ORIENTING ATTENTION FOR PAIN ATTENUATION IN PATIENTS WITH CHRONIC LOW BACK PAIN: A STUDY OF MECHANISM USING EVENT-RELATED POTENTIAL

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Orienting Attention for Pain Attenuation in Patients with Chronic Low Back Pain: A Study of Mechanism Using Event-Related Potential

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CERTIFICATE OF ORIGINALITY

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ABSTRACT

Orienting attention between one's internal and external environments involves both top-down control and bottom-up control, particularly when the external-to-internal (E–I) difference increases among patients with chronic pain (specifically chronic lower back pain (CLBP)). The three event-related potential components (ERP), i.e., N1 (100-200 ms), P2 (260-380 ms), and P3 (340-400 ms) can be markers reflecting the attention disengagement, shifting and re-engagement sub-processes of E–I orienting attention, respectively. This thesis aims to investigate how the neural processes underlying E–I orienting attention are modulated by 1) the salience level of the external stimulus, 2) the salience level of the internal representation, and 3) the pain experience of CLBP patients.

A total of 19 healthy individuals (9 females) volunteered in the first ERP Study and 15 CLBP patients (12 females) volunteered in the second ERP Study. The participants were to perceive a fleeting (50 ms) external nociceptive stimulus (ES) at the ankle in Study 1 and at the ankle (non-painful site (S_{NP})) and lower back ("painful" site (S_P)) in Study 2. The salience level of the ES was either Low (E_L) or High (E_H). Next, the participants were required to mentally rehearse a Low (I_L) or High (I_H) salient internal representation (IR) of the self-generated sub-nociceptive image for 3s. This was followed by assigning a numeric rating scale (NRS) score to indicate the pain intensity of the perceived nociceptive stimulus in Study 1 or perceiving another external stimulus and then comparing it with a self-generated/maintained image in Study 2. Electroencephalography (EEG) signals were captured throughout the process.

Among the healthy individuals, a three-way repeated measures ANOVA on the amplitudes of the three ERP components in the first study revealed that the ES × IR× electrode interaction was not significant, but the ES × IR interaction effect was significant in all the three components ($F(1,28) = 5.781$, $p = .016$ and $F(1,28) = 4.947$; $p = .025$ for the SP3, and SP3/P2 time window of the N1 component; $F(28,504) = 2.204$, $p < .001$ for the P2 component; and $F(28,504) = 2.374$, $p < .001$ for the P3 component). Further analysis indicated that the differences between the I_H image and the I_L image were only significant in the E_H condition. Besides, a two-way repeated measures ANOVA on the NRS scores revealed that the ES and IR main effects were significant ($F(2,36)= 215.80$, $p = .001$ and $F(2,36) = 4.17$, $p = .012$, respectively). Additionally, significant and positive correlations between the attenuation in NRS scores and the P3 component were revealed by Pearson correlation analysis (the r- values were from .517 to .638, $p < .050$).

Among the CLBP patients, a four-way repeated measures ANOVA on the amplitudes of all the three ERP components in the second study revealed that 1) the ES × IR × electrode × stimulation site (SS) four-factor interaction effect was not significant, but ES × IR ×SS three-factor interaction was significant ($F(2,28) = 3.678$, $p < .038$) in the N1 component; 2) only a marginally significant ES × IR interaction effect ($F(2,28) = 3.129$, $p = .059$) was significant for the P2 component; 3) the ES × IR × electrode × stimulation site (SS) four-factor interaction effect was significant ($F(16,224) = 2.484$, $p < .002$) for the P3

component. Further analysis indicated that 1) the N1 amplitudes were more negative-going in the S_P condition than that in the S_{NP} condition, 2) the P3 amplitudes were more positively-going for an E_H stimulus in the I_H condition at the S_P site, but not the S_{NP} site. Besides, significant correlations between the attenuation in NRS scores and the amplitude changes of all the three components were revealed by Pearson correlation analysis as well (the r- values were from .541 to .652, $p < .050$).

These findings suggest that the sub-processes underlying E–I orienting attention serve different roles. The disengagement sub-process tends to be stimulus dependent, which is bottom-up in nature. Shifting and reengagement tend to be top-down sub-processes, which involve more cognitive control. These sub-processes may account for the attenuation effects on perceived pain intensity after orienting attention.

PUBLICATIONS AND CONFERENCE

PRESENTATIONSARISING FROM THIS THESIS

Journals

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Conferences

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LIST OF ABBREVIATIONS

ACC = anterior cingulate cortex

AMY= amygdala

CLBP = chronic low back pain = chronic pain at the lower back

CN = color naming

E–I = external (stimulus) to internal (interpresentation)

EH = high salient external nociceptive stimulus

EL= low salient external nociceptive stimulu

EEG =electroencephalography

EO = orienting attention to an external stimulus

EOG = electrooculograph

ES = external stimuli

ERP = event-related potential

ICN = incongruent color naming

IH= high salient internal representation of the sub-nociceptive image

IL= low salient internal representation of the sub-nociceptive image

IO = orienting attention to an internal stimulus

IR= internal representations

JPS = just painful sensation

NDS = minimum detectable sensation

NRS = Numeric Rating Scale

PAG = periaqueductal grey

PFC = prefrontal cortex

PIQ = personal information questionnaires

PSES = pain self-efficacy scale

RVM = rostroventral medulla

S1 = the first external stimulus in a trial

S2 = the second external stimulus in a trial

SD = standard deviation

SEP = somatosensory-evoked potential

SI = primary somatosensory cortex

SII = secondary somatosensory cortex

SNP = non-painful stimulation Site

SP = painful stimulation Site

SS=Stimulation Sites

SPL= superior parietal lobe

VPS = very painful sensation

WR= word reading

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Chapter I

INTRODUCTION

The first chapter presents an outline of the research studies on the external-to-internal (E–I) orienting attention among people with chronic lower back pain, and how this E–I orienting attention process is modulated by the salience of both external stimulus and internal representation, as well as the patient's past pain experience. This chapter consists of three major sections. The first section provides background information on patients with chronic pain, attentional modulation of chronic pain, and the rationales for writing this dissertation. This is followed by the objectives of the dissertation. After that, the structure of the chapter is addressed.

1.1 Background

In recent years, increasing attention has been drawn to chronic pain because it has become a burden to society. Chronic pain, which refers to pain that persists for more than three months (Treede et al., 2015), has a high prevalence rate, ranging from 30.7% to 51.3% based on different populations(Azevedo, Costa-Pereira, Mendonça, Dias, & Castro-Lopes, 2012; Fayaz, Croft, Langford, Donaldson, & Jones, 2016; Johannes, Le,

Zhou, Johnston, & Dworkin, 2010; Raftery et al., 2011; Wong & Fielding, 2011). To the best of the author's knowledge, for example, the lowest prevalence rate was reported to be 30.7% in the United States with a sample of 27,035 adults (Johannes et al., 2010), while the highest prevalence rate was shown in a systematic review based on the data from 139,933 adults in the United Kingdom (Fayaz et al., 2016). The prevalence rate in Hong Kong was found to be 35% based on interviews with 5,001 adults (Wong & Fielding, 2011). Chronic pain severely affects patients' daily life in multiple ways. For instance, De, Maree, and Van (2015) pointed out that chronic pain causes daily suffering, such as impeding patients in everyday activities, for example, walking. Raftery et al. (2011) suggested that chronic pain may lead to emotional distress, and particularly, 15% of patients are diagnosed with depression. According to Gaskin and Richard (2012), chronic pain may also cause reduced income, job loss, and massive utilization of medical services.

In clinical practice, pharmaceutical interventions are frequently applied to help relieve pain. Medications, such as selective serotonin reuptake inhibitors and tricyclic antidepressants, are preferred by doctors (Nüesch, Häuser, Bernardy, Barth, & Jüni, 2013). However, pharmaceutical interventions are frequently reported to be accompanied by undesirable side-effects, such as nausea and constipation (Benyamin et al., 2008; Boldt et al., 2014; Furlan et al., 2006; Porreca &O ssipov, 2009). For example, a meta-analysis of the side-effects of using opioids for relieving chronic noncancer pain suggested that side effects such as nausea (14%) and constipation (9%) occur significantly more frequently in patients taking opioids than patients in the

placebo group (Furlan et al., 2006). In recent decades, increasing numbers of researchers have become interested in applying non-pharmaceutical treatments (e.g., aerobic exercise, cognitive behavioral therapy) to attenuate chronic pain (Nüesch et al., 2013). Unfortunately, the mechanism of non-pharmaceutical treatments remains unclear (Amatya, Young, & Khan, 2017), and there has not been consistent and robust evidence on their effectiveness (Boldt et al., 2014).With the development of neuroimaging techniques, cognitive factors (e.g., memory, anticipation, orienting attention), have been reported to play an essential role in mediating pain perception (Bushnell, Ceko, & Low, 2013). Among all of these cognitive factors, orienting attention is one of the most reported components in studies of non-pharmaceutical treatments (also can be seen in a recent review, Subnis, Starkweather, & Menzies, 2016). Researchers have revealed that orienting attention away from or towards the source of the pain influences the intensity of the perceived pain (e.g., Dunckley et al., 2010; Moseley, Zalucki, & Wiech, 2008).These changes were found to be associated with modulation of the early attentional process as reflected by the Event-Relative Potential (ERP) component such as the fronto-centrally distributed N1 component, and the centrally distributed P2 component (see Chapter 2 for an elaboration). In conclusion, it seems that attention-based interventions are promising in the attenuation of chronic pain.

Attention can either be oriented to a stimulus in external environments (i.e., External Attention, EA) or to an internal representation in the working memory (i.e., Internal Attention, IA) (Chun, Golomb, & Turkbrowne, 2011). According to the

three-step orienting attention model which was proposed by Posner (Petersen& Posner, 2012; Posner, Walker, Friedrich, & Rafal, 1984), there are three theorized steps during orienting attention between two external targets, which are to disengage attention from the first target, shift attention to a second target, and engage attention to the second target. Posner's model elucidates orienting between two stimuli in the external world, but not orienting attention between an external stimulus and an internal representation. The E–I orienting attention process is crucial because human beings are required to process perceptual information (e.g., words, sounds) available in the external world to proceed to other internal high-level cognitive processes, such as discrimination and appraisal. Studies show that orienting attention between the external and internal worlds involves cognitive control, particularly when the E–I orienting attention difference increases (Chan, Chan, Kwan, Ting, & Chui, 2012; Legrain, Crombez, Plaghki, & Mouraux, 2013).Legrain, Iannetti, Plaghki, and Mouraux (2011) proposed that orienting attention from a nociceptive stimulus includes both goal-directed top-down control and stimulus-driven bottom-up control (see Chapter II) and also suggested a salience system which plays an essential role in this model. However, how the neural mechanism underlying how the bottom-up control (the salience of the external stimulus) and the top-down control (the salience of the internal representation) modulate the E–I processes is still not clear. Salience refers to the extent to which target information prevails over background information (Yantis, 2008). More importantly, research on the attention modulation of pain among patients with chronic pain remains inconsistent and inconclusive (Damme, Legrain, Vogt, &Crombez,

2010), particularly on the neural mechanism of pain experience modulating E–I orienting.

1.2 Purpose of the study

This thesis aims to examine the neural mechanism underlying the modulation of E–I orienting in regard to pain perception among patients with chronic pain. To achieve this ultimate purpose, the author conducted two ERP studies. The first study gathered fundamental knowledge on this issue. Only healthy individuals were recruited in the first ERP study. The second study examined the neural mechanism of this topic. Only patients with chronic pain of the lower back (CLBP) were recruited to control the heterogeneity of chronic pain. The specific objectives of each study reported in this thesis were:

For the first study：

1) To examine the neural process underlying the bottom-up modulation of the salience of an external stimulus on the sub-processes of E–I orienting attention, i.e., the processes of disengagement, shifting and re-engagement among healthy individuals;

2) To examine the neural process underlying the top-down modulation of the salience of an internal representation on the sub-processes of E–I orienting attention, i.e., the processes of disengagement, shifting and re-engagement among healthy individuals;

For the second study：

1) To examine the neural process underlying the bottom-up modulation of the salience of an external stimulus on the sub-processes of E–I orienting attention, i.e., the processes of disengagement, shifting and re-engagement among CLBP patients;

2) To examine the neural process underlying the top-down modulation of the salience of an internal representation on the sub-processes of E–I orienting attention, i.e., the processes of disengagement, shifting and re-engagement among CLBP patients;

3) To examine the neural process underlying the top-down modulation of the experience of chronic pain on the sub-processes of E–I orienting attention, i.e., the processes of disengagement, shifting and re-engagement among CLBP patients.

1.3 The Structure of Chapters

This thesis consists of six chapters. The first chapter provides brief background knowledge, objectives and the outline of this research. The second chapter reviews literature on the concepts of chronic pain, orienting attention and attentional modulation of pain.

The third chapter describes the methods of this research. It is divided into two parts. The first part describes the methods used for the first study which aimed to examine the neural process of E–I orienting attention among healthy individuals. The second part describes the methods of the second study which aimed to examine the neural process of E–I orienting attention among CLBP patients.

The fourth chapter describes the results obtained from the two studies. It consists of three parts. The first part comprises findings on E–I orienting attention among healthy individuals. The second part comprises the results on E–I orienting attention among CLBP patients. The differences between healthy individuals and CLBP patients will be described in the last part of this chapter.

The interpretations of the obtained findings and the contribution of this thesis will be discussed in the fifth chapter. The limitations of this study and implications for future studies will be discussed in the final chapter.

Chapter II

LITERATURE REVIEW

In this chapter, prior literature concerning the objectives of this thesis stated in the first chapter will be discussed. With the theoretical framework, I will address the issues regarding the attentional modulation of chronic pain, and identify the knowledge gap in previous studies. Specifically, this chapter will start by reviewing the literature on the concepts of orienting attention, followed by the area of pain and chronic pain. In section 2.3, previous studies on the modulation of pain by orienting attention, and the underlying neural mechanism will be reviewed. In section 2.4,one of the most significant knowledge gaps will be discussed: E–I orienting attention for attenuating chronic pain is not fully explored in the literature. Lastly, the hypotheses of this thesis will be presented in the last section of this chapter.

2.1 Orienting Attention

2.1.1 Attention

The topic of attention has been studied for decades by cognitive scientists. It is a complex concept, but "everyone knows what attention is" (James, 1890). According to William James (1890), attention is defined as "the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible

objects or trains of thought" (pp. 403–404). By this definition, James pointed out that attention can be directed to two kinds of targets, i.e., the objects and the thought. Chun et al. (2011) endorsed this view and further proposed that attention can be divided into external attention (EA) and internal attention (IA). External attention refers to the processes of selecting and modulating the sensory information, for example, the selection of spatial location or time points in the perceptual world. Internal attention refers to the processes of selecting, modulating and maintaining internally generated information (i.e., internal representation), including task rules and working memory. In Chun et al.'s (2011) framework of attention (Figure 2.1), external attention includes modality-specific input, spatial locations, time points, features and objects; while internal attention includes task rules or responses, content in working memory or long-term memory.

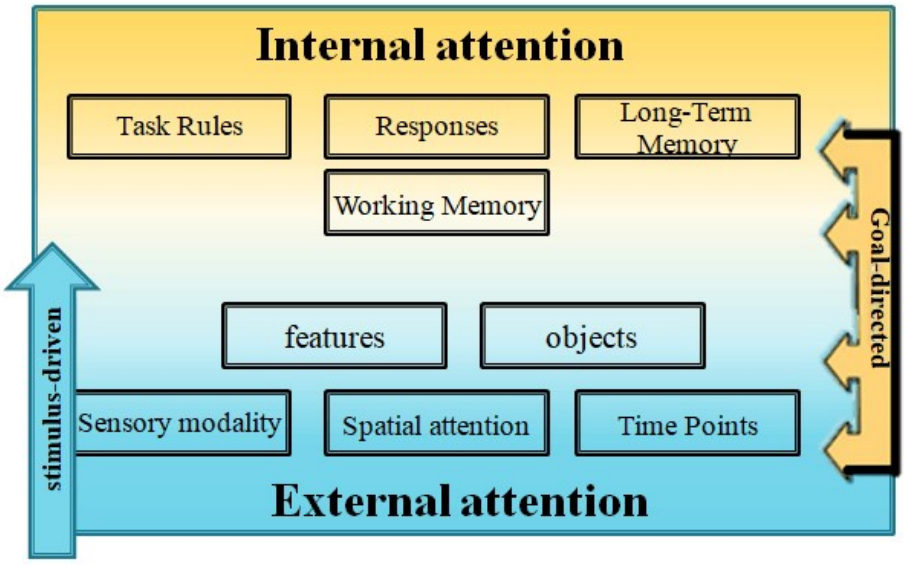


Figure 2.1 Chun et al. (2011)'s framework of attention

2.1.2 Definition of orienting attention

In daily life, people are bombarded by different kinds of information: external information (e.g., sounds, light) from the external environment and internal information (e.g., thoughts, memory) from the brain. It is the orienting attention that dynamically guides the selection of useful information from the bombarded information and optimizes our perception and action (Lepsien & Nobre, 2006). Orienting attention refers to the primary process of selecting one or more piece of information for further processing (Petersen & Posner, 2012; Posner et al., 1984). Orienting attention is crucial not only because it enables individuals to perceive perceptual (e.g., visual, audio) information from the external environment, but also because it allows internal processing such as discrimination and decision-making (Chun et al., 2011; Lepsien & Nobre, 2006). Specifically, orienting attention to an external stimulus (i.e., external orienting attention) filters or inhibits distraction and noise from different kinds of external stimuli(Kane & Engle, 2003). For example, using a visual cue (e.g., the icon of a "arrow") presented before the stimulus array to orient attention to the perceptual target (e.g., location) optimizes participants' performance, such as reducing the response time and increasing the accuracy to detect the cued items (Griffin & Nobre, 2003; Posner, 1980). On the other hand, orienting attention to internal representation (i.e., internal orienting attention) shields perception against interference from internal sources such as irrelevant information from memory (e.g., Griffin & Nobre, 2003) or emotional impulse (e.g., Tangney, Baumeister, & Boone, 2004). For example, researchers found that using a visual cue presented after

the stimulus array to orient attention to the perceptual target (e.g., location) remaining in the working memory can improve participants' performance in detecting the cued items (Astle, Summerfield, Griffin, & Nobre, 2014; Griffin & Nobre, 2003; Kuo & Astle, 2014).

2.1.3 Sub-processes under orienting attention

A large number of studies have been conducted to understand the orienting attention between two external stimuli in the last few decades (Dowman, 2007; Dowman, 2011; Dowman, Darcey, Barkan, Thadani, & Roberts, 2007; Kuo & Astle, 2014). Posner and his colleagues (Petersen & Posner, 2012; Posner et al., 1984) theorized three sub-processes underlying orienting attention from one target to another target, namely disengagement, shifting, and re-engagement. Disengagement refers to the initial process of drawing attention away from where it is. Re-engagement refers to allocating attention to a new target. Shifting is defined as the process of attention being assigned from one target to another. For example, in the study of Kuo et al. (2014), a visual cue was presented simultaneously with the stimulus array of four items to guide the participants to orient their attention to the perceptual target in this array. According to Posner's three steps model (Petersen & Posner, 2012; Posner et al., 1984), orienting attention from the cue to the cued target includes three sub-processes: the disengagement attention from the cue, followed by shifting the attention to the array of four items, and finally re-engaging attention to the cued item.

2.2 Chronic Pain

2.2.1 Concepts of chronic pain

Chronic pain refers to pain that persists after a person's healing period which is usually 3 to 6 months (Treede et al., 2015). As for the concept of pain, the International Association for the Study of Pain (IASP) has defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (IASP, 2017). This definition identifies two crucial components of pain—the sensory component and the emotional component. Specifically, the sensory component is known as “ nociception”, which is a neural process when information about a noxious stimulus is encoded by the primary afferent neurons, represented and transformed through the peripheral nervous system and ultimately emerges in the primary sensory cortex where the “nociceptive sensation” is produced (Prescott, Ma, & Koninck, 2014). Then the nociceptive sensation is interpreted as “pain” in associative somatosensory and related areas (Goldstein, 2010). These transformation and interpretation processes can be “abnormally modulated or disrupted by the cognitive factors (such as memory or attention), which results in a misinterpreted representation or contaminated perception of the nociceptive stimulus” (Prescott, Ma, & Koninck, 2014). Another crucial component of pain that the IASP (2017) has emphasized is the emotional component. Unquestionably, pain is a sensation because it can be accompanied by actual or potential tissue damage. It is also an emotional experience as well, which usually causes unpleasant feelings and fear. It should be noted that feelings such as pricking

and numbness should not be classified as “pain” due to a lack of unpleasant feelings although it seems similar to the sense of pain (IASP, 2017).

Unlike acute pain, chronic pain usually occurs without tissue damage, in many cases, particularly those with chronic back pain, patients are found to tend to experience “pain” which cannot be corroborated by positive results from objective assessments such asphysical examination (e.g. X-ray, CT) (Coates et al., 2012).Walsh and Radcliffe (2002) further concluded that “there is nothing wrong bodily”. Coates et al. (2012) proposed a sensitization model for the purpose of explaining the behavior of these patients. They further explained that due to the potential neurophysiologic changes in the central nervous system, patients with chronic lower back pain tend to feel pain due to stimuli that are not normally painful. Musculoskeletal (including spinal stenosis and arthritis) and neuropathic dysfunctions are the major causes of chronic pain (Merskey&Bogduk,1994; Sara et al. 2012; Azevedo et al.,2012). For example, a cross-sectional epidemiological study with a sample size of 2,213 conducted in Portugal by Azevedo et al. (2012) found that the most reported type of chronic pain is musculoskeletal pain (e.g., osteoarthritis,47% of patients). Merskey and Bogduk (1994) categorized chronic pain into four types based on its mechanism: 1) nociceptive pain, which emerges when the nociceptors in the somatic (e.g., muscles) or visceral (e.g., small intestine) tissues are stimulated; 2) neuropathic pain, which is caused by the misperception of the peripheral or the central nervous system; 3) psychogenic pain, which is always accompanied with psychological disorder (e.g., anxiety, depression); and 4) idiopathic pain, which has no obvious underlying cause.

Thanks to the heterogeneity of chronic pain, the interpretation of the findings are difficult and incomparable, leading to a limited number of studies on this topic (Chan et al., 2012; Moseley et al., 2008; Nouwen, Cloutier, Kappas, Warbrick, & Sheffield, 2006). Hence, this thesis focuses on chronic lower back pain to control the heterogeneity in order to be comparable with the previous studies (e.g., Chan et al., 2012; Hulle, 2013).

2.2.2 Cortical changes in pain perception among chronic pain patients

Generally, a nociceptive stimulus is perceived by the ascending pain pathways, which involves multiple cortical areas such as the primary somatosensory cortex (SI) and secondary somatosensory cortex (SII) (Chudler, Anton, Dubner, & Jr, 1990; Greenspan, Lee, & Lenz, 1999; Ploner, Freund, & Schnitzler, 1999), the anterior cingulate cortex (ACC) and insula, etc.(Craig, Ichesco, Quintero, & Schmidtwilcke, 2011; Ostrowsky et al., 2002; Rainville, Duncan, Price, Carrier, & Bushnell, 1997; Tölle et al., 2010), as well as sub-cortices such as the thalamus, cerebellum and periaqueductal gray (PAG), etc.(Apkarian, Bushnell, Treede, & Zubieta, 2005; Schnitzler & Ploner, 2000). This brain network has been called the “Pain Matrix” (Ingvar, 1999; Legrain et al., 2011; Rainville, 2002; Tracey & Mantyh, 2007).

Ohara, Vit, and Jasmin (2005) proposed that there are two ascending pain pathways, which are the peripheral pathways and central pathways. In the peripheral pathways (shown in black in Figure 2.2), nociceptive stimulation first activates the nociceptors, which are the free nerve endings of the diameter non-myelinated C or

thinly myelinated (Aδ) fibers in the periphery. After that, the sensory component of the nociceptive stimulus (e.g., the location and intensity of the stimulus) is transmitted to the dorsal horn of the spinal cord where its central branch terminates. And then at the spinal cord, sensory informationis received by the axons of the second-order neurons, and transmitted to the thalamus via the spinothalamic pathway before terminating in SI and SII in the cerebral cortex. In the central pathways (indicated in red in Figure 2.3), the nociceptive projections from the spinal cord are received by the parabrachial nuclei in the brainstem and eventually terminate in the ACC directly or through the thalamus or amygdala (AMY).Ohara et al. (2005) suggested that the emotional and motivational component of pain (e.g., fear, helplessness) is transmitted via the central pathways.

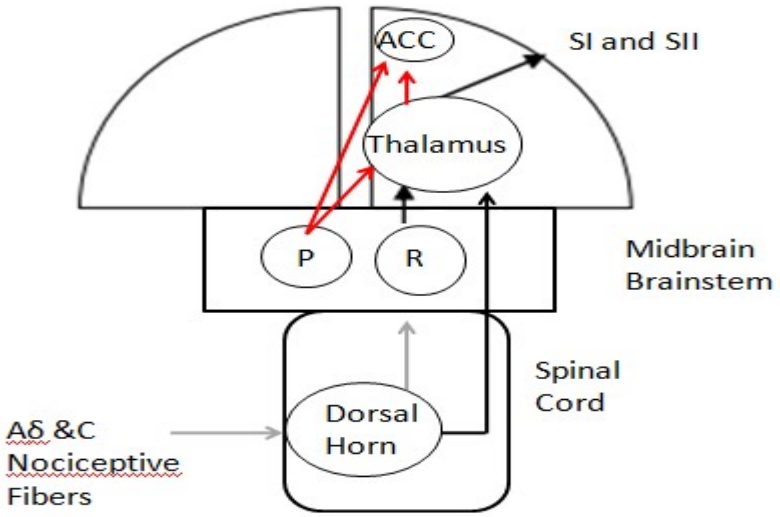


Figure 2.2 Ascending pain pathway

Note: This pathway includes the peripheral pathway (black arrows) and the central pathway (red arrows). SI: primary sensory cortices; SII: secondary sensory cortices; ACC: anterior cingulate cortex; P: parabrachial nuclei; T: Thalamus; P: Periaqueductal Gray; R: Raphe Nuclear & Locus Coeruleus.

However, as for patients with chronic pain, neuroimaging studies have consistently found functional and structural changes in the pain modulation systems, particularly in the ACC, the prefrontal cortex (PFC), and the insula (Bushnell et al., 2013). For example, a meta-analysis study summarized that abnormal activation of the thalamus and SII in patients with chronic pain (e.g., headache, neuropathic pain) has been found to be concomitant with decreased cerebral blood flow in the ACC (Peyron, Laurent, & García-Larrea, 2000). In addition to the diminished activity in the ACC, the PFC, and the insula, a large amount of evidence suggests a reduction of the gray matter (Apkarian et al., 2004; Schmidtwilcke et al., 2006; Seminowicz et al., 2011) and disruptions in white matter tracts (Gerstner, Ichesco, Quintero, & Schmidtwilcke, 2011; Lutz et al., 2008) in these brain regions in patients with chronic pain, compared with those in healthy individuals. Furthermore, Apkarian et al. (2004) examined brain morphology in CLBP patients and healthy individuals and found a 5-11% reduction in the bilateral dorsolateral PFC in CLBP patients, and suggested that the longer that chronic pain persists, the more that gray matter that is lost.

2.2.3 Hypervigilance to pain among chronic pain patients

Hypervigilance is a state in which an organism remains excessively vigilant. For patients suffering from chronic pain, hypervigilance to pain refers to attention bias to pain information (Hulle, 2013). The hypervigilance to pain among chronic pain patients has frequently been reported in behavioral studies(Apkarian, Baliki, & Geha, 2009; Tiemann et al., 2012). For example, Tiemann et al. (2012) reported that people

with chronic pain tend to rate higher scores of hypervigilance to pain than healthy people. A behavioral study using a visual-probe task which included both sensory and affective pain words revealed that participants with chronic headaches exhibited significantly greater attention bias towards pain-related words than the healthy control group (Liossi, Schoth, Bradley, & Mogg, 2009). Furthermore, two recent meta-analytic studies summarized the results from five experimental studies which implemented the modified Stroop task (Roelofs, Peters, Zeegers, & Vlaeyen, 2002) and 50 studies using the modified Stroop task, spatial cueing task, and dot-probe task (Crombez, Ryckeghem, Eccleston, & Damme, 2013), and suggested that individuals with chronic pain appear to attend to sensory pain words (e.g. “burning”, “pinching”) selectively and pictures associated with somatosensory pain (Crombez, et al., 2013; Roelofs et al., 2002). Crombez et al. (2013) suggested that attention bias to sensory pain-related information in a chronic pain group is because this pain-related information is what chronic pain patients are concerned about.

2.3 Attentional Modulation of Pain

Pain is an alarm system. Perceiving and reacting to pain promptly and correctly protects people from potential danger (Prescott et al., 2014). For example, the feeling of pain in the ankle after a sprain will stop the person running and prevent further fracture. However, prolonged pain (i.e., chronic pain) always persists or recurs without tissue damage (Coates et al., 2012b), and thus loses its warning function as an

alarm system (Treede et al., 2015). Hence, it is unwanted and requires attenuation. One of the most commonly used ways to attenuate chronic pain by clinicians is the use of medications. However, medications are frequently reported to be accompanied by undesirable side-effects, such as nausea and constipation (Benyamin et al., 2008; Boldt et al., 2014; Furlan et al., 2006; Porreca &O ssipov, 2009). Nowadays, an increasing number of patients with chronic pain have turned to non-pharmaceutical treatments including aerobic exercise and cognitive behavioral therapy to cope with the pain. Among all the non-pharmaceutical interventions for chronic pain, attention-based interventions have been proved to be promising. Researchers found that directing attention away from or towards the source of the pain could reduce the pain intensity (e.g., Dunckley et al., 2010; Moseleyet al., 2008; details will be reviewed in the next paragraph). Although the non-pharmaceutical treatments show no side-effects compared to medication, their effectiveness to manage the pain tends to be weak and inconsistent, and their underlying mechanism remains unclear (Boldt et al., 2014; Amatya et al., 2017).

2.3.1 Research studies on the attention modulation of pain

Pain attracts people's attention, and in return, attention can modulate pain perception (Troche et al., 2015). There are two commonly used attention-based strategies to down-regulate pain, which are distraction and focused attention.

In prior studies, researchers found that pain can be attenuated when people draw their attention away from the pain, or to other demands or non-painful stimuli (Dunckley et al., 2010; Fors, Sexton, & Götestam, 2002; Nouwen et al., 2006; Tsao, Fanurik, & Zeltzer, 2003). This diversion of attention is called distraction. For example, in the study of Freeman, Barabasz, Barabasz, & Warner (2000), the participants were subjected to cold pressor-induced pain, and the experimental group was instructed to memorize a sequence of colored lights (as a distraction), while the control group kept their eyes open and relaxed. The results revealed that the distraction group exhibited a lower perception of pain compared with the control group, suggesting that attention diversion contributes to pain attenuation.

Instead of diverting attention away from the pain, other researchers suggested focusing on the sensory component of the nociceptive sensation, which is called focused attention (Moseley et al., 2008; Nouwen et al., 2006; Roelofs, Peters, Van, & Vlaeyen, 2004). In the study of Moseley et al.(2008), 13 patients with chronic pain were instructed to focus their attention on the objective aspect of tactile stimulation by discriminating the diameter and location of tactile stimuli in the discrimination condition. Compared with the tactile stimulation condition, the researchers found that the self-reported intensity of their chronic pain was significantly lower in the discrimination condition suggesting that focusing on the sensory component of pain helps suppress the processes of the emotional component, and consequently reduces chronic pain.

The effectiveness of orienting attention to down-regulate pain remains controversial. A number of studies have suggested that distraction is superior to focused attention (Dunckley et al., 2010; Fors et al., 2002). For example, Dunckley et al. (2010) compared the usages of distraction with that of focused attention in attenuating electrically induced pain among healthy individuals and found that the pain intensity was reduced in the distraction condition compared with the focused attention condition. On the contrary, other studies have proved distraction to be inferior to focused attention (Hadjistavropoulos, Hadjistavropoulos, & Quine, 2000; Keogh, Hatton, & Ellery, 2000). For example, Keogh et al.(2000) compared the usage of focused attention with that of distraction in attenuating cold pressor-induced pain among male participants. A better pain attenuation effect in terms of self-reported sensory pain was found in the focused attention condition. Others have suggested that distraction and focused attention play equally important roles in attenuating pain in different situations (Mccaul & Haugtvedt, 1982; Roelofs et al., 2004). For instance, it has been shown that focused attention down-regulates pain better among participants with high scores in the Fear of Pain Questionnaire, but distraction down-regulates pain better among participants with low scores (Roelofs et al., 2004).These findings suggest that orienting attention away from the painful source or forced attention on the sensory aspect of the stimulation is a useful way to down-regulate pain in a certain context.

2.3.2 Theories of the attentional modulation of pain

There are a few theories or models trying to explain how pain perception is modulated by pain. Some of the most popular ones will be reviewed here, which are the load theory, the motivational theory, the emotion theory and the bottom-up and top-down attention models.

2.3.2.1 Load theory

Load theory was proposed by Lavie, Hirst, De Fockert, & Viding (2004) to explain attention modulation sensory perception. According to Lavie et al. (2004), attention affects the sensory perception of the cognitive load (which refers to the extent that the task demands cognitive engagement) and the perceptual load (which refers to the difficulty of detecting the stimulus according to its perceptual features). In the study of Linnell and Caparos (2011), the cognitive load was the number of items to be memorized (including high and low cognitive load conditions) and the perceptual load was the distance between the target and distraction(including high and low perceptual load conditions) in a flanker task. The results showed that the high cognitive load hindered the orienting attention processes only in the high perceptual load condition, suggesting that more attention was consumed by the difficult cognitive task, and it, in turn, became less capable of processing the perceptual features. In studies related to pain, a difficult cognitive task occupies the majority of the attention resource, which leads to less attention to process the nociceptive stimulus (Legrain et al., 2013; Romero, Straube, Nitsch, Miltner, & Weiss, 2013). This could be the reason

why a better pain attenuation effect was reported in a highly cognitive demanding task (Romero et al., 2013).

2.3.2.2 Motivational theory

The motivational theory (Damme et al., 2010) stresses the importance of the role of motivational factors (e.g., goal pursuit) in the attentional modulation of pain perception. There are two basic arguments in this theory. The first point is that pain is able to draw attention away from ongoing goals, and this ability depends on the characteristics of both the pain and goal. The second is that the pain-related goal will enhance the attention to the processing of pain information.For example, Seminowicz, Mikulis, and Davis (2004) recorded participants performing the Stroop Test in painful and non-painful conditions, and found that attention-dominated participants exhibited more reaction time but pain-dominated participants performed the task better during painful stimulation. These results show that pain can still capture attention even when the pain is irrelevant to the current goal (i.e., the task requirements) among attention-dominated participants. Besides, it was able to enhance the attentional process when pain becomes a pain-related goal among pain-dominated participants.

2.3.2.3 Emotion theory

Emotion theory of pain emphasizes the importance of emotional factors in the attentional processes of nociception information (Bushnell et al., 2013). Some researchers believe that it is the emotional factor (e.g., negative emotions) that contributes to the transition of acute pain to chronic pain (Baliki et al., 2015). Others agree and suggest that emotional factors such as fear and catastrophizing thinking might enhance the attentional processing of nociceptive input (Dillmann, Miltner, & Weiss, 2000; Godinho, Magnin, Frot, Perchet, & Garcia-Larrea, 2006; Vlaeyen et al., 2004; Peters, Vlaeyen, & Van, 2000). For instance, Peters et al. (2000) manipulated the levels of pain-related fear of participants for sub-nociceptive stimuli and found that the participants tended to detect stimuli faster in a higher fearful condition than in the control condition, suggesting that fear enhanced the response of the participants to pain-related information.

2.3.2.4 Bottom-up and top-down attention models

Legrain et al.(2011) proposed that nociceptive information is modulated by attention via bottom-up control and top-down attention control. They also claimed that there is a salience detection system in bottom-up attention selection of pain. Salience refers to the extent to which target information prevails over background information (Yantis, 2008). The salience detection system was found to be mediated by the operculo-insular and cingulate network. The function of this network is to

orient attention to the most salient stimulus which guides the subsequent perceptual processes (Legrain et al., 2009). This is supported not only by studies on attentional modulation of visual, emotional stimulus, but also by attentional modulation of somatosensory stimulus (e.g., Dowman, 2011; Legrain et al., 2009, 2011; Peng, Qu, Gu, & Luo, 2012).

In the somatosensory domain, during bottom-up attention selection, the processing of nociceptive information which triggers the salience detector will be prioritized. On the other hand, the top-down attention selection is driven by goals defined by the attentional set and attentional load in the working memory. Goal-relevant processing will be facilitated, and goal-irrelevant information will be inhibited during the top-down selection. This bottom-up and top-down attention model might be able to explain the failures of using visual distractors to direct attention away from the pain source. This is because a salient nociceptive stimulus can still capture attention even though pain is goal-irrelevant.

2.3.3 Neural mechanism of the attentional modulation of pain

2.3.3.1 Neural substrates

As can be seen in section 2.2.2 in Chapter 2, the sensory component of pain (i.e., information such as intensity and location) is transmitted via the peripheral pathways while the emotional and motivational component of pain (e.g., fear and helplessness) is transmitted via the central pathways and is finally projected to the “pain matrix”,

including the SI, SII, insula, and amygdala (AMY). During the transmission process, pain perception is modulated by the descending pathway, which includes the ACC, PFC, superior parietal lobe (SPL), SI, SII, insula, AMY, PAG, and the rostroventral medulla (RVM). The output from the PFC and ACC goes through the SI, SII, and insula and then to the amygdale (Cavada & Goldmanrakic, 2010; Prevosto, Graf, &Ugolini, 2011). After that, it reaches the PAG in the midbrain and is further projected onto the RVM or locus coeruleus in brainstem nuclei. Eventually, it inhibits or facilitates transmission in the dorsal horn of the spinal cord (Basbaum & Fields, 1978).

Among all of these neural substrates, the PFC and ACC are the core brain regions pertaining to pain modulation (Bushnell et al., 2013). Brain imaging studies have found that the activation of the medial PFC, including the rostral ACC is associated with increased activation in the brain regions that process pain perception (e.g., SI & SII) (Baliki et al., 2006; Petrovic& Ingvar, 2002). And the lateral PFC, including the dorsolateral PFC and the ventrolateral PFC, was found to be correlated with the analgesic effect of perceived control (Wiech et al., 2005) and the decrease in pain-sensitive brain regions (e.g., SI & SII) (Wager et al., 2004). These studies suggest that the PFC and ACC are able to down-regulate pain by controlling the functional connectivity in the pain-related brain regions (e.g., SI & SII) during pain perception (Tracey & Mantyh, 2007).

2.3.3.2 Neural processes

Electroencephalography (EEG) is a non-invasive electrophysiological monitoring method to record the electrical activity of the brain (Teplan, 2002). Event-related potential (ERP) measures the brain response that is the direct result of a specific sensory, cognitive, or motor event. It is measured by means of EEG (Luck & Kappenman, 2011). Somatosensory evoked potentials (SEPs) are ERP components that measure the brain response to the stimulation of touch. Researchers using ERP in conjunction with electrically induced pain consistently found a series of ERP components (see Table 2.1) that might reflect the neural processing during the attentional modulation of pain. These ERP components are called Somatosensory Evoked Potential (SEP). There are three commonly found SEP components, N1, P2, and P3. According to the time course, the first attention-related component of interest is a mid-latency negative potential, Fronto-centrally distributed N1 (also called FCN), with a time window from 100 to 200 ms, and is a stimulus-driven automatic process. The N1 amplitude is more negative-going when the nociceptive stimulus is unattended, which reflects pain's ability to capture attention even when it is unattended (Dowman, 2004, 2007, 2011; Dowman et al., 2007). Additionally, the N1 amplitude increases when a change in attentional control is required, reflecting an early process of orienting attention (i.e., disengagement of attention from pain) (Dowman et al., 2007).

Table 2.1 Somatosensory Evoked Potential

Components		Duration	Distribution	Sources	Mental Processes
MNP	CN 70–110	SP1&2 70–110	Central	S1,&supplementary (medial wall of the parietal cortex)	-a. Increased when the nociceptive stimulus is unattended
	CTN 100–180	SP3 & SP3/P1 100–180	Contra-lateral temporal	Somatosensory association areas located in the parietal operculum (e.g. S2, Brodmann area 7b, insula)	-b. Automatic & stimulus-driven process
	FCN 130–200	SP3& SP3/P1 130–200	Fronto-central	mPFC(including the supplementary motor area &ACC),&S1	- a. b. -c. Increased when a situation requires a change in attentional control
P2		280–320	Fronto-central positivity	ACC, inferior parietal cortex/temporal parietal junction, & dorsolateral prefrontal cortex	-Attention shift -Pain intensity
P3a		320–400	Fronto-central positivity	Dorsolateral and medial prefrontal (ACC) cortices	Involuntary orienting response
			Parietal positivity	Inferior parietal cortex, and the posterior hippocampus	Stimulus evaluation and categorization

Note: SP: stable period; S1: primary sensory cortices; S2: secondary sensory cortices; PFC: Prefrontal cortex; ACC: anterior cingulate cortex; AMY: amygdala; BG: basal ganglia; PB: parabrachial nuclei; PAG: periaqueductal gray

The second attention-related component is the P2 component. The time window for the P2 component ranges typically from 260 to 380 ms, and the amplitudes are most positive-going at the fronto-central electrodes. The P2 component is believed to be sensitive to the non-pain-specific attention shift process (Dowman, 2004, 2007, 2011; Dowman, et al., 2007). For example, researchers found an increase in the positive-going P2 component when shifting attention from an external nociceptive

stimulus to a self-generated internal sub-nociceptive image (Chan et al., 2012). Another crucial attention-related component is fronto-central P3 (also called P3a). The P3a component is commonly found during 340 to 400 ms after the onset of a nociceptive stimulus and is most positive-going in the fronto-central electrodes. The P3a component is claimed to be sensitive to the involuntary orienting response (Dowman, 2004, 2007, 2011; Dowman et al., 2007).

2.4 Knowledge gaps

Previous studies mainly focused on the attentional orientation between two external stimuli (Dowman, 2004, 2007, 2011; Dowman, et al., 2007) rather than between an external stimulus and an internal representation. The E–I orienting attention process is essential because, in real-life situations, we are required to rapidly orient between the external and the inner environment to optimize our actions (Henseler, Krüger, Dechent, & Gruber, 2011). In fact, the information processing in internal processes, such as decision-making and reading requires encoding of the perceptual information from the external world in the first place (Peng, Chan, Chau, Yu, & Chan, 2017).

Numerous researchers have suggested that attention can be directed from an external stimulus to an internal representation (Astle, Scerif, Kuo, & Nobre, 2009; Astle et al., 2014; Gosling & Astle, 2013; Lepsien & Nobre, 2006). Similar to orienting attention to an external stimulus (EO), orienting attention to an internal stimulus (IO) has been found to influence information processing and hence

behavioral responses (Mysore & Knudsen, 2013). For example, it was reported that participants respond faster and more accurately when guided to orient their attention to a cued item in their working memory (i.e., internal representation) (Griffin& Nobre, 2003). Besides, the neural processes associated with EO and IO were found to be comparable, both of them consisting of an early sensory-evoked component and a later negative component (Backer & Alain, 2014). For example, a visually evoked negative-going N1 component (120–200 ms) contralateral to the stimulus elicited in the postero-lateral regions was reported for both EO and IO trials (Griffin & Nobre, 2003). More recent studies also revealed visually evoked contralateral N2pc (180 to 300 ms) after the onset of the stimulus array or after the onset of the target for both EO and IO trials (Astle, et al., 2009; Backer & Alain, 2014; Eimer & Kiss, 2010; Backer etal., 2014).

Although EO and IO share similar neural processes, there are still some differences in their function and the neural processes (Backer et al., 2014). Sauce, Wass, Smith, Kwan, and Matzel (2014) proposed that EO inhibits the perception of distraction from the external world (e.g., the letter "F" is distracting as it is similar to the target letter "T" in shape), whereas the function of IO is to shield the targeted perception against distraction from the internal world, such as an irrelevant memory or emotional impulses. Besides, IO differs from EO in terms of the underlying neural processes. A more negative-going N1 component was elicited in the IO condition compared with the EO condition in the frontal brain region in the time window of 120 to 200 ms and in central regions in the time window of 160 to 200 ms (Griffin &

Nobre, 2003). The additional frontal N1 process suggested that IO might involve more attentional control in the orienting process than EO. Concordant with the previous ERP studies, Tanoue, Jones, Peterson, and Berryhill (2012) reported that electrical stimulation of the frontal region resulted in a significantly greater impact on the performance of responding to the target in the IO condition than in the EO condition, suggesting that IO may involve more frontal lobe functions than EO. Griffin and Nobre (2003) as well as Tanoue et al. (2012) have consistently found that, when compared with attention to external stimulus, attention to internal representation tends to achieve a higher level of attentional control as part of the frontal function (Griffin& Nobre, 2003; Tanoue et al., 2012). These studies, however, have not explored the orienting attention process by dividing it into its three sub-processes (disengaging - shifting - engaging) as in the case of E–I orienting attention.

Notably, in the pain-related studies, researchers found that the N1 component could be a marker reflecting orienting between external somatosensory-stimuli (Dowman, 2004, 2007, 2011; Dowman et al., 2007), but their findings were contradictory. On one hand, prior studies on cross-modal attention found that the N1 component is less negative-going when disengaging attention from an external nociceptive stimulus to an external visual stimulus (Ohara, Lenz, & Zhou, 2006; Staines, Popovich, Legon, & Adams, 2014) or from an external visual stimulus to an external nociceptive (Dowman, 2004, 2007, 2011; Dowman et al., 2007). On the other hand, Katus, Andersen, and Müller (2012) reported a more negative-going N1 component when directing attention from an external stimulus to a different external

stimulus delivered at a different spatial location and resulted in a more negative-going N1. Besides, previous studies showed that the fronto-central P2 and the central P3 components are associated with the processes of shifting and reengaging attention to an external nociceptive stimulus (Dowman, 2004, 2007, 2011; Dowman, et al., 2007). Taking these results together, N1, P2, and P3 components play significant roles in orienting attention between an external stimulus, and they might reflect different sub-processes of orienting attention

So far, to the best of the author's knowledge, only a few studies have addressed the E–I orienting process in the somatosensory system. In one of those studies, Legrain et al. (2013) examined the neural processes of orienting attention from nociceptive or non-nociceptive stimulation (external stimuli) to images of visual dots (internal representations). The results showed that E–I orienting attention processes are associated with reduced N1 amplitudes and P2 amplitudes. This finding contradicted what was found in previous studies on orienting attention between two external stimuli, in which more enhanced N1, P2 and P3a components were found (Dowman, 2004, 2007, 2011; Dowman et al., 2007). Another study on the E–I orienting process in the somatosensory system was the study of Chan et al. (2012). In this study, they implemented nociceptive electrical stimulations as the external stimuli and used images of the sub-nociceptive electrical stimuli as the internal representations. Differing from the research of Legrain et al. (2013), Chan et al. (2012) found the E–I orienting process to be associated with more enhanced P2 amplitudes. It is unfortunate that the findings from Legrain et al. (2013) and Chan et al. (2012) were

inconsistent and they only investigated healthy individuals. In conclusion, research on E–I orienting attention processes in pain, particularly chronic pain, is limited and inconclusive. The neural processes of E–I orienting attention among chronic pain patients and how these neural processes differ from that of healthy individuals remain unclear.

As we can see from the previous literature, patients with chronic pain tend to be hypervigilant to pain (Tiemann et al., 2012; Roelofs et al., 2002; Crombez et al., 2013). However, the underlying mechanism of hypervigilance remains controversial. Some researchers believe that the attentional biases to pain information in chronic pain patients are due to the difficulty of disengaging attention from the existing pain sensation or experience (Haggman, Sharpe, Nicholas, & Refshauge, 2010; Sharpe, Dear, & Schrieber, 2009). For instance, a behavioral study conducted by Sharp et al. (2009) examined the attentional biases among 100 patients with chronic pain caused by rheumatoid arthritis with the dot-probe task, in which the participants were required to respond to a word (e.g., sensory words) after the perception of a dot. It was found that patients reacted slowly to the incongruent trials with sensory words, not the other trials (e.g., emotional words, disability words), suggesting that patients with chronic pain have difficulty in disengaging their attention from sensory information. However, it was argued that patients with chronic pain are excessively vigilant to pain information because of their abnormality in engaging with the updated pain information (Liossi, Schoth, Godwin, & Liversedge, 2014; Yang, Jackson, Gao, & Chen, 2012). Liossi et al.'s (2014) study corroborated this argument by using an

eye-tracking approach to record eye movements when viewing pictures (e.g., facial expressions of pain) among patients with chronic pain. The results showed that, compared with their healthy counterparts, patients showed hypervigilance in the process of engaging attention to pictures of pain but not in the process of maintaining attention to those pictures, suggesting that the characteristic of hypervigilance is probably caused by the abnormality of engaging with pain information.

However, the proposal of the engagement against the disengagement mechanisms for explaining the hypervigilance to pain among patients with chronic pain was based on findings from behavioral studies (Haggman et al., 2010; Sharpe et al., 2009) or eye-tracking studies (Liossi et al., 2014; Yang et al., 2012). As we all know, the engagement and disengagement mechanisms are two related but distinct cognitive processes and these studies need to be refined with methods beyond the analysis of observable behaviors. The ERP is one of the refined research methods which has a high temporal resolution (Kessels, Ruiter, & Jansma, 2010). With this refined research method, the time course of the brain activity can be examined one millisecond at a time. Therefore, in order to better understand the mechanism of hypervigilance to pain, the ERP method was used in this study to examine the neural processes of E–I orienting among patients with chronic pain. Besides, according to the bottom-up and top-down attention models proposed by Legrain et al. (2011) to explain the modulation effect of attention to pain, the salience detection system has played an important role in this modulation. The salience detection system was found to be mediated by the operculo-insular and cingulate network. The function of this

network is to orient attention to the most salient stimulus which guides the subsequent perceptual processes (Legrain et al., 2009). This is supported not only by studies on attentional modulation of a visual, emotional stimulus, but also by attentional modulation of a somatosensory stimulus (e.g., Dowman, 2011; Legrain et al., 2009; Legrain et al., 2011; Peng et al., 2012). Dowman (2011) revealed that amore salient external somatosensory stimulus (in terms of intensities) resulted in a more negative-going N1component, suggesting that the level of salience influences the processes of orienting attention between external stimuli. However, how the salience detection system modulates the neural processes of E–I orienting among patients with chronic pain is still unclear.

2.5 Hypotheses

To address the literature gap, this thesis reports on two ERP studies conducted to examine the underlying neural mechanism of the E–I orienting attention processes (i.e., the disengagement-shifting-reengagement process) among healthy individuals and patients with CLBP. The first ERP study aimed to investigate how these processes are influenced by the salience levels of an external stimulus (bottom-up) and the salience levels of an internal image (top-down) among healthy individuals. The second ERP study was to determine how these processes are modulated by the salience levels of an external stimulus (bottom-up) and the salience levels of an internal image (top-down) and the pain experienced by patients with CLBP.

The hypotheses for the first ERP study were:

1) Compared with a lower salience level of external nociceptive stimuli, a more highly salient one will lead to a higher level of bottom-up attention control for initiating the attentional disengagement process, which will induce a more negative-going N1 component among healthy individuals;

2) Compared with a lower salience level of the internal sub-nociceptive representation, shifting attention to a more highly salient one will lead to a higher level of top-down attention control for the shifting and reengagement process, which will induce more positive-going fronto-central P2 and centro-parietal P3 components among healthy individuals.

The hypotheses for the second ERP study were:

1) Compared with a lower salience level of external nociceptive stimuli, a more highly salient one will lead to a higher level of bottom-up attention control for initiating the attentional disengagement process, which would induce a more negative-going N1 component among patients with CLBP;

2) Compared with a lower salience level of the internal sub-nociceptive representation, shifting attention to a more highly salient one will lead to a higher level of top-down attention control for the shifting and reengagement process, which will induce more positive-going fronto-central P2 and centro-parietal P3 components among patients with CLBP;

3) Compared with stimulation located at a non-painful site, stimulation located at the "painful" site will result in dysfunction of the bottom-up attention control for

initiating the disengagement process, which will induce a more negative-going N1 component among patients with CLBP;

4) Compared with stimulation located at a non-painful site, stimulation located at the "painful" site will result in dysfunction of the top-down control for the shifting and reengagement process, which will induce more positive-going fronto-central P2 and centro-parietal P3 components among patients with CLBP;

5) The E-I modulations correlate with significant attenuation of the intensity of the pain perception for external nociceptive stimulations, and with an increase of self-chronic pain severity and with higher pain self-efficacy among patients with chronic lower back pain.

Charter III

METHODS

This chapter includes the methodologies of the two ERP studies. It first introduces the electrical stimuli, pre-experimental preparation and training, experimental tasks, EEG recording and pre-processing information, as well as data analysis used in the first ERP study to examine the External-to-Internal (E–I) orienting attention processes among the healthy individuals. The second part introduces the methodology of the second ERP study which was resembled that of the first ERP study to examine the E–I orienting attention processes among the patients with CLBP.

3.1 Methods of Study One: E–I Orienting Attention Among Healthy Individuals

3.1.1 Participants

Twenty-two pain-free individuals (13 females) participated in this research study. All the participants were recruited by posting the subject recruitment poster in The Hong Kong Polytechnic University. Their ages ranged from 25 to 54 years with an average of 36.4years and standard deviation (SD) of 12.4 years. All the participants should be at the age 25 ~ 55 and had at least obtained the secondary level of education. Participants who showed potential cognitive deficits which measured executive

control function or complained about any pain were excluded from this study. Two participants were excluded because they failed to achieve the training requirement and another one was excluded because of the bad quality of EEG data. In the end, data of 19 healthy individuals were investigated in the subsequent analysis. The research committee of the Department of Rehabilitation Sciences of The Hong Kong Polytechnic University has approved this study. The completed Consent Form (Appendix III) was obtained from each participant after they read the Information Sheet describing the details of this study (Appendix II).

3.1.2 Electrical stimuli

The nociceptive stimuli, which were painful, and sub-nociceptive stimuli, which were non-painful, were the two types of electrical stimulations used in the pre-experimental training and the formal experiment. These electrical stimulations were a 25-pulse train of electrical square-wave pulses, meaning a pulse duration of 0.5ms and a frequency of 500 Hz. S88K Dual Output Square Pulse Stimulator (Grass Technologies, Grass-telefactor, West Warwick, RI) and Constant Current Unit (CCU), which were implemented in the study of Chan et al. (2012), were adopted in this study to produce and control the intensities of electrical stimulations. The bipolar electrodes of the pain stimulator were attached to the smooth skin with the anode up and cathode down at the lateral malleolus of the left ankle to stimulate the sural nerve (L5-S1 dermatome; Dowman, 2007). Both nociceptive and sub-nociceptive stimuli were

delivered to the left ankle during the pre-experimental training and the formal experiment.

3.1.3 Pre-experimental preparation

Before the formal experimental, all the participants have completed a Personal Information Questionnaires (PIQ, See Appendix III), the Stroop test (see Appendix IV) and then completed the calibration for electrical stimuli and the pre-experimental training.

3.1.3.1 Personal Information Questionnaires

The PIQ was designed to obtain the demographic data of the participants It covered various aspects of the participants, including age, education level, gender, marital status, and employment status. The questionnaire was written in Chinese. Details about the questionnaire can be found in Appendix III.

3.1.3.2 Stroop test

Stroop test is one of the most commonly used neuropsychological tests. The Chinese version of the Stroop Test was used, and it aimed to test the participants 'ability to cope with cognitive conflicts and to inhibit unrequited response in this thesis study. As can be found in Appendix IV, it consisted of three subtests. The first subtest was word reading test (WR), in which four Chinese characters "綠", "紅", "黃", "藍"(i.e., Green, Red, Yellow, Blue, respectively, in English) were

arranged into a 10 x 10 matrix (i.e., totally 100 items). The second subtest was a color naming test (CN), in which four single colors (Green, Red, Yellow, Blue) solid rectangles were arranged into a 10 x 10 matrix. The third subtest was incongruent color naming test (ICN), in which four single-color Chinese characters “綠” “紅” “黃” “藍”(i.e., Green, Red, Yellow, Blue) were arranged into a 10 x 10 matrix. The semantic meaning of these characters in ICN subtest was always incongruent with its color, for example, a word with a meaning of Green was written as “绿” in red color. The participants were asked to read the semantic meaning of the Chinese character in the WR subtest or name the color of the rectangles in CN subtest and ICN subtest as quickly as possible in the premise of keeping a high accuracy rate. Three kinds of measures including the total response time, number of errors, and number of self-corrected errors were obtained for each subtest. The total response time refers to the time the participants used to complete the subtest. The number of errors refers to the number of errors (e.g., misreading Green to Red in Word Reading subtest) that a participant made during a subtest and did not realize until the end of the subtest. The number of self-corrected errors refers to the number of error (e.g., misreading Green to Red in Word Reading test) that a participant made during a subtest, but they realized and corrected themselves immediately before the end of the subtest. Difference scores (e.g., CN –WR difference score) was calculated by subtracting the total response time of an earlier subtest (i.e., the WR subtest) from a latter subtest (i.e., the CN subtest). Proportional scores (e.g., (CN –WR) / WR proportional score) which were calculated by dividing the difference scores (i.e., CN –WR difference score)

between the total response time of two subtests by the total response time of earlier one (i.e., WR).

3.1.3.3 Calibration

A calibration procedure that is adopted from the previous studies (Chan, et al., 2012; De Pascalis, Cacace, & Massicolle, 2008) was employed to calibrate the nociceptive and sub-nociceptive stimuli for each participant. Details of this procedure can be found in the Calibration Recording Sheet (see Appendix V). Three thresholds were generated for each participant after the procedure. The first one was the Minimum Detectable Sensation (MDS). It is the weakest stimulation intensity level that can be detected, in other words, the stimulation can hardly be noticed. The second one is the Just Painful Sensation (JPS)—the minimal pain intensity level at which one started to perceive the stimulation as "painful". Based on the Numeric Rating Scale (NRS) (Jensen, Karoly, & Braver, 1986; Williamson & Hoggart, 2005) (Jensen, Karoly, & Braver, 1986; Williamson & Hoggart, 2005), where pain level was categorized on a scale of 0 (non-painful) to 10 (extremely painful), JPS was rated as "1" for the pain intensity. The third one is the Very Painful Sensation (VPS). It is a maximum pain intensity level adopted in this dissertation. With this pain intensity level, a participant perceives the stimulation as "very painful" and rates the pain intensity level as "7" on the NRS. Mean voltages and standard deviation (SD) for these three thresholds were $Mean_{MDS}$ = 3.32 milliamperes (mA), SD_{MDS} = 5.24 mA for the MDS; $Mean_{JPS}$ =19.11 mA, SD_{JPS}= 6.38 mA for the JPS, and $Mean_{VPS}$ =41.27

mA, SD_{VPS} = 12.60 mA for the VPS. The sub-nociceptive stimuli included two salience (intensity) levels which were distributed between the MDS and the JPS. To be more specific, the intensity of a low salience sub-nociceptive stimulus was defined as one-third of the difference of MDS and the JPS ((MDS- JPS)/3), and the intensity of a high salience sub-nociceptive stimulus was defined as two-thirds of the difference of MDS and the JPS ((MDS- JPS) x 2/3). Similarly, six different intensity levels of the nociceptive stimuli were distributed between the JPS and the VPS. Specifically, the difference between the JPS and the VPS was divided evenly into six levels, which were labeled as L1 to L6. Mean voltages and SD of these SN and N stimuli were described in Table 3-1.

Table 3.1 Mean Levels of Voltages and NRS Ratings for The Six Levels of Nociceptive and The Two Levels of Sub-nociceptive Stimuli in Study One (n = 19)

		Sub-nociceptive		**Nociceptive**					
		SN_L	**SN_H**	**L1**	**L2**	**L3**	**L4**	**L5**	**L6**
Voltage	Mean	3.4	16.1	20.7	24.2	28.0	32.6	36.7	41.0
	SD	5.3	6.1	7.1	7.6	8.6	9.6	10.9	12.3
NRS	Mean	-	-	1.6	2.7	3.6	4.7	5.3	5.7
	SD	-	-	0.7	0.8	1.0	0.7	0.6	0.8

Note: SN_L refers to lower intensity of the sub-nociceptive stimulus; SN_H refers to higher intensity of the sub-nociceptive stimulus. L1 to L6 refer to six levels of nociceptive stimulus, and L1 is the lowest intensity while L6 is the highest intensity. NRS (Numeric Rating Scale), ranging from 0 to 10, is used for rating the level of pain intensity felt by the participant.

3.1.3.4Pre-experimental Training

During the pre-experimental training, all the participants had to go through the procedure of familiarization with pain rating using NRS for the nociceptive stimuli, the procedure of familiarization with the sub-nociceptive stimuli, the procedure of E–I orienting training and testing.

3.1.3.4.1 Familiarization with pain rating using NRS for nociceptive stimuli

Participants received training in rating pain intensity level based on the NRS to ensure the accuracy and validity of the NRS scores. This is important for the subsequent formal experiment because, by the end of each trial, participants were asked to rate a certain external nociceptive stimulus based on the 11-point NRS within a limited timeframe of 50 ms. During the training, participants were asked to perceive the intensity of the randomly selected nociceptive stimuli applied to the left ankle, after which they rated the presented nociceptive stimulus with the NRS. The NRS scores given by the participants to indicate the intensity of the nociceptive stimuli were recorded using the Familiarization Recording Sheet of Nociceptive Stimulus (Appendix VI). Participants took at least 24 trials in the training for the nociceptive stimuli.

3.1.3.4.2 Familiarization with sub-nociceptive stimuli

Since each trial in the formal experiment required the participants to recall a specific internal sub-nociceptive image (which was either high salient (I_H) or low salient (I_L) after perceiving an external nociceptive stimulus, the participants'

familiarization with sub-nociceptive stimuli was important. During the training, one level of the sub-nociceptive stimuli was applied to the left ankle, after which participants were asked to identify which salience levels this sub-nociceptive stimulus and named it as I_H or I_L according to its salient level. This ensured the participants to be able to associate the two descriptors (I_H and I_L) with the sensation of the two sub-nociceptive stimuli respectively. The participants' responses to the sub-nociceptive stimuli were recorded with the Familiarization Recording Sheet of Sub-nociceptive Stimuli (Appendix VII). The participants took at least 27 trials until the accuracy rate reached 80% in the training session for sub-nociceptive stimuli.

3.1.3.4.3 E–I orienting training and testing

E–I orienting training and testing aimed to help the participants learn how to shift attention from the external nociceptive stimulus to a self-generated sub-nociceptive image by pair learning. In the training, when receiving a nociceptive stimulus, the participants were asked to self-generate an image of the sub-nociceptive sensation which was either I_H or I_L. Then, the participants adjusted the image with the given true nociceptive stimuli.

After the training, the participants learned about three rules that were employed in the second steps of the experimental task. Rule 1 (I_L blocks) is to orient attention to the I_L image, in which the participants were required to recall the image of I_L after perceiving an external nociceptive stimulus, of which the salient level could be high (E_L) or low (E_H), i.e., orienting attention from E_L/E_H to I_L. Rule 2 (I_H blocks) is to

orient attention to the I_H image, in which the participants were required to recall the image of I_H after perceiving an external nociceptive stimulus (E_L / E_H),i.e., orienting attention from E_L/E_H to I_H. In Rule 3 (control blocks), they just need to retain the image of the stimulus in their mind, i.e., from E_L to E_L or from E_H to E_H.

Next, the participants were asked to complete the test on attention orientating, in which they needed to self-generate an I_L or I_H image when receiving a nociceptive stimulus (i.e., S1), until they perceived a randomly selected second stimulus (S2) and then they were asked to match the salient level of this self-generated image with that of S2. The performance of the participant in this training was recorded using the Orienting Attention Task Sheet (see Appendix VIII).

3.1.4 Experiment tasks of the formal experiment

The experiment tasks in this dissertation study were adapted from the study of Chan and his colleagues (2012). The six levels of nociceptive stimuli were classified into two salience levels. Specifically, the three lower intensity stimuli were classified as the external low salience level (E_L), and the other three higher intensity stimuli were classified as the external low salience level (E_H). There was a significant difference between E_L and E_H in intensity (salience) indexed by the NRS scores ($t(1,18) = -16.138$, $p < .001$) and voltages ($t(1,18) = -12.134$, $p < .001$) in the present study. The two salient levels of internal representations referred to the two self-generated images of sub-nociceptive stimuli, of which the salient (intensity) level was either low (i.e., I_L) or high (i.e., I_H).

All of the participants need to complete an experimental task and a control task. In each trial of the experimental task, all the participants were involved in the three mental processes. The first one was the detection process, in which the participants were required to attend to a fleeting external nociceptive stimulus of either E_H or E_L (i.e., S1). The second one was the image generation process, in which the participants were required to generate a learned sub-nociceptive image (either I_H or I_L). The participants were required to disengage their attention from a relatively strong external nociceptive stimulus, and then quickly shift and re-engage the attention with a self-generated internal image of a relatively weak sub-nociceptive sensation. The third step was the response process, in which the participants were required to recall the previous perceived S1 and give an NRS score to indicate the intensity for their pain experience in that trial (Figure 3.1, left panel).

In each trial of the control task, all the participants were involved in three similar mental processes. The first and the third processes were the same as those in the experimental trial. However, the second process was maintaining image process instead of image generation process for the control trials. In this step, the participants were required to maintain the nociceptive image of S1 in their working memory (Figure 3.1, right panel).

The timing, presentation of output stimulus, and sequence for each trial in both the experimental and the control tasks were programmed by the E-prime 2.0 (Psychology software tools, Inc). Specifically, in the experimental tasks, for each trial, a fixation ("+") was first presented in the center of the computer screen for 500 ms to

signal the beginning of a trial. After a black screen with a varied interval from 1100 to 1300 ms was presented, a fleeting electrical nociceptive stimulus (i.e., S1, lasting for 50 ms) was delivered at the lateral malleolus of the left ankle of the participant. The nociceptive stimuli were randomly selected from the six intensity levels (L1–L6) in each trial. The participant was required to attend to it (Step 1). After that, the screen remained black for 3000 ms. During this period, the participant was required to generate and rehearse a learned I_H or I_L image depending on the rules (Step 2). At the end of each trial (Step 3), a letter "S1"11-point scale appeared on the screen to signal the participant to give a score based on the NRS to indicate the intensity of pain that they perceived. They gave an NRS score by pressing a certain number key ranging from "1" to "10" on the keyboard. The response screen lasted for 6000 ms or until responded. The design for the Step 1 and Step 3 of the control task was same with that of the experimental task. Different from the experimental task, the Step 2 in the control task required the participants to receive the external nociceptive stimulus (S1), retain this image of S1 for 3000 ms, and then give an NRS score to indicate the intensity of pain that they perceived for S1. In order to ensure the participants to engage in the E–I orienting attention task, one-third of the trials in each block asked the participants to do comparing response instead of the rating response. In the comparing response trial, the second stimuli (S2, nociceptive in the control blocks, sub-nociceptive in the I_H or I_L blocks) were delivered at the ankle of the participant, and a question "Is this stimulus similar to the image in your brain in term of the

intensity?" appeared to encourage the participant to compare it with the image maintained mentally.

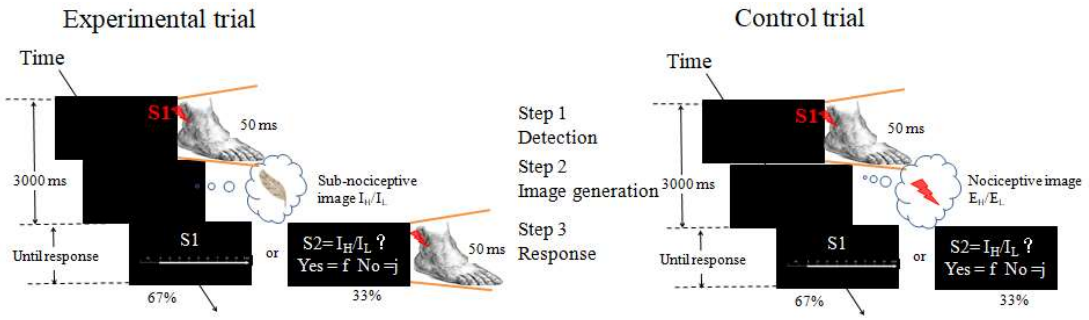


Figure 3.1 Schematic Representation of the Experimental Paradigm of Study One

Notes: Left panel is Schematic representation of an experimental trial. The participant first attended to an 50 ms external nociceptive stimulus (S1) which is either high salient (E_H) or external low (E_L) and maintained the image (Step 1). After that, in Step 2, they generate a pre-trained internal sub-nociceptive image with either high (I_H) salience or low salience (I_L) according to the rules. The Rule in Step 2 was that the participant was to recall a low salient sub-nociceptive image (I_L) once perceived an external nociceptive stimulus in I_L blocks and a highly salient sub-nociceptive image (I_H) in I_H blocks. During the responsephase (Step 3), 67% of trials required the participant to assign a rating against Numeric Rating Scale (scores from zero to 10, in which, "0" = "non-painful","10" = "extremely painful") for the perceived pain intensity for the S1; while occasionally, a second stimulus (S2) which was sub-nociceptive appeared and the participant judged whether the perceived intensity of S2 was comparable with that of the I_H or I_L just generated in the other 33% of trials. Right panel show the flow in a control trial. The control trial only contains Step 1 and Step 3. In Step 3, the same procedure with the experiment trial except that the S2 delivered to the participant was nociceptive and was to comparable with that of S1.

The experimental design for this study was a 2 (external stimuli) × 3 (internal representations) two-factor within-subject design. The first factor was external stimuli (ES), which manipulated the salience of the perceived external nociceptive stimuli at the beginning of each trial. The ES factor included an E_H condition and an E_L condition. Only a nociceptive stimulus which ranged from L4 to L6 was delivered in the E_H condition. Similarly, only a nociceptive stimulus ranging from L1 to L3 was

delivered in the H_L condition. The second factor was internal representations (IR), which manipulated the salience of an internal representation (a self-generated sub-nociceptive image). This IR factor included an I_H condition, an I_L condition, and a control condition. The participants were required to generate and rehearse a learned high salient sub-nociceptive image in the I_H condition. They were also required to generate and rehearse a learned low salient sub-nociceptive image in the I_L condition. However, in the control condition, they were required to just maintain the mental image from the perceived nociceptive stimulus. Therefore, the 2 (ES: E_H VS. E_L) × 3 (IR: I_H, I_L, and control) combinations yielded a total of 324 trials which were organized into 9 experimental blocks:3 I_H blocks, 3 I_L blocks, and 3 control blocks. There were 36 trials in each experimental block. Completion of one experimental block took approximately five minutes. The sequences of the blocks and trials within each experimental block were pseudo randomized. The sequence of the stimulus presentation was counterbalanced across subjects and the sequence of the blocks was pseudo randomized across subjects as well.

3.1.5 EEG data recording and pre-processing

The EEG signals during the formal experiment were recorded in the Applied Cognitive Neuroscience Laboratory in the Hong Kong Polytechnic University. A 64-channel cap based on the 10–20 system was attached to the participants' scalps. The EEG signals were recorded and preprocessed by CURRY Neuroimaging Suite software (Neuroscan, Compumedics Ltd., Melbourne, Australia). The

electrooculograph (EOG) was recorded by two pairs of electrodes which was attracted 1cm around the eyes vertically and horizontally. The EOG signals were used for monitoring the eye blinks and eye movements. The electrodes which were attached to a flat skin area on the left and right mastoids were served as reference electrodes. The sample rate to record the EEG signal was 1024 Hz. The impedances for all the recorded EEG/EOG electrodes were less than 10kΩ. At the beginning of the EEG pre-processing, the average of EEG signals from the two referenced electrodes was used as a reference for the EEG signals recorded from other EEG/EOG electrodes. The continuous EEG signal for each electrode was segmented with 200 ms before the onset of each electric shock and continuing for 900 ms. Ocular artifact reduction was conducted. The parameters of low-pass of 30 Hz and 24 dB/Oct were applied in the zero-pass filter.

3.1.6 Data Analysis

The Descriptive Analysis in SPSS20 was used to compute the means and standard deviations of NRS ratings for the perceived pain intensity for S1. The possible ES effect (E_L vs. E_H) and IR effect (I_L, I_H vs.Control) on the NRS scores were tested by a two-way repeated-measures ANOVA. Post-hoc comparisons were conducted to explore significant interaction effects between the factors of ES and IR.

In this study, a stable period for SEP method used in previous studies (Dowman 2007, 2011) was applied to determine the time windows of each ERP component. The stable period refers to the time window between the onset and offset

latencies. The onset and offset latencies were first roughly identified by visual inspection, and then verified by conducting an r^2 statistical analysis on the amplitudes of the EEG signals captured from the scalp electrodes. Time points at which the r^2 values between its amplitudes and peak (or midpoint) amplitudes ≥ 0.85 were clumped into the same stable period (Dowman, 2011). Based on the stable period method, in this study, the identified time windows ranged from128 to180 ms for N1. In fact, it consisted of two sub-windows: SP3 (128-152 ms) and SP3/P2 (152-180 ms).The time windows for P2 ranged from 200 to 260 ms, and the time windows for P3 ranged from 280 to 380 ms (Figure 3.2). Three-way repeated-measures ANOVA was conducted to test the main effects of the ES factor, the IR factor, and Electrode factors, and, interactions among them on each of the N1, P2 and P3 time window. In these GLM models, the ES factor included one E_H condition and one E_L condition; the IR factor included one I_H condition (i.e., a high salient self-generated sub-nociceptive image), and one I_L, (i.e., a low salient self-generated sub-nociceptive image). The Electrode factor included 15 electrodes—five electrodes in the left hemisphere (F3, FC3, C3, CP3, P3), five in the midline (Fz, FCz, Cz, CPz, Pz), and five in the right hemisphere (F4, FC4, C4, CP4, P4). In this GLM model, the significance level was set at .050, and each pair-wise contrast within the significant interaction effects was corrected by Bonferroni correction.

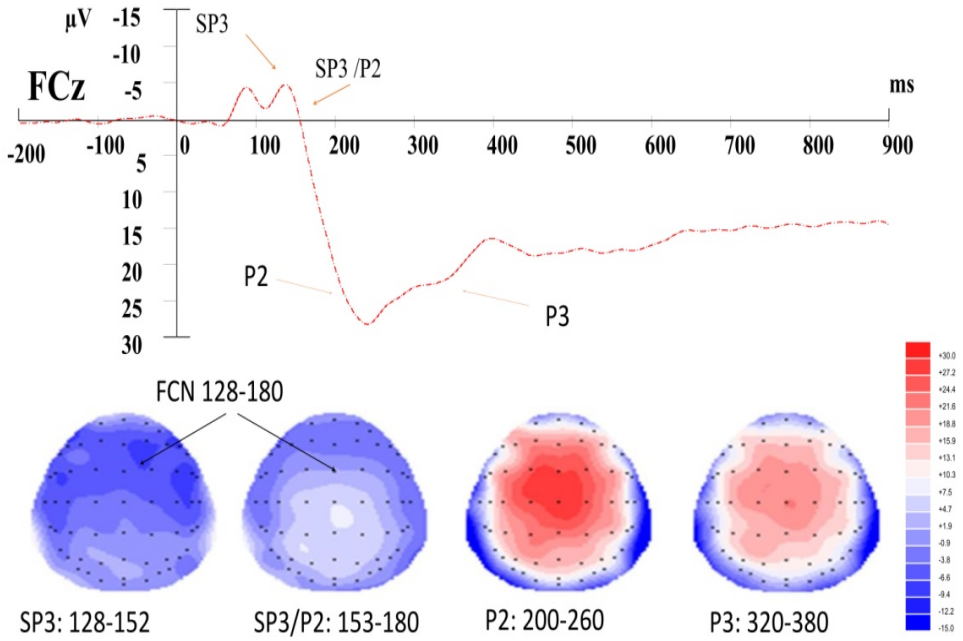


Figure 3.2 ERP Waveforms and Topographic Maps in Study One

Note: The upper panel of the figure illustrates nociceptive ERPs recorded at the scalp frontal-central electrode. The time t = 0 refers to the onset of the nociceptive stimulus. The bottom part of the figure represents topographic maps (top view) of nociceptive ERP magnitude at the its corresponding of N1(SP3, SP3/P2), P2& P3 waves respectively.

The relationships between the change in amplitude for each ERP component and the change in NRS scores, and between the changes in the amplitude of ERP component and the Stroop score were tested by Pearson correlation. The change in the amplitude referred to the difference between the mean amplitudes of the experimental external condition and control condition. For example, changes of amplitudes of N1 elicited by E_H stimulus in I_H condition were computed by subtracting amplitude of N1 elicited by E_H stimulus in control condition from that elicited by E_H stimulus in I_H condition. A similar calculation was conducted to investigate the changes in NRS scores. The significance level was set at .05.

3.2 E–I Orienting Attention Among Patients with Chronic Low Back Pain

3.2.1 Participants

In the second dissertation study (Study Two), there were twenty-two patients with Chronic low back pain (CLBP) (17 females). All the patients were recruited by reading the advertisement posted in The Hong Kong Polytechnic University or recommended by their doctors or therapist or referred by Workers' Health Centre. The selection criteria for the CLBP participants were:1) age from 25 to 55; 2) a secondary level of education or above; 3) CLBP duration of 6 months and above; 4) CLBP with a musculoskeletal origin (supported by a formal diagnosis from their doctors or therapist); 5) CLBP with a particular "painful" site (i.e., the reported most "painful" site should be located on the left side of lumbar region and between L3 and S1). The exclusion criteria included: 1) demonstrable nerve or spinal impingement, 2) pain caused by malignancy,3) presentation of cognitive deficits or neurological impairment, and 4) failure to pass the training. Selection criteria 3 to 5 and exclusion criteria 1 and 2 were screened according to the results of items in Pain History Questionnaire (PHQ, Appendix XII). Three of the patients dropped out after completing the first day's experiment, and four patients failed to continue participating in the study because they were unable to pass the training session. In the end, data of 15 CLBP patients (first 15 patients in Table 3.2) were investigated in the subsequent analysis. The average age of them was 39.0 years with an SD of 11.6, ranging from 25 to 55 years. The research committee of the Department of Rehabilitation Sciences of the Hong Kong Polytechnic University has approved this study. All participants completed the written

Consent Form (See Appendix X) after reading the Information Form (see Appendix XI) where the purpose of the study was explained.

Table 3. 2 Demographic characteristics and pain-related information of the patient participants

Patient No. /Age/Gender	Diagnosis	Pain Duration (years)	Medication
1/40/Female	Lumbar Degeneration at L4	15	Paracetamol
2/56/Female	Lumbar Degeneration at L4 & L5	30	None
3/53/Female	Lumbar Degeneration at L4 & L5	6	Paracetamol
4/52/Female	Muscle and Ligament Injuries at L4 & L5	7	Paracetamol
5/51/Female	Muscle and Ligament Injuries at L4 & L5	20	None
6/54/Female	Muscle and Ligament Injuries at L4 & L5	17	None
7/44/Female	Lumbar Degeneration at L3 - L5	1	None
8/53/Female	Muscle and Ligament Injuries at L4 & L5	2	Paracetamol
9/52/Female	Lumbar Degeneration at L3	20	None
10/55/Male	Muscle and Ligament Injuries at L4 & L5	13	Not Available
11/46/Male	Muscle and Ligament Injuries at L4 & L5	2	None
12/49/Female	Muscle and Ligament Injuries at L4 & L5	15	None
13/51/Female	Muscle and Ligament Injuries at L4 & L5	3	None
14/54/Male	Muscle and Ligament Injuries at L4 -S1	10	Celecoxib
15/31/Female	Muscle and Ligament Injuries at L3 - L5	18	None
16/51/Female	Lumbar Degeneration at L4 & L5	7	None
17/55/Female	Lumbar Degeneration at L4 & L5	8	Aspirin
18/35/Male	Lumbar Degeneration at L4	10	None
19/31/Female	Muscle and Ligament Injuries at L4 & L5	6	Not Available
20/43/Male	Lumbar Degeneration at L3 - L5	3	None
21/52/Female	Lumbar Degeneration at L4 & L5	2	None
22/34/Female	Lumbar Degeneration at L4 & L5	4	None

Note: Medication refers the medication taken by the patient participants within the recent six months. Not Available refers to patient participants failed to recall the name of the medication.

3.2.2 Electrical stimuli

Similar to the first study, the nociceptive stimuli and sub-nociceptive stimuli were the two types of electrical stimulations used in the pre-experimental training, the ERP experiment and behavioral experiment. The methods of control and implementation of electrical stimuli were the same as that in Study One, except that anode and cathode electrodes of the stimulator were attached either to the lateral malleolus of the left ankle in non-painful condition or to the left lateral lumbar region, 2 cm near lumbar vertebrae (L5) in "painful" condition, and along the distribution of the sural nerve (L5-S1 dermatome; Dowman, 2007).

3.2.3 Procedures

The study took place on any two days within one week. All the CLBP patients had to go through a pre-experimental preparation and training session, an ERP experiment session and a behavioral experiment session in both experimental days. These experimental procedures in each day were same except for the sites to where the electrodes of the stimulator were attached. For half of the participants, stimulator electrodes were assigned to the non-painful site (i.e., the lateral malleolus of the left ankle) on the first experimental day and to the "painful" site (i.e., the left lateral lumbar region, 2 cm near the fifth lumbar vertebrae) on the second experimental day. For the other half of the participants, the stimulator electrodes were attached to the "painful" site (S_P) first, and then to the non-painful site (S_{NP}).

3.2.3.1 Pre-experimental Preparation

In the pre-experimental preparation, they completed the PIQ and Neuropsychological Tests—Stroop Tests as in Study One. Besides, the experimenter and/or an occupational therapist with a Doctor of Philosophy degree in Rehabilitation Medicine interviewed the participants about their pain history (including the pain duration, intensity, possible trigger, etc.) with the Pain History Questionnaire (PHQ, see Appendix XII) and the Body Chart (see Appendix VIII). After the interview, all the participants completed the Pain Self-efficacy Scale (PSES, see Appendix XIII).

3.2.3.1.1 Pain History Questionnaire

The PHQ was used to gather information on the self-perceived pain of the patient participants. The questionnaire includes possible triggers or causes of the chronic pain, the duration of the pain history, medical treatments currently received, involvement of self-help groups, the severity of chronic pain in the past six months (including maximum and average of the pain intensity perceived in the past six months, pain intensity perceived during the interview) etc. Details of the questionnaire can be found in Appendix XII. The results of the PHQ are part of the inclusion criteria of this study.

3.2.3.1.2 Pain Self-efficacy Scale

The PSES was a chronic pain related scale. It aimed to measure the patients' beliefs about self-efficacy and how confidence tackled daily life activities when suffering the chronic pain (Lim et al., 2007). The PSES consisted of 10 items. Each

item was scored from “0” (not confident at all) to “6” (extremely confident). A higher score indicated a better self-efficacy in handling the pain experience.

3.2.3.1.3 Calibration

The procedure used for calibrating the nociceptive and sub-nociceptive stimuli for each participant and each body site (i.e., both S_{NP} and S_P) was the same as that in Study One. The mean voltages and NRS scores of the three thresholds, the six levels of nociceptive stimuli and two levels of sub-nociceptive stimuli at the S_{NP} (ankle) and S_P (lumbar) for the present study are shown in Table 3-3.

3.2.3.2 Pre-experimental Training

3.2.3.2.1 Familiarization with nociceptive stimuli

In this study, the procedure used to ensure that the participants were familiar with using the NRS to rate the perceived pain from the nociceptive stimuli was similar to that in Study One, except that the timing was programmed by the E-prime 2.0 (Psychology software tools, Inc). Mean NRS scores of six levels of nociceptive stimuli at the S_{NP} (ankle) and S_P (lumbar) for the present study are shown in Table 3.3.

After the training of NRS rating, at the end of this session, the participants were asked to categorize the individualized calibrated nociceptive stimuli as E_L, (including Level 1 & 2) or E_H, (including Level 5 & 6) based on the pain intensity they perceived.

Table 3. 3 Mean Levels of Voltages and NRS Ratings for The Three Thresholds, The Six Levels of Nociceptive and The Two Levels of Sub-nociceptive Stimuli in Study Two in Study Two (n = 15)

			MDS	Sub-nociceptive		JPS	Nociceptive						VPS
				SN_L	SN_H		L1	L2	L3	L4	L5	L6	
Voltages	Ankle	Mean	3.9	4.0	9.2	18.1	19.3	21.4	24.8	28.3	31.4	34.9	34.9
		SD	5.7	5.8	5.1	5.5	5.6	4.6	6.5	7.4	8.1	9.3	9.3
	Lumbar	Mean	2.8	3.1	8.4	16.3	17.3	19.9	22.7	26.5	29.4	32.0	32.6
		SD	4.5	5.0	5.0	5.0	5.2	6.1	7	9	10	11.1	10.8
NRS Scores	Ankle			Null		1	2.0	2.3	3.3	4.3	5.1	5.3	7
							1.0	1.0	1.0	1.0	0.9	0.9	
	Lumbar						1.5	2.0	2.8	3.9	4.7	4.7	
							0.8	0.7	1.0	0.8	1.2	1.1	

Note: NRS (Numeric Rating Scale), ranging from 0 to 10, is used for rating the level of pain intensity felt by the participant. MDS refers to the minimum detectable sensation, the weakest stimulation intensity level with which participant detected a tactile sensation; JPS refers to the just painful sensation which participant perceived stimulation as painful and rated "1" on the NRS; VPS refers to very painful sensation, the intensity with which participant perceived a stimulation as very painful and rated "7" on the NRS. SN_L refers to the External of the non-painful sub-nociceptive stimulus is low, SN_H refers to the External of the non-painful sub-nociceptive sensation is relative high but still under the just painful sensation.L1-L6 refers to the 6 levels of painful nociceptive stimulus, increasing number means that the External of the electrical pulse increases.

3.2.3.2.2 Familiarization with sub-nociceptive stimuli

The familiarization with sub-nociceptive stimuli procedure used in this study was similar to that in Study One, except that the timing was programmed by the E-prime 2.0 (Psychology software tools, Inc).

3.2.3.2.3 E–I orienting training and testing

According to the rules of experimental tasks, the participants were required to learn to generate a specific internal sub-nociceptive representation (I_L or I_H) or to retain the image of the nociceptive stimulus after perceiving the external nociceptive stimulus. After the image generation / maintaining, a feedback stimulus appeared to reinforce the learning of E–I orienting. The feedback stimulus was sub-nociceptive if the self-generated image was sub-nociceptive (no matter whether it was I_L or I_H, while the feedback stimulus was nociceptive if the image was nociceptive. After the training, the participant was supposed to be clear about the three rules. Specifically, in Rule 1, the participant was asked to recall the image of I_L if the external nociceptive stimulus was E_L and to recall the image of I_H if the external nociceptive stimulus was E_H (i.e., orienting attention from E_L to I_L or from E_H to I_H). Rule 2 was the reverse of Rule 1 (i.e., orienting attention from $E_L$to I_H or from E_H to I_L). In Rule 3, the participants only need to retain the image of the stimulus (e.g., from E_L to E_L or from E_H to E_H). There were at least 24 training trials for each step and the E–I orienting training did not

proceed to the ERP experiment until the accuracy rate for each step reached at least 80%.

3.2.3.3 Experimental tasks

In Study One, the experimental task for EEG recording included two kinds of responses—to rate the perceived the nociceptive stimulus after orienting attention to a self-generated internal image and to compare the intensity of an image maintained in working memory with that of a second external stimulus. However, this dual-response task was found to be too difficult for the CLBP patients in previous research (Chan etal., 2012) and author's pilot study (A conference paper, Pang, Chan, &Chan, 2014). Therefore, in Study Two, the experimental task was divided into two parts—one was for recording ERP signal during processes of E–I orienting, and one was for recoding NRS to measure the pain attenuation effect.

3.2.3.3.1 Experimental tasks for the ERP Experiment

The experimental tasks on each experimental day in Study Two were similar to those in Study One. In Study Two, three mental processes were involved in each experimental trial. The first two processes, the detection, and image generating processes were same as those in Study One. However, the third processes (i.e., the responding process) of Study Two were different from that in Study One. In the responding process of Study Two, the participants were required to match the image with the perceived external stimulus (i.e., S2) (Figure 3.3, left panel). In the control

task, three similar mental processes were involved. The first and the third processes were exactly same as those in the experimental trial. The only difference between the experimental task and the control task was that, in the second step, where the participants were required to maintain an image of the perceived nociceptive stimulus (i.e., S1) instead of generating an I_L or I_H image. (Figure 3.3, right panel). Noteworthy, the electrical stimulation was delivered at a non-painful site (ankle) throughout the whole experimental and control task on the first day, and the procedures were repeated at a "painful" site (lower back) on the second day or the other way around.

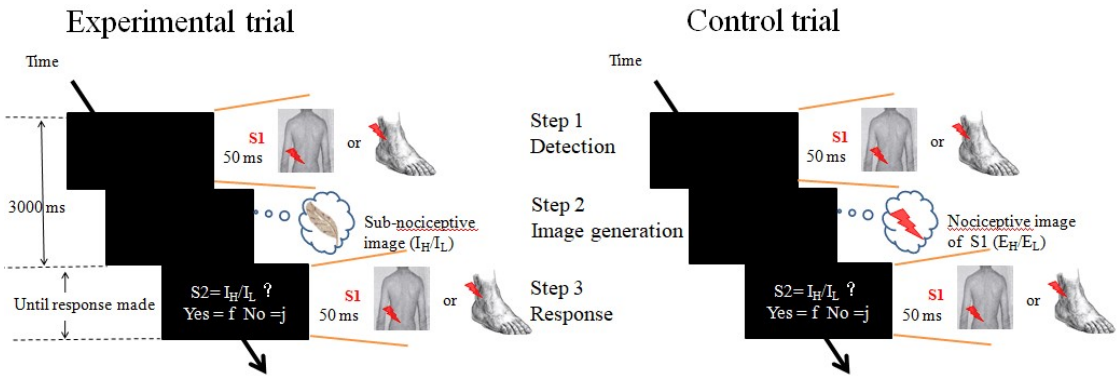


Figure 3.3 Schematic Representation of The Experimental Paradigm in Study Two

Note: The design was resemble to that in Study One. Left panel is schematic representation of an experimental trial. The participant first attended to an 50 ms external nociceptive stimulus (S1) which is either high salient (E_H) or external low (E_L) was delivered either at "painful" site (lower back) or non-painful site (ankle) and maintained the image (Step 1). After that, in Step 2, they were required to generate a pre-trained internal sub-nociceptive image with either high (I_H) salience or low salience (I_L) according to the rules. There were two rules in Step 2. In Rule 1, the participant was to recall a low salient sub-nociceptive image (I_L) if the external nociceptive stimulus was low salient (E_L) and a highly salient sub-nociceptive image (I_H) if the external nociceptive stimulus was highly salient(E_H), i.e., E_L - I_L & E_H - I_H. Rule 2 was the reverse of Rule1, i.e., E_L - I_H & E_H - I_L. During the response phase (Step 3), a second stimulus (S2) which was sub-nociceptive appeared and the participant judged whether the perceived intensity of S2 was comparable with that of the I_H or I_L just generated. Right panel show the flow in a control trial. The control trial only contains Step 1 and Step 3. In Step 3, the same procedure with the experiment trial except that the S2 delivered to the participant was nociceptive and was to comparable with that of S1.

Similar to Study One, the timing, the presentation of output stimulus, and the sequence of each trial in both the experimental tasks and the control task were programmed by the E-prime 2.0 (Psychology software tools, Inc). The design for each trial in the experimental and control tasks on each experimental day in Study Two was similar to that in Study One, except for the rules of Step 2 and the response step (Step 3). In Study Two, according to Rule 1 in Step 2, the participants were supposed to recall the image of I_L if the external nociceptive stimulus was E_L and to recall the image of I_H if the external nociceptive stimulus was E_H. Rule 2 was the reverse of Rule 1. In Rule 3, the participants only need to maintain the image of nociceptive stimulus in their working memory.

The experimental factor designed for this study was a 2 ES × 3 IR × 2 (stimulation sites) three-factor within-subject design. The first factor was ES, which manipulated the salience of the perceived external nociceptive stimuli at the beginning of each trial. The ES factor included an E_H condition and an E_L condition. Only a nociceptive stimulus of L5 & L6 was delivered in the E_H condition. Similarly, only a nociceptive stimulus of L1 & L2 was delivered in the E_L condition. The second factor was IR, which manipulated the salience of the internal representation (i.e., a self-generated sub-nociceptive image). The IR factor included one I_H condition, one I_L condition, and one condition. The participants were required to generate and rehearse a learned I_H image in the I_H condition. Similarly, they were required to generate and rehearse a learned I_L image in the I_L condition. However, in the control condition, the participants were only required to maintain the image from the perceived nociceptive

stimulus. The third factor was stimulation sites (SS) which manipulated the pain experience. The SS factor included one S_P condition and one S_{NP} condition and manipulated the effects of the chronic pain. In the S_P condition, the external stimulus was delivered to the left lateral lumbar region, 2 cm near the lumbar vertebrae (L5), where the major painfulness was reported when they consented to participate in this study. In the S_{NP} condition, the external stimulus was delivered at the lateral malleolar of the left ankle where no perception of pain was reported when they consented to participate in this study.

The 2 (ES: E_H VS. E_L) × 3 (IR: I_H, I_L, and control) × 2 (SS: S_P VS. S_{NP}) combinations yielded a total of 648 trials which were organized into nine blocks: three blocks (Rule 1), three blocks (Rule 2), and three control blocks (Rule 3) on the first experimental day and another similar nine blocks on the second experimental day. There were 36 trials in each experimental block. Completion of one experimental block took around five minutes. The sequence of the blocks and the trials within each experimental block was pseudo randomized. The sequence of stimulus presentation was counterbalanced across patients, and the sequence of the blocks was pseudo randomized across patients as well.

3.2.3.3.2 Experimental task for Behavioral Experiment

Experimental tasks for the behavioral experiment were same as that in the ERP experiment except for the response step. In the experimental tasks (including the control task), for the behavioral experiment, each trial involved the participants in three

mental processes as well. The first two processes, detection and image generation processes, were the same as those in the ERP experiment of the Study Two. However, the response process (third process) was as same as that in Study One, where the participants were required to recall the previously perceived nociceptive stimulus (i.e., S1) and to rate the intensity of the pain for S1 with an NRS score. Same as the experimental task for ERP study in Study Two, the experimental factor design for the behavioral experiment was a 2 ES × 3 IR × 2 SS, a total of three factors within the subject design as well. The 2 × 3 × 2 combinations yielded a total of 96 trials. The trials were organized into nine blocks: three blocks (Rule 1), three blocks (Rule 2), and three control blocks (Rule 3) on the first experimental day and another similar nine blocks on the second experimental day. The completion of 16 trials in each block took approximately two minutes. The sequences of the blocks and the trials within each experimental block were pseudo randomized.

3.2.4 EEG recording and pre-processing

The EEG recording and pre-processing procedures, as well as the parameters used in Study Two, were exactly the same as those in Study One.

3.2.5 Data analysis

Descriptive Analysis in SPSS20 was used to compute the means and standard deviations of the reaction time (RT), the accuracy rate of the participants' matching

the internally self-generated image with the second external stimuli (i.e., S2) in the ERP experiment, and the NRS ratings of the perceived pain intensity for S1 in the behavioral experiment. The possible ES effect (E_L vs. E_H) and the IR effect (I_L vs. I_H) were tested by a two-way repeated-measures ANOVA for the NRS scores, the RT, and the accuracy rate respectively. Post-hoc comparisons were conducted to explore the significant interaction effects among the ES, the IR, and SS factors.

Regarding the EEG data, similar to Study One, a stable period for SEP method which was used in previous studies (Dowman, 2007, 2011) was applied to determine the time window of each ERP component in Study Two. According to the stable period method, the time window varied: For N1, it was 110–130 ms in the S_P condition and 130–150 in the S_{NP} condition; For P2, it was 170–230 ms in the S_P condition and 200–260 ms in the S_{NP} condition; For P3, it was 280–380 ms (Figure 3.4).

A four-way repeated-measures ANOVA was conducted to test the effects of the ES (E_L vs. E_H), the IR (I_L vs. I_H), the SS (S_P vs. S_{NP}), and the Electrode (F3/z/4, FC3/z/4, C3/z/4) factors on mean amplitudes and latencies for each of the N1, P2 and P3 time window. The main effects of the ES factor, the IR factor, the stimulation sites and Electrodes factors and the interactions among them were conducted by a four-way repeated-measures ANOVA on each of the N1, P2 and P3 time window. In this GLM model, the ES factor included one E_H condition and one E_L condition; the IR factor included one I_H condition (i.e., a high salient self-generated sub-nociceptive image) and one I_L condition (i.e., a low salient self-generated sub-nociceptive image); the

stimulation sites included one S_P condition (lower back) and one S_{NP} (ankle); the Electrode factor included nine electrodes—three electrodes in the left hemisphere (F3, FC3, C3), three in the midline (Fz, FCz, Cz), and three in the right hemisphere (F4, FC4, C4). The significance level was .05, and each pair-wise contrast within the significant interaction effects was corrected by Bonferroni correction

The relationships between the change in amplitude for each ERP component and the change in including NRS scores, and the relationship between in change in each ERP amplitudes with other instruments (e.g., the Stroop score were tested, the pain severity scores and PSES scores) were analyzed by Pearson correlation. The calculation of the change in amplitude and the change in NRS scores were same with that in Study One.

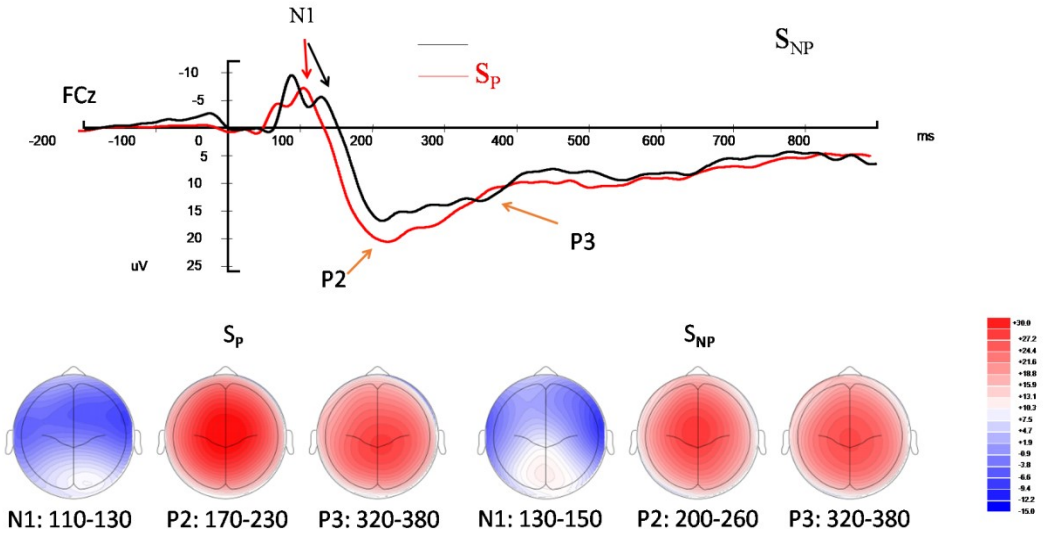


Figure 3.4 ERP Waveforms and Topographic Maps in Study Two

Note: The upper panel of the figure illustrates nociceptive ERPs recorded at the scalp frontal-central electrode. The time t = 0 corresponds to the onsetof the nociceptive stimulus. The bottom part of the figure represents topographic maps (top view) of nociceptive ERP magnitude at the its corresponding of the N1, P2& P3 for "painful" site (S_P)and non-painful site (S_P)waves respectively.

Chapter IV

RESULTS

In this chapter, the results for the healthy individuals (Study One) were first described and then followed by the description of results for the CLBP patients (Study Two). At the end of this chapter, the results compared between the healthy individuals and the CLBP patients during the experiments were presented.

4.1 Results of E–I Orienting Attention Among Healthy Individuals (Study One)

4.1.1 Demographics data

Demographic data for the healthy individuals was shown in Table 4.1. Twenty-two healthy individuals had volunteered to be the participants of Study One. Nine of them were male (40.9 %). Slightly more than half (54.9%) of the participants were married. Majority of them had a bachelor's (54.4%) or above (13.6%). Additionally, 9 (40.9 %) of the participants had a full-time job, 6 (27.3%) of them had a part-time job, 5 (22.7%) of them were undergraduate or postgraduate students.

Table 4.1 Demographics Data Among Healthy Individuals in Study One (n = 22)

	Number	Percentage (%)
Gender		
Male	9	40.9
Female	13	59.1
Marital Status		
Single	9	40.9
Married	12	54.5
Divorced	0	0
widowed	1	4.5
Educational Level		
Middle School	1	4.5
high School	6	27.3
Undergraduate	12	54.5
Postgraduate	3	13.6
Employment Status		
Unemployed	1	4.5
Part-time	6	27.3
Full-time	9	40.9
Student	5	22.7
Housewife	1	4.5

Table 4.2 Mean Scores and Standard Deviation for Stroop Test Among Healthy Individuals in Study One (n = 22)

Subtest	Mean	SD
Word Reading Sub-test		
Total Response Time (second)	45.2	7.5
No. of Error	0.2	0.5
No. of Self-corrected Error	0.7	0.9
Color Naming Sub-test		
Total Response Time (second)	63.9	14.7
No. of Error	0.5	0.9
No. of Self-corrected Error	1.0	1.3
Incongruent Color Naming Sub-test		
Total Response Time (second)	105.9	26.0
No. of Error	1.0	1.6
No. of Self-corrected Error	2.0	2.7
Difference Score (second)		
ICN – WR	59.1	22.4
ICN – CN	42.0	18.6
CN – WR	18.4	11.5
Proportional Score (second)		
(ICN – WR) / WR	1.3	0.4
(ICN – CN) / CN	0.7	0.3
(CN – WR) / WR	0.4	0.2

Notes: SD = Standard Deviation; CN = Color Naming; INC = Incongruent color naming. Different scores are computed by subtracting the reaction time score of the earlier from the later test. Proportional scores are computed by dividing the difference scores by the total time of the earlier test.

4.1.2 Results of Stroop Test

Table 4.2 shows the results of the descriptive analysis for the Stroop Test for the healthy individuals. The Stroop Test consists of three subtests, the Word Reading (WR) subtest, the Color Naming (CN) subtest, and the Incongruent Color Naming (ICN) subtest. For the WR subtest, the mean of the total response time was 45.2 s with standard deviation (SD) of 7.5; the mean error was 0.2 with SD of 0.5; the mean self-corrected error (SCE) was 0.7 with SD of 0.9. For the CN subtest, the mean of the total response time was 63.9 s with SD of 14.7; the mean error was 0.5 with SD of 0.9; the mean SCE was 1.0 with SD of 1.3. For the CN subtest, the mean of the total response time was 105.9 s with SD of 26.0; the mean error was 1.0 with SD of 1.6; the mean SCE was 2.0 with SD of 2.7. As for the difference scores, the mean of ICN – WR was 59.1 s with SD of 22.4; the mean of ICN – CN was 42.0 s with SD of 18.6; the mean of CN – WR was 18.4 s with SD of 11.5. In terms of the proportional scores, the mean of (ICN – WR) / WR was 1.3 s with SD of 0.4; the mean of (ICN – CN) / CN was 0.7 s with SD of 0.3; the mean of (CN – WR) / WR was 0.4 s with SD of 0.2.

4.1.3 Accuracy rate in training

The average accuracy rate of familiarization with the nociceptive stimulus was 85.1 %, ranging from 59.0 % –100.0 % with SD of 13.9%. The average accuracy rate of identifying low salient external sub-nociceptive stimulus (I_L) was 89.3%, ranging from 69.0 % –100.0 % and the SD was 10.2 %. The average accuracy rate of

identifying high salient sub-nociceptive stimulus (I_H) was 94.1 %, ranging from 78.0 % –-100.0 % and the SD was 6.5 %.

4.1.4 Results of NRS scores

Table 4.3 shows the results of the descriptive analysis (Mean and SD) on the NRS scores for the first external nociceptive stimuli in the beginning of each trial (i.e., S1) among the healthy individuals. Results from the three-way repeated measures ANOVA (Table 4.4) has shown that the main effects of the External Stimuli (ES) factor and the Internal Representations (IR) factor on the NRS scores for the S1 were statistically significant ($F_{(2,36)}$= 215.80, p <.001, and $F_{(2,36)}$ = 4.17, p <.012, respectively). For the ES factor, the NRS scores in high salient external nociceptive stimulus (E_H) condition (Mean = 5.1) were significantly higher than that in low salient external nociceptive stimulus (E_L) condition (Mean = 2.9). For the IR factor, the NRS scores for S1 when participants rehearsing an I_L t image (Mean = 4.1) were significantly higher than those when participants rehearsing an I_L image (Mean = 3.9). However, the interaction effect between ES and IR was not significant (p < .789).

Table 4.3 The Mean (and Standard Deviations) of NRS Ratings Among Healthy Individuals in Study One (n = 19)

		External Stimuli		
		E_L	E_H	Mean
Internal	I_L	3.0 (0.2)	5.247 (0.2)	4.134 (0.2)
Representations	I_H	2.7 (0.2)	4.984 (0.2)	3.859 (0.2)
	Mean	2.9 (0.2)	5.116 (0.2)	

Note: E_L refers to the low salient external nociceptive condition, E_H refers to the high salient external nociceptive condition. I_L refers to recall an internal low salient sub-nociceptive image. I_H refers to recall a relatively internal high salient sub-nociceptive image. NRS scores are ranging from 0 to11(from non-painful to extremely painful).

Table 4.4 Tests of Within-Subjects Effects for NRS Scores Among Healthy Individuals in Study One (n = 19)

	df	*F*	*Sig.*
ES	1	211.479	< .001
IR	1	7.775	.012
ES × IR	1	0.074	.789

Note: NRS scores for Numeric Rating Scale, refers the perceived pain rating for the first external stimulus; ES = External Stimuli; IR = Internal Representations; the two-factors interaction between ES and IR.

4.1.5 Results of the ERP components

Figure 4.1 shows the ERP waveforms for the external nociceptive stimulus among each condition at the frontal-central electrode (FCz) and the vertex electrode (Cz). Results from the three-way repeated measures ANOVA on the mean amplitude of the N1, which included time window SP3 and SP3/P2 (see Table 4.5), on the mean

amplitude of P2 (see Table 4.6) and on the mean amplitude of P3 (see Table 4.7) were described in the following paragraphs.

Table 4.5 Tests of Within-Subjects Effects for Mean Amplitudes of N1 Components Among Healthy Individuals in Study One (n = 19)

		df	*F*	*Sig.*
SP3	**Electrode**	2	11.317	< .001
	IR	2	0.291	.749
	ES	1	24.641	< .001
	Electrode× IR	28	3.032	< .001
	Electrode× ES	3	9.610	< .001
	ES× IR	1	5.797	.016
	Electrode × ES × IR	28	0.902	.612
SP3/P2	**Electrode**	2	23.151	< .001
	IR	2	1.346	.273
	ES	1	5.335	.033
	Electrode× IR	28	1.621	.024
	Electrode× ES	3	5.091	.006
	ES × IR	1	4.947	.025
	Electrode × ES × IR	28	0.967	.516

Note: ES refers to External Stimuli; IR refers to Internal Representations, ES × IR refers to the two-factors interaction between External Stimuli and Internal Representations. Electrode × ES × IR refers the three-factors interaction among External Stimuli, internal Representations and Electrode.

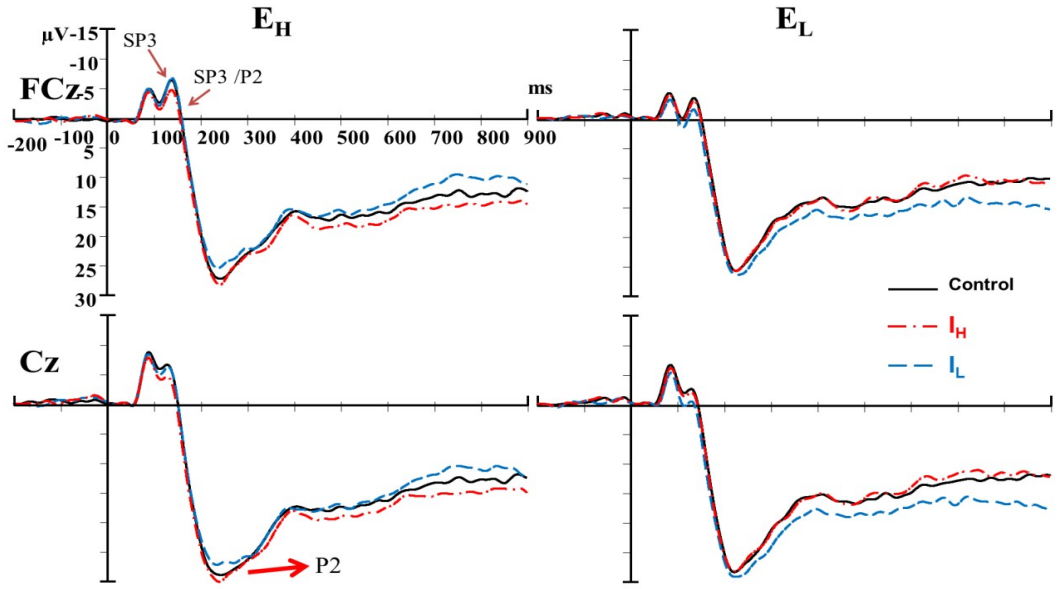


Figure 4. 1 Nociceptive event-related potentials recorded at the FCz andCz

Note: Superimposition of black, red and blue waveforms represents the ERPs elicited by the external nociceptive stimuli during the control condition, during the internal highsalience condition (I_H), and during the internal low salience condition (I_L) respectively, distinctly for the external high salience nociceptive stimuli (left panel) and the external low salience nociceptive stimuli (right panel).

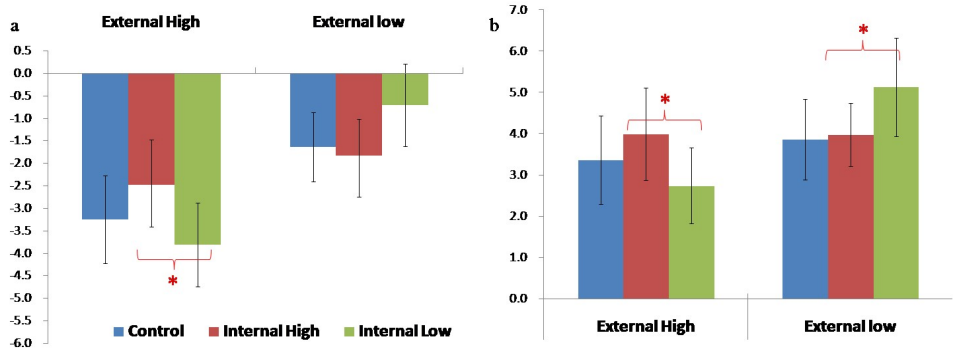


Figure 4. 2 The external-to-internal interactive effects on the disengagement process among the healthy individuals.

Note: The simple-effect analysis of this interaction was conducted on the amplitudes of the SP3 (a) and the SP3/P2 (b) separately. Error bars represent standard errors. * refers to $\alpha < 0.050$.

4.1.5.1 Results of the N1 components

Table 4.5 shows results from the three-way repeated measures ANOVA, on the amplitudes of SP3. The two-factor interaction effect between the ES factor and the IR factor was significant ($F(1,28) = 5.781$; $p = .016$). Results of the simple-effect analysis (Figure 4.2a) on this interaction showed that the mean amplitude elicited by the E_H stimuli were significantly more negative-going during disengaging attention from an E_H stimulus to an I_L image (Mean = -3.81 μV) than that to an I_H image (Man = -2.49 μV) with *p*-value of .021. However, the difference between the two IR conditions was not significant in the E_L condition. The two-factor interaction effect between the Electrode factor and the IR factor was significant ($F(28, 504) = 3.032$, $p < .001$); the mean amplitude at electrode C4 was significantly more negative-going in the I_L condition (Mean = -5.1 μV) than that in the I_H condition (Mean = -4.4 μV) and control condition (Mean = -2.9 μV) with *p*-value of .001 and .032, respectively. The two-factor interaction effect between the Electrode factor and the ES factor was significant ($F(14, 525) = 9.610$; $p < .001$) as well; the enhanced (significantly negative-going) amplitude was found in the E_H condition than in the E_L condition at all the 12 electrodes ($ps < .050$) with exceptions of electrodes P3, Pz, and P4. The main effect of the ES factor was significant ($F(1,18) = 24.641$; $p < .001$), and the enhanced amplitude was found in the E_H condition (Mean = -3.18 μV) than in the E_L (Mean = -1.39). Besides, the main effect of Electrode factor was also found significant ($F(2,42) = 11.317$; $P \leq .001$), specifically, the amplitude was most negative-going at FC4 (Mean = -5.10 μV), compared with those at other electrodes

(*ps* < .050). No other significant main effects or interaction effects were found in the time window of SP3.

Table 4.5 shows results from the three-way repeated measures ANOVA, on the amplitudes of SP3/P2. Similar to results showed in the time window of SP3, in the time window of SP3/P2, the two-factor interaction effect between the ES factor and the IR factor was significant ($F(1,28) = 4.947$; $p = .025$). Results of the simple-effect analysis (Figure 4.2b) on this interaction showed that the mean amplitude elicited by the E_H stimuli was significantly more negative-going in the I_L condition (Mean = 2.7 μV) than to the I_H condition (Man = -2.5 μV) with *p*-value of .021; in contrast, the mean amplitude elicited by the E_L stimuli was significantly less negative-going in the I_L condition (Mean = 5.1 μV) than that in the I_H condition (Mean = 3.9 μV) with *p*-value of .018. The two-factor interaction effect between the Electrode factor and the IR factor was significant ($F(28, 504) = 1.621$, $p = .024$). Further analysis indicated that the mean amplitude at electrode F3 was slightly less negative-going in the I_H condition (Mean = 0.4 μV) than in the control condition (Mean = -0.8μV), $p = .076$. The two factor interaction effect between the Electrode factor and the ES factor was significant ($F(14, 525) = 5.091$; $p = .006$) as well; the more enhanced amplitude was found in the E_H condition than in E_L condition at left-lateral frontal and central electrodes (i.e., Fz ($p = .029$), FC3 ($p = .010$), FCz ($p = .005$), and Cz ($p = .005$)). The main effect of the ES factor was significant ($F(1,18) = 5.335$; $p = .033$), the enhanced amplitude was found in the E_H condition (Mean =3.4 μV) than in the E_L (Mean = 4.3 μV). Besides, the main effect of the Electrode factor was also found

significant ($F(2,42) = 11.317$; $P \leq .001$), specifically, the amplitude was most negative-going at F4 (Mean = -0.60 μV) and most positive-going at Cz (Mean = 9.6 μV), compared with those at other electrodes (*ps* < .050). No other significant main effects or interaction effects were found in the time window of SP3/P2.

Table 4.6 Tests of Within-Subjects Effects for Mean Amplitudes of P2 Components Among Healthy Individuals in Study One (n = 19)

	df	F	Sig.
Electrode	3	21.411	< .001
IR	2	0.368	.695
ES	1	1.770	.200
Electrode× IR	28	1.178	.244
Electrode× ES	3	4.586	.009
ES × IR	1	3.695	.059
Electrode × ES × IR	28	2.208	< .001

Note: ES refers to External Stimuli; IR refers to Internal Representations, ES × IR refers to the two-factors interaction between External Stimuli and Internal Representations. Electrode × ES × IR refers the three-factors interaction among External Stimuli, internal Representations and Electrode.

4.1.5.2 Results of the P2 components

Table 4.6 shows results from the three-way repeated measures ANOVA on the amplitudes of the P2 component. The three-factor interaction effect among the Electrode factor, the ES factor and the IR factor was found significant ($F(28,504) = 2.204$, $p < .001$). Results of the simple-effect analysis (Figure 4.3) on this interaction showed that the mean amplitude elicited by the E_H stimuli at FCz were significantly attenuated (less positive-going) in the I_L condition (Mean = 21.6 μV) than in the I_H

condition (Man = 23.79 μV, p = . 017); and the difference between the two IR conditions was found at electrodes F3, Fz, F4, FC4, Cz, and CPz as well (ps < .050); however, no significant difference between the I_H condition and the I_L condition was found in the E_L condition. The two-factor interaction effect between the Electrode factor and the ES factor was significant (F(14, 525) = 4.586; p = .009) as well; the enhanced amplitudes were found in E_H condition than in E_L condition at central and parietal electrodes (i.e., C4 (p = . 003), CP4 (p =.002), CPz (p = .047), P3 (p = .035), P4 (p = .001), and Pz (p = .005)). The main effect of the ES factor was significant (F(1,18) = 5.335; p = .033), the more enhanced amplitude was found in the E_H condition (Mean =3.4 μV) than in the E_L (Mean = 4.3 μV). Besides, the main effect of the Electrode factor was also found significant (F(3,54) = 21.411; $P \leq .001$) as well, specifically, the amplitude was most positive going at Cz (Mean = 25.6 μV), compared with those at other electrodes (ps < .050). No other significant main effects or interaction effects were found in the time window of P2.

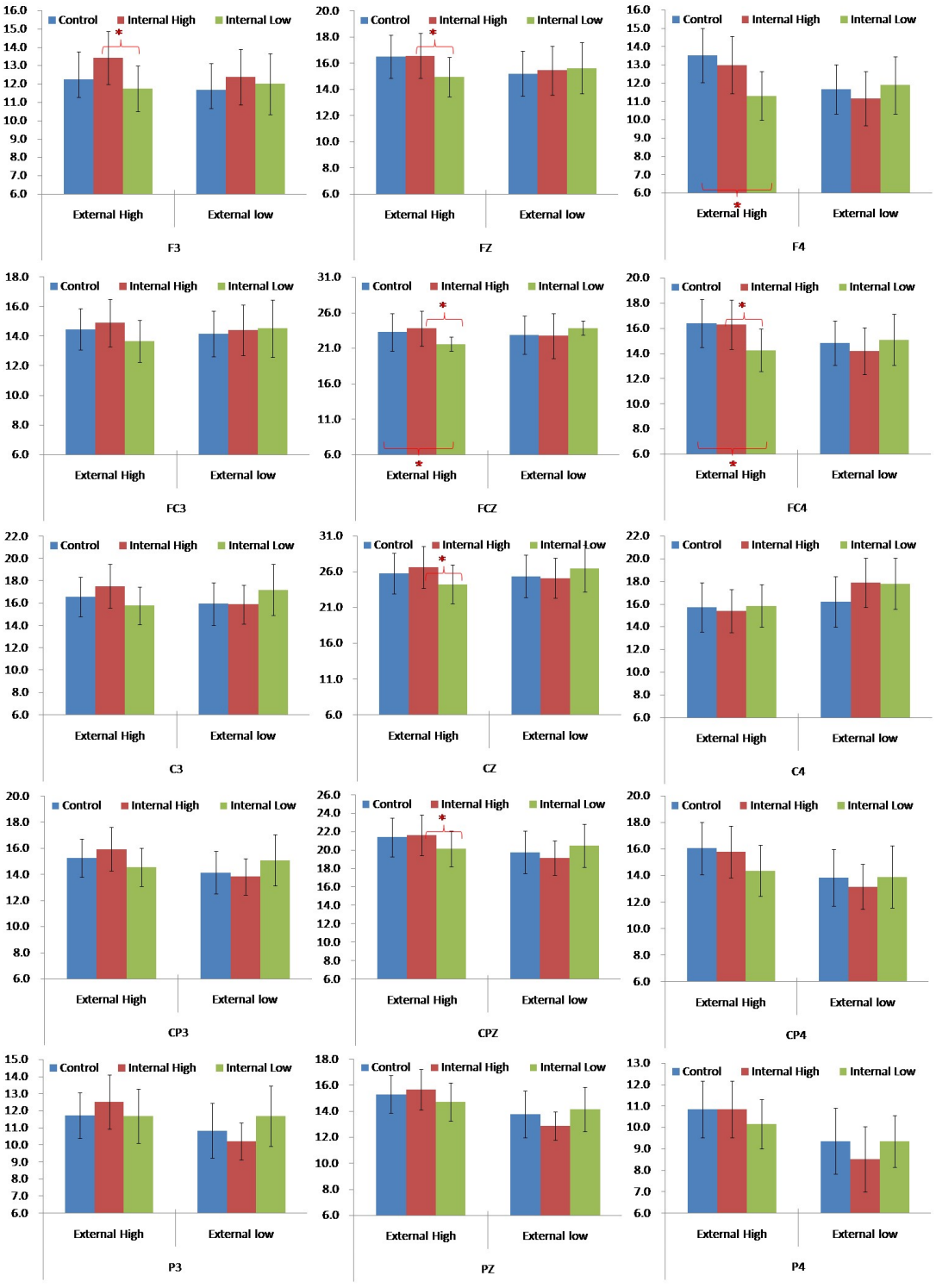


Figure 4.3 The external-to-internal interactive effects on the shifting process among the healthy individuals.

Note: The simple-effect analysis of this interaction was conducted on the amplitudes of the P2 component. Error bars represent standard errors. * refers to $\alpha < 0.050$.

4.1.5.3 Results of the P3 components

Table 4.6 shows results from the three-way repeated measures ANOVA on the amplitudes of the P3 component. Similar to the results showed in the time window of P2, in the time window of P3, the three-factor interaction effect among the Electrode factor, the ES factor and the IR factor was found significant ($F(28,504) = 2.374$, $p < .001$). Results of the simple-effect analysis (Figure 4.4) on this interaction showed that the mean amplitude elicited by the E_H stimuli at C4 was significantly enhanced (more positive-going) in the I_L condition (Mean = 12.8 μV) than those in the I_H condition (Mean = 10.0 μV) and the control condition (Mean = 10.6) with *p*-value of .067 and .004, respectively; however, no significant difference between the I_H condition and the I_L condition was found in the E_L condition. The two-factor interaction effect between the Electrode factor and the IR factor was significant ($F(28, 504) = 1.588$, $p = .030$); the mean amplitude at electrode C4 was significantly more positive-going in the I_L condition (Mean = 13.2 μV) than in the I_H condition (Mean = 11.6 μV) and the control condition (Mean = 11.2 μV) with *p*-value of. 039. and .001, respectively. The two-factor interaction effect between the Electrode and the ES was significant ($F(2, 42) = 3.870$; $p = .023$); the enhanced amplitude was found in the E_H condition when compared to the E_L condition at all the 14 electrodes (*p*s < .050) except electrodes F3. The main effect of the ES factor was significant ($F(1,18) = 20.963$, $p < .001$), the more enhanced amplitude was found in the E_H condition (Mean = 12.2 μV) when compared to the E_L (Mean = 10.4 μV). Besides, the main effect of Electrode factor was also found significant ($F(3,54) = 17.259$; $P \leq .001$). Specifically,

the amplitude was most positive going at FCz (Mean = 25.6 μV), compared with those at other electrodes (*ps* < .050). No other significant main effects or interaction effects were found in the time window of P3.

Table 4.7 Tests of Within-Subjects Effects for Mean Amplitudes of P3 Components Among Healthy Individuals in Study One (n = 19)

	df	*F*	*Sig.*
Electrodes	3	17.259	< .001
IR	2	0.859	.432
ES	1	20.963	<.001
Electrodes × IR	28	1.588	.030
Electrodes × ES	3	3.870	.023
IR × ES	1	1.550	.231
Electrodes × IR × ES	28	2.374	<.001

Note: ES refers to External Stimuli; IR refers to Internal Representations, ES × IR refers to the two-factors interaction between External Stimuli and Internal Representations. Electrode × ES × IR refers the three-factors interaction among External Stimuli, internal Representations and Electrode. Same rules apply for other abbreviation.

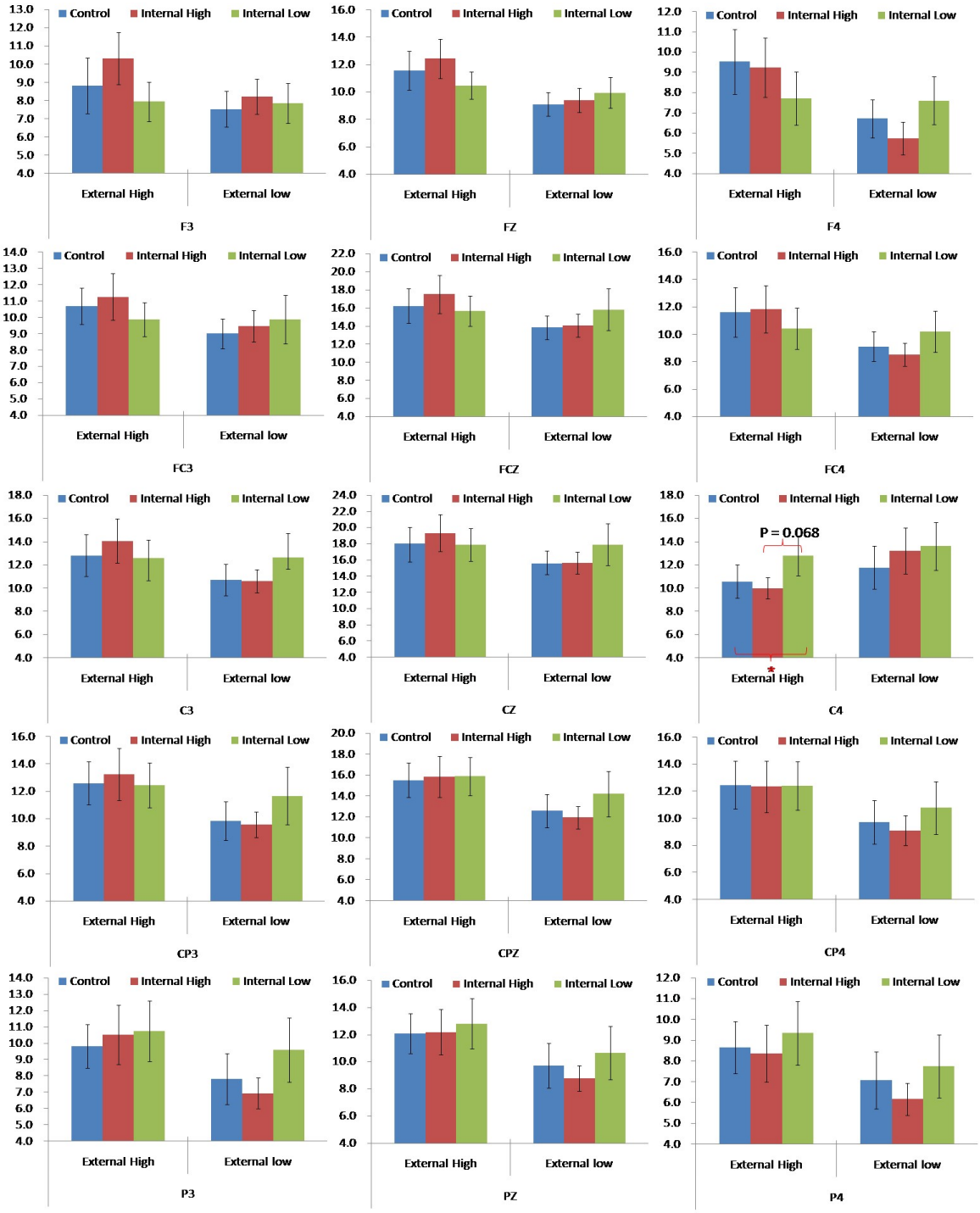


Figure 4.4**The external-to-internal interactive effects on the re-engagement process among the healthy individuals.**

Note: The simple-effect analysis of this interaction was conducted on the amplitudes of the P2 component. Error bars represent standard errors. * refers to $\alpha < 0.050$.

4.1.6 Results of correlations

4.1.6.1 Correlations between changes in the NRS scores and the ERP amplitudes

Among the four E–I orienting attention conditions, correlations between the changes in amplitude and the changes in NRS scores (ΔNRS) were only significant when the external S1 was an E_H stimulus in the I_L condition (E_H/I_L) in the P3 component. These correlations were found to be moderate and positive at the centro-parietal electrodes (i.e., C4 (r = .633, *p*= .004), CP3 (r = .537, *p*= .018), CP4 (r = .638, *p*= .003), and CPz (r = .592, *p*= .008).

ΔNRS in the E_H/I_L condition were calculated by scores for the E_H/I_L condition minus that in the control condition (E_H/control), i.e., $\Delta E_H/I_L = E_H/I_L - E_H$/control. The same formulas were conducted to calculate the amplitude changes in the P3 amplitudes in E_H/I_L condition.

4.1.6.2 Correlations between the proportional scores in Stroop Test and changes in the ERP components

Among the four E–I orienting attention conditions, the correlations between the changes in amplitude and the proportional score of (ICN – WR) / WR for the Stroop Test were only significant when the external S1 was an E_H stimulus in the I_L condition (E_H/I_L) in the P2 component.

The proportional score, which was calculated by dividing the difference scores between the total response time of two sub-test (i.e., ICN – WR) by the total response time of earlier one (i.e., WR) were moderately and positively correlated with the amplitudes changes in P2 components recorded at the centro-parietal electrodes in the

right hemisphere (i.e.,CP4 (r = .499, *P* = .030), and P4 (r = .517, *P* = .023)) in the E_H/I_L condition. Amplitudes changes in the E_H/I_L condition $\Delta E_L/I_L$ was calculated by the amplitude elicited by the E_L stimuli in the I_L condition (I_L/E_L) minus that in control condition (Control/E_L), i.e., $\Delta\ I_L/E_L = I_L/E_L$ - control/E_L.

4.2 Results of E–I Orienting Attention Among Patients with Chronic Low Back Pain (Study Two)

4.2.1 Demographics data

Demographic data for CLBP patients were shown in Table 4.8. Fifteen CLBP patients have completed the two-day ERP experiments. Three of them were males (20.0%). More than half (60.0 %) of the participants were married. Half of them were well-educated. To be more specific, 8 of them had a degree of bachelor (33.2%) or above (20.0%). For the employment status, 9 of the participants had a full-time job (60.0 %), 6 of them had a part-time job (20.0%), and 3 of them were unemployed (20.0%).

4.2.2 Results of Stroop Test among CLBP patients

The results of the descriptive analysis for Stroop Test for CLBP patients were shown in Table 4.9. For the WR subtest, the mean of the total response time was 56.9 s and its standard SD was 12.5; the mean error was 0.5 with SD of 0.7; the mean SCE was 0.7 with SD of 1.2. For the CN subtest, the mean of the total response time was 76.0 s and its SD was 23.8; the mean error was 1.7 with SD of 3.1; the SCE was 1.5

with SD of 2.5. For the ICN subtest, the mean of the total response time was 132.6 s and its SD was 39.7; the mean error was 1.3 with SD of 2.6; the mean SCE was 2.1 with SD of 2.8.

Table 4.8 Demographics Data Among Patients with Chronic Low Back Painin Study Two (n = 15)

	Number	Percentage(%)
Gender		
Male	3	20.0
Female	12	80.0
Marital Status		
Single	4	26.7
Married	9	60.0
Divorced	2	13.3
widowed		
Educational Level		
Middle School	3	20.0
high School	4	26.7
Undergraduate	5	33.3
Postgraduate	3	20.0
Employment Status		
Unemployed	3	20.0
Part-time	3	20.0
Full-time	9	60.0

Table 4.9 Mean Scores and Standard Deviation for Stroop Test Among Patients with Chronic Low Back Pain in Study Two (n = 15)

Subtest	Mean	SD
Word Reading Sub-test		
Total Response Time (second)	56.9	12.5
No. of Error	0.5	0.7
No. of Self-corrected Error	0.7	1.2
Color Naming Sub-test		
Total Response Time (second)	76.0	23.8
No. of Error	1.7	3.1
No. of Self-corrected Error	1.5	2.5
Incongruent Color Naming Sub-test		
Total Response Time (second)	132.6	39.7
No. of Error	1.3	2.6
No. of Self-corrected Error	2.1	2.8
Difference Score (second)		
ICN – WR	75.7	30.7
ICN – CN	56.6	27.0
CN – WR	19.1	16.2
Proportional Score (second)		
(ICN – WR) / WR	1.3	0.4
(ICN – CN) / CN	0.8	0.3
(CN – WR) / WR	0.3	0.2

Notes: SD = Standard Deviation; CN = Color Naming; INC = Incongruent color naming. Different scores are computed by subtracting the reaction time score of the earlier from the later test. Proportional scores are computed by dividing the difference scores by the total time of the earlier test.

Table 4.10Summary of Results from Pain History Questionnaire Among Patients with Chronic Low Back Painin Study Two (n = 15)

Item	Possible Range	Mean	SD
Pain Duration (year)		12.6	8.7
Pain Severity			
Average Pain	0-10	3.6	2.5
Worst Pain	0-10	6.9	2.2
Current Pain	0-10	4.7	1.8
General Health	0-5	4.1	0.8
Professional Visits			
Medical Doctors		0.9	3.1
Clinical Psychologist		0.7	1.9
Community Nurses		0.2	0.8
Physiotherapy / Occupational Therapy		9.5	19.7
Visit at Accident / Emergency Department		0.8	1.3
	Number		**Percentage （%）**
Pain Reason			
Muscle and Ligament Injuries	7		46.7
Lumbar Degeneration	8		53.3
Pain Pattern			
Persists in same intensity	3		20.0
Persists. Sometimes, it is more serious	12		80.0
Medicine			
Yes	6		40.0
NO	9		60.0
"painful" sites			
Only Lumbar	10		66.7
Multiple including Lumbar	5		33.3

For the difference scores, the mean of ICN – WR was 75.7 s with SD of 30.7; the mean of ICN – CN was 56.6 s with SD of 27.0; the mean of CN – WR was19.1 s with SD of 16.2. For the proportional scores, the mean of (ICN – WR) / WR was 1.3 s with SD of 0.4; the mean of (ICN – CN) / CN was 0.8 s with SD of 0.4; the mean of (CN – WR) / WR was 0.3 s with SD of 0.2.

4.2.3 Results of Pain History Questionnaire among the CLBP Patients

The results from the Pain History Questionnaire (PHQ) among the CLBP patients were summarized in Table 4.10. Among these CLBP patients, the mean Pain Duration that the patients were suffering from was 12.6 years and the SD was 8.7, ranging from 1 to 30 years. In terms of the Pain Severity, the mean intensity of Average Pain the patients perceived in the last six months was 3.6 (out of 10), and the SD was 2.5; the mean intensity of the Worst Pain the patients perceived in the last six months was 6.9 (out of 10) and the SD was 2.2; the mean intensity of the Current Pain the patients perceived currently was 4.7 (out of 10) and the SD was 1.8. As for the General Health, the mean scores the patients reported was 4.1 (out of 5, a higher score indicates a worse health condition) and the SD was 0.8. For the causes of the pain, nearly half of the patients reported that their pain was caused by the "Muscle and Ligament Injuries" (46.7%), and the others reported that their pain was caused by the "Lumbar Degeneration" to be the cause of their pain. Regarding the Response Pattern for the occurrence of pain in the past six months, the majority of them (80.0 %) reported the pain as "persists and sometimes, it is more serious", while only a few of them

(20.0 %), reported the pain as " persists in same intensity ". In terms of the medication, most of the patients (60.0%) did not take any medicine currently, while some of them were taking medicines such as Panadol. For the locations of their chronic pain, the majority of them (66.7 %) reported the pain to be at the lower back, while the rest of them (33.3 %) reported multiple "painful" sites including shoulder or neck. As for the number of times to visits the professionals for the treatment in the last six months, the most frequent professionals from whom they sought help were physiotherapy and occupational therapy (Mean = 9.5 times; SD = 19.7), followed by the meeting with the medical doctors (Mean = 0.9 times; SD = 3.1).The mean number of times of visiting the clinical psychologists was 0.7 times with SD = 1.9 and the mean number of times of visiting the community nurses was 0.2 times with SD = 0.8. The mean number of times of being in an accident/emergency department was 0.8 times with SD = 1.3.

4.2.4 Results of the performances in training

As for the performances in the familiarization of nociceptive stimulus, in which the patients were required to categorize the salience level of the nociceptive stimuli as E_L or E_H, the mean accuracy rate at non-painful site (S_{NP}) was 92.2 %, ranging from 75.0 % – 100 % and the SD was 7.8 %, while at "painful" site (S_P) the mean accuracy rate was 92.4 %, ranging from 79.0 % – 100 % and the SD was 6.2 %; the mean response time in the S_{NP} condition was 732.9 s, and the SD was 206.0, while in the S_P condition, the mean response time was761.1 with SD being 206.9.

In terms of the performances in the familiarization of sub-nociceptive stimulus, in which the patients were required to identify the salience levels of the two sub-nociceptive stimuli, the mean accuracy rate for low salient sub-nociceptive stimulus in the S_{NP} condition was 95.6 %, ranging from 75.0 % – 100 % and the SD was 7.4 %, whilst in the S_P condition, the mean accuracy rate for was 91.4 %, ranging from 60.0 % – 100 % and the SD was 11.1 %; and the mean accuracy rate for the high salient sub-nociceptive stimulus in the S_{NP} condition was 90.7 %, ranging from 79.0 % – 100 % and the SD was 8.4 %, and the mean for high salient sub-nociceptive stimulus in the S_P condition was 84.7 %, ranging from 64.0 % – 100 % and the SD was 12.8 %; the mean response time for low salient sub-nociceptive stimulus in the S_{NP} condition was 691.1s, and the SD was 279.9, and the mean in the S_P condition, was 638.4, and the SD was 197.7; the mean response time for high salient sub-nociceptive stimulus in the S_{NP} condition was 710.3 s, and the SD was 321.6, and the mean in the S_P condition was 845.5, and the SD was 259.8.

4.2.5 Behavioral Performances in ERP experiment

The results of the descriptive analysis (Mean and SD) on the Accuracy Rate, the Reaction Time (RT) and the efficiency (calculated by RT divided by Accuracy Rate) of matching an internal image with the second external stimulation (i.e.,S2) which appeared at the end of a trial among the CLBP patients were shown in Table 4.11. Table 4.12 shows the results of the three-way repeated measures ANOVA for Accuracy Rate, RT and, efficiency of the matching performances separately.

Table 4.11 Mean Scores and Standard Deviation of Performance in ERP Experiment Among Patients with Chronic Low Back Pain in Study Two (n = 15)

			Control		I_H		I_L	
			Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Accuracy	E_H	S_{NP}	81.70%	13.30%	86.10%	9.90%	84.40%	8.20%
		S_P	79.60%	12.10%	79.20%	9.70%	78.30%	11.80%
	E_L	S_{NP}	95.30%	3.30%	86.10%	12.50%	85.50%	16.70%
		S_P	93.50%	3.90%	81.50%	13.30%	80.40%	13.80%
		S_{NP}	1344.2	1463.7	1380.7	265.7	540.7	507.8
RT	E_H	S_P	1507	1892.8	1562.3	682	752.1	581.3
		S_{NP}	1064.4	1570.4	1357.6	250.3	605.8	619.1
	E_L	S_P	1097.6	1721.8	1519.2	263.4	538.7	580.3
Efficiency	E_H	S_{NP}	1544.7	1615.6	1512.9	359	602.7	602.9
		S_P	1679.7	2130.4	1721	700.2	844.9	593.5
	E_L	S_{NP}	1090.4	1688.5	1516.5	257.4	650.5	855.7
		S_P	1130.4	1923.5	1729.2	258.7	666.5	895

Note: RT refers to the Reaction Time; Efficiency was calculated by RT divided by accuracy rate; $E_L$refers to the low salient external nociceptive condition; E_H refers to the high salient external nociceptive condition; S_{NP} refers to the external nociceptive stimuli were placed at the CLBP patients' non-painful site (ankle); $S_{P,}$ refers to the external nociceptive stimuli were placed at the CLBP patients' "painful" site, i.e., lower back; I_L refers to recall an internal low salient sub-nociceptive image. I_H refers to recall a relatively internal high salient sub-nociceptive image.

4.2.5.1 Accuracy Rate of behavioral performances

For the Accuracy Rate, the three-factor interaction effect among the ES, the IR and the SS was not significant, but the two-factor interaction effect between the ES factor and the IR factor was statistically significant ($F(2,28) = 13.403$, $p < .001$). Further analysis indicated that in the E_L condition, accuracy rate was significantly higher in the control condition (94.4 %) than that in the two experimental conditions (the mean was 83.8 % ms for the I_H condition, and was 82.9% ms for the I_L condition with

p-values of .032 (I_H) and .016 (I_L), respectively). In the E_H condition, the differences among those three conditions were not significant. The main effect of the ES factor and the IR factor were significant ($F(2,28) = 10.883$, $p = .005$ and $F(2,28) = 4.896$, $p = .015$, respectively), however, the main effect of the SS factor was only marginally significant ($F(1,14) = 3.422$, $p = .086$). For the ES factor, the Accuracy Rates were significantly higher for the E_L stimuli (Mean = 87.0 %) than that for the E_H stimuli (Mean = 81.5 %) with *p*-values of .005. For the IR factor, the Accuracy Rate for the I_H condition (Mean = 87.5 %) was significantly higher than those for the control condition (Mean = 83.2 %). For the SS factor, the Accuracy Rate at the S_{NP} (Mean = 86.5 %) was significantly higher than that at the S_P (Mean = 82.1). The two-factor interaction effects (i.e., SS × ES and SS × IR) were not significant.

Table 4.12Tests of Within-Subjects Effects for Performance in ERP Among Patients with Chronic Low Back Pain in Study Two (n = 15)

	ACC		RT		ACC/RT	
	F	***Sig.***	***F***	***Sig.***	***F***	***Sig.***
SS	3.422	.086	2.375	.146	2.764	.119
ES	10.883	.005	7.064	.019	8.961	.010
IR	4.896	.015	20.554	.001	13.031	.001
SS× ES	0.143	.711	1.152	.301	0.764	.397
SS ×IR	0.942	.402	1.922	.165	3.254	.054
ES × IR	13.403	.001	10.986	.001	9.650	.001
SS × ES × IR	0.063	.940	2.287	.120	1.837	.178

Note: RT refers to the Reaction Time; Efficiency was calculated by RT divided by accuracy rate; SS refers to Stimulation Sites; ES refers to External Stimuli; IR refers to Internal Representations; ES × IR refers to the two-factors interaction between External Stimuli and Internal Representations; SS × ES × IR refers the three-factors interaction among Stimulation Sites External Stimuli, and internal Representations. Same rules apply for other abbreviation..

4.2.5.2 Reaction Time of behavioral performances

The results for the RT were similar to those for Accuracy Rate, the three-factor interaction effect among the ES factor, the IR factor and the SS factor was not significant, but the two-factor interaction effect between the ES factor and the IR factor was statistically significant ($F(2,28) = 10.986$, $p < .001$). Further analysis suggested that in the E_L condition, the differences among those three IR conditions were significant. To be more specific the RT in the I_H condition (Mean = 1646.1 ms) was significantly longer than that the I_L condition (Mean = 1438.4 ms) and that in the control condition (Mean = 1081.0 ms), the *p*-values were .001 for the contrasts of I_H and I_L and .008 for the contrast of I_L and control. In the E_H condition, the RT in the I_H condition (Mean = 1678.2 ms) was significantly longer than that in the I_L condition (Mean = 1471.5 ms) and that in the control condition (Mean =1425.5 ms), the *p*-values were .016 for the I_H-I_L contrast and was .008 for the I_H-control contrast , but the I_L-control contrast was not significant. Besides, the main effects of the ES factor and the IR factor were significant ($F(2,28) = 7.064$, $p = .019$, and $F(2,28) = 20.554$, $p < .001$, respectively). For the ES factor, the RT was significantly longer for the E_H stimuli (Mean = 1525.1ms) than that for the E_L stimuli (Mean =1388.5 ms), $p < .005$. For the IR factor, the RT for the I_H image condition (Mean = 1662.2 ms) was significantly longer than that for the I_L image condition (Mean = 1455.0 ms) and also significantly longer than those for the control condition (Mean = 1253.3 ms), *ps* < .001. No other significant main effects or interaction effects were found in RT.

4.2.5.3 Efficiency of behavioral performances

The results for the efficiency were similar to those for Accuracy Rate and RT, the three-factor interaction effect among the ES, the IR and the SS was not significant, but the two-factor interaction effect between ES factor and IR factor was statistically significant, $F(2,28) = 9.650$, $p < .001$. Further analysis revealed that in the E_H condition, it was significantly less efficient in the two experimental conditions (the mean was 1646.1 ms for I_H condition, and was 1622.8 ms for I_L condition) than that in the control condition (Mean = 1110.4 ms), with the *p*-values of .001 and .034, respectively. In the E_L condition, it was significantly less efficient in the I_H conditions (Mean = 1873.0 ms) than that in the I_L condition (Mean = 1616.9 ms) and that in control condition (Mean = 1612.2 ms) with the *p*-values of .014 and .038, respectively. The two-factor interaction effect between the SS factor and the IR factor was marginally significant ($F(2,28) = 3.254$, $p = .054$). Further analysis suggested that at S_{NP}, it was significantly less efficient in the I_H conditions (Mean = 1652.1 ms) than in the control condition (Mean = 1317.6; ms) with *p*-value of.035 while there was no significant difference between the two experimental conditions. At S_P, it was significantly less efficient in the I_H condition (Mean =2026.9 ms) than in the control condition (Mean = 1405.1; ms), and also significantly less efficient than that in the I_L conditions (Mean = 1725.1 ms), *ps* <.001. The main effects of the ES factor and the IR factor were significant ($F(2,28) = 8.961$, $p = .010$, and $F(2,28) = 13.031$, $p < .001$, respectively). For the ES factor, it was significantly less efficient in the E_H condition (Mean = 1700.8 ms) than that for the E_L stimuli (Mean = 1513.1 ms), $p = .010$. For

the IR factor, it was significantly less efficient in the two experimental conditions (the mean was 1839.5 ms for I_H condition, and was 1361.3 ms for I_L condition) than in the control condition (Mean = 1361.3 ms), *ps* < .001. No other significant main effects or interaction effects were found in the efficiency.

4.2.6 NRS Scores in behavioral experiment

Table 4.13 shows the results of the descriptive analysis (Mean and SD) on the NRS scores for the first external nociceptive stimuli (S1) in the behavioral experiment among CLBP patients. Results from the three-way repeated measures ANOVA (Table 4.14) had shown that there are not significant three-factor interaction effects among the ES factor, the IR factor and the SS factor, but the two-factor interaction effect between the ES factor and the IR factor was marginally significant ($F(2,28) = 2.646$, $p = .089$). Further analysis suggested that in the E_L condition, the NRS score in I_L condition (Mean = 2.3 (out of 10)) was significantly lower than that in the I_H condition (Mean = 2.6 (out of 10)) and that in the control condition (Mean = 2.9 (out of 10)) with the *p*-values of .039 and .043, respectively. No significant difference was found among these three IR conditions in the E_H condition.

Table 4.13 Mean Scores and Standard Deviation of NRS Rating in Behavioral Experiment Among Patients with Chronic Low Back Pain in Study Two (n = 15)

		Control		I_H		I_L	
		Mean	SD	Mean	Mean	SD	Mean
E_H	S_{NP}	4.6	1.0	4.1	1.1	4.4	1.3
	S_P	4.4	1.3	3.9	1.7	4.1	1.6
E_L	S_{NP}	3.0	1.1	2.8	0.9	2.5	0.8
	S_P	2.8	1.5	2.5	1.1	2.1	1.0

Note: E_L refers to the low salient external nociceptive condition; E_H refers to the high salient external nociceptive condition; S_{NP} refers to the external nociceptive stimuli were placed at the CLBP patients' non-painful site (ankle); $S_{P,}$ refers to the external nociceptive stimuli were placed at the CLBP patients' "painful" site, i.e., lower back; I_L refers to recall an internal low salient sub-nociceptive image. I_H refers to recall a relatively internal high salient sub-nociceptive image. NRS scores are ranging from 0 to11(from non-painful to extremely painful).

Table 4.14 Tests of Within-Subjects Effects for NRS Rating in Behavioral Experiment Among Patients with Chronic Low Back Pain in Study Two (n = 15)

	NRS	
	F	***Sig.***
SS	1.620	.224
ES	131.694	.001
IR	3.398	.077
SS× ES	0.332	.574
SS ×IR	0.337	.717
ES × IR	2.646	.089
SS × ES × IR	0.058	.944

Note: SS refers to Stimulation Sites; ES refers to External Stimuli; IR refers to Internal Representations; ES × IR refers to the two-factors interaction between External Stimuli and Internal Representations; SS × ES × IR refers the three-factors interaction among Stimulation Sites External Stimuli, and internal Representations. Same rules apply for other abbreviation..

The main effect of the ES factor was significant ($F(2,28) = 131.694$, $p < .001$), the post-hoc analysis revealed that the NRS score for the E_H stimuli (Mean = 4.3) was significantly higher than that for the E_L stimuli (Mean = 2.6, $p < .001$). For the IR factor, no statistically significant difference on the NRS score was found among those three IR conditions though the main effect was marginally significant ($F(2,28) =$

3.398, p =.077). No other significant main effects or interaction effects were found in the NRS scores.

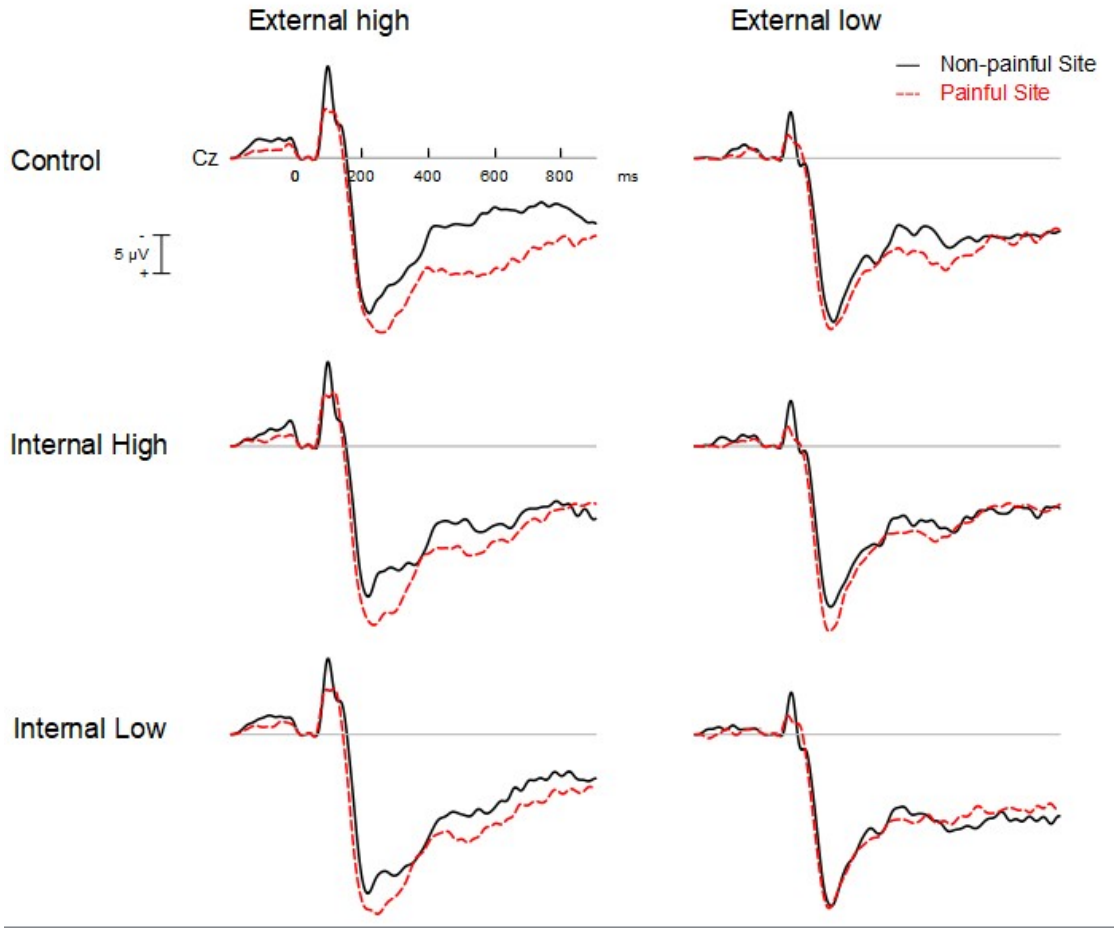


Figure4.5 Nociceptive event-related potentials recorded at Cz

Note: Nociceptive event-related potentials recorded at the frontal-central electrode (Cz) when stimulation at Lumbar part (upper panels) and at Ankle (bottom panels). Superimposition of black, red and blue waveforms represents the ERPs elicited by the external nociceptive stimuli during the control condition, during the internal high salience condition (IH), and during the internal low salience condition (IL) respectively, distinctly for the external high salience nociceptive stimuli (left panels) and the external low salience nociceptive stimuli (right panels).

4.2.7 Results of the ERP components

Figure 4.5 shows the ERP waveforms for the external nociceptive stimulus among each condition at the vertex electrode (Cz). Results from the four-way repeated measures ANOVA to investigate the mean amplitude and latency of the N1 (see Table 4.15), for the mean amplitude of P2 (see Table 4.16) and for the mean amplitude of P3 (see Table 4.17) were described in the following paragraphs.

4.2.7.1 Results of the N1 components

Table 4.15 shows results from the four-way repeated measures ANOVA on the amplitudes of the N1 component. For the mean amplitudes of the N1 component, the four-factor interaction effect among the ES factor, the IR factor, the SS factor and the Electrodes factor was not significant, but the three-factor interaction effect among the ES factor, the IR factor, and SS factor was statistically significant($F(2,28) = 3.678$, $p < .038$). Further analysis indicated that among all the four E–I conditions at both S_P and S_{NP}, the mean amplitudes were extremely and significantly more negative-going in the E_H condition than those in the E_L condition ($ps \leq .009$) with an exception of those in the control condition at S_{NP} ($p = .010$). The two-factor interaction effect between Electrodes factor and SS was significant $F(8, 112) = 4.709$; $p = .003$. Further analysis revealed that the mean amplitudes recorded at Cz were significantly more negative-going in the S_P condition (Mean = -2.25 μV) than those in the S_{NP} (Mean = .85 μV) with the *p*-values of .050. The two-factor interaction effect between the Electrodes factor and the ES factor was found significant, $F(8, 112) = 4.208$, $p = .012$.To be more specific, the mean amplitude was extremely significantly more

negative-going in the E_H condition than those in the E_L condition at all electrodes (*ps*≤ .001) except those in the control condition at the non-painful site. For the ES factor, a more negative-going N1 was found in the E_H condition (Mean = -4.63 μV) than that in the E_L condition (Mean = -1.51 μV), $F(1,14) = 26.234$; $p < .001$. The main effect of the Electrodes factor was also found significant as well ($F(8, 112) = 8.203$, $p < .001$), the most negative-going N1 was recorded at FC4 (Mean = -4.66 μV) compared with that at other eight electrodes, *P*s< .050. No other significant main effects or interaction effects were found for the amplitudes of the N1 component.

Table 4.15 Tests of Within-Subjects Effects for the External-to-Internal Orienting Attention on The Mean Amplitudes and Latencies of N1 Component Among Patients With Chronic Low Back Pain in Study Two(n = 15)

	Mean amplitudes		**Latencies**	
	F	***Sig.***	***F***	***Sig.***
Electrodes	8.203	.001	11.801	.001
ES	26.234	.001	0.369	.553
IR	0.261	.772	0.946	.364
SS	0.473	.503	243.672	.001
IR × ES	0.422	.660	0.934	.405
SS × IR	0.770	.473	0.078	.925
SS × ES	0.065	.803	2.846	.114
Electrodes × IR	1.229	.247	0.843	.636
Electrodes × ES	4.208	.012	2.478	.086
Electrodes × SS	4.709	.003	1.687	.178
ES × IR × SS	3.678	.038	1.935	.179
Electrodes × IR × ES	0.365	.989	1.058	.398
Electrodes × SS × IR	0.730	.762	0.639	.850
Electrodes × SS × ES	0.300	.795	1.052	.382
Electrodes × SS × IR × ES	0.699	.794	1.078	.377

Notes: SS refers to Stimulation Sites; ES refers to External Stimuli; IR refers to Internal Representations; Electrodes × SS × IR × ES refers to the four-factors interaction among Electrode, Stimulation Sites External Stimuli, and internal Representations. Same rules apply for other abbreviation.

For the latencies, there was no any significant interaction effect among all the four factors, but the main effects of the SS factor and the Electrode factor were significant ($F(1,14) = 243.672$, $p < .001$ and $F(8,112) = 11.801$; $p < .001$, respectively). For the SS factor, the peaks of N1 appeared significantly earlier at the S_P (Mean=119.51 ms) than that the S_{NP} (Mean = 138.16 ms). For the Electrode factor, the peak of N1 was first appeared at Cz (Mean = 124.52 ms).

4.2.7.2 Results of the P2 components

Table 4.16 shows results from the four-way repeated measures ANOVA on the amplitudes of the P2 component. For the mean amplitudes of the P2 component, the four-factor interaction effect among the among the ES factor, the IR factor, the SS factor and the Electrodes factor ($F(2,28) = 3.129$, $p = .059$). Further analysis suggested that in the E_H condition, an enhanced P2 (more positive-going) was revealed in the I_L condition (Mean =11.91 μV) compared with the control condition (Mean = 10.77μV), $p = .016$; whilst in the E_L condition, no significant differences among the mean amplitudes in all the IR conditions. The main effect of the Electrodes factor was also found significant ($F(8, 112) = 30.044$, $p < .001$), and the most positive-going P2 was recorded at Cz (Mean = 19.44 μV) compared with that at other eight electrodes, $ps < .050$. No other significant main effects or interaction effects were found for the mean amplitudes of the P2 component.

For the latencies, there was no any significant interaction among all the four factors, but the main effects of the SS factor and the ES factor were significant ($F(1,14) = 8.944$, $p = .010$ and $F(8,112) = 11.426$; $p = .004$, respectively). For the SS factor, the peaks

of P2 appeared significantly earlier in the S_P condition (Mean = 211.16 ms) than that in the S_{NP} (Mean= 220.24 ms). For the ES factor, peaks of the P2 component appeared significantly later in the E_H condition (Mean=217.83 ms) than in the E_L condition (Mean=213.54 ms).

Table 4.16 Tests of Within-Subjects Effects for the External-to-Internal Orienting Attention on The Mean Amplitudes and Latencies of P2 Component Among Patients With Chronic Low Back Pain in Study Two(n = 15)

	Mean amplitudes		Latencies	
	F	***Sig.***	***F***	***Sig.***
Electrodes	30.044	.001	2.453	.069
ES	0.907	.357	11.426	.004
IR	2.162	.134	0.764	.475
SS	0.398	.538	8.944	.010
IR × ES	3.129	.059	2.118	.139
SS × IR	2.539	.126	1.071	.356
SS × ES	0.037	.850	0.004	.949
Electrodes × IR	0.951	.511	0.878	.596
Electrodes × ES	0.499	.675	2.411	.076
Electrodes × SS	1.088	.367	0.689	.600
ES × IR × SS	0.266	.768	1.060	.360
Electrodes × IR × ES	0.465	.961	1.178	.287
Electrodes × SS × IR	1.156	.306	0.643	.847
Electrodes × SS × ES	0.509	.629	0.693	.697
Electrodes × SS × IR × ES	1.126	.332	1.032	.424

Notes: SS refers to Stimulation Sites; ES refers to External Stimuli; IR refers to Internal Representations; Electrodes × SS × IR × ES refers to the four-factors interaction among Electrode, Stimulation Sites External Stimuli, and internal Representations. Same rules apply for other abbreviation.

4.2.7.3 Results of the P3 components

Table 4.17 shows results from the four-way repeated measures ANOVA on the amplitudes of the P3 component. Different from the results of the two earlier components, results of the mean amplitudes of the P3 component indicated a

significant four-factor interaction effect among the ES factor, the IR factor, the SS factor and the Electrodes factor ($F(16,224) = 2.484$, $p < .002$). Further analysis revealed that in the I_H condition, an enhanced P3 component were found in E_H condition compared with that in the E_L condition at electrode FCz (Mean E_H=12.10 μV vs. Mean E_L=9.15 μV, $p = .033$) & Cz (Mean E_H= 15.55μV vs. Mean E_L= 12.17 μV, $p = .033$) at the S_P but not the S_{NP}; whilst in the I_L condition, compared with the E_L stimuli, the enhanced P3 component elicited by E_H stimuli was only found at electrode Cz (Mean E_H=15.98μV vs. Mean E_L= 12.14 μV, $p = .035$) in the S_P condition, but in the S_{NP} condition, this enhanced P3 components were found at electrode Fz (Mean E_H= 9.54μV vs. Mean E_L= 5.59 μV, $p = .003$), F4 (Mean E_H= 6.60μV vs. Mean E_L= 2.21 μV, $p = .006$), FCz (Mean E_H=13.37 μV vs. Mean E_L= 10.03 μV, $p = .033$), FC4 (Mean E_H=8.44μV vs. Mean E_L= 5.79 μV, $p = .047$) & C4 (Mean E_H= 9.54μV vs. Mean E_L= 10.03 μV, $p = .032$). The two-factor interaction effect between the Electrode and ES was also found significant ($F(8, 112) = 4.208$, $p = .013$). To be more specific, only at Cz electrodes, the mean amplitude of the P3 component was enhanced in the E_H condition (Mean = 15.12 μV) than those in E_L condition (Mean = 12.39 μV, $p = .059$). The main effect of Electrodes was also significant, $F(8, 112) = 21.294$, $p < .001$, the most enhanced P3 was recorded at Cz (Mean = 13.76 μV) compared with that at other eight electrodes (ps< .050). No other significant main effects or interaction effects were found for the mean amplitudes of the P3 component.

Table 4. 17 Tests of Within-Subjects Effects for the External-to-Internal Orienting Attention on The Mean Amplitudes and Latencies of P3 Component Among Patients With Chronic Low Back Pain in Study Two(n = 15)

	Mean amplitudes		Latencies	
	F	***Sig.***	***F***	***Sig.***
Electrodes	21.294	.001	2.772	.070
ES	2.189	.161	12.302	.003
IR	0.030	.971	1.390	.265
SS	0.006	.939	8.282	.012
IR × ES	2.214	.128	2.611	.091
SS × IR	0.087	.917	0.025	.976
SS × ES	0.061	.809	2.182	.162
Electrodes × IR	0.937	.527	1.107	.349
Electrodes × ES	4.235	.013	2.577	.046
Electrodes × SS	0.928	.430	1.425	.194
ES × IR × SS	3.248	.054	1.100	.347
Electrodes × IR × ES	1.040	.415	2.454	.002
Electrodes × SS × IR	1.150	.311	0.397	.982
Electrodes × SS × ES	0.968	.414	1.002	.439
Electrodes × SS × IR × ES	2.484	.002	1.150	.311

Notes: SS refers to Stimulation Sites; ES refers to External Stimuli; IR refers to Internal Representations; Electrodes × SS × IR × ES refers to the four-factors interaction among Electrode, Stimulation Sites External Stimuli, and internal Representations. Same rules apply for other abbreviation.

For the latencies, the three-factor interaction among Electrodes, ES and IR was significant, ($F(16, 224) = 2.454$, $p = .002$). Further analysis suggested that in E_H condition, the peaks of P3 appeared significantly earlier when engaging attention with an I_L image (Mean =333.40 ms at Fz and 332.30 ms at F4) than that with an I_H image (Man = 340.00 ms at Fz and 341.00 ms at F4, *ps* < .050). By contrast, in the E_L condition, the peaks of P3 appeared significantly later when engaging attention with an I_L image (Mean =349.37 ms, 355.00 ms, 354.60 ms, and 356.17 ms at Fz, F4, FC4, and C4, respectively) than that with an I_H image (Mean =341.00 ms, 341.96 ms, 341.400 ms, or 345.70 ms, at Fz, F4, FC4, and C4, respectively, *ps* < .050). The

two-factor interaction effect of the ES factor and the Electrodes factor was found significant ($F(8, 112) = 2.577$, $p = .046$); peaks of P3 appeared significantly earlier in the E_H condition than those in the E_L condition at most of the nine electrodes, particularly, the largest difference between the E_H condition (Mean=336.44 ms) and E_L condition (Mean=344.21 ms) was found at Electrode F4 ($p < .001$). The main effect of SS was significant, $F(1,14) = 243.672$, $p < .001$, the peaks of P3 appeared significantly earlier at the S_P (Mean = 335.94 ms) than that the S_{NP} (Mean = 343.88 ms), Other main and interaction effects were not significant. No other significant main effects or interaction effects were found for the latencies of the P3 component.

4.2.8 Results of Correlations

4.2.8.1 Correlations between changes in the NRS score and the ERP amplitude

Among the eight E–I orienting attention conditions, correlations between the change in the N1 amplitude (ΔN1) and change in the NRS score (ΔNRS) were only significant in the I_H condition for an E_L stimulus located at the S_{NP} site ($S_{NP}/E_L/I_H$). These correlations were found to be moderate and negative at the electrode Fz (r = -.563, $p = .029$), FCz (r = - .652, $p = .008$) and C3(r = - .547, $p = .035$). The ΔNRS in the $S_{NP}/E_L/I_H$ condition were calculated by scores for the $S_{NP}/E_L/I_H$ condition minus that in the control condition (S_{NP}/E_L/control), i.e., $\Delta S_{NP}/E_L/I_H = S_{NP}/E_L/I_H - S_{NP}/E_L$/control. Similar formulas were applied for the calculations of changes in NRS score and ERP amplitudes in this thesis study.

Among the eight E–I orienting attention conditions, correlations between the changes in the P2 (ΔP2) amplitudes and the ΔNRS were only significant in the I_H condition for an E_H stimulus located at the S_{NP} site ($S_{NP}/E_H/I_H$). These correlations were found to be moderate and positive at the electrode Fz (r = .623, *p* =.013), F3 (r = .541, *p* =.037), FCz (r = .591, *p* =.020) and Cz (r = .613, *p* =.015).

Among the eight E–I orienting attention conditions, the correlations between the changes in P3 (ΔP3) amplitudes and ΔNRS were only significant in the I_L condition for an E_L stimulus located at the S_P site ($S_P/E_L/I_L$). This correlations was found to be moderate and positive at the electrode FC4 (r = .598, *p* = .018).

4.2.8.2 Correlations between the severity scores and changes in the ERP amplitudes

For the CLBP patients, among the eight E–I orienting attention conditions, correlations between the ΔN1 and the severity scores of the patients' CLBP they were currently experienced during the interview were only significant in the I_H condition for an E_H stimulus located at the S_P site ($S_P/E_H/I_H$). These correlations were found to be moderate and negative at the electrode FC4 (r = - .561, *p* = .030).

Among the eight E–I orienting attention conditions, correlations between the ΔP2 and the severity scores were not only significant in the I_H condition for an E_L stimulus located at the S_P site ($S_P/E_L/I_L$), but also in the I_L condition for an E_L stimulus located at the S_P site ($S_P/E_L/I_H$). These correlations were found to be moderate and positive at the electrodes Fz (r = .590, *p* = .021), FCz (r = .594, *p* = .020), FC3 (r = .538, *p* = .039), C4 (r = .515, *p* = .049) and Cz (r = .619, *p* = .014) in the $S_P/E_L/I_L$ condition.

Similarly, these correlations were found to be moderate and positive at the electrodes F4 (r = .604, p = .017), FCz (r = .563, p = .029), FC3 (r = .627, p = .012), FC4 (r = .612, p = .015) and C4 (r = .549, p = .034) in the $S_P/E_L/I_H$ condition.

Among the eight E–I orienting attention conditions, correlations between the ΔP3 and the severity scores were not only significant in the I_L condition for an E_L stimulus located at the S_P site ($S_P/E_L/I_L$), but also in the I_H condition for an E_L stimulus located at the S_P site ($S_P/E_L/I_H$). These correlations were found to be moderate and positive at the electrodes FCz (r = .557, p = .031) in the $S_P/E_L/I_L$ condition. Similarly, these correlations were found to be moderate and positive at the electrodes Fz (r = .583, p = .022) in the $S_P/E_L/I_H$ condition.

Table 4. 18 Correlations Between Proportional Scores in Stroop Test and Changes in ERP Amplitudes Among Patients With Chronic Low Back Pain in Study Two (n = 15) s

	Non-painful Site				Painful Site			
	E_L		E_H		E_L		E_H	
	I_L	I_H	I_L	I_H	I_L	I_H	I_L	I_H
ΔN1	CZ：-.536	CZ：-.516*	\	\	\	F4：-.532* FZ：-.522* FC4：-.598* C4：-.685** CZ：-.611**	FCZ：-.521* C4：-.652** CZ：-.705**	FC4：-.522*
ΔP3	C4：-.530*	FCz：-.519* Cz：-.549*	Cz：-.643**	F4：-.553* FC4：-.519* Cz：-.563*	F4：-.554* Fz：-.572*	\	\	F4：-.663** FC4：-.558*

Note: CN = Color Naming; INC = Incongruent color naming. (ICN-CN)/CN = proportional scores, which were computed by dividing the difference reaction time between INC and CN by the total time of CN.ΔN1 = Changes in N1 amplitudes,ΔP1 Changes in N1 amplitudes,,ΔP3 = Changes in P3 amplitudes, which were computed by subtracting the mean amplitudes of the control condition from the experimental condition.

4.2.8.3 Correlations between the proportional scores of Stroop Test and changes in the ERP component

Table 4.18 shows significant correlations between the proportional scores of (ICN – CN) / CN in the Stroop Test and the changes in ERP component amplitudes among the CLBP patients. Among the eight E–I orienting attention conditions, the proportional scores were significantly and negatively correlated with the ΔN1 for an E_L stimulus at the S_{NP} site in both the I_L condition and the I_H condition (i.e., $S_{NP}/E_L/I_L$ and $S_{NP}/E_L/I_H$, respectively), and for an E_H stimulus at the S_P site in both the I_L condition and the I_H condition (i.e., $S_P/E_H/I_L$ and $S_P/E_H/I_H$, respectively) and for an E_L stimulus at the S_P site in the I_H condition ($S_P/E_L/I_H$) at the electrodes Fz, F4, FCz, FCz, C4, and Cz (the r-values was from -.516 to -.705, *p*s < .050, see Table 4.18).

The proportional scores were significantly and positively correlated with the ΔP3 in all four E–I orienting attention conditions at the S_{NP} site (i.e., $S_{NP}/E_L/I_L$, $S_{NP}/E_L/I_H$, $S_{NP}/E_H/I_L$, $S_{NP}/E_H/I_H$) and also for an E_H stimulus in I_H condition or for an E_L stimulus in the I_L condition at the S_P site (i.e., $S_P/E_H/I_H$ and $S_P/E_L/I_L$) at the electrodes Fz, F4, FCz, FCz, C4, and Cz (the r-values was from -.519 to -.663, *p*s < .050, see Table 4.18).

4.2.8.4 Correlations between Pain Self-efficacy Scale and changes in the ERP amplitudes

For the CLBP patients, among the eight E–I orienting attention conditions, correlations between the ΔN1 amplitudes and the Pain Self-efficacy Scale (PSEQ) scores of CLBP patients were only significant in the I_L condition for an E_N stimulus

located at the S_{NP} site ($S_{NP}/E_H/I_L$). The PSEQ scores were moderately and negatively correlated with the ΔN1 in the $S_{NP}/E_H/I_L$ condition at the electrodes F4 (r = .536, *p* = .039), Fz (r = .664, *p* = .007), FCz (r = .576, *p* =. 025), C3 (r = .559, *p* =.018), C4 (r = .581, *p* = .023) and Cz (r = .533, *p* = .041).

Among the eight E–I orienting attention conditions, correlations between the ΔP2 and the PSEQ scores were not only significant in the I_L condition for an E_L stimulus located at the S_P site ($S_P/E_H/I_L$), but also in the I_H condition for an E_L stimulus located at the S_P site($S_P/E_H/I_H$). The PSEQ scores were moderately and positively correlated not only with the ΔP2 in the $S_P/E_H/I_L$ condition at the electrodes F4 (r = .556, *p* = .031), Fz (r = .609, *p* = .016), FCz (r = .524, *p* =. 045), FC4(r = .628, *p* =. 005), C3 (r = .524, *p* =.045). Similar correlations were found in the $S_P/E_H/I_H$ condition at the electrodes FCz (r = .552, *p* = .046) and FC4 (r = .561, *p* =. 029).

Among the eight E–I orienting attention conditions, the correlations between the ΔP3 amplitudes and the PSEQ scores were significant in I_H condition for an E_L stimulus located at the S_{NP} site ($S_{NP}/E_L/I_H$), in I_L condition for an E_L stimulus located at the S_{NPP} site ($S_{NP}/E_L/I_L$), and in I_H condition, for an E_H stimulus located at the S_{NP} site ($S_{NP}/ E_H/I_H$). The PSEQ scores were moderately and positively correlated with 1) the ΔP3 in the $S_{NP}/E_L/I_H$ condition at the electrodes F3 (r = -0.532, *p* = .041) and FC4(r = -0.549, *p* = .034); 2) the ΔP3 in the $S_{NP}/E_L/I_L$ condition at the electrodes F3, (r = - .552, *p* = .033) and FC4 (r = - .536, *p* = .039); and 3) the ΔP3 in the $S_{NP}/E_H/I_H$ condition at the electrodes F3(r = -0.576, *p* = .025) and C4 (r = -0.557, *p* = .031).

4.3 Results of The Comparison Between The Healthy Individuals and CLBP Patients

4.3.1 Differences in the demographics data between the healthy individuals and CLBP patients

Table 4.19 shows the different demographic distribution between the healthy individuals and CLBP patients. The data suggested that almost half of the healthy participants in Study One were females, while the majority (80.0%) of the patient participants in Study Two was females. In both studies, more than half of the participants were married (54.5 % in Study One, 60.0 % in Study Two). In terms of the educational level, the majority of the healthy participants in the Study One had a bachelor's degree (54.4%) or above (13.6%), while slightly more than half of the patient participants in Study Two had a bachelor's degree (33.2%) or above (20.0%). Additionally, 63.6 % of the participants healthy participants in the Study One were currently working (the percentages for having a part-time and full-time job were 27.3% and 22.7%), while most of the patient participants in Study Two had a full-time job (60.0 %) and 20.0% of the patient participants had a part-time job.

Table 4.19 The Comparison Between The Healthy Individuals and The Patients With Chronic Low Back Pain in The Demographics Data

	Healthy individuals		CLBP patients	
	Number	**Percentage**	**Number**	**Percentage**
Gender				
Male	9	40.9	3	20.0
Female	13	59.1	12	80.0
Marital Status				
Single	9	40.9	4	26.7
Married	12	54.5	9	60.0
Divorced	0	0	2	13.3
Widowed	1	4.5	0	0
Educational Level				
Middle School	1	4.5	3	20.0
High School	6	27.3	4	26.7
Undergraduate	12	54.5	5	33.3
Postgraduate	3	13.6	3	20.0
Employment Status				
Unemployed	1	4.5	3	20.0
Part-time	6	27.3	3	20.0
Full-time	9	40.9	9	60.0
Student	5	22.7	0	0
Housewife	1	4.5	0	0

Table 4.20The comparison Between The Healthy Individuals and The Patients With Chronic Low Back Pain in Stroop Test

Subtest	Healthy		Patient		*t*	Sig
	Mean	SD	Mean	SD		
Word Reading Sub-test						
Total Response Time (second)	45.2	7.5	56.9	12.5	-3.397	0.044
No. of Error	0.2	0.5	0.5	0.7	-1.208	0.075
No. of Self-corrected Error	0.7	0.9	0.7	1.2	-0.254	0.419
Color Naming Sub-test						
Total Response Time (second)	63.9	14.7	76.0	23.8	-1.707	0.325
No. of Error	0.5	0.9	1.7	3.1	-1.367	0.009
No. of Self-corrected Error	1.0	1.3	1.5	2.5	-0.711	0.436
Incongruent Color Naming Sub-test						
Total Response Time (second)	105.9	26.0	132.6	39.7	-2.246	0.051
No. of Error	1.0	1.6	1.3	2.6	-0.238	0.534
No. of Self-corrected Error	2.0	2.7	2.1	2.8	-0.029	0.671
Difference Score (second)						
ICN – WR	59.1	22.4	75.7	30.7	-1.708	0.221
ICN – CN	42.0	18.6	56.6	27.0	-1.793	0.273
CN – WR	18.4	11.5	19.1	16.2	-0.017	0.392
Proportional Score (second)						
(ICN – WR) / WR	1.3	0.4	1.3	0.4	1.164	0.944
(ICN – CN) / CN	0.7	0.3	0.8	0.3	-0.008	0.975
(CN – WR) / WR	0.4	0.2	0.3	0.2	-0.86	0.505

Notes: SD = Standard Deviation; CN = Color Naming; INC = Incongruent color naming. Different scores are computed by subtracting the reaction time score of the earlier from the later test. Proportional scores are computed by dividing the difference scores by the total time of the earlier test.

4.3.2 The differences in the performances in the Stroop Test between the healthy individuals and CLBP patients

Table 4.20 shows the results of the differences in terms of the performances in the Stroop Test between the healthy individuals and CLBP patients. For the WR Subtest, the mean of the total response time of CLBP patients (Mean = 56.9 s) was significantly longer than that of the healthy individuals (Mean = 45.2 s) with the *p*-value of.044; while the difference between patients and healthy individuals in terms of the number of error and self-corrected error was marginally significant or not significant (*p*= .075 and .419, respectively). For the CN Subtest, the mean number of error of CLBP patients (Mean = 1.7) was significantly more than that of the healthy individuals (Mean = 0.5) with the *p*-value of.009; while the difference between patients and healthy individuals in the total response time and the number of self-corrected error were not significant (*ps*> .050). For the ICN subtest, the mean of the total response time of CLBP patients (Mean =132.6 s) was marginally longer than that of the healthy individuals (Mean =105.9 s) with the *p*-value of .051; whilst the difference between patients and healthy individuals in the number of error and self-corrected error were not significant (*ps*> .050). The difference between patients and healthy individuals in the difference scores and the proportional scores was not significant.

Table 4.21 The Comparison Between The Healthy Individuals and The Patients With Chronic Low Back Pain in Voltages and Pain Intensities During Calibration

			MDS	Sub-nociceptive		JPS	Nociceptive						VPS
				SN_L	SN_H		L1	L2	L3	L4	L5	L6	
Voltages	Healthy	Mean	3.32	3.4	16.1	19.11	20.7	24.2	28	32.6	36.7	41	41.27
		SD	5.24	5.3	6.1	6.38	7.1	7.6	8.6	9.6	10.9	12.3	12.6
	Patients	Mean	3.9	4	9.2	18.1	19.3	21.4	24.8	28.3	31.4	34.9	34.9
		SD	5.7	5.8	5.1	5.5	5.6	4.6	6.5	7.4	8.1	9.3	9.3
Pain Intensities	Healthy	Mean					1.6	2.7	3.6	4.7	5.3	5.7	
		SD					0.7	0.8	1	0.7	0.6	0.8	
	Patients	Mean					2	2.3	3.3	4.3	5.1	5.3	32.6
		SD					1	1	1	1	0.9	0.9	10.8

Note: MDS refers to the minimum detectable sensation, the weakest stimulation intensity level with which participant detected a tactile sensation; JPS refers to the just painful sensation which participant perceived stimulation as painful and rated "1" on the NRS; VPS refers to very painful sensation, the intensity with which participant perceived a stimulation as very painful and rated "7" on the NRS. SN_L refers to the External of the non-painful sub-nociceptive stimulus is low, SN_H refers to the External of the non-painful sub-nociceptive sensation is relative high but still under the just painful sensation.L1-L6 refers to the 6 levels of painful nociceptive stimulus, increasing number means that the External of the electrical pulse increases.

Table 4.22 Results of T-Test for The Comparison Between The Healthy Individuals and The Patients With Chronic Low Back Pain in Voltages and Pain Intensities during Calibration

		MDS	Sub-nociceptive		JPS	Nociceptive						VPS
			SN_L	SN_H		L1	L2	L3	L4	L5	L6	
Voltages	***t***	0.339	0.445	2.769	-0.075	-0.899	-1.482	-1.366	-1.580	-1.701	-1.921	-1.440
	Sig.	0.829	0.648	0.770	0.323	0.038	0.042	0.151	0.245	0.240	0.221	0.191
Pain Intensities	***t***					1.122	-1.317	-1.087	-1.868	-0.960	-1.639	
	Sig.					0.156	0.298	0.981	0.449	0.299	0.324	

Note: MDS refers to the minimum detectable sensation, the weakest stimulation intensity level with which participant detected a tactile sensation; JPS refers to the just painful sensation which participant perceived stimulation as painful and rated "1" on the NRS; VPS refers to very painful sensation, the intensity with which participant perceived a stimulation as very painful and rated "7" on the NRS. SN_L refers to the External of the non-painful sub-nociceptive stimulus is low, SN_H refers to the External of the non-painful sub-nociceptive sensation is relative high but still under the just painful sensation.L1-L6 refers to the 6 levels of painful nociceptive stimulus, increasing number means that the External of the electrical pulse increases.

4.3.3 The differences in the Voltages and the Pain Intensities during the Calibration between the healthy individuals and CLBP patients

Table 4.21 shows the difference in the Voltages and the Pain Intensities for the different levels of the electrical pulse during the calibration between the healthy individuals and CLBP patients. The t-test results (see Table 4.22) revealed that the voltages at the lowest two levels of the nociceptive stimuli (20.7 mA for L1 and 24.7 mA for L2) were only significantly lower in CLBP patients than the healthy individuals (p= .038 and .042, respectively). No other significant difference between these two groups of participants was found.

Table 4.23 The Comparison Between The Healthy Individuals and The Patients With Chronic Low Back Pain in NRS scores (Mean and Standard Deviation)

		Healthy		Patients	
		Mean	**SD**	**Mean**	**SD**
E_H	**Control**	5.3	0.2	4.6	1.0
	I_H	5.0	0.2	4.1	1.1
	I_L	5.3	0.2	4.4	1.3
E_L	**Control**	2.9	0.2	3.0	1.1
	I_H	2.7	0.2	2.8	0.9
	I_L	3.0	0.2	2.5	0.8

Note: E_L refers to the low salient external nociceptive condition; E_H refers to the high salient external nociceptive condition; I_L refers to recall an internal low salient sub-nociceptive image. I_H refers to recall a relatively internal high salient sub-nociceptive image. NRS scores are ranging from 0 to11(from non-painful to extremely painful).

Table 4.24 Results of ANOVA for The Comparison Between The Healthy Individuals and The Patients With Chronic Low Back Pain in NRS Scores

	F	*Sig.*
ES	302.937	0.000
IR	5.080	0.009
Group	2.865	0.100
ES * IR	0.990	0.366
ES * Group	9.951	0.003
IR * Group	2.370	0.102
ES * IR * Group	1.282	0.284

Notes: ES refers to External Stimuli; IR refers to Internal Representations; ES × IR refers to the two-factors interaction between External Stimuli and Internal Representations; Group × ES × IR refers the three-factors interaction among Group, External Stimuli, and internal Representations. Same rules apply for other abbreviation.

4.3.4 The differences on NRS score between the healthy individuals and CLBP patients

Table 4.23 shows the Mean and SD of the healthy individuals and CLBP patients in NRS scores, which were given at the end of each trial to indicate the intensity of the participants' pain experience for the external nociceptive electrical stimulation (S1) in both Studies. Results from the ES (E_L vs. E_H) × IR (control, I_L vs. I_H) × Group (Healthy vs. Patients) three-way repeated measures ANOVA (see Table 4.24) on the NRS Scores revealed that only the two-factor interaction between the ES factor and the group factor was significant ($F(2,64) = 9.951$, $p = .003$). Further analysis indicated that in the E_H condition, the NRS scores of the patients (Mean = 5.2 (out of 10)) were significantly higher than that of the healthy individuals (Mean = 4.3(out of 10)) with

the *p*-value of .013; whilst no significant difference was found between the healthy individuals and the patients in the E_L condition.

4.3.5 The differences in the ERP components between the healthy individuals and CLBP patients

The differences between the healthy individuals and CLBP patients on the mean amplitudes and the latencies of N1, P2, and P3 component during the pain perception process were shown in Tables 4.25- 4.27. The mean amplitudes and the latencies of each ERP components were from those at the non-painful site (ankle) during the control tasks in each of the two ERP studies. The control tasks in both Study One and Study Two required the participants to maintain the image of a fleeting (50ms) nociceptive sensation in their working memory.

Three-way repeated measures ANOVA models (2 Group × 2 ES × 9 Electrodes) on the mean amplitudes and the latencies for each ERP components separately were conducted to test the neural processes underlying the pain perception. The group factor included one healthy group who were the healthy participants from Study One and one patient group who were the CLBP patients from the Study Two. The ES factor included an E_H condition and an E_L condition.The Electrode factor included nine electrodes—three electrodes in the left hemisphere (F3, FC3, C3), three in the midline (Fz, FCz, Cz), and three in the right hemisphere (F4, FC4, C4). The time windows for the N1, P2, and P3 was 130–150 ms, 200–260 ms and 320–380 ms

respectively. The significance level was .050, and each pair-wise contrast within the significant interaction effects was corrected by Bonferroni correction.

4.3.5.1 The differences in the N1 components

Table 4.25 shows the difference between the healthy individuals and the CLBP patients in the mean amplitudes and the latencies of N1 component during perception. Results of ANOVA (see Table 4.28) on the mean amplitudes revealed that the main effects of the ES factor and the Electrode factor were significant (*ps* = .001). For the ES factor, the mean amplitudes were extremely significantly more negative-going in the E_H condition (Mean = -4.9 μV) than those in E_L condition (Mean = -1.7 μV). For the Electrode factor, the most negative-going N1 was recorded at FC4 (Mean = -4.9 μV) compared with those at other eight electrodes (*P*s< .050). However, the main effect of group and any interaction effects were not significant.

Results of ANOVA (see Table 4.28) on the latencies were similar to that on the mean amplitudes. To be more specific, only the main effect of the Electrode factor was found significant (*p* = .001), the peak of N1 first appeared at Cz (Mean = 134.9 ms) among all other eight electrodes, *p*s <.050. No other main and interaction effects were found significant.

Table 4.25 The Mean and Standard Deviation for The Amplitudes and Latency of the N1 components During the Control Task at Non-painful Site Among The Healthy Individuals and The Patients With Chronic Low Back Pain

			Amplitudes				Latency			
			E_H		E_L		E_H		E_L	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD
Left	**F3**	**Patients**	-3.7	4.6	0.2	5.0	137.9	7.1	140.8	8.0
		Healthy	-4.0	5.5	-2.8	4.8	143.4	6.6	144.9	4.3
	FC3	**Patients**	-4.7	5.2	-1.3	3.5	138.4	7.2	138.5	8.0
		Healthy	-5.1	5.2	-3.0	4.4	140.5	6.8	142.3	5.7
	C3	**Patients**	-4.5	5.0	-0.7	3.2	138.4	7.8	138.0	8.3
		Healthy	-4.6	5.2	-2.9	4.1	138.9	6.6	139.6	6.5
Middle	**Fz**	**Patients**	-4.6	6.7	0.2	3.9	134.7	6.8	135.7	7.3
		Healthy	-5.6	7.0	-2.4	4.8	137.5	6.5	137.8	6.8
	FCz	**Patients**	-4.1	6.0	-0.9	3.6	138.6	7.9	138.9	8.2
		Healthy	-5.1	6.2	-3.0	5.3	143.1	5.9	143.7	4.9
	Cz	**Patients**	-1.2	8.8	3.1	5.0	133.9	6.8	135.1	7.1
		Healthy	-4.1	7.1	-0.7	5.5	135.0	5.3	135.5	6.5
Right	**F4**	**Patients**	-6.0	5.8	-2.1	4.6	139.0	7.4	140.7	8.2
		Healthy	-5.4	6.0	-3.4	5.3	143.6	5.1	144.5	5.3
	FC4	**Patients**	-6.6	6.6	-2.3	5.0	137.1	6.3	138.4	7.2
		Healthy	-6.5	5.5	-4.1	4.5	140.3	6.0	141.8	5.4
	C4	**Patients**	-6.1	6.1	-2.1	5.2	138.0	7.4	138.1	6.8
		Healthy	-5.4	4.6	-3.5	3.6	138.6	6.4	140.0	5.4

Note: E_L refers to the low salient external nociceptive condition; E_H refers to the high salient external nociceptive condition; Left refers to the electrodes distributed in the left hemisphere; Middle refers to the electrodes distributed in midline; Right refers to the electrodes distributed in the right hemisphere.

Table 4.26 The Mean and Standard Deviation for The Amplitudes and Latency of the P2 components During the Control Task at Non-painful Site Among The Healthy Individuals and The Patients With Chronic Low Back Pain

			Amplitudes				Latency			
			E_H		E_L		E_H		E_L	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD
Left	**F3**	**Patients**	15.1	6.6	13.9	6.5	217.3	17.2	214.9	14.8
		Healthy	9.1	7.9	11.2	10.0	226.0	21.6	228.6	15.3
	FC3	**Patients**	16.7	6.6	16.1	7.5	216.5	16.7	221.9	15.7
		Healthy	10.5	6.9	11.4	6.3	231.1	16.3	224.6	15.1
	C3	**Patients**	18.7	8.3	18.0	8.7	214.5	17.1	220.3	16.5
		Healthy	12.4	7.3	13.1	7.6	231.0	18.6	224.2	15.7
Middle	**Fz**	**Patients**	26.3	12.0	25.1	12.2	229.0	19.5	224.1	18.8
		Healthy	18.9	9.7	20.2	10.4	236.0	16.1	229.2	15.1
	FCz	**Patients**	19.6	7.8	17.5	7.8	230.9	18.2	225.5	19.4
		Healthy	13.8	8.4	13.9	8.0	236.2	16.3	230.0	14.9
	Cz	**Patients**	28.6	12.8	27.7	13.5	223.0	17.8	217.5	16.9
		Healthy	21.0	9.8	22.7	12.1	240.1	18.4	228.8	19.5
Right	**F4**	**Patients**	16.3	7.0	13.9	5.9	228.5	20.8	218.6	17.6
		Healthy	9.2	7.4	10.5	9.6	235.5	17.7	228.8	17.1
	FC4	**Patients**	18.9	9.0	16.9	8.1	225.9	20.7	222.3	19.2
		Healthy	12.2	7.5	13.3	9.6	234.9	17.8	227.7	18.6
	C4	**Patients**	20.1	10.0	17.9	9.8	219.1	18.6	218.3	16.9
		Healthy	13.0	8.6	14.1	11.2	241.7	19.0	229.9	20.3

Note: E_L refers to the low salient external nociceptive condition; E_H refers to the high salient external nociceptive condition; Left refers to the electrodes distributed in the left hemisphere; Middle refers to the electrodes distributed in midline; Right refers to the electrodes distributed in the right hemisphere.

Table 4.27 The Mean and Standard Deviation for The Amplitudes and Latency of the P3 components During the Control Task at Non-painful Site Among The Healthy Individuals and The Patients With Chronic Low Back Pain

			Amplitudes				Latency			
			E_H		E_L		E_H		E_L	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD
Left	**F3**	**Patients**	3.9	6.2	5.8	6.3	338.5	19.6	345.1	22.3
		Healthy	8.8	6.7	7.5	4.3	346.9	23.7	347.9	21.4
	FC3	**Patients**	5.7	4.7	6.6	4.2	339.9	21.6	344.9	19.2
		Healthy	10.7	4.9	9.0	4.0	336.4	19.6	343.1	21.3
	C3	**Patients**	7.6	4.9	8.0	5.7	343.8	19.8	349.6	19.4
		Healthy	12.8	7.9	10.7	5.9	331.9	17.7	336.4	21.0
Middle	**Fz**	**Patients**	10.7	5.4	11.3	6.8	337.5	21.9	344.8	18.5
		Healthy	16.2	8.3	13.8	5.6	332.6	18.7	337.4	20.0
	FCz	**Patients**	7.3	5.6	7.7	5.3	340.7	23.0	344.8	19.4
		Healthy	11.6	6.1	9.1	3.8	344.4	21.8	345.7	20.2
	Cz	**Patients**	12.9	6.3	12.4	7.5	340.0	21.1	345.3	20.6
		Healthy	18.0	8.7	15.6	7.0	330.8	19.0	330.6	17.1
Right	**F4**	**Patients**	3.6	5.6	4.4	5.7	339.3	21.1	348.0	19.7
		Healthy	9.5	6.9	6.7	4.1	340.8	21.6	343.2	20.9
	FC4	**Patients**	6.3	5.3	6.8	5.9	337.9	20.9	350.9	20.4
		Healthy	11.6	7.9	9.1	4.7	332.0	18.8	338.1	19.2
	C4	**Patients**	7.9	6.0	7.9	7.0	341.0	21.3	354.2	19.9
		Healthy	13.2	8.7	10.6	6.3	332.4	19.4	333.0	17.2

Note: E_L refers to the low salient external nociceptive condition; E_H refers to the high salient external nociceptive condition; Left refers to the electrodes distributed in the left hemisphere; Middle refers to the electrodes distributed in midline; Right refers to the electrodes distributed in the right hemisphere.

Table 4.28 Results of ANOVA for The Amplitudes and Latency of the N1 components During the Control Task at Non-painful Site Among The Healthy Individuals and The Patients With Chronic Low Back Pain

	Mean amplitudes		Latencies	
	F	Sig.	F	Sig.
Electrodes	9.599	0.001	17.945	0.001
Group	0.797	0.379	2.266	0.142
ES	19.137	0.001	2.588	0.118
Electrodes × Group	1.378	0.206	1.911	0.059
Electrodes × ES	2.377	0.083	1.088	0.367
Group × ES	1.468	0.235	0.015	0.903
Electrodes × Group × ES	0.634	0.749	0.865	0.546

Notes: ES refers to External Stimuli; Group × ES refers to the two-factors interaction between Group and External Stimuli; Electrode × Group × ES refers the three-factors interaction among Electrode, Group, and External Stimuli,. Same rules apply for other abbreviation.

4.3.5.2 The differences in the P2 components

Table 4.26 shows the difference between the healthy individuals and the CLBP patients in the mean and the latencies of P2 component during perception. Results of ANOVA (see Table 4.29) on the mean amplitudes revealed that the main effects of the group factor and the Electrode factor were significant ($p \leq .050$ and .001, respectively). For the Group factor, an attenuated P2 (significantly less positive-going) was found among the CLBP patients (Mean = 11.5 μV) compared with the P2 among the healthy individuals (Mean=16.9 μV). For the Electrode factor, the most positive-going P2 was recorded at Cz (22.2 μV) compared with that at other eight electrodes (ps< .050). However, the other main effect and any interaction effects were not significant.

Same with results of ANOVA on the mean amplitudes., results of ANOVA (see Table 4.29) on the latencies revealed that only the main effect of the Group factor and

the Electrode factor were found significant (p = .017 and .006, respectively). For the Group factor, the peak of P2 appeared significantly earlier among the CLBP patients (Mean = 221.6 ms) than healthy individuals (Mean=231.4 ms). For the Electrodes factor, the peak of P2 first appeared at F3 (Mean = 221.71 ms) among all other eight electrodes (ps< .050). No other main and interaction effects were found significant.

Table 4.29 Results of ANOVA for The Amplitudes and Latency of the P2 components During the Control Task at Non-painful Site Among The Healthy Individuals and The Patients With Chronic Low Back Pain

	Mean amplitudes		Latencies	
	F	***Sig.***	***F***	***Sig.***
Electrodes	41.654	0.001	3.979	0.006
Group	4.162	0.050	6.395	0.017
ES	0.002	0.962	2.765	0.106
Electrodes × Group	0.461	0.883	1.548	0.141
Electrodes × ES	1.185	0.308	1.652	0.158
Group × ES	0.083	0.245	0.637	0.431
Electrodes × Group × ES	0.784	0.617	1.531	0.147

Notes: ES refers to External Stimuli; Group × ES refers to the two-factors interaction between Group and External Stimuli; Electrode × Group × ES refers the three-factors interaction among Electrode, Group, and External Stimuli,. Same rules apply for other abbreviation.

4.3.5.3 The differences in the P3 components

Table 4.27 shows the difference between the healthy individuals and the CLBP patients in the mean and the latencies of P3 component during the pain perception stage. Results of ANOVA (see Table 4.30) on the mean amplitudes revealed that the main effects of the group factor and the Electrode factor were significant ($p\leq$ .035 and .001, respectively). For the Group effect, an attenuated P3 (significantly less

positive-going) was found among CLBP patients (Mean = 7.6 μV) compared with the P2 among the healthy individuals (Mean =11.4 μV). For the Electrode factor, the most positive-going P3 was recorded at CPz (14.71μV), compared with that at other eight electrodes (*p*s< .050). Besides, the two-factor interaction effect of Group factor and ES factor was marginally significant (*p* = .079). Further analysis revealed that in the E_H condition, the attenuated P3 was found among the CLBP patients (Mean = 7.3μV) compared with the P3 among the healthy individuals (Mean =12.5 μV); while the difference between two groups in EL condition was not significant. The other main effect and any interaction effects were not significant. Results of ANOVA (see Table 4.30) on the latencies revealed that the two-factor interaction effect of the Group factor and Electrodes factor was significant *(p* ≤ .001). Further analysis revealed that peaks of P3 appeared significantly later among the CLBP patients than the healthy individuals at Electrodes C3, Cz, and C4 (ps <.050); but no significant difference was found between the two groups at other electrodes. Besides, the main effects of the ES factor and the Electrode factor were found significant (*p*≤ .023 and .027, respectively). For the ES factor, the peak of P3 appeared significantly later in the E_H condition (Mean = 338.2 ms) than in E_L condition (Mean = 343.5 ms). For the Electrodes factor, the peak of P3 first appeared at F3 Cz (Mean = 336.7 ms) among all other eight electrodes (*p*s <.050). No other main and interaction effects were found significant.

Table 4.30 Results of ANOVA for The Amplitudes and Latency of the P3 components During the Control Task at Non-painful Site Among The Healthy Individuals and The Patients With Chronic Low Back Pain

	Mean amplitudes		Latencies	
	F	***Sig.***	***F***	***Sig.***
Electrodes	33.186	0.001	2.994	0.027
Group	4.854	0.035	1.050	0.313
ES	1.182	0.285	5.699	0.023
Electrodes× Group	0.192	0.992	5.526	0.001
Electrodes × ES	1.701	0.161	0.880	0.494
Group × ES	3.287	0.079	1.083	0.306
Electrodes × Group × ES	0.333	0.953	0.761	0.637

Notes: ES refers to External Stimuli; Group × ES refers to the two-factors interaction between Group and External Stimuli; Electrode × Group × ES refers the three-factors interaction among Electrode, Group, and External Stimuli,. Same rules apply for other abbreviation.

4.3.6The differences on E–I orienting attention processes between the healthy individuals and the CLBP patients

The differences between the healthy individuals and the CLBP patients in the mean amplitudes and the latencies of N1, P2, and P3 component during the E–I orienting attention stage was shown in Appendix XIV. These mean amplitudes and latencies of each ERP components were from those at non-painful site during the experimental tasks in each of the two ERP studies. The experimental tasks in the experimental design in both Study One and Study Two required the participants to disengage their attention away from a relatively strong nociceptive sensation from the external world, shift and re-engage the attention with a weak, self-generated and learned sub-nociceptive image. According to these tables, relatively attenuated N1, P2,

and P3 were showed among the CLBP patients when compared to the healthy individuals.

Chapter V

DISCUSSION

In this chapter, the findings in regard to the neural mechanism of E–I orienting attention among healthy individuals and CLBP patients are first discussed, followed by a general discussion of the findings from the comparisons between the two groups of participants. At the end of this chapter, the contributions of this thesis to the literature and the implications for clinical practice are discussed.

5.1 The neural mechanism of E–I orienting attention

5.1.1 Disengaging attention from external stimuli

Among healthy individuals, similar to the previous studies, the attention disengagement between two external stimuli as investigated by Dowman (2007, 2011), and N1 amplitudes elicited by high-salience-level nociceptive stimuli (E_H) were more negative-going than those elicited by the low-salient ones (E_L) at the fronto-centrally distributed electrodes (e.g. FCz). This fronto-central N1 component was believed to reflect an early bottom-up process and to be stimulus-driven, i.e., highly salient nociceptive stimuli capture a higher level of attention compared with low-salient

stimuli (Dowman, 2004, 2007, 2011; Dowman et al., 2007). Additionally, this finding further endorses those revealed by Legrain et al. (2013) that the N1 component evoked by somatosensory stimuli is less negative-going when the orienting attention process involves visualization of a heavier load of visual images in the working memory. It is noteworthy that the salience levels of both external stimulus (ES) and internal representation (IR) conditions were manipulated in the studies reported in this thesis, different from previous studies (Dowman, 2004, 2007, 2011; Legrain et al., 2013). By doing so, a significant interaction between the ES and IR was found during the disengagement process (reflected by the N1 component). This significant E–I interactive effect showed that the disengagement process is modulated by high-salience external nociceptive stimuli. During the disengagement process, the participants needed to process the nociceptive stimulus from the external world (i.e., the pain generator in these studies) and internal representation from the internal world (i.e., the self-generated learned sub-nociceptive image in their mind) at the same time. In particular, processing the external nociceptive stimulus (called external processing) would have involved encoding and recognition of the nociceptive stimulus felt at the ankle, which predominantly was bottom-up in nature. In contrast, processing the internal representation (called internal processing) would have involved recalling and generating the sub-nociceptive images, which is top-down in nature. A larger incongruence between the external processing and internal processing was found in the E_H condition than that in the E_L condition. The larger incongruence could have

created larger mental conflicts, leading to a higher level of top-down control to resolve them (Egner, Jamieson, & Gruzelier, 2005; Kerns & Carter, 2004).

Similar to the first study on E–I orienting attention among healthy individuals, an enhanced N1 component elicited by an E_H nociceptive stimulus at frontal and central electrodes was also found in the second study on E–I orienting attention among CLBP patients. The frontal-central N1 component was claimed to be associated with the stimulus-driven bottom-up process of disengaging attention away from a nociceptive stimulus (Dowman, 2007, 2011). A more negative-going N1 component suggested that more mental resources were needed in order to disengage from the nociceptive stimuli, and to proceed to the next step (Egner et al., 2005; Kerns & Carter, 2004).

One of the critical purposes of the second study was to investigate the modulation effect of the patients' chronic pain experience on E–I orienting attention. To achieve this goal, the location where a nociceptive stimulus was placed was manipulated ("painful" site (S_P) vs. non-painful site (S_{NP})) in the second study. As expected, the N1 component was found to be significantly more negative-going in amplitude and shorter in latency in the S_P condition than in the S_{NP} condition in the second study. Among CLBP patients, in the S_P condition, the electrical stimulation was located at the lower back where they had been preoccupied by pain, while in the S_{NP} condition, the electrical stimulation was located at the ankle which was assumed to be free of pain. According to the Motivational Theory of pain (Damme et al., 2010), stimulating their painful site would motivate the patients to disengage from the painful source due to the previous pain experience in their daily life, compared with stimulating their

non-painful site. This might explain why a more negative-going N1 component was found in the S_P condition during the disengagement among the CLBP patients.

5.1.2 External-to-Internal Shifting

Among the healthy individuals, the interaction effect between the ES and IR was also found to be significant at the fronto-central electrodes for the P2 component. Interestingly, the modulation of the IR on the fronto-centrally distributed P2 component was only observed in the E_H condition but not in the E_L condition. The P2 component has been illustrated to reflect the shifting attention process involving somatosensory stimuli (Chan et al., 2012; Legrain et al., 2013). However, inconsistent findings were reported on both enhanced and attenuated P2 amplitude as a result of the modulation. The enhanced P2 amplitudes were found to be associated with unattended contrasted and attended somatosensory stimuli (Dowman, 2011). Chan et al. further added that the enhanced P2 component reflects the process of shifting attention from the nociceptive stimulus to a rapid self-generated sub-nociceptive image. The attenuated P2 amplitude was found to be associated with the process of shifting attention from a nociceptive stimulus to internally generated visual images of dots (Legrain et al., 2013). The difference in the task design between the study of Legrain et al. and that of Chan et al. (2012) is that the generation of sub-nociceptive images in the former study was anticipatory while that in the study of Chan et al. (2012) was not anticipatory. In the experimental task in Study One of this thesis, the

healthy individuals were given prior knowledge of the salience level of the sub-nociceptive images to be generated after perceiving an external stimulus. In contrast, the healthy individuals in the study of Chan et al. (2012) were required to generate a sub-nociceptive image at a salience level contingent upon that of the nociceptive stimulus that they perceived. In other words, Study One would have involved more top-down control than the study of Chan et al. (2012) when the sub-nociceptive images were generated. Such top-down processes are comparable to those in the study of Legrain et al. (2013) in which the participants were required to maintain the visual dot images in their working memory for generation and visualization after the shock of a nociceptive stimulus. The top-down processes underlying the process of shifting attention from a strong ES to a weak IR among healthy individuals is a plausible explanation for the attenuated P2 amplitude being associated with the significant E–I interactive effects obtained in this study.

One might notice that the amplitude of the P2 component was attenuated when the perception of an E_H stimulus was coupled with the generation of an I_L image among healthy individuals. This E–I interaction effect of the P2 component is similar to that in the N1 component and it is argued that this P2 effect could have been due to the carrying over of the significant N1 component effect which occurred prior to the shifting attention process. It is true that carry over effects are not uncommon as nearby event-related components can overlap each other (Luck & Kappenman, 2011). However, this proposition is excluded because our results showed that the most negative-going differences in amplitude of the N1 component were at F4 and FC4

when compared with those of the P2 component at Cz. It is therefore plausible that the P2 component which reflects the goal-directed top-down process of shifting attention to a sub-nociceptive image was likely to interact with the N1 component which reflects the stimulus-driven bottom-up process of disengaging attention away from the nociceptive stimulus. In fact, previous behavioral studies on visual perception have reported the interaction effect of the top-down process and the bottom-up process on attentional shift (Caparos & Linnell, 2010; Linnell & Caparos, 2011). For example, Linnell et al. (2011) manipulated both effects of perceptual load (high load vs. low load) of an external stimulus and the items maintained in the working memory (high load vs. low load) on the performance in a visual flanker task. The results showed that the increase in memory load (a top-down process) impeded the attention shifting process only when the perceptual load (a bottom-up process) was high. In contrast, the increase in the perceptual load impeded the attention shifting process only when the working memory load was low. The finding in this thesis further corroborates this interaction and provides evidence that such interactions occur during the shifting process (reflected by the P2 component) at around 200 to 260 ms after onset of the stimulus.

Similar to the findings from healthy individuals in the first study, a significant E–I interaction effect in the P2 amplitude was also found among CLBP patients in the second study. Differently, instead of being less positive-going among the healthy individuals in the first study, the P2 amplitudes were found to be more positive-going in the I_L condition compared with the control condition among the CLBP patients.

Although the task design in both studies required the participants to generate and maintain the internal representations in their working memory which involves more top-down control to resolve the cognitive conflicts (Egner et al., 2005; Kerns & Carter, 2004), the result was a less positive-going P2 component among the healthy individuals but a more positive-going P2 component among the CLBP patients. This inconsistency in P2 amplitudes might be due to the dysfunction of CLBP patients in regard to attentional control (Apkarian et al., 2004; Eccleston & Crombez, 1999). In other words, the adaptive brain response (a less positive-going P2 component) did not appear in the shifting process among patients with chronic pain.

5.1.3 Re-engaging attention with internal representations

Among healthy individuals, the significant E–I interaction was also found in the P3 component at the central electrode as well as in Study One. The centrally distributed P3component (or called P3a component) was believed to reflect the process of attention re-engagement in previous studies on orienting attention between two external stimuli (Dowman, 2007, 2011). Therefore, the enhancement in P3 amplitude revealed in Study One can be the result of the top-down process of re-engaging attention with an internal sub-nociceptive stimulus after successfully disengaging attention from the external nociceptive stimulus. However, we should be cautious when drawing this conclusion because this P3 effect was marginally significant (P = .067), so further studies are necessary in order to confirm the P3 effect.

Similar to findings from the healthy individuals in the first study, a significant E–I interaction effect in the P3 amplitude was also found among the CLBP patients in the second study as well. As discussed, the P3 component reflected the process of attention re-engagement (Dowman, 2004, 2007, 2011; Dowman et al., 2007). Hence, the P3 interaction effect in the second study among the CLBP patients might be due to the top-down process of re-engaging attention with the sub-nociceptive image among the CLBP patients. It is noteworthy that the P3 amplitude elicited by the E_H stimuli in the I_H condition was more positive-going than that by the E_L stimuli, but this E–I effect only appeared when stimulating the patients' painful site, but not the non-painful site suggesting that the re-engagement process was modulated by patients' preoccupied pain experience, which concurs with the findings that the patients' pain experience modulated the process of attention being allocated to the nociceptive stimulus in previous behavioral studies (Bushnell et al., 2015; Haggman et al., 2010; Villemure & Bushnell, 2002). The findings of the second study provide evidence that the modulation effect of pain experience was in the process of re-engaging attention with a sub-nociceptive stimulus among the CLBP patients.

One might notice that the peaks of the P3 component obtained in this study appear not to be distinctive in the patient group. A distinct and sharp P3 peak is usually found in studies adopting an oddball paradigm. Besides the oddball paradigm, the P3 component can also be elicited during the emotion regulation tasks (e.g. Peng et al., 2013; Krompinger et al., 2008) or during working memory tasks (e.g. Vogel and Luck, 2002; Saliasi et al., 2013). Similar to the previous studies, the time window

for the P3 component in this study was identified according to the method used in Dowman (2011). A smaller P3 amplitude was found in the CLBP patients than the healthy individuals (Gordeev, 2006). A small and non-distinct P3 component was also found in chronic lower back patients who had attention deficits (e.g. Liossi et.al., 2009; Tiemann et al., 2012; Apkarian et al., 2004; Schmidtwilcke et al., 2006) in this study.

5.1.4 Correlation between the change in ERP components and pain attenuation

Among the healthy individuals, the less positive-going P3 component was found to be significantly correlated with the larger attenuation of the NRS scores. The NRS scores were assigned by the participants at the end of a trial to indicate the pain intensity they felt for the perceived nociceptive stimulus after the E–I orienting attention. In other words, the reduced P3 component signified a better attenuation effect in terms of the pain intensity. Interestingly, the significant correlation was observed at both central electrodes (C3 & C4) and parietal electrodes (CP3, CP4, & CPz). Previous studies suggested that the anterior P3 component and the posterior P3 component reflect different mental processes (Donchin, 1981; Pontifex, Hillman, & Polich, 2009; Dowman, 2004, 2007, 2011). The anterior P3 component was reported to be associated with reengaging attention with the external nociceptive stimulus (Dowman, 2004, 2007, 2011), while the posterior P3 component reflected the process of maintaining a mental representation (Donchin, 1981; Pontifex, Hillman, & Polich, 2009). The findings on the correlations between the changes in the NRS scores and the P3 component might provide a plausible mechanism for understanding the

modulation of orienting attention to pain intensity, which has been frequently reported in previous behavioral studies (e.g., Chan et al., 2012; Fors et al., 2002).

Similarly, significant correlations were found between the ERP components and the attenuation effect on the NRS scores among the CLBP patients. Indeed, the NRS scores were significantly reduced in the I_L condition for an E_L stimulus while they were not significant for E_L stimulus among the CLBP patients. Caution should be exercised during interpretation of this finding as the interaction of external stimulus and internal representation was marginally significant ($p = .089$). And the attenuation effect was found to be significantly correlated with amplitude changes in the N1 component at the S_{NP} site and with the amplitude change in the P3 component at the S_P site. As it was found that the N1 component is associated with the process of attention disengagement and the P3 component is associated with the process of attention re-engagement (Dowman, 2007, 2011; Legrain et al., 2013, Chan et al., 2003), these correlational findings indicate that the pain attenuation effect at the S_{NP} site might be the result of the successful disengagement process and the pain attenuation effect at the S_{NP} site might be due to the successful re-engagement process. Our findings might provide a plausible explanation for CLBP patients being hypervigilant to pain (Tiemann et al., 2012; Vania, Baliki, & Geha, 2009; Roelofs et al., 2002; Crombez et al., 2013), due to their dysfunction in disengaging attention from the painful stimulus when the stimulus did not trigger their pain or being unable to engage with the updated non-pain information when the stimulus triggered their pain.

5.1.5 Correlation between change in ERP components and the Stroop Test

As expected, significant correlations between the performance in the Stroop Test and the changes in ERP amplitudes were both found among the healthy individuals and CLBP patients. To be more specific, the scores in the Stroop Test were positively correlated with amplitude changes in the P2 component among healthy individuals and negatively correlated with the N1 and P3 components among the CLBP patients. Previous studies suggested that the Stroop Test reflects the ability to monitor and solve cognitive conflict (Floden, Vallesi, & Stuss, 2011; Swick & Jovanovic, 2002). In the incongruent color naming trials of the Stroop Test, both semantic meaning and color naming processes are initiated which are incongruent with each other. However, the rule is to energize the process of color naming, which triggers the top-down control process to cope with the cognitive conflict and to inhibits the semantic meaning analysis. In these two studies, the rule was to self-generate a sub-nociceptive internal image after the onset of a nociceptive stimulus. However, both external processes (the perception of an external stimulus) and internal process (the processing of an internal representation) were initiated during E–I orienting attention. The participants were required to inhibit the external process and engage in the internal process which requires the ability to solve cognitive conflicts (Floden et al., 2011; Swick & Jovanovic, 2002). Hence, the significant and positive correlations obtained in the first study suggested that the healthy individuals who were worst at coping with the cognitive conflicts in the Stroop Test would require more top-down control to shift attention away from the nociceptive stimulus to the internal sub-nociceptive image.

The significant and negative correlations obtained in the second study suggested that the CLBP patients who were worst at coping with the cognitive conflicts in the Stroop Test were less devoted to the disengagement and re-engagement process during E–I orienting attention.

5.1.6 Correlation between the changes in ERP components and self-reported scores among CLBP patients

To investigate the relationships between the E–I orienting attention processes and the characteristics of CLBP patients, correlation analysis between the self-reported scores (e.g., the severity score and the Pain Self-Efficacy Scale (PSES) scores) and the changes in ERP amplitudes was conducted. The severity score which was reported by the CLBP patients to indicate their currently experienced pain intensity during the interview was significantly positively correlated with the changes in all of the three ERP components recorded at the painful site. This suggested that the patients who were suffering from more serious CLBP conditions required more top-down control to orient attention from the nociceptive stimulus to the internal sub-nociceptive image. These correlation findings, together with the ERP findings, once again provide evidence on the modulation effect of the patients' pain experience on the E–I orienting attention processes. Moreover, significant positive correlations between the PSES score and the changes in the P2 and P3 amplitudes recorded at the non-painful site were found among the CLBP patients as well. Prior correlation

studies reported that the PSES is a risk factor in the management of chronic pain (Börsbo, Gerdle, & Peolsson, 2009; Edwards, Telfair, Cecil, & Lenoci, 2001; Jackson, Wang, & Fan, 2014). Besides, the prior study also suggested that the attention function might correlate with the pain self-efficacy among chronic musculoskeletal pain patients (Dehghani et al., 2003). Therefore, these correlation findings in the second study indicate that the patients who believed that they were able to handle their pain required more top-down control to orient attention from the nociceptive stimulus to the internal sub-nociceptive image.

5.2 General discussion

5.2.1 The characteristics of the patient participants

One of the most important purposes of this thesis is to examine how the E–I orienting attention processes are modulated by chronic pain. However, studies on chronic pain are limited due to the fact that chronic pain is heterogeneous in nature (Nouwen et al., 2006; Moseley et al., 2008; Chan et.al., 2012). To control the heterogeneity of the participants, the author only recruited CLBP patients for the patient group in these two studies. Besides, recruiting the CLBP patients enabled the author to compare the neural process at the "painful" site (lower back) and that at the non-painful site (ankle). Because both electrical stimulation at the non-painful site and "painful" site was along the distribution of the sural nerve (L5-S1 dermatome), the observed difference between the non-painful site and painful site in the E–I orienting attention processes could be attributed to the modulation effect on chronic pain. However, as the patients were only those who were suffering from CLBP, the finding that pain experience modulates the E–I orienting attention processes could be a specific characteristic of these CLBP patients. Therefore, caution should be exercised when generalizing to other chronic pain patients such as patients with chronic headache or neuropathic pain.

Besides, in these two studies, it appears that the demographic distribution of the CLBP patients was comparable with that of the healthy individuals in terms of educational level, marital status, and employment status. However, the male-female ratio among the CLBP patients was imbalanced. The majority (80.0%) of the CLBP participants were females, which might be due to the fact that the prevalence of CLBP is higher in females than males (Fayaz, et al., 2016; Hoy et al., 2014).

5.2.2 The hypervigilance to pain of CLBP patients

The findings in this thesis might provide the neural mechanism to understand the characteristic of the CLBP patients being hypervigilant to pain or pain-related information. The hypervigilance to pain was assumed to be the characteristic of chronic pain patients due to their persistent experience of chronic pain (Pincus & Morley, 2001; Vlaeyen & Linton, 2000). The fact that chronic pain patients abnormally and excessively deploy attention to pain information has been reported in previous behavioral studies (Roelofs, et al., 2002; Vangronsveld et al., 2007). For example, Roelofs et al. (2002) summarized studies comparing the performance of chronic pain patients with healthy individuals during the modified Stroop task and found that chronic pain patients are distracted by task-irrelevant information compared with healthy individuals. Additionally, the results reported in this thesis indicate that the performances of the CLBP patients were significantly worse than healthy individuals in the word reading task and color naming task, while only slightly worse (marginally significant) in the incongruence color naming task, suggesting that the general attention function of CLBP patients is impaired. However, researchers claim that this behavioral finding that the behavioral indexes such as the response time, accuracy rate of chronic pain patients are inferior to that of healthy individuals is not robust and convincing (Crombez, et al., 2013; Damme, et al., 2010; Pincus & Morley, 2001). They argued that it is unclear whether the increase of reaction time and decrease in accuracy among chronic patients are due to dysfunction in perceptual processing or other biases.

In this thesis, the author also compared the ERP components of the CLBP patients with that of healthy individuals in the control task, in which the participants were required to perceive nociceptive stimuli and maintain them. The results from the repeated measures ANOVA yielded that an enhanced P2 component (more positive-going in amplitude and shorter in latency) and enhanced P3 amplitudes were found among the CLBP patients compared to those among the healthy individuals, suggesting that they over-reacted to the nociceptive stimulus. The Motivational Theory of Pain (Damme et al., 2010) might provide a plausible interpretation of the over-reaction among patients with chronic pain. According to the Motivational Theory, pain information will be enhanced if it is relative to their goal. For patients with chronic pain, the goal in their daily life is to control or manage their pain, which triggers stronger brain reactivity to respond to a nociceptive stimulus than they usually do to manage pain information according to their previous pain experience (Damme et al., 2010). Besides, when comparing the NRS scores between the CLBP patients and healthy individuals, the results indicate that the patients had significantly higher scores for pain intensity than the healthy individuals did, but this difference was only found when the external nociceptive stimulus was highly salient. These findings once again provide convincing evidence on the characteristics of CLBP patients being hypervigilant to pain or pain-related information, particularly, to highly salient types.

5.2.3 Behavioral performance on the E–I orienting attention among the CLBP patients

When comparing the performance (including the accuracy rate, reaction time and efficacy) for the purpose of matching the response in the E–I orienting attention among the CLBP patients, it was found that the patients responded slower and less accurately in the two E–I conditions than in the pain perception condition. These findings are consistent with prior studies comparing internal orienting attention and external orienting attention in regard to visual modality in healthy individuals (Astle, et al., 2009; Griffin & Nobre, 2003; Henseler, et al., 2011). The findings in this thesis suggest that orienting attention to the internal representation involves more top-down processes and result in extra reaction time and less accuracy.

Furthermore, significant differences were found between two E–I conditions among the CLBP patients as well. Specifically, CLBP patients responded slower but slightly more accurately after rehearsing with highly salient images than after rehearsing with low-salient images. It appears that there might be a trade-off between the reaction time and the accuracy rate. The analysis of the efficiency which was calculated by dividing the reaction time by the accuracy rate aimed to solve this trade-off. The results of the analysis of the efficiency suggested that the patients were less efficient in rehearsing with the I_H image than the I_L image, indicating that the CLBP patients might find it more difficult to orient their attention from an external nociceptive stimulus to an I_H image. The reason could be that the low salience level of the sub-nociceptive stimulus was more related to the goal of the CLBP patients which was to down-regulate their pain (Van Damme et al., 2009).

5.3 The significance of this thesis

5.3.1 The theoretical contribution

This thesis aimed to investigate how the neural processes underlying E–I orienting attention among chronic pain patients (specifically CLBP) is modulated by 1) the salience level of the external stimulus, 2) the salience level of the internal representation, and 3) the pain experience of CLBP patients. The findings from the two ERP studies contribute to the theories on the attentional modulation of chronic pain, specifically CLBP in the following ways.

First of all, the finding in this thesis extends Posner's Three Steps Model (Petersen & Posner, 2012; Posner, et al., 1984) on orienting attention between two external stimuli and orienting attention between an external stimulus and the internal representation among chronic pain patients, specifically CLBP patients. In this model, three sub-processes of disengagement, shifting, and re-engagement are theorized to underlie orienting attention from two visual targets (Petersen & Posner, 2012; Posner et al., 1984; Kuo et al., 2014). This model was supported by prior studies on cross-modalities of orienting attention (from visual modality to somatosensory modality or vice versa), in which the N1 component, the P2 component, and the P3 component could be the "ERP markers" that reflect the attentional orienting between a visual stimulus and nociceptive stimulus among healthy individuals (Dowman, 2004, 2007, 2011; Dowman et al., 2007; Chan etal., 2012). To the best of the author’s knowledge, limited studies have investigated the orienting attention between an

external nociceptive stimulus and internal representation (Legrain et al. 2013; Chan et al., 2012). The findings of these limited studies suggest that the N1 component, the P2 component, and the P3 component reflect the neural processes underlying the E–I orienting attention among healthy individuals. The two ERP studies reported in this thesis examined the neural processes of E–I orienting attention process not only among healthy individuals but also CLBP patients. It was found that the N1 component, the P2 component, and the P3 component could be the ERP markers for the neural process of attention disengagement, shifting and reengagement between an external nociceptive stimulus and the internal representation.

Secondly, the findings in both studies have provided new insight on the bottom-up and top-down attention models proposed by Legrain et al. (2011), which was supported not only by studies on attentional modulation of visual emotional stimuli, but also by attentional modulation of somatosensory stimuli (e.g., Peng et al., 2013; Legrain et al., 2009, 2011; Dowman, 2011). In this model, the deployment of attention to the nociceptive stimulus is modulated not only by the stimulus-driven bottom-up process but also by the goal-directed top-down process. And they also claimed that there is a salience detection system in the bottom-up process to select salient nociceptive information to further process it, while the nociceptive information is filtered by the function of the attentional set and the attentional load in the working memory during the top-down processes. The finding in this thesis reveals that the P2 component and the P3 component which reflect the top-down processes of the shifting and reengagement are modulated by the salience level of the internal image

suggesting that the salience detection system is also crucial in top-down processes. Besides, results from the CLBP patients also revealed significant differences in ERP amplitudes between the non-painful site and painful site, indicating that the patients' previous pain experience is also one of the most important factors during the top-down modulation of pain.

Last but not least, the finding in the second study might have provided a plausible mechanism for explaining the hypervigilance to pain among chronic pain patients, specifically CLBP patients. Chronic pain patients show hypervigilance to pain due to their persisting experience of pain (Pincus & Morley, 2001; Vlaeyen et al., 1995). However, the underlying mechanism of chronic pain patients, specifically CLBP patients, being hypervigilant to pain is still unclear. Some researchers believe that the chronic pain patients are biased to pain information because they find it difficult to disengage their attention from the existing pain sensation or experience (Haggman et al., 2010; Sharp et al., 2009), while others disagree and suggest that it is because chronic pain patients have difficulty in engaging with updated pain information (Liossi et al., 2014; Yang et al., 2013). In order to solve this disengagement vs. engagement argument, in this thesis, the ERP, which has a high temporal resolution, was used to examine the neural processes of attention disengagement and re-engagement. The findings of the second ERP study among CLBP patients reported in this thesis show that the amplitudes of the N1 component (reflects the processes of disengagement) and the P3 component (reflects the processes of reengagement) are modulated by their experience of pain. Besides, the amplitude changes in these ERP components were significantly correlated with attenuation in NRS scores for the perception of pain intensity. These findings suggest the reasons why chronic pain patients, specifically CLBP patients exhibit

hypervigilance to pain to varying degrees depending on their pain experience. In other words, the CLBP patients showed dysfunction in disengaging their attention from a nociceptive stimulus if it did not trigger their pain experience and showed dysfunction in engaging with updated non-pain information when a nociceptive stimulus triggered their pain experience.

5.3.2 The clinical implications

The findings in these two studies provide theoretical guidance for applying attentional-based strategies to down-regulate the influence of chronic pain, specifically CLBP, in clinical treatment. Previous studies that instructed patients to direct their attention away from their pain to pain-unrelated targets (the distraction strategy) or to focus on the objective component of the pain (the focused attention strategy) have shown an attenuated effect in terms of pain intensity (Moseley et al., 2008; Nouwen et al., 2006). However, the distraction strategy is not always effective to down-regulate pain especially for chronic pain due to the characteristics of hypervigilance to pain among chronic pain patients (Chan et al., 2012). They proposed to use a sub-nociceptive image to replace the pain-unrelated target and encouraged CLBP patients to focus on this image. According to the bottom-up and top-down model (Legrain et al., 2011), information that resembles the attentional set in the working memory would have the priority to proceed to the further processes (e.g., appraisal of the intensity of the stimulus). A sub-nociceptive image is more pain-related compared with a pain-unrelated visual image (Tsao, et al., 2003). Hence, chronic pain patients might find it easier to orient their attention from a nociceptive

stimulus to a sub-nociceptive image (Chan et al., 2012). However, in the study of Chan et al. (2012), only some (6 out of 17) of the patient participants exhibited an attenuation effect on pain intensity after focusing on this sub-nociceptive image. This thesis study refined the previous study by manipulating the salience levels of the sub-nociceptive image and found alarger attenuation effect on pain intensity after rehearsing with a low-salient sub-nociceptive image. Therefore, in clinical practice, therapists might guide their patients to focus on low-salient sub-nociceptive images by encouraging them to down-regulate their pain experience. Besides, the performances in the Stroop Test and the self-reported scores (e.g., the pain severity scores and PSES score) were found to be correlated with the changes in ERP components, suggesting that the performances in the Stroop test might predict the ability to orient their attention from a nociceptive stimulus to a sub-nociceptive image among CLBP patients. Therefore, clinicians may apply the Stroop Test to screen patients who are suitable focusing the E–I orienting attention-based strategy.

Chapter VI

CONCLUSION

6.1 Summary of the significant findings

This thesis investigated the neural processes of external-to-internal (E–I) orienting attention among healthy individuals and patients with chronic lower back pain (CLBP). To achieve this goal, the author manipulated the levels of salience of both an external nociceptive stimulus and internal sub-nociceptive representation into high and low salience levels in Study One and Study Two. Additionally, the electrical stimulation site in Study Two was manipulated as well. The stimulus was either at a non-painful site (S_{NP}) or "painful" site (S_P) among the CLBP patients in Study Two. In these two studies, the participants were required to self-generate an internal representation of a sub-nociceptive sensation after perceiving an external nociceptive stimulus in the experimental task and to perceive an external nociceptive stimulus and maintain it in their working memory in the control task.

Among the healthy individuals, the ERP results in the first study indicated the differences between the highly salient internal representation (I_H) and the low-salient internal representation (I_L) in the amplitudes of the N1, P2 and P3 components, which might be the ERP components reflecting the neural processes of attention

disengagement, shifting and re-engagement, which were only significant when the salience of external nociceptive stimulus was high (E_H) but not when it was low (E_L). Besides, the results from the correlation analyses between the behavioral self-reported scores and the ERP data show that the changes of the P3 component were correlated with the attenuation in NRS scores for the perceived pain intensity. This suggested that the P3 component might be responsible for the attenuation effect on pain intensity. Additionally, correlation analyses also yielded that the changes in the P2 component correlated with the performance in the Stroop Test, which provided convincing evidence that the E–I orienting attention process involves a top-down process to solve the conflict created by the perception of the external stimulus and shifting to the internal representation (Egner et al., 2005; Kerns & Carter, 2004). These findings in the first study suggest that the E–I processes orienting attention among healthy individuals involve both a bottom-up and top-down process.

Among the CLBP patients, the ERP results in the second study indicate that the disengagement process (reflected by the N1 component) is bottom-up dominated. More enhanced N1 amplitudes were found for the E_H stimulus than the E_L one. Besides, the disengagement process was also modulated by pain experience (top-down process) among the CLBP patients. The N1 amplitude was more negative-going when the electrical stimulations were located at their S_P site than when at their S_{NP} site. The E–I interaction was found during the shifting process. An enhanced P2 component was found when rehearsing with the low-salient internal representation compared to the control condition among the CLBP patients, different

from that among the healthy individuals. This finding suggests a dysfunction of the CLBP patients in the top-down process of E–I orienting attention. Besides, an enhanced P3 amplitude when rehearsing with the highly salient internal representation was revealed at the S_P site, but not the S_{NP} one among the CLBP patients as well, indicating that the re-engagement process was also modulated by pain experience. These ERP findings in the second study suggest that the E–I orienting attention processes among the CLBP patients is not only modulated by a bottom-up process (the salience of the external nociceptive stimulus), but also a top-down process (the salience of the internal representation and pain experience).

Behaviorally, the better attenuation effect in terms of the NRS score for the perception of pain intensity was found when the patients rehearsed with an I_L image. However, this was true only for the E_L stimulus among the CLBP patients. These findings suggest that the down-regulation of internal representation is modulated by the salience level of the external nociceptive stimulus. Additionally, the attenuation effect in the NRS score was found to be associated with the amplitude changes in the N1 component at the S_{NP} site and with the amplitude change in the P3 component at the S_P site. The results from the correlation analysis also show that the two ERP components are associated with the performance in the Stroop Test and the severity scores for their current CLBP condition. The correlations between amplitudes changes in the ERP components (P2 and P3) and the PSES scores when the stimulations were delivered at the S_P site. These correlational findings suggest that the N1 component and P3 component are important ERP markers for E–I orienting attention among

CLBP patients and might offer a possible neural mechanism for understanding the attentional dysfunction among CLBP patients (Fors et al., 2002; Hart, Martelli, & Zasler, 2000).

6.2 Limitations in this thesis

This thesis has several limitations. These include the experimental design, the electrical stimulation, and the participating CLBP patients.

It is noted that the experimental design had some drawbacks. First, the experimental design was not a "true experimental design", in which the treatment group and the control group should be comparable in all aspects except the experimental manipulation (Gribbons & Herman, 1997). The CLBP patients and the healthy individuals volunteered in the two independent ERP experiments which were different from each other in terms of the task design. In the first study, the healthy individuals were asked to give two kinds of responses—to recall the previous perceived nociceptive stimulus and then give an NRS score to indicate the intensity of their pain in that trial, and to compare the intensity of the image maintained in their working memory with that of the second external nociceptive stimulus. In the second study, this dual-response task was divided into two parts — the CLBP patients were required to compare the intensity of the self-generated image with that of a second external stimulus in the first part of the study, and to give a NRS score for the perceived pain intensity in the second part. The reason for this different implementation of the task design was because the dual-response task was found to be too difficult for the CLBP patients in the previous research (Chan et al., 2012) and the pilot study (see the conference paper, Peng et al., 2014). Although the author may argue that the task requirement which was to rehearse with a self-generated internal image after

perceiving a nociceptive stimulus was the same for both groups of participants and the major difference between the two experimental tasks was in the response requirement, which would not affect the neural process of E–I orienting attention. Unfortunately, the rules for the experimental tasks between these two ERP studies were different as well, which was the second drawback of the task design. The rule in the first study for the healthy individuals was to generate a specific internal image according to the instruction given at the beginning of each block, while the rule in the second study for the CLBP patients was to generate an internal image the salience level of which was the same or opposite to the external stimulus according to the instruction given at the beginning of each block. Therefore, one should be cautious when comparing the findings between these two groups of participants directly. Besides, in the experimental task design for both studies, the time at which the participants began to generate the internal images was not controlled. This could be a confounding factor that might affect the latency of the P3 component, resulting in a marginally significant interaction between the external stimulation and internal representation. With refined experimental tasks, future studies might have a better understanding of the neural mechanism of orienting attention to down-regulate chronic pain.

The major limitation of the stimulation was the short duration of the electrical stimulation. The purpose of this thesis is to investigate the modulation of orienting attention in regard to chronic pain, particularly CLBP. However, the external electrical stimulus was delivered to each participant for only 50 ms. The fleeting electrical stimulus created an instantaneous nociceptive stimulus while CLBP is

long-lasting in nature. This difference may reduce the validity of this thesis. The reason for applying such a short period is to avoid the artifacts of the electrical pulses affecting the ERP components of interest in these studies. Previous studies suggested that the N1 component, P2 component, and P3 component are sensitive to the modulation of orienting attention with regard to pain perception (Dowman, 2004, 2007, 2011; Dowman et al., 2007; Legrain et al., 2013). Among these components, the onset timing of the N1 component is usually reported as early as 100 ms (Dowman, 2004, 2007, 2011; Dowman et al., 2007). Therefore, in order to record a clean N1 component, the timing for the external electrical pulse was set as 50 ms. Besides, an electrical pulse might not be the best approach to induce nociception because an electrical pulse may not only activate the nociceptors, but also other receptors, such as mechanoreceptors (Kakigi, Watanabe, & Yamasaki, 2000). Future studies can employ a cold-pressor (Veldhuijzen, Kenemans, De Bruin, Olivier, & Volkerts, 2006) or laser (Legrain, Bruyer, Guérit, & Plaghki, 2005) to induce nociception to overcome the shortcomings of the electrical stimulation in these studies.

There are many types of chronic lower back pain: nociceptive pain, neuropathic pain, psychogenic pain and idiopathic pain. This heterogeneity of chronic lower back pain made the interpretation of the findings difficult and incomparable, leading to a limited number of studies on this topic (Chan et al., 2012; Moseley et al., 2008; Nouwen, Cloutier, Kappas, Warbrick, & Sheffield, 2006). To control the heterogeneity and be able to compare with the previous studies (e.g., Chan et al., 2012; Hulle, 2013), only chronic musculoskeletal origin nociceptive lower back pain

patients were recruited for the present thesis study. However, to the best of my knowledge, due to the lack of direct evidence, the effect of different types of lower back pain on the neural processes of orienting attention is still unclear. Further studies could consider comparing the neural processes of orienting attention of patients' chronic nociceptive lower back pain with other kinds of lower back pain to examine whether the findings from the chronic nociceptive lower back pain patients can be generalized to other kinds of lower back pain (e.g., the neuropathic pain). Actually, in the this thesis study, there was still not homogeneity within the CLBP patients in terms of the duration of CLBP. According to the common clinical guidelines (Hart, Martelli, & Zasler, 2000), one of the inclusion criteria is "CLBP duration of 6 months and above", which results in a wide range of variation in terms of the pain duration that they were suffered due to CLBP, ranging from 1 to 30 years. And significant correlations between the pain duration and amplitudes changes in the P3 components were found when the external stimulus has high salience ($r = -.664$, $p = .026$ at FC3 in the internal low salience condition and $r = -.622$, $p = .041$ at C4 in the internal high salience condition). Previous studies suggest that chronic pain patients who experience long-lasting pain for more than three months show plastic changes in their brain (Apkarian, et al., 2009; Zhuo, 2008). Therefore, the varied duration of the chronic pain might be a confounding factor which might affect the patients' response to E–I orienting attention. Further studies might consider controlling the pain duration during the screening session to improve the with-in subjects' heterogeneity. Besides, the sample size of the effective patients was small. Statistical analyses were based on

valid data obtained from 15 patients who had completed the two-day training and experimental task. This small sample size undermines the power of the statistical analyses, resulting in failures in detecting a true experimental effect, particularly the pain attenuation effect which was measured by self-reported scores. Future studies should increase the sample size to confirm the effectiveness of orienting attention in regard to down-regulating the experience of pain.

Another limitation of the patient participants is the imbalanced male-female ratio among the CLBP patients. As the majority of the CLBP participants were females in this study, one might worry that the gender difference in pain thresholds might have affected the results of the study. This study adopted two measures to minimize the effect of the potential gender effects. First, calibration of the pain thresholds was carried out for each of the participants. Second, the thresholds obtained for the participants were compared to test for the gender effects. The results did not show significant differences between females and males in both the healthy group and patient group. A better control for the gender factor should be considered in the future study.

6.3 Suggestions for future studies

This thesis provides some basic understandings of the neural processes underlying the modulation effect of E–I orienting attention on the perception of pain among healthy individuals and CLBP patients. A lot of efforts are still needed to enrich the knowledge on the topic.

First of all, future studies can consider using healthy individuals as the control group and comparing the difference in the neural processes between healthy individuals and chronic pain patients in regard to E–I orienting attention to better understand the dysfunction of chronic pain in E–I orienting attention. For example, a more positive-going P2 component was found during E–I orienting attention among the CLBP patients which was different from that among healthy individuals. This enhanced P2 component could be due to their compensatory enhanced brain response to the E–I orienting attention or because they were biased by the nociceptive stimulus.

Secondly, clinical studies with a randomized controlled trial design can be conducted to examine the effectiveness of E–I orienting attention strategies to down-regulate the perception of pain or even their chronic pain situation. Besides, instruments such as the Stroop Test and the PSES can be used as selection criteria for chronic pain patients to increase the effectiveness of E–I orienting attention strategy to down-regulate the perception of pain.

Furthermore, the neural processes underlying the E–I orienting attention was examined by employing the ERP method in this thesis. The results show that fronto-central distributed N1, P2, and P3 components were found to be modulated

during the top-down process of the E–I orienting attention. These ERP components are believed to be generated by the prefrontal cortex such as the dorsolateral and medial prefrontal cortex (Dowman, 2004, 2007, 2011; Dowman et al., 2007). Therefore, future studies can employ other neuroimaging approaches with high spatial resolution, for example, functional magnetic resonance imaging, to examine the important role of the frontal lobe in E–I orienting attention.

Additionally, findings on the neural processes of E–I orienting attention were based on the modality of somatosensory stimulus in this thesis, so generalization to other modalities (e.g., auditory and visual modalities) should be done with caution. Future studies need to test the robustness of the three sub-processes of E–I orienting attention using stimuli in other modalities such as auditory and visual stimuli.

Besides, these thesis study only compared neural processes between the "painful" (means sites within the painful lower back region) and non-painful sites are based on the assumption that both types of sites are covered under the same L5-S1 dermatomes (sural nerve, Dowman, 2007). The differences in the contrasts between the ERPs obtained from the "painful" and non-painful sites would inform the modulation due to the pain experience effects. To my knowledge, there has been no attention-related study on the site effect within the painful body region. This woud be an interesting study to conduct in the future.

APPENDIXES

Appendix I Consent Form for Study One

a. Chinese Version

香港理工大學復康治療科學系

研究同意書
研究題目
專注轉移對痛覺感知的影響——ERP 研究
研究成員
陳智軒教授, 陳子頌博士及彭家欣女士
同意書
本人 _____（香港身分證號碼：_____）明白此項研究之細節，並聲明自願參加此項研究。我明白可以隨時在不需作出解釋之情況下退出此項研究，而將不會受到處罰或歧視。我悉知參與本研究當中可能引致的不適。我明白本人之個人資料將不會向本研究以外之人士公開，並且我的姓名或照片將不會出現於任何研究之報告內。所有資料會於研究完成後銷毀。

本人可致電 2766 4310 向研究員陳子頌博士查詢本研究事宜。若果我對研究員有任何投訴，可致電 2766 5397，與 Ms. Michelle Leung 接洽。我將受予簽署同意書副本一份。

參加者簽署：_____日期：_____
見證人簽署：_____日期：_____

b. English Version

The Hong Kong Polytechnic University
Department of Rehabilitation Sciences
Research Project Informed Consent Form

Project title:

Orienting Attention for Intervening Pain Perception

Investigators:

Prof. Chetwyn C. H. Chan; Dr. Sam C. C. Chan, Mr. Eddie Y. K. Hai

Consent:

I, _____ (HKID no. _____), 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 withdrawal will not lead to any punishment or prejudice against me. I am aware of any potential discomfortduring the 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. All personal information will be discarded upon the completion of the study.

I can contact the project investigators, Professor Chetwyn Chan (Tel.: 2766 6727), Dr. Sam Chan (Tel: 2766 4310) or Mr Eddie Hai (Tel: 2766 4842) for any questions about this study. If I have complaints related to the investigator(s), I can contact Mrs. Michelle Leung, Secretary of Department Research Committee, at 2766 5397. I know I will be given a signed copy of this consent form.

Subject's Signature: _____ Date: _____

Witness' Signature: _____ Date: _____

Appendix II Information Form for Study One

a. Chinese Version

香港理工大學復康治療科學系

研究項目介绍

研究題目
專注轉移對痛覺感知的影響——ERP 研究
研究成員
陳智軒教授, 陳子頌博士,及彭家欣女士
研究目的
探討運用感覺意象(專注轉移)的技巧調節痛楚時的腦機制。
研究內容
本研究實驗包括兩部分：
在第一部分中，你需要先填寫有關個人資料、痛症的病歷（如適用）、痛楚有關的問卷，及認知功能的測試，之後你將會接受接受感覺意象的訓練。
在第二部分中，你將參與一項有關的實驗，期間腦電活動將同時記錄下來。

研究員會帶領你進行每個部份的實驗程序。若在過程中感到覺疲倦或不適時，你可稍作休息。
潛在危險及權利
縱使在實驗中涉及痛楚之刺激，我的身體將不會受到任何的損傷。參與本研究項目乃純屬自願性質。我有權利在任何時間及任何理由下終止實驗。

b. English Version

The Hong Kong Polytechnic University
Department of Rehabilitation Sciences

Research Project Information Sheet

Project title:

Orienting Attention for Pain Attenuation

Investigators:

Prof. Chetwyn C. H. Chan; Dr. Sam C. C. Chan, Mr. Eddie Y. K. Hai, Ms. JiaxinPeng.

Purpose of the study:

To investigate the effect of attention orientation on pain perception of people with chronic low back pain

Project information:

The experiments including two sessions.

The first session is screening session, in which, you need to complete a series of questionnaires concerning personal particulars, pain history, pain-related questionnaires, and cognitivefunction assessment.

The second part is training session, in which, you will receive a range of electrical stimuli transmitted by an electrical stimulatorat your left ankle and you will be trained to rate painful sensations and remember tactile sensations. In the end, you will be trained to generate the imagery of previously learned tactile sensationswhere painful stimulation is received. The total time will be 3-4 hours.

The study investigator will guide you through the procedures in all sessions. I will be provided with breaks in case of tiredness or discomfort.

Potential Risks and Rights:

Although the study involves painful stimuli, no damages to your body will be the consequence of the experiments and you will not experience any unnecessary painful sensation. Participation is completely on voluntary basis and you have the right to withdraw from study at any time or with any reason.

Appendix III Personal Information

參加者個人資料問卷

姓名 :_____ 日期 :_____

1. 年齡 _____
2. 性別 □1.男 □2.女
3. 婚姻狀況 □1.未婚 □2.已婚 □3.分居 / 離婚 □4.喪偶 □5.其他 _____
4. 教育程度：
   □1.小學程度或以下 □2.小學畢業
   □3.中學程度 □4.中學畢業
   □5.預科 □6.大專 / 大學 □7.大學以上
5. 就業情況
   □1. 失業 / 沒有工作
   □2. 兼職工作, 你的工作是 _____
   □3. 全職工作, 你的工作是 _____
   □4. 學生
   □5. 家庭主婦
   □6. 退休

Appendix IV Stroop Test

a. Word Reading Sub-test

綠 紅 黃 藍 黃 紅 藍 綠 紅 黃

綠 藍 紅 黃 紅 綠 黃 綠 紅 綠

黃 紅 藍 黃 紅 黃 藍 綠 藍 綠

藍 紅 黃 藍 紅 綠 藍 紅 藍 紅

綠 藍 紅 綠 藍 黃 藍 綠 黃 綠

黃 藍 紅 黃 綠 藍 黃 藍 綠 紅

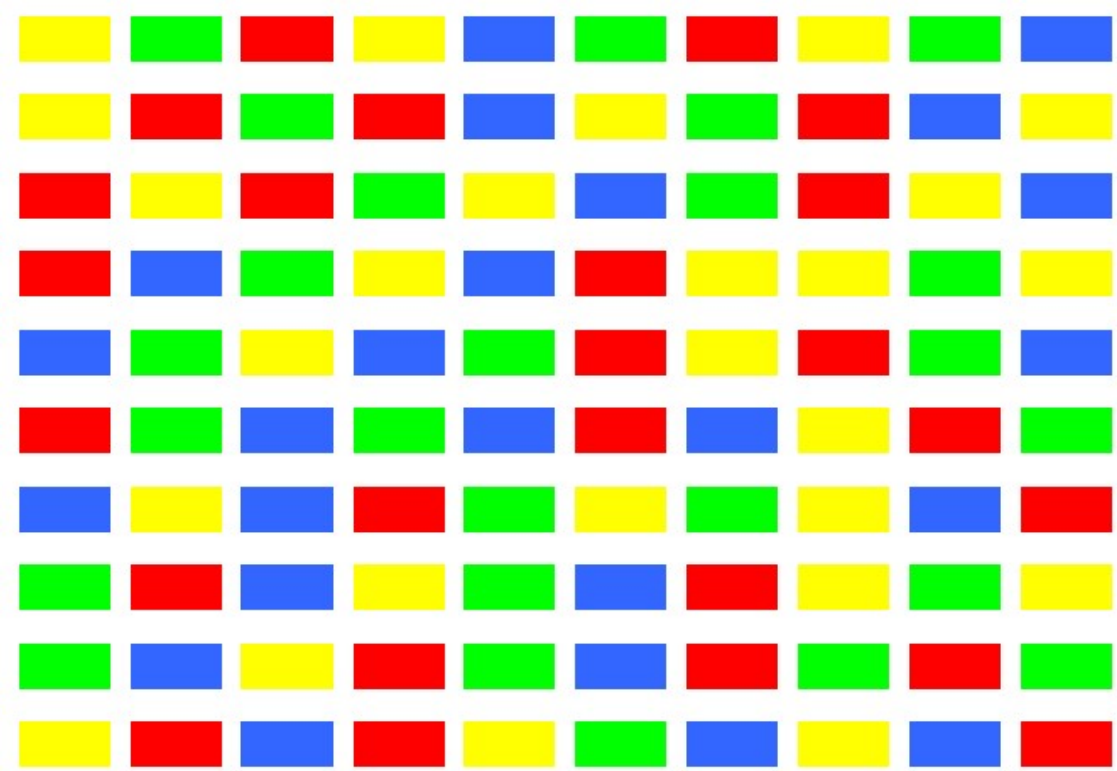
綠 藍 黃 綠 紅 藍 黃 綠 黃 藍

紅 黃 紅 綠 藍 紅 黃 綠 藍 紅

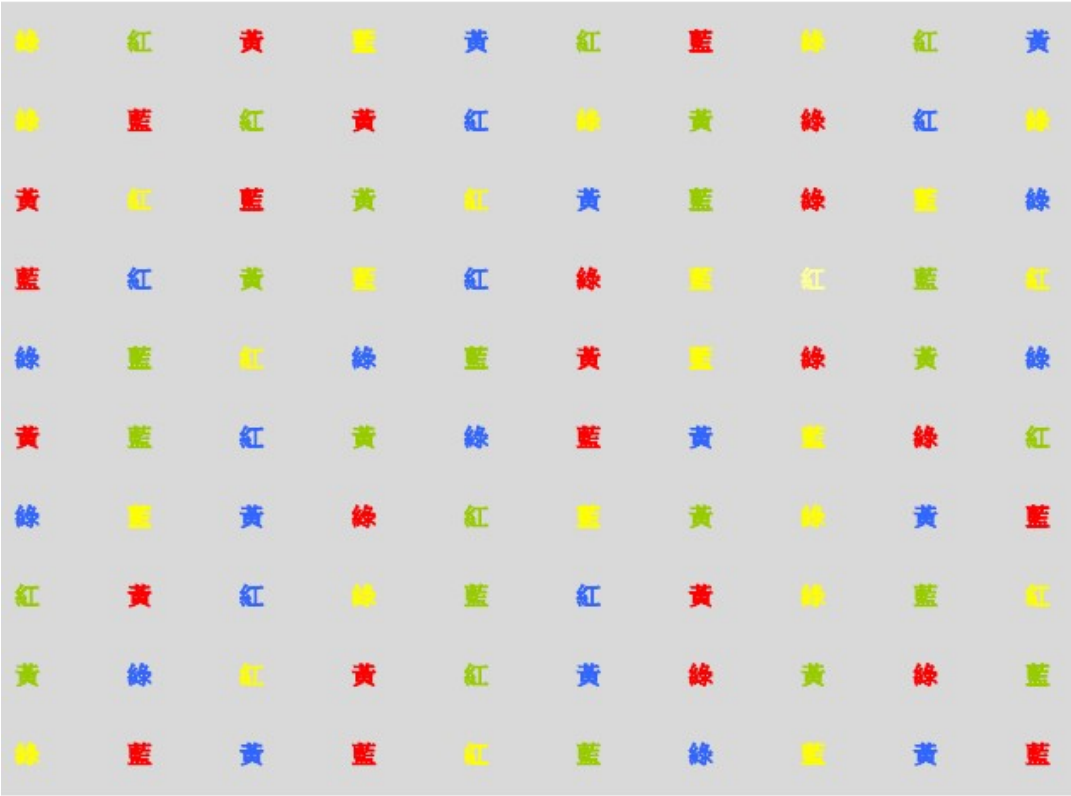
黃 綠 紅 黃 紅 黃 綠 黃 綠 藍

綠 藍 黃 藍 紅 藍 綠 藍 黃 藍

b. Color Naming Sub-test



c. Incongruent Color Naming Test



Appendix V Calibration Recording Sheet

Subj Name:_____ Date:_____

Calibration

Ascending:

Ints	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Y/N										
Ints	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**
NRS										
Ints	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**
NRS										
Ints	**30**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**	**39**
NRS										

Descending:

Ints	**39**	**38**	**37**	**36**	**35**	**34**	**33**	**32**	**31**	**30**
NRS										
Ints	**29**	**28**	**27**	**26**	**25**	**24**	**23**	**22**	**21**	**20**
NRS										
Ints	**19**	**18**	**17**	**16**	**15**	**14**	**13**	**12**	**11**	**10**
NRS										
Ints	**9**	**8**	**7**	**6**	**5**	**4**	**3**	**2**	**1**	**0**
Y/N										

Min Detectable Sensation			Just Painful Sensation			Very painful Sensation (NRS=7)
Ascending	Descending	Average	Ascending	Descending	Average	

Get 3levels' of N stimuli

The five levels' of non-nociceptive stimuli are evenly distributed between MDS and JPS.

SN_L____ SN_H ____

Get 6levels' of P stimuli

P1____ P2____ P3____ P4____ P5____ P6____

Appendix VI: Familiarization Recording Sheet of Nociceptive stimulus

a. Familiarization of pain rating using NRS

No.1	Stimu	**P3**	**P5**	**P1**	**P6**	**P4**	**P2**	**Score**
	Respond							
No.2	Stimu	**P5**	**P1**	**P3**	**P2**	**P6**	**P4**	**Score**
	Respond							
No.3	Stimu	**P1**	**P3**	**P5**	**P4**	**P2**	**P6**	**Score**
	Respond							
No.4	Stimu	**P4**	**P6**	**P2**	**P1**	**P5**	**P3**	**Score**
	Respond							
No.5	Stimu	**P2**	**P4**	**P6**	**P5**	**P3**	**P1**	**Score**
	Respond							
No.6	Stimu	**P6**	**P2**	**P4**	**P3**	**P1**	**P5**	**Score**
	Respond							
No.7	Stimu	**P1**	**P6**	**P3**	**P2**	**P4**	**P5**	**Score**
	Respond							
No.8	Stimu	**P5**	**P4**	**P1**	**P6**	**P2**	**P3**	**Score**
	Respond							
No.9	Stimu	**P3**	**P2**	**P5**	**P4**	**P6**	**P1**	**Score**
	Respond							
No.10	Stimu	**P2**	**P1**	**P4**	**P3**	**P5**	**P6**	**Score**
	Respond							

b. Numeric Rating Scale:

Appendix VII: Familiarization Recording Sheet of sub-nociceptive stimuli

	Sub-nociceptive									
Level	2	2	1	1	3	1	3	2	3	Score
1Responds										
Level	1	2	3	2	3	1	1	3	2	Score
2. Responds										
Level	1	2	1	3	1	3	2	2	3	Score
3. Responds										
Level	2	2	3	1	1	1	3	2	3	Score
4. Responds										
Level	3	2	2	1	3	3	1	1	2	Score
5. Responds										

Note: 1 refers to SN_L，2 refers to SN_M，3 refers to SN_L.

Appendix VIII: Orienting Attention Training and Tasting sheet

SN_L____ SN_M ____SN_H ____ (P1____ P2____ P3____ P4____ P5____ P 6 ____)

Part 1 Pair training:

S1 [P1…6] →I[SN_L]→S2[SN_L]……S1 [P1…6]→I[SN_H]→S2[SN_H]

Note: 1 it would be better if each pair repeats three times before going to next pair.

2 Note the time interval and the introduction should be the same.

Part 2 Imagery

Instruction: when you feel a electric stimuli, Please generate a non-painful image immediately, and keep the image in your brain and compare it with the second electric stimuli, tell me whether the second stimuli is similar to the first one, please tell me "similar " or not as soon as possible.

For each trail, give the instruction "Please generate a SN_L(or 2 or3) and keep it in mind", meanwhile give a electric stimuli(P1……6), 3000s later, give the instruction "compare with this".

I	s1	s2	R	I	s1	s2	R	I	s1	s2	R
SN_H	P4	SN_L		SN_H	P5	SN_L		SN_L	P5	SN_H	
SN_H	P2	SN_H		SN_L	P5	SN_L		SN_L	P3	SN_L	
SN_H	P3	SN_L		SN_H	P6	SN_L		SN_L	P2	SN_H	
SN_L	P6	SN_L		SN_L	P3	SN_H		SN_H	P1	SN_H	
SN_L	P4	SN_M		SN_H	P4	SN_M		SN_L	P1	SN_M	
SN_H	P5	SN_H		SN_H	P2	SN_M		SN_L	P6	SN_H	

I	s1	s2	R	I	s1	s2	R	I	s1	s2	R
SN_L	P3	SNM		SN_L	P5	SN_M		SN_H	P3	SN_H	
SN_H	P4	SN_H		SN_H	P1	SN_L		SN_L	P1	SN_H	
SN_L	P4	SN_H		SN_H	P6	SN_H		SN_H	P1	SN_M	
SN_L	P6	SN_M		SN_H	P2	SN_L		SN_H	P3	SN_M	
SN_L	P4	SN_L		SN_H	P6	SN_M		SN_H	P5	SN_M	
SN_L	P2	SN_L		SN_L	P2	SN_M		SN_L	P2	SN_M	

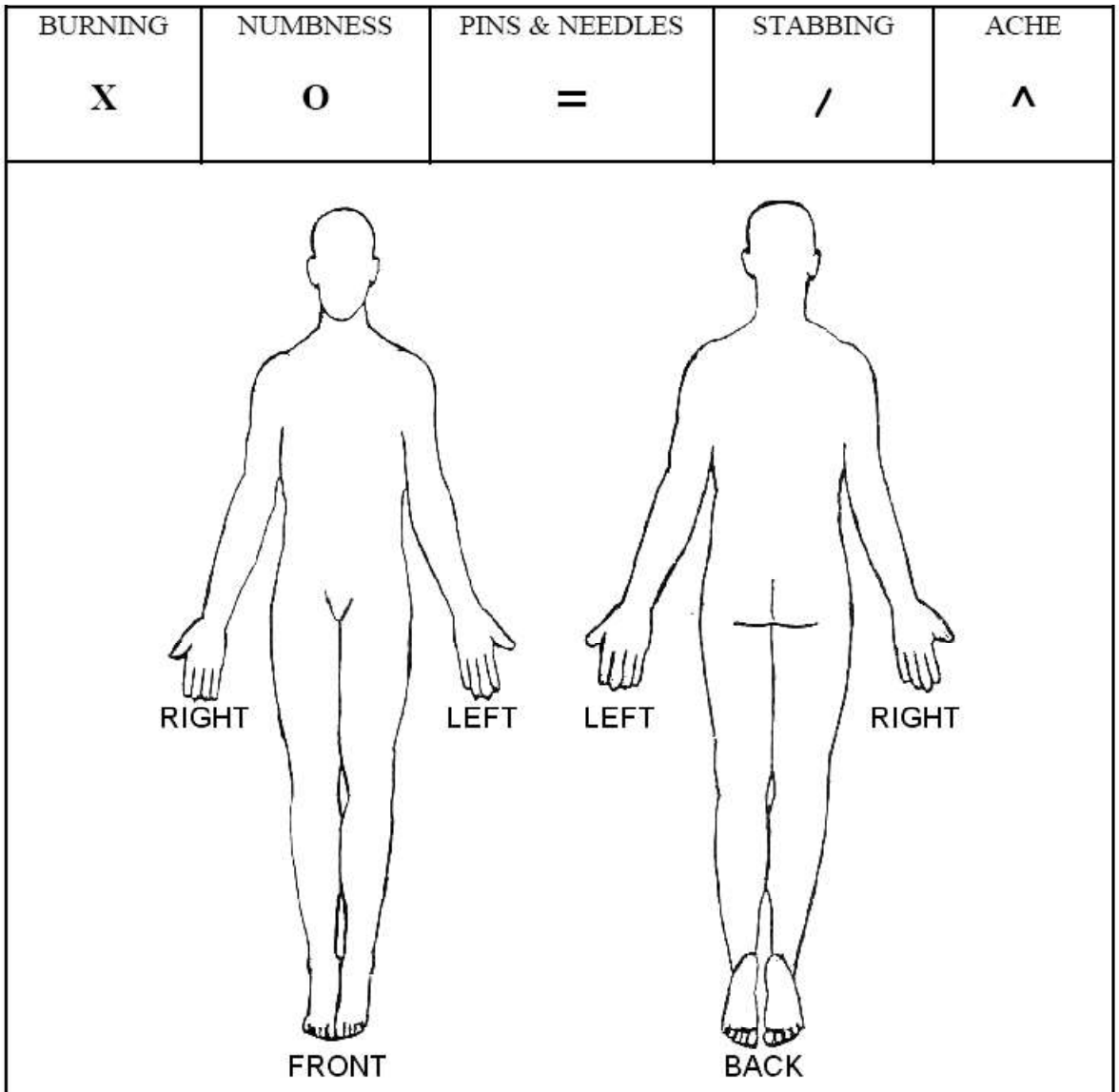
Note: Each successful case of matching the self-generated sub-nociceptive image with the actual given sub-nociceptive stimuli was scored as "2", and each case of mismatching (i.e., matching the self-generated image with the actual given stimuli in the near level) was scored as "1". and the accuracy rate was calculated by dividing the correct score (i.e., sum of matching score and mismatching score) by the total score.

Appendix IX Body Chart

請以下列的符號表示出身體上所有的不適，並寫下該部份的痛楚程度 (1 – 10)。

Use the symbols below to mark the areas on your body where you feel the following sensations. Include ALL affected areas. And give your pain ratings for that particular body part.

BURNING	NUMBNESS	PINS & NEEDLES	STABBING	ACHE
X	O	=	/	^



Numeric Rating Scale (NRS) of Pain (11-point scale)

完全沒有痛楚 0 1 2 3 4 5 6 7 8 9 10 極度痛楚

Appendix X Consent Form for Study Two

a. Chinese Version

香港理工大學康復治療科學系

研究同意書

研究題目
專注轉移對長期腰痛人士疼痛的調節
研究成員
彭家欣女士, 陳智軒教授, 及陳子頌博士
同意書
本人 _____ （香港身分證號碼：_____）明白此項研究之細節, 並聲明自願參加此項研究。我明白可以隨時在不需作出解釋之情況下退出此項研究，而將不會受到處罰或歧視。我悉知參與本研究當中可能引致的不適。我明白本人之個人資料將不會向本研究以外之人士公開, 並且我的姓名或照片將不會出現於任何研究之報告內。所有資料會於研究完成後銷毀。

本人可致電向研究員陳智軒教授(Tel.: 2766 6727)或者陳子頌博士(Tel: 2766 4310)查詢本研究事宜。若果我對研究員有任何投訴,可致電 2766 4394, 與 Ms. Gloria Man 接洽。我將受予簽署同意書副本一份。

參加者簽署：_____日期：_____
見證人簽署：_____日期：_____

Appendix X Consent Form

b. English Version

The Hong Kong Polytechnic University

Department of Rehabilitation Sciences
Research Project Consent Form

Project title:
Orienting Attention for Pain Attenuation in Patients with Chronic Low Back Pain
Investigators:
Ms.JiaxinPeng;Prof. Chetwyn C. H. Chan; Dr. Sam C. C. Chan
Consent:
I, _____ (HKID no. _____), 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 withdrawal will not lead to any punishment or prejudice against me. I am aware of any potential discomfortduring the 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. All personal information will be discarded upon the completion of the study.
I can contact the project investigators, Professor Chetwyn Chan (Tel.: 2766 6727) or Dr. Sam Chan (Tel: 2766 4310)for any questions about this study. If I have complaints related to the investigator(s), I can contact Ms. Gloria Man, Secretary of Department Research Committee, at 2766 4394. I know I will be given a signed copy of this consent form.
Subject's Signature: _____ Date: _____
Witness' Signature: _____ Date: _____

Appendix XI A: Information Form for Study Two

a. Chinese Version

香港理工大學康復治療科學系

研究項目介紹

研究題目
專注轉移對長期腰痛人士疼痛的調節
研究成員
彭家欣女士, 陳智軒教授, 及陳子頌博士
研究目的
探討運用感覺意象(專注轉移)的技巧調節痛楚時的腦機制。
研究內容
本研究分成三節進行。
第一節是實驗前的準備階段。在這環節中，你需要先填寫有關個人資料、痛症的病歷（如適用）、痛楚有關的問卷，及認知功能的測試。這一環節大概需要 1 小時。
第二節是專注轉移技巧的第一次訓練和測試。在這環節中，你的腳踝非疼痛部位將會接受不同程度的電刺激。在研究員的指導下，你先須要熟悉如何對這些痛覺刺激進行評分，以及記憶兩種不同程度的觸覺。然後在接受不同電刺激的情況下，你須要在腦海想像出之前記住的感覺意象，以代替真實的感覺，期間腦電活動將被同時記錄下來。總共需要耗時 3 小時。
第三節是專注轉移技巧的第二次訓練和測試。在這環節中，你的腰部疼痛部位將會接受不同程度的電刺激，除此以外，整個過程同第二節一致。總共需要耗時 3 小時。
研究員會帶領你進行每個環節的實驗程序。第二和第三環節中有較長的時間吃飯和休息。除此以外，你若在過程中感覺疲倦或不適時，你亦可稍作休息。
潛在危險及權利
縱使在實驗中涉及痛楚之刺激，我的身體將不會受到任何的損傷。參與本研究項目乃純屬自願性質。我有權利在任何時間及任何理由下終止實驗。

b. English Version

The Hong Kong Polytechnic University
Department of Rehabilitation Sciences
Research Project Information Sheet

Project title:
Orienting Attention for Pain Attenuation in Patients with Chronic Low Back Pain

Investigators:
Ms. JiaxinPeng, Prof. Chetwyn C. H. Chan; Dr. Sam C. C. Chan

Purpose of the study:
To investigate the effect of attention orientation on pain perception of people with chronic low back pain

Project information:

The study takes place in two days.

The study on the first day includes two parts. The first part is a screening session, in which, you need to complete a series of questionnaires concerning personal particulars, pain history, pain-related questionnaires, and cognitivefunction assessment. The second part is a training session, in which, you will receive a range of electrical stimuli transmitted by an electrical stimulatorat thenon-painful site and you will be trained to rate painful sensations and remember tactile sensations. The total time taken for completion will be 3-4 hours.

The study on the second day includes two parts as well. The first part is a training session which is similar to that in the first day, except that the stimulation site would be located at the pain-full body site at lumbar and orienting attention training would be added.The second part is the formal experiment session, in which you will be given different intensities of sensory stimuli and you will be required to generate different sensory imagery learned in the first part while electroencephalogram (EEG) is being recorded. The total time taken for completion will be 4 hours.

The study investigator will guide you through the procedures in all sessions. It will be provided with breaks in case of tiredness or discomfort.

Potential Risks and Rights:
Although the study involves painful stimuli, no damages to your body will be the consequence of the experiments and you will not experience any unnecessary painful sensation. Participation is completely on voluntary basis and you have the right to withdraw from study at any time or with any reason.

Appendix XII Pain History Questionnaire

有關病況的資料

1. (Duration)你腰痛咗幾久？_____年

2.(Reason)系點樣開始痛？_____

3.(Diagnose from Dr) 醫生診斷

3a 有沒有見過醫生，如果有，醫生診斷的原因是_____？

1）沒有，

2）有，Muscle and Ligament Injuries (sprain or strain) 肌肉或韌帶損傷

3）有，Spinal Nerve Irritation 神經壓迫

4）有，Lumbar Degeneration (Spondylosis,Spondylolisthesis, Spinal stenosis) 退化（椎关节强硬，脊椎前移，椎管狭窄）

5）有，Osteoporosis (collapsed vertebrae)骨质疏松

6）有，其他_____

3b (Body check)有沒有做過檢查？例如拍過 Xray / CT/MRI

1）沒有； 2）Xray； 3） CT；4）MRI

3c (Site)哪些位置疼痛？請描述如何疼（結合 body chart）

@ Lumbar :from Dr._____（範圍）self-claim._____（範圍）

@其它_____

4. (Intensity)疼痛的程度

4.aNow：0 系完全沒有痛楚，10 極度痛楚，你覺得你現在幾痛？ @ Lumbar: ___ @ _____

完全沒有痛楚 0 1 2 3 4 5 6 7 8 9 10 極度痛楚

Maximum：同樣，0 系完全沒有痛楚，10 極度痛楚，你最痛時幾痛？@ Lumbar: ___ @ _____

完全沒有痛楚 0 1 2 3 4 5 6 7 8 9 10 極度痛楚

Average：同樣，0 系完全沒有痛楚，10 極度痛楚，平均來講，最近 6 個月內你有幾痛？

@ Lumbar: ___ @ _____

完全沒有痛楚 0 1 2 3 4 5 6 7 8 9 10 極度痛楚

5. (Pattern)現在需要了解你最近 6 個月痛的情況，請問你的腰痛符合以下邊一種情況？

1）持續痛，痛的程度差不多

2）持續痛，有些時候會特別痛

3）有時候痛，平時不痛

4）平時不痛，但是有時會很痛（有點週期性）

6. 一般來說，你認為自己的健康狀況是．．．

1 極佳 2 非常好 3 好 4 普通 5 惡劣

7. 在**過去六個月內**，你有冇吃药？

1 没有 2 有药名_____

8. 在**過去六個月內**，你有冇見過下列的醫療專業人士？ **（留院期間次數不計）**

1. 精神科醫生 【 】1.沒有 【 】2.有，總共多少次 _____
2. 心理學家或心理輔導員【 】2.沒有 【 】2.有，總共多少次 _____
3. 社康護士 【 】1.沒有 【 】2.有，總共多少次 _____
4. 物理／職業治療師 【 】1.沒有 【 】2.有，總共多少次 _____

9. 在**過去六個月內**，你有冇去過急症室嗎？

【 】1.沒有 【 】2.有，總共多少次：_____

往急症室的原因：_____

10. 在**過去六個月內**，你總共留院（有過夜的）多少次？共多少晚？

【 】1.沒有 【 】2.有，總共多少次：_____ 總共多少晚：_____

原因：____

11. 你是否病人自助組織的會員？

□1. 是 □2. 否

Appendix XIII Chinese Version of Pain Self-Efficacy Questionnaire (PSEQ-HK)

即使痛楚，請評估你**現在**有幾多信心能夠做到以下的事情，請你在量表上，圈出適當的答案。
請記著，這問卷不是問你有沒有做過那些事情，而是**即使痛楚**，你現在有幾多信心能夠做到以下的事情。

		完全沒有信心						非常有信心
1.	即使痛楚，我仍能享受日常生活中的事物。	0	1	2	3	4	5	6
2.	即使痛楚，我仍能做大部份的家務。(如打掃、洗碗碟等)	0	1	2	3	4	5	6
3.	即使痛楚，我仍能與我的朋友或家人如常交往。	0	1	2	3	4	5	6
4.	在大多數情況下，我都能應付我的痛楚。	0	1	2	3	4	5	6
5.	即使痛楚，我仍能做一些工作。(「工作」包括家務、有薪金或無薪金的工作)	0	1	2	3	4	5	6
6.	即使痛楚，我仍能做很多我享受做的事情。(如我的興趣及娛樂活動)	0	1	2	3	4	5	6
7.	不用藥物，我仍能應付我的痛楚。	0	1	2	3	4	5	6
8.	即使痛楚，我仍能完成我生命中大部份的目標。	0	1	2	3	4	5	6
9.	即使痛楚，我能過一個正常的生活。	0	1	2	3	4	5	6
10.	即使痛楚，我能漸漸變得更加活躍。	0	1	2	3	4	5	6

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Appendix XIV The Mean and Standard Deviation for The Amplitudes and Latency of the ERPs During the experimental Task at Non-painful Site Among The Healthy Individuals and The Patients With Chronic Low Back Pain

a. For N1 component

			Amplitudes				Latencies			
			E_H		E_L		E_H		E_L	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD
F3	I_H	**Patients**	-3.3	4.3	-1.3	4.0	140.6	7.6	138.6	7.1
		Healthy	-3.0	6.1	-2.2	5.1	144.2	5.6	145.1	4.2
	I_L	**Patients**	-3.5	4.3	-0.7	3.6	141.7	7.3	139.6	7.4
		Healthy	-4.7	5.8	-1.7	4.5	145.1	4.8	144.8	5.3
FC3	I_H	**Patients**	-4.1	5.0	-1.8	4.5	139.7	7.0	137.8	7.5
		Healthy	-4.5	5.0	-2.5	4.4	142.0	6.1	142.8	5.7
	I_L	**Patients**	-4.4	5.2	-1.7	3.9	141.3	7.4	137.5	7.4
		Healthy	-5.6	4.9	-2.0	4.3	142.5	5.4	142.2	6.7
C3	I_H	**Patients**	-3.8	4.9	-1.5	4.1	140.5	7.7	137.8	8.0
		Healthy	-3.5	5.1	-2.4	4.4	139.7	7.1	140.3	6.6
	I_L	**Patients**	-4.2	5.0	-1.4	3.8	140.8	7.8	138.3	8.0
		Healthy	-5.0	4.6	-1.2	4.3	140.6	6.6	140.3	6.8
FZ	I_H	**Patients**	-3.3	5.0	-1.0	4.1	138.0	7.6	137.5	7.4
		Healthy	-4.3	5.6	-2.8	5.3	143.5	6.1	143.9	4.9
	I_L	**Patients**	-3.5	5.5	-0.8	3.9	138.3	8.1	138.0	7.8
		Healthy	-5.8	5.9	-1.9	4.7	143.2	6.3	142.7	6.6
FCZ	I_H	**Patients**	-3.4	5.9	-0.3	4.8	135.4	7.4	135.3	7.0
		Healthy	-4.1	6.1	-1.9	5.2	136.7	7.0	138.1	7.5
	I_L	**Patients**	-4.0	6.7	0.5	4.3	135.7	6.8	135.1	7.3
		Healthy	-5.9	5.2	-0.4	5.7	137.3	6.7	137.1	6.6
CZ	I_H	**Patients**	-0.5	7.7	2.1	5.7	135.0	7.7	134.9	7.1
		Healthy	-2.3	7.2	-0.2	5.7	134.5	5.9	135.5	6.8
	I_L	**Patients**	-1.6	8.3	3.2	4.3	136.1	8.3	134.8	7.4
		Healthy	-4.1	5.8	1.4	6.7	135.6	6.4	134.1	6.1
F4	I_H	**Patients**	-5.1	4.3	-3.3	4.2	140.5	7.4	139.5	7.4
		Healthy	-5.2	5.3	-4.3	4.9	144.0	5.0	144.2	4.6
	I_L	**Patients**	-5.9	5.5	-3.1	4.0	140.1	7.0	141.1	6.6
		Healthy	-6.3	5.1	-3.2	4.2	143.4	5.6	142.9	5.8
FC4	I_H	**Patients**	-5.7	5.2	-3.4	5.1	139.2	7.4	137.3	5.8
		Healthy	-5.8	5.2	-4.7	4.4	140.2	6.1	141.0	6.2
	I_L	**Patients**	-6.8	6.7	-3.2	4.4	137.9	6.8	139.5	5.9
		Healthy	-7.4	4.4	-3.5	3.8	140.0	5.6	139.6	5.4
C4	I_H	**Patients**	-5.5	5.3	-3.2	5.0	140.3	7.8	137.7	6.4
		Healthy	-4.6	5.0	-3.8	3.7	138.1	6.2	139.5	5.7
	I_L	**Patients**	-6.3	7.0	-2.9	4.3	139.6	7.6	139.5	6.8
		Healthy	-6.1	4.2	-2.9	3.6	138.6	5.6	137.9	5.0

b. For P2 component

			Amplitudes				Latencies			
			E_H		E_L		E_H		E_L	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD
F3	I_H	Patients	7.9	7.3	9.2	6.3	217.2	18.5	213.5	15.2
		Healthy	16.4	6.9	14.8	6.9	223.5	19.2	224.5	20.7
	I_L	Patients	9.3	6.7	10.0	6.2	218.8	17.1	217.5	12.8
		Healthy	14.1	5.5	14.4	7.5	226.7	20.6	225.8	22.1
FC3	I_H	Patients	10.2	6.3	11.3	6.0	221.1	19.5	218.4	21.2
		Healthy	17.1	7.6	16.6	7.9	228.4	13.3	224.0	20.9
	I_L	Patients	11.1	6.2	11.6	6.2	220.3	19.8	218.1	17.4
		Healthy	15.6	6.5	16.6	9.0	227.8	13.3	228.8	16.9
C3	I_H	Patients	12.1	6.9	12.8	7.3	217.0	16.4	219.9	23.1
		Healthy	19.5	9.1	17.9	8.2	232.6	18.5	228.7	19.3
	I_L	Patients	12.8	7.2	13.4	7.2	220.3	21.4	215.3	13.5
		Healthy	17.9	7.9	19.0	10.1	230.2	18.1	227.4	17.5
FZ	I_H	Patients	12.9	7.8	13.7	7.3	226.6	20.3	223.2	21.4
		Healthy	19.8	8.6	18.2	8.6	234.1	15.0	228.4	21.9
	I_L	Patients	14.5	7.8	13.5	7.1	230.7	22.1	215.8	13.4
		Healthy	17.8	7.2	18.1	9.1	233.3	16.6	231.2	20.6
FCZ	I_H	Patients	18.3	9.0	19.7	8.9	225.1	20.4	218.3	20.4
		Healthy	26.9	13.0	25.4	12.6	237.6	15.2	229.0	21.8
	I_L	Patients	20.0	9.1	20.2	9.9	232.3	21.3	217.9	18.5
		Healthy	24.5	11.8	26.2	14.2	235.2	15.4	229.5	21.0
CZ	I_H	Patients	20.7	8.9	22.0	8.2	218.4	16.9	217.9	20.7
		Healthy	29.5	13.6	27.4	13.0	239.2	17.7	225.4	20.8
	I_L	Patients	22.1	9.6	22.9	9.9	222.8	22.4	213.6	15.0
		Healthy	27.1	12.4	28.6	14.5	240.5	17.0	226.1	21.1
F4	I_H	Patients	8.8	6.5	9.4	6.1	218.1	19.1	212.7	16.8
		Healthy	15.7	7.7	13.5	7.0	233.3	15.6	230.7	19.8
	I_L	Patients	9.4	6.9	9.4	6.4	226.7	23.2	213.0	13.2
		Healthy	14.0	6.3	14.0	7.1	230.7	16.9	230.1	17.3
FC4	I_H	Patients	11.8	6.6	12.8	6.6	219.8	20.1	218.5	20.2
		Healthy	18.6	9.5	16.4	8.8	233.8	16.1	227.2	19.9
	I_L	Patients	12.8	7.5	13.1	7.3	226.8	24.1	213.3	12.6
		Healthy	16.8	8.2	17.0	9.2	230.7	19.5	227.8	17.8
C4	I_H	Patients	12.8	8.2	13.6	7.8	213.5	15.8	223.0	22.1
		Healthy	20.0	10.6	17.2	9.0	236.6	18.4	229.6	20.4
	I_L	Patients	14.3	9.0	13.9	9.1	225.7	24.2	213.8	14.9
		Healthy	18.3	8.9	17.9	9.8	235.8	21.6	228.2	19.3

c. For P3 component

			Amplitudes				Latencies			
			E_H		E_L		E_H		E_L	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD
F3	I_H	Patients	5.9	7.6	6.0	6.5	346.7	20.9	338.8	18.0
		Healthy	13.2	7.2	10.8	4.8	338.1	15.4	348.4	21.6
	I_L	Patients	7.5	7.9	4.9	6.9	345.9	22.7	348.7	21.3
		Healthy	11.7	5.4	10.5	5.4	335.8	21.2	342.1	19.5
FC3	I_H	Patients	8.9	6.1	8.0	5.9	339.5	21.6	339.8	20.8
		Healthy	15.0	6.7	12.4	4.7	330.7	15.5	346.2	22.8
	I_L	Patients	9.6	7.0	7.2	5.8	343.4	23.6	347.6	20.0
		Healthy	14.4	5.3	12.5	6.8	333.3	20.7	339.6	20.0
C3	I_H	Patients	11.1	6.9	9.5	6.4	338.5	21.8	343.9	20.7
		Healthy	18.1	8.8	13.5	4.8	328.6	13.9	340.6	22.4
	I_L	Patients	11.7	7.5	8.7	5.9	339.4	22.7	350.6	16.4
		Healthy	17.2	7.6	15.1	9.0	331.8	18.6	333.1	19.3
FZ	I_H	Patients	10.4	7.8	9.1	6.7	347.4	21.6	337.7	18.0
		Healthy	15.8	7.0	12.5	4.5	336.0	15.5	347.4	21.3
	I_L	Patients	12.2	9.2	7.5	7.1	338.7	21.8	351.5	24.2
		Healthy	14.8	5.1	12.9	5.7	335.5	21.7	343.2	20.9
FCZ	I_H	Patients	14.8	6.8	12.7	6.4	338.9	22.4	335.1	18.4
		Healthy	21.4	9.1	17.4	6.4	330.9	14.6	339.3	20.1
	I_L	Patients	16.4	8.1	12.0	6.9	340.5	23.1	343.3	20.2
		Healthy	20.5	8.1	18.7	10.3	331.5	18.9	337.0	20.2
CZ	I_H	Patients	17.0	7.7	14.0	5.6	340.1	23.3	341.8	18.7
		Healthy	24.4	9.5	19.4	6.4	328.2	12.9	335.3	18.6
	I_L	Patients	18.8	8.5	13.7	6.5	344.1	22.5	345.0	17.6
		Healthy	23.8	8.8	21.2	11.0	329.6	18.3	327.8	17.5
F4	I_H	Patients	6.8	6.4	5.3	5.3	350.1	24.4	343.0	20.6
		Healthy	12.6	6.8	8.9	3.9	334.4	17.0	346.8	22.0
	I_L	Patients	8.0	7.2	4.2	6.5	335.7	21.3	356.3	24.2
		Healthy	12.1	5.7	10.3	5.8	335.3	21.7	344.7	22.8
FC4	I_H	Patients	9.7	6.0	8.2	4.7	340.1	23.1	341.5	18.7
		Healthy	15.7	8.0	11.6	4.4	332.2	14.4	339.6	20.4
	I_L	Patients	10.8	7.3	7.4	5.1	340.7	22.7	356.1	22.0
		Healthy	15.2	7.0	12.8	7.0	329.6	18.0	335.2	20.5
C4	I_H	Patients	11.6	7.5	9.3	5.6	343.9	24.5	350.5	17.9
		Healthy	17.9	9.2	13.1	4.9	327.4	12.8	336.2	19.1
	I_L	Patients	13.0	8.0	8.6	5.7	342.0	23.2	356.4	17.7
		Healthy	17.8	8.4	14.8	8.5	331.5	19.0	332.8	19.6

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