mattay et al., 2002).

Besides the r-LRP amplitude, the s-LRP amplitude was also significantly less negative-going in the multisensory condition compared to uni-sensory conditions in both younger and older groups. The s-LRP amplitude measured the difference of activation level between the relevant and irrelevant motor cortex and the s-LRP amplitude is related to the evidence accumulation in the motor cortex that favors the initiation of a certain response (Jepma et al., 2009; Van Vugt et al., 2014). Therefore, less negative-going LRP amplitude can indicate a higher level of general motor preparation or a decreased threshold of motor response between the two options at the motor cortex level (Wild-Wall et al., 2008). As the s-LRP amplitudes were significantly correlated with the P2 amplitude with the present data, this kind of decreased threshold could be a consequence of the modulation of multisensory integration in the perceptual and feedback process. Additionally, in the AV condition, the presentation of both visual and auditory information could provide more detailed spatial evidence for a choice to be made, further decreasing the competition level between the two hands. As the s-LRP amplitude measured the difference of activation level between the relevant and irrelevant motor cortex, the decreased competition between the two motor cortices could increase the s-LRP amplitude. The decreased onset latency of s-LRP in the AV condition also supported the fact that the competition level between the two hands decreased. The decreased competition further causes a shorter time to make a decision on choosing the response hand. For the s-LRP onset latency, no significant age effect was observed and this result is consistent with previous studies (Falkenstein et al., 2006; Yordanova et al., 2004). Yordanova et al. (2004) argued that the increased response time in older adults is not contributed by the response selection process. In summary, audiovisual integration can decrease the response selection onset latency, but the aging effect does not modulate the response

selection process.

No significant difference of EMG amplitude and onset latency was found between the multisensory and uni-sensory conditions which indicates the multisensory process may not be able to modulate the peripheral motor execution, such as the motor unit action potential. Previous studies demonstrated that the response force can be enhanced when an accessory auditory signal is provided simultaneously with visual stimulus in a letter discrimination task and go-no go task (Kiesel & Miller, 2007; Stahl & Rammsayer, 2005). The reason may be because the accessory sound can modulate the arousal system which can further activate more motor muscle units (Jaskowski et al., 2000; Miller et al., 1999; Ulrich & Mattes, 1996; Wlodarczyk et al., 2002). However, the stimulus in both modalities used in this study conveyed congruent information rather than a neutral sound which may not be able to increase the attention and arousal level. Hence, the response force which belongs to the peripheral motor process may not be modulated by the multisensory process. No significant difference of r-LRP onset latency between multisensory and uni-sensory conditions also proved that the peripheral motor process may not be influenced by multisensory integration.

CHAPTER 6

GENERAL DISCUSSION AND CONCLUSIONS

6.1 General discussion

To investigate the impact of aging when receiving congruent multisensory information simultaneously, two studies were conducted. The aim of the first study (Study 1) was to validate the audiovisual discrimination task used in this thesis. In the first study (Study 1, Chapter 4), only younger participants were recruited and the results of Study 1 were consistent with previous findings, indicating that the audiovisual discrimination task is valid for investigating multisensory integration. The aim of the second study (Study 2) was to investigate the impact of aging in multisensory integration from the perceptual and feedback processes to response selection and generation processes. Hence, in the second study (Study 2, Chapter 5), older adults were recruited. The results of older adults in Study 2 were compared with the results of younger adults in Study 1. The results of comparison demonstrated that the older adults exhibited better behavioral improvements in terms of IES in the multisensory condition compared with their younger counterparts. Furthermore, the increased gain could be due to the modulation of multisensory integration in the perceptual and feedback processes and response generation process.

In the perceptual and feedback processes, a larger degree of super-additive neural response in the P2 component was found to be related to larger degrees of behavioral improvements in the multisensory condition in older adults. Additionally, significant correlation was found between fronto-central P2 amplitude and the attention function in older adults, suggesting that multisensory

integration compensated for the declined attention function in older adults when performing spatial discrimination tasks. The impact of aging on multisensory integration could also be observed in the response generation process. Specifically, multisensory integration modulated both response selection and generation while aging modulated the response generation process. The multisensory integration effect was reflected by the less negative-going s-LRP amplitude in the AV condition in both groups while the aging effect was reflected by the less negative-going r-LRP amplitude in the AV condition in the older group but not in the younger group. Furthermore, the less negative-going r-LRP amplitude was correlated with beneficial behavioral performance in the older adults. As the amplitude of fronto-central P2 was significantly correlated with the amplitude of the s-LRP, the results indicated that multisensory integration modulates the response selection as a consequent effect of modulation on the perception and feedback process. Furthermore, aging modulates multisensory integration in motor response generation indicating that the increased benefit from multisensory integration in the older group could be due to the modulation of motor response generation. These findings support the claim that multisensory integration plays an important role in compensating for the deterioration in motor generation in older adults. The correlations among the amplitude of different ERP components and the behavioral performance were regarded as weak. The weak correlations could be due to the relatively large variations of the amplitudes of the ERP components among the participants, which tended to limit the strengths of the correlations. Our results concur with those reported in previous studies in this area of which the correlations were around 0.40 (Dayan et al., 2017; Jones et al., 2017; Li et al., 2017; Meade et al., 2017).

The thalamic-cortical loop may be the neural pathway which contributes to this kind of compensation (Cappe et al., 2012). Prior evidence showed that the thalamus, which relays information between sensory and motor areas, is

involved in multisensory integration as well as integrating different sensory modalities with motor attributes (Cappe et al., 2009a, 2009b). Therefore, the thalamus may integrate the information from heteromodal cortices and relay the integrated information to the motor cortex (cortico-thalamo-cortico route) and further enhance behavioral performance. Taking all the results together, the aging effect modulates the audiovisual integrative process in both perceptual and feedback processes as well as the response generation process.

6.2 Conclusions

In summary, the results of this thesis demonstrate that the more enhanced behavioral performance in older adults compared with their younger counterparts when receiving multisensory information is related to the audiovisual modulation of the perceptual and feedback processes as well as response generation process. These modulations serve an important role to compensate for the deteriorated attention function as well as response generation function in older adults. Furthermore, the results of this thesis imply that audiovisual integration helps older adults in their daily activities. Moreover, this study can also serve as a basis for further work focusing on the multisensory integration in the patient population, for example, the post-stroke patients who suffered motor deficits. As providing information from different modalities can facilitate motor preparation, enriching the information or instructions provided to patients in rehabilitation treatment may increase the motor ability, like walking or reaching.

6.3 Limitations

The behavioral response was given by wrist extension and flexion in both Study 1 and Study 2, which may contaminate the ERP results because of the movement of the wrist. Further studies are needed to explore if other response

types could also replicate the results. As only auditory and visual information was provided in the task, further studies with other modalities such as olfactory modality are needed to explore multisensory integration. Also, cautions should be made when generalizing the results of this thesis to other types of multisensory integration with different modalities. Limited by the high difficulty level of this task, participants older than 75 years old were not recruited which limits the generalization of the results to people older than 75. This thesis mainly focused on the neural process in audiovisual integration and peripheral process modulation such as the tract of movement was not investigated. Future studies could collect kinesiology data and focus on the influence of multisensory integration on the movements.

APPENDICES

Appendix I Annett Handedness Questionnaire

Annett Handedness Questionnaire

ANNETT 慣用手問卷

Please indicate which hand you habitually use for each of the following questions.

針對以下事項，請註明你習慣用邊隻手

| | Question 事項 | Left 左 | Right 右 | Either 任何 |
|----|--|-----------|------------|--------------|
| 1 | To write a letter legibly? 你用邊隻手寫字? | | | |
| 2 | To throw a ball to hit a target? 你用邊隻手拎住個波，掙向一個目標? | | | |
| 3 | To hold a racket in tennis, squash or badminton? 你用邊隻手揸球拍打波? | | | |
| 4 | To hold a match whilst striking it? 你劃火柴既時候用邊隻手拎住支火柴? | | | |
| 5 | To cut with scissors? 你用邊隻手揸鉸剪? | | | |
| 6 | To guide a thread through the eye of a needle? 你穿針既時候用邊隻手揸住條線? | | | |
| 7 | At the top of a broom while sweeping? 揸掃把既時候，兩隻手你會用邊隻手揸上面? | | | |
| 8 | At the top of a shovel when moving sand? 劇沙既時候，兩隻手你會用邊隻手揸上面 | | | |
| 9 | To deal playing cards? 派啤牌時，你會用邊隻手派牌出去? | | | |
| 10 | To hammer a nail into wood? 踏釘時，你用邊隻手揸錘? | | | |
| 11 | To hold a toothbrush while cleaning your teeth? 刷牙既時候，你用邊隻手揸牙刷? | | | |

12 To unscrew the lid of a jar?

開樽蓋嗰陣，你用邊隻手擰開個樽蓋？

If you use the **right / left hand for all of the above actions**, are there any one-handed actions for which you use the other hand?

Please indicate:

如果全部以上的事項，你都用右/左手，有沒有任何單手的動作是用另外一隻手的？

請註明：

Appendix II Montreal Cognitive Assessment (Hong Kong version, MoCA-HK)

Montreal Cognitive Assessment Hong Kong version (HK-MoCA)
蒙特利爾認知評估香港版

姓名: _____
教育程度: _____
性別/年齡: _____ 日期: _____

| 視覺空間/執行性 | | 複製圖形 | | 畫時鐘 (十一點十分) (3分) | | | 分數 | | |
|--|--|---|--|---|--------|--------|--------|---|--------------------|
| | | | | [] [] [] 鐘面 數字 時分針 | | | | ___/5 | |
| 命名 | | | | | | | | | |
| | | | | | | | ___/3 | | |
| 記憶 | | 讀出詞語再由病者重複 以上步驟做兩次 5分鐘後回憶 | | 圓孔 | 絲絨 | 教堂 | 雛菊 | 紅色 | 不用 計分 |
| 專注 | | 讀出數字 (每秒一個) | | 第一次嘗試 | | | | | |
| | | 病者須把數字向前重複 [] 2 1 8 5 4 病者須把數字向後重複 [] 7 4 2 | | 第二次嘗試 | | | | | ___/2 |
| | | 讀出數字: 當數字 '1' 出現時病者必須用手敲打桌面 (如≥2分鐘便不給予分數) | | | | | | | ___/1 |
| | | 由100開始連續 7 減算 | | [] 93 | [] 86 | [] 79 | [] 72 | [] 65 | ___/3 |
| | | 4 或 5 個正確減算得 3 分, 2 或 3 個正確得 2 分, 1 個正確得 1 分, 沒有正確得 0 分 | | | | | | | |
| 語言 | | 重複: 橫文買賣講 [] 西施四十四歲 [] | | | | | | | ___/2 |
| | | 流暢: 一分鐘內能說出的動物名稱的數目 [] (N ≥ 11 個名稱) | | | | | | | ___/1 |
| 抽象 | | 相似點: 例如: 香蕉 - 橙 - 生菜 [] 火車 - 單車 [] 手錶 - 開尺 | | | | | | | ___/2 |
| 延遲記憶 | | 須回憶詞語 不可給提示 | | 圓孔 | 絲絨 | 教堂 | 雛菊 | 紅色 | 分數只給予沒有 提示的正確回憶 |
| | | 單項提示 (見下表) | | [] | [] | [] | [] | [] | |
| | | 多項選擇 (見下表) | | | | | | | |
| 定向 | | [] 日 [] 月 [] 年 [] 星期 [] 地點 [] 地區 | | | | | | | ___/6 |
| © Headline MD Hong Kong version 08 June 2010 Translated by Wing A and Mok V http://www.mocatest.org | | | | 延遲記憶備註表 題目提示 多項選擇 圓孔 身體的一部分 桌子, 圓孔, 手 絲絨 紡織品的一種 牛仔布, 棉花, 絲絨 教堂 建築物的一種 教堂, 學校, 醫院 雛菊 花的一種 玫瑰, 雛菊, 鬱金香 紅色 一種顏色 紅色, 藍色, 綠色 | | | | 總分 如≥26年教育加1分 22分或以上為正常 ___/30 | |

Appendix III Consent form used in this experiment

The Hong Kong Polytechnic University

Department of Rehabilitation Sciences

Research Project Informed Consent Form

Project title: The Effect of Audiovisual Spatial Information Integration on Motor Preparation & Execution

Investigator(s): Professor Chetwyn Chan (chief supervisor), Dr. Eric Tsang (co-supervisor), Zou Zhi (1290)

Project information:

The aim of this study is to investigate the mechanisms underlying cross audio-visual processing for modulating preparation and execution of motor actions in the upper limbs. Data capturing includes brain electrical activities called event-related potential (ERP) and muscle electrical activities called electromyography (EMG), and motor movements of the upper limbs.

Project content:

You will first be asked to provide some personal information. You will need to complete two cognitive tests - Mini-Mental State Examination and Montreal Cognitive Assessment, one hearing test (staircase audiogram test) and one visual acuity test before the experiment. You will go through a “Bat-ears” sound training session for discriminating four different sounds, which takes about 40 minutes to complete. This will be followed by a visual calibration session on the blurry level of visual stimuli, which takes about 20 minutes. The main experiment involves you to simultaneously listen to the sound and view visual stimuli. Based on the information received, you are required to make different movement responses with the upper limbs via the right and left joysticks. At the same time, the electrical signals produced from the brain and muscles will be recorded. The entire experiment will take about one hour to complete. *The study involves no risk* to participants.

Consent:

I, _____, have been explained the details of this study. I voluntarily consent to participate in this study. I understand that I can withdraw from this study at any time without giving reasons, and my withdrawal will not lead to any punishment or prejudice against me. I am aware of any potential risk in joining this study. I also understand that my personal information will not be disclosed to people who are not related to this study and my name or photograph will not appear on any publications resulted from this study.

I can contact the co-investigator Miss Zou at 2766 6764 or e-mail: jojo.zou@ . And you can also contact the chief investigator, Prof Chetwyn Chan at 2766 6727 or co-investigator, Dr Eric Tsang at 2766 6746 for any questions about

this study. If I have complaints related to the investigator(s), I can contact Ms Gloria Man, secretary of Departmental Research Committee, at 2766 4394. I know I will be given a signed copy of this consent form.

Signature (subject): _____ Date: _____

Signature (witness): _____ Date: _____

香港理工大學康復治療科學系科研同意書

研究題目

視聽聯合對運動準備及運動執行過程的影響：事件相關電位研究

研究員

主要科研人員：陳智軒教授，曾偉謙博士，鄒智

研究目的

本課題目的在於研究視聽聯合對於上肢運動準備及運動執行之影響機制。實驗將會利用事件相關電位（ERP）記錄腦部電活動，利用肌電圖（EMG）記錄肌肉電活動以及上肢的其他運動參數。

研究內容

在實驗開始前您需要首先填寫個人資料。之後您需要完成兩項認知測試，即簡易智能精神狀態檢查量表及蒙特利爾認知評估量表、一項聽覺測試（進階聽力測試）及視覺測試。此後，我們需要培訓您區分4種不同的“蝙蝠耳”聲音並通過測試（約耗時40分鐘）。另外，您還需要完成視覺校準測試（約耗時20分鐘）。在主實驗部份您會同時接受聽覺及視覺的位置信息，您需要按照信息內容通過雙手操縱左右兩側的遊戲桿來給出反饋。與此同時我們會記錄腦電活動及肌電活動。主實驗部份約耗時1小時。

潛在危險性：無。

同意書

本人_____已瞭解此項研究的具體情況。本人自願參與這項研究，本人有權在任何時候、毫無理由地退出這項研究，而此舉不需要我承擔任何後果。本人明白參加此項研究的潛在危險性以及本人的資料將不會洩露給與此研究無關的人員，名字或相片不會出現在任何出版物上。

本人可以用電話 2766 6764 或電郵 1290 @ _____來聯繫此次研究課題的研究人員鄒智女士或2766 6727來聯繫此次研究課題負責人陳智軒教授或2766 6746來聯繫課題負責人曾偉謙博士。若本人對此研究人員有任何投訴，可以聯繫文女士（部門科研委員會秘書），電話：2766 4394。本人亦明白，參與此研究課題需要本人簽署一份同意書。

簽名（參與者的名字）：_____ 日期：_____

簽名（證人）：_____ 日期：_____

Appendix IV Ethics approval for this study



THE HONG KONG
POLYTECHNIC UNIVERSITY
香港理工大學

To Chan Che Hin (Department of Rehabilitation Sciences)
From TSANG Wing Hong Hector, Chair, Departmental Research Committee
Email rshtsang@ Date 04-Jul-2014

Application for Ethical Review for Teaching/Research Involving Human Subjects

I write to inform you that approval has been given to your application for human subjects ethics review of the following project for a period from 07-Jul-2014 to 30-Dec-2016:

Project Title: The Effect of Audiovisual Spatial Information Integration on Motor Preparation & Execution
Department: Department of Rehabilitation Sciences
Principal Investigator: Chan Che Hin
Reference Number: HSEARS20140627001

Please note that you will be held responsible for the ethical approval granted for the project and the ethical conduct of the personnel involved in the project. In the case of the Co-PI, if any, has also obtained ethical approval for the project, the Co-PI will also assume the responsibility in respect of the ethical approval (in relation to the areas of expertise of respective Co-PI in accordance with the stipulations given by the approving authority).

You are responsible for informing the Departmental Research Committee in advance of any changes in the proposal or procedures which may affect the validity of this ethical approval.

You will receive separate email notification should you be required to obtain fresh approval.

TSANG Wing Hong Hector
Chair
Departmental Research Committee

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