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The Influence of Sex, Age and Psychological Traits on Experimental Heat Pain Experience

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For all my friends and my family

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ABBREVIATIONS

°C	Grad Celsius
ANOVA	Analysis of Variance
AUs	Action Units
BAS	Behavioral Activation System scales
BIS	Behavioral Inhibition System
BVP	Blood Volume Pressure
ECG	Electrocardiography
EDA	electrodermal activity
EEG	Electroencephalography
EMG	Electroencephalography
EMG_{corr}	Electromyography of *corrugator supercilii*
EMG_{trap}	Electromyography of *trapezius*
EMG_{zyg}	Electromyography of *zygomaticus major*
ERQ	Emotion Regulation Questionnaire
FACS	Facial Action Coding System
FDC	Facial distance change
FS	Fun-seeking
GSI	Global Severity Index
HRV	Heart Rate Variability
Hz	Hertz
IASP	International Association for the Study of Pain
IS	Interpersonal Sensitivity
ms	Millisecond
mV	Millivolt
Neo-FFI	Neo Five-Factor Inventory
NRS	Numerical Rating Scales
OC	Obsessive Compulsive
PA	Phobic Anxiety
PI	Paranoid Ideation
PSDI	Positive Symptom Distress Index
PST	Positive Symptom Total
s	Second
RR	Reward Responsiveness
SCL	Skin Conductance Level
SCL-90-R	Symptom Checklist-90- Revised

std	standard deviation
SVM	Support Vector Machine
P1	Pain threshold
P4	Pain tolerance threshold
VAS	Visual Analogue Scale
VRS	Verbal Rating Scales
PI	Paranoid Ideation
µS	Microsiemens
µV	Microvolt

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CHAPTER 1

INTRODUCTION

1.1 Forward

Although a common experience, pain is a complex phenomenon and a very personal sensation at the same time, and as a dynamic process, pain is always subjective and difficult to measure and interpret objectively (Melzack, 1988). According to the International Association for the Study of Pain (IASP), the definition of pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Merskey and Bogduk, 1994). According to this definition, the experience of pain is influenced by a combination of several factors which include cultural learning, the meaning of the situation, attention, the individual's thoughts and secondary behaviors, and other psychological variables (Melzack, 1988; Hadjistavropoulos et al., 2011; Craig, 2018).

To better understand pain, the biopsychosocial model of pain arose during the 1980s, which incorporates physiological, psychological, and social factors associated with pain, and highlights the connection between the mind and body when interpreting the pain experience (Duncan, 2000). Based on this popular model, a recent review of the definitions of pain highlighted pain as "a distressing experience associated with actual or potential tissue damage with sensory, emotional, cognitive, and social components" (Williams and Craig, 2016). This definition supports the easy use of experimental (artificial) pain stimulation for experimental and clinical research and the application of brief and clearly defined pain stimulation. Furthermore, it underscores the physiological processing of pain, incorporates the essential subjectivity of pain experience and the crucial social influence on pain communication, especially at an advanced level, and takes the emotional component as a significant understanding of pain.

1.2 Physiology of pain

As a complex experience, the perception of pain and its thresholds are the final result of the complicated interactions between the sensory of the noxious input, personality, emotional, cultural, and behavioral factors (Williams and Craig, 2016). Noxious stimuli that can potentially induce damage (e.g., thermal, mechanical, electrical, or chemical stimuli) elicit pain by acting on nociceptors which are free, unencapsulated peripheral nerve endings widely found in most tissues of the body including the skin, blood vessels, deep somatic tissue (e.g., muscles and joints) and the viscera (Bridgestock and Rae, 2013; Bourne, Machado and Nagel, 2014). Two main types of nociceptors respond to noxious stimuli. C-fiber polymodal nociceptors are the most numerous type and respond to different modes of stimuli including mechanical, thermal (general above approximately 45°C), and noxious chemical stimuli (Bridgestock and Rae, 2013). The other primary type of nociceptors is Aδ-

fibres. C-fibres (<2 mm diameter) are unmyelinated with slow conduction (<3 m/second) and associated with slow pain which is perceived as a dull, poorly localized, and burning type of pain; while Aδ-fibres with a diameter of 2-5 mm are thinly myelinated and are more rapidly conducting (5-30 m/second) associated the fast pain which is perceived as a shorting-lasting, pricking type of pain (Machado and Nagel, 2014). The information from nociceptors is relayed via the spinal cord to the brainstem and thalamus, then in the spinothalamic tracts to the brain, and connections between the thalamus and higher cortical areas of the brain control the perception of pain and integrate the response to pain. The widely distributed cerebral activities indicate the complex nature of pain involving discriminative, affective, autonomic, and motor components (Bridgestock and Rae, 2013).

Many different studies have shown that pain can induce changes in the autonomic nervous system. Heart rate variability (HRV) has been reported to correlate with pain intensity, and it is considered as an objective pain assessment variable (Jeanne et al., 2009; Boselli et al., 2014). Loggia et al. (2011) found EDA increased with more intense painful stimulation evoked by heat in healthy volunteers and it is more sensitive to relative changes in perception than heart rate, and Chapman et al. (2001) discovered the same performance of EDA in pain elicited by electrical stimulation. Storm (2008) suggested that EDA can detect nociceptive pain fast and continuously, specific to the individual, with higher sensitivity and specificity than other available objective methods. Guglielminotti et al. (2013) reported that changes in pupil diameter and pupillary dilatation reflex correlated with pain brought about by a uterine contraction, however, the clinical application of this method remains uncertain along with issues of practicality, especially in uncooperative patients (Cowen et al., 2015).

Treister et al. (2012) conducted the first study to compare a combination of multiple autonomic parameters and each parameter alone in their ability to differentiate among four categories of heat pain intensity (No, low, medium, and high pain). Electrocardiogram (ECG), blood volume pulse (BVP), and EDA were recorded, and the following parameters were extracted and calculated: heart rate, HRV, EDA, number of EDA fluctuations, and BVP amplitude. The results indicated that all the parameters successfully differentiated between no pain and all other pain categories, but none of the parameters differentiated between all three pain categories (i.e., low and medium; medium and high; low and high). In contrast, the linear combination of parameters significantly differentiated not only between pain and no pain but also between all pain categories. Ben-Israel et al. (2013) replicated the study of Treister et al. (2012) in patients under general anesthesia, and also found the superiority of a multiparameter approach over any individual parameter in the evaluation of pain. These studies suggest that a multiparameter model based on autonomic nervous system changes could be a reliable tool for pain assessment.

1.3 Conventional diagnosis of pain

Outside research in the clinical setting, the examining therapist has to rely on the patients' subjective statements of their pain as a conventional diagnosis of pain. Currently, a person's self-report is the most reliable measure of pain, i.e. the patient is asked to quantify the experienced pain (Prkachin, Solomon and Ross, 2007). Usually, this kind of measurement

is acquired by the description of pain intensity, pain relief, pain interference, pain quality, pain site, affect/unpleasantness, and the temporal aspects of pain, among which pain intensity accounts for the majority suffering of the pain and is recognized as one of the most relevant clinical dimensions of the pain experience (Frampton and Hughes-Webb, 2011). To measure pain intensity reliably and validly, a large number of pain measurement tools have been invented, and patients are asked to rate their pain on one-dimensional scales that can transform patients' subjective pain intensity into numerical values. The most often used conventionally diagnostic tools make use of verbal descriptions, visual analog metaphors, and numeric rating.

Verbal Rating Scales: the VRS has been used for nearly 70 years and includes lists of descriptors that represent different degrees of pain intensity. The least intense descriptor is usually given a score of 0, and the more intense the pain, the higher the score. The patient chooses the most appropriate descriptor from the list, and the chosen descriptor is the number associated with the patient's pain intensity score. The four-point VRS is most widely used clinically, and the five-point scale is usually used for treatment outcome study (Frampton and Hughes-Webb, 2011).

Visual Analogue Scale: the VAS is considered to be one of the best methods available for the estimation of the intensity of pain, which usually consists of a 10-centimeter-long line, anchored at the ends by two descriptors: "no pain" on the extreme left and "the worst possible pain" on the extreme right. The patient is asked to put a mark on the line that can best indicate the intensity of their perceived pain at the time of completion or over the previous time interval (e.g., the past 24 h). The distance from the "No pain" end to the marked point is measured as the score of the pain intensity (Frampton and Hughes-Webb, 2011).

Finally, the Numerical Rating Scale is similar to the VAS, which also consists of a numerical scale, but the difference is that the former's estimate point is changeable, from 0 to 100 (101-point scale), 0 to 10 (11-point scale), or 1 to 10 (10-point scale), with 0 or 1 represents no pain and 100 or 10 represents the worst pain. Patients are informed to write down or present the number which can best describe their pain intensity (Salaffi, Sarzi-Puttini, and Atzeni, 2015).

1.4 Methods of experimental pain stimulation

As pain is the most prevalent health care problem and characterization of pain is essential in the diagnosis and choice of treatment (Melzack, 1988; Prkachin, Solomon and Ross, 2007), the development of human experimental pain models are of importance and essential in studying the pain mechanisms. In experimental pain stimulation models, nature, localization, intensity, frequency, and duration of the pain are controllable during the experimental stimulation, which can present quantitative measurements of the psychological, behavioral, or neurophysiological responses of pain (Olesen et al. 2012). Experimental pain stimulation can be conducted through different tissues which include skin, muscle, viscera, and the stimulations of skin are extensively used, because of the easy access to the skin (Olesen et al. 2012). According to Reddy et al. (2012), there exist four different kinds of pain

stimulation methods for the skin, which include mechanical stimulation, electrical stimulation, chemical stimulation, thermal stimulation.

1.4.1 Mechanical stimulation

Mechanical stimulation methods of the skin can be grouped into three categories, which include touch (assessed by applying light pressure with a von Frey hair or a finger; pinprick (by stimulating the skin gently with a needle or thick von Frey filaments; and pressure (induced by pressure algometers) (Curatolo, Petersen-Felix and Arendt-Nielsen, 2000; Reddy et al., 2012; Olesen et al., 2012). The advantages of these methods are that the stimulation of pressure can be reproducible and precise and that the pain response can be measured quantitatively (Olesen et al. 2012). However, each method has limitations: for touch, this kind of light stimulation cannot elicit pain, and it can only explore allodynia (Curatolo, Petersen-Felix and Arendt-Nielsen, 2000), furthermore, von Frey hair stimulation is not specific which activates both low threshold mechanoreceptors and nociceptors (Le Bars, Gozariu and Cadden, 2001); for pinprick and pressure, the onset and termination of pain are both too rapid to be easily controlled (Olesen et al. 2012).

1.4.2 Electrical stimulation

Many stimulator devices connected to electrodes can evoke electrical stimulation through the application to the skin surface or the intracutaneous tissue (Reddy et al., 2012). The advantages are that the electrical stimuli are easily controlled on-line and off-line by digital systems, and stimulator devices can produce various stimulation paradigms with different waveforms, frequencies, and durations, which are used to activate different afferents and nervous structures selectively, and hence evoke various pain sensations (Olesen et al. 2012). This stimulation method is suitable for neurophysiological assessments of the pain (Olesen et al. 2012). The limitations are that electrical stimulation bypasses the receptors and activates the nerve fibers directly which cause a loss of information on receptor functioning in the periphery, and the method is not a specific activation of the nociceptors (Reddy et al., 2012; Olesen et al., 2012).

1.4.3 Chemical stimulation

Capsaicin, as the pungent agent of chili peppers, is one of the most usually used chemical pain induction methods, which can evoke pain and hyperalgesia by intradermal injection or direct application via central and peripheral mechanisms (Olesen et al. 2012). Capsaicin-induced pain has been considered as a substitute model to represent changes observed in neuropathic pain (Reddy et al., 2012). Another stimulation material is mustard oil, as a topical application, the topical administration of which can induce a burning pain as well as secondary allodynia and hyperalgesia in the surrounding unaffected area, similar to the topical capsaicin administration (Curatolo, Petersen-Felix and Arendt-Nielsen, 2000). The advantages of chemical stimulation include that these experimental models inducing allodynia and/or hyperalgesia have been used to show the effect of analgesics, and can be used to investigate the effect and mechanisms of drugs as they can produce long-lasting allodynia and hyperalgesia for up to several days (Reddy et al., 2012; Olesen et al. 2012). The limitations are: these models induce not only allodynia and/or hyperalgesia but also

inflammatory responses (Le Bars, Gozariu and Cadden, 2001), besides, inducing allodynia and/or hyperalgesia are more difficult to control with respect to reproducibility compared with the phasic pain models (Curatolo, Petersen-Felix and Arendt-Nielsen, 2000; Olesen et al. 2012).

1.4.4 Thermal stimulation

Cold

Cold stimulation can be conducted by ice, a cold gel bag, a wet alcohol sponge, or a cooling thermode to the skin. In addition, immersing the forearm or other extremities in ice water can induce the formation of cold pressor pain (Olesen et al. 2012). The advantage is that warming and cooling are considered to be conveyed by different peripheral nerve fibers, so the measurement of the threshold for warming and cooling can be used to study the functional integrity of these fibers which are inaccessible to clinically electrophysiological investigations (Staahl et al., 2009). The limitations include that the stimulation response is influenced mainly by the vascular reactions and cold pressor pain has shown variable results in the measurement of pain threshold, withdrawal threshold, and subjective pain in some subjects, moreover, there exists no standardization of the duration of extremity cooling and how the response is rated (Kumar Reddy et al., 2012; Olesen et al. 2012).

Contact heat

Heat pain can be evoked by heat/cold contact stimulators. To prevent injuries to the skin, the stimulating temperature should be controlled with a high limit of 50 °C and a low limit of 5 °C (Kumar Reddy et al., 2012). The advantage is that this method can evoke pain rapidly with an adjustable heat pulse. The limitations are that the comparisons between different experiments are difficult as the intracutaneous temperature profiles may rely on wavelength or type of contact stimulator (Handwerker and Kobal, 1993).

Laser

As a particular light source, laser pulses can evoke heat pain in the skin by noncontact radiation pulses emitted by CO_2 lasers, thulium lasers, or diode lasers (Arendt-Nielsen and Chen, 2003). An advantage of the utilization of laser is that eliciting lots of energy fast to the skin controllably and reproducibly can be conducive to study quantitative sensory testing; another is that this method avoids direct contact to the skin with a merely thermal stimulation (Arendt-Nielsen and Chen, 2003; Kumar Reddy et al., 2012; Olesen et al. 2012). The limitations include that different responses between the individuals have been reported, and all laser equipment is expensive and cumbersome (Staahl et al., 2009; Olesen et al. 2012).

1.5 Facial expressions of pain

During the social communications of human beings, facial expressions transport lots of information, particularly for the expressions of emotions and pain (Craig, 2018). The research on facial expressions of pain got more and more attention recently, and a general agreement has been made that facial activities during pain are not unspecific grimacing but

convey pain-specific information, and it is characterized by substantial inter-individual differences (Williams, 2002; Hadjistavropoulos et al., 2011).

Most studies on emotion and increasingly on pain utilizing facial expressions have used the Facial Action Coding System (FACS), which is based on anatomical analysis of facial movements and distinguishes 44 different action units (AUs) produced by single muscles or combinations of muscles. FACS is considered the criterion standard when decoding facial expressions, including the facial expression of pain, and numerous studies reported a set of actions, which tend to occur consistently during acute pain and acute exacerbation of persistent pain (Craig, Prkachin and Grunau, 2011). A more recent research conducted by Kurz and Lautenbacher (2014) revealed that there is no uniform set of facial actions, but instead, there are at least four "faces of pain" during pain, which include: (1) narrowed eyes with furrowed brows and wrinkled nose; (2) opened mouth with narrowed eyes; (3) raised eyebrows; and (4) furrowed brows with narrowed eyes. Some studies suggest that there is no prototypical facial expression of pain; instead, more and more researchers in this area have agreed on the existence of several facial expression patterns during pain stimulation (Craig, Prkachin, and Grunau, 2011; Kurz and Lautenbacher 2014; Craig, 2018).

However, several shortcomings of FACS have been reported from the studies on facial expressions of pain, which include that manually coded action units from the FACS system is too time-consuming for pain assessment, and it is not objective enough; moreover, it is definitely influenced by the observer's own subjective factor, the relationship between the observer and the subject and the subjects' facial attractiveness; besides, it cannot effectively detect faked facial expressions from genuine expressions of pain (Craig, Prkachin and Grunau, 2011; Bartlett et al., 2014). For these reasons, the automatic recognition methods of facial expressions in pain have become more and more necessary and promising.

1.6 Objective measurements of pain experience

As an important experience, pain has shaped human evolution and helps us to avoid dangerous stimuli (Williams, 2002). Pain assessment is a key point in the pain study, especially fundamental to measure the existence and severity of pain in clinical settings.

As the current "gold-standard" pain measurement methods, self-report scales are the most often used tools in experimental and clinical pain study (Frampton and Hughes-Webb, 2011). The VRS, VAS, and NRS are the three most commonly used tools to assess pain intensity. The main advantage of these three tools is that they are relatively quick and straightforward to use, but the validity of these tools depends on the administration method and the instructions given to patients (Frampton and Hughes-Webb, 2011; Salaffi, Sarzi-Puttini and Atzeni, 2015). Moreover, this kind of self-report measurement is a subjective description of patients' pain intensity which cannot allow for objective comparison with other patients. Besides, these tools are not available for small children and patients with cognitive impairment (Frampton and Hughes-Webb, 2011).

For the purpose of assessing pain intensity in cognitively impaired people, a variety of observational measurement tools have been developed and used in clinical practice and

research; however, most studies have indicated that these tools have failed to gain validity and reliability (Hadjistavropoulos, 2005). Developing an objective measurement method for pain intensity detection should be essential and necessary (Cowen et al., 2015; Gruss et al., 2015, Werner et al., 2017).

Cowen et al., (2015) conducted a comprehensive review and divided the objective parameters of pain measurements into five groups, which include autonomic nervous system changes; biopotentials; neuroimaging parameters; biological markers, and composite algorithms. Neuroimaging methods are currently less applied, as they need expensive equipment and take long measurement time with an easily affected image (Cowen et al., 2015). As for biological markers, until now it still lacks enough evidence to support its objectivity and practicality for pain assessment (Cowen et al., 2015). Composite algorithms that integrate several parameters from changes of the autonomic nervous system and other biopotentials provide a substitute choice (Treister et al., 2012; Ben-Israel et al., 2013; Gruss et al., 2015). Besides, with the application and advancement of facial expression recognition technology, automatic composite algorithms encompassing the facial change information can be another objective tool for pain measurement (Bartlett et al., 2014; Werner et al., 2017).

1.6.1 Objective measurements of pain experience via biopotentials

Biopotential refers to the electric potential, which is measured between points in living cells, tissues, and organisms, and is produced by electrochemical activity in a specific class of excitable cells (Reilly and Lee, 2010). Biopotentials can be measured as electrocardiography (ECG), electroencephalography (EEG), or electromyography (EMG).

EEG signal amplitudes are thought to correlate with nociceptive stimulus intensity and can reflect both peripheral and central processing of nociceptive inputs, however, the measurement methods of EEG are remaining within the research setting and need further development in the extraction process and computation for the clinical application of assessment of pain in the future (Cowen et al., 2015).

Facial muscles are innervated by cortical motor pathways and brainstem emotive pathways, and the universal facial expressions can be recorded during a pain stimulation in a conscious individual (Prkachin, 1992). Facial EMG, especially the corrugator supercilii and the zygomatic major, present an increased activity during painful stimulation; additionally, trapezius, which can indicate a high-stress level is also thought to correlate with pain (Gruss et al., 2015). The measurements of the biopotentials of the three muscles may be helpful for the assessment of pain.

1.6.2 Objective measurements of facial expressions during pain

Based on computer vision and machine learning techniques, several automatic systems for facial recognition in pain have been developed. The Computer Expression Recognition Toolbox (Bartlett et al., 2014), the Active Appearance Models (Cootes, Edwards, and Taylor, 2005) and the Supervised Descent Method (Xiong and De la Torre, 2013), Automatic Pain Recognition with Facial Activity Descriptors (Werner et al., 2017) have been employed and reported to be more objective and can acquire the dynamics of facial expressions in pain, and can be more sensitive to little changes and grasp more complex dynamics than FACS.

In the future, the automatic recognition systems of facial expressions will be more and more popular for the assessment of pain in both experimental and clinical settings and should need better improvement (Bartlett et al., 2014; Werner et al., 2017).

1.7 The influence of sex and age on pain experience

1.7.1 The influence of sex on pain experience

In clinical settings, more females complain about pain with more frequent clinical visits compared with males (Fillingim et al., 2009; Mogil, 2012; Bartley and Fillingim, 2013). In the experimental area, many research results support that females are more sensitive to pain with lower pain threshold and tolerance. However, a critical 2012 review failed to find clear and consistent sex differences in pain perception across all stimulation modalities, which suggested that females and males have comparable thresholds for cold and ischemic pain but females can tolerate less pressure and thermal pain (Racine et al., 2012a). In terms of the sex difference in facial responses of pain, little research has explored the problem. Kunz et al. conducted a facial encoding of 40 healthy participants during tonic heat stimulation and found that there was no difference between males and females in the facial expression of pain (Kunz, 2006). However, females seem to be better at decoding facial expressions of pain (Keogh, 2014), and there are sex differences in the encoding and decoding of facial expressions of emotions (Kring and Gordon, 1998; Thompson and Voyer, 2014). Concerning the sex differences in the physiology of pain, the previous studies failed to support sex-related differences in heart rate and skin conductance level during experimental pain (Racine et al., 2012b), besides, there is no study exploring the sex difference in EMG activity during experimental pain.

1.7.2 The influence of age on pain experience

The clinical implications indicate that chronic pain prevalence increases with aging, which can be conceptualized as reductions of the functional activities in the pain system (Gibson, Farrell, 2004). Therefore, it is hypothesized that age-related changes also exist in experimental pain. As for experimental pain perception, a recent systematic review firmly concluded that aging reduces pain sensitivity for lower pain intensities (Lautenbacher, 2017), besides, the decrease of heart activity was confirmed in the older population (Abhishekh, 2013; Lautenbacher, 2017; Holzman and Bridgett, 2017), however, the age-related facial expression of pain was not reported, and Kunz et al. (2008) found that during pressure-induced and electrical induced pain older participants presented no different facial expression compared with the young.

1.8 Psychological traits and pain

1.8.1 Psychological traits and chronic pain

As a prevalent condition, population studies suggest that between 11% and 30% of individuals experience chronic pain at some point in their lives (Whal, 2009), and

psychological comorbidity is a frequent complication of chronic pain, which can strongly influence the prognosis and course of chronic pain (Tunks, Crook, and Weir, 2008). Engel (1959) presented the theory of "pain-prone patients" who are more prone than others to use pain as a psychic regulator with several psychological features including "depression, or pessimism, or conscious and unconscious guilt, or suppressed hostility, or masochistic character structure, etc. A wealth of researchers have tried to identify the relationship between psychological traits and chronic pain, and a growing number of studies indicate that certain personality characteristics such as high hypochondriasis, hysteria, neuroticism, and depression, are related to chronic pain (Conrad, 2013).

Based on the study of the influence of specific psychological traits on chronic pain, recently more and more researchers tried to identify several particular personality types of chronic pain. Chronic pain is found to be significantly related to several personality types (see Table 1), which include Type D personality (Cond D, 2013; van Middendorp, 2016), a neuroticism personality profile (Esteban, 2012), Cluster C personality disorders (Gustin, 2015) and a personality profile characterized by a heavy emotional burden (Montoro and del Paso, 2015). These findings may help to improve the psychological treatment of chronic pain and shift the treatment target from a sensory and psychological state focused to a personality type focused and may lead to more comprehensive treatment outcomes (Gustin, 2015).

Undoubtedly, many studies have suggested that there exists a relationship between affective, cognitive, and behavioral patterns and the experience and maintenance of pain. However, the hypotheses related to the interaction between pain and personality issues are somewhat contradictory. A review conducted by Vendrig concludes that psychological problems could mediate chronic pain, but not acute pain (Vendrig, 2000), whereas the majority of the results suggests that personality can mediate acute pain to an extent (Pud et al., 2006; Klauenberg et al., 2008; Paine et al., 2009). Indeed, this dispute indicates caution in generalizing the influence of personality on chronic and acute pain and in understanding why the interaction of personality and pain may vary between acute and chronic pain conditions. Compared with the healthy population, patients with chronic pain have relatively elevated scores on specific psychological traits such as pessimism, moody, anxiety, and depression (Gustin, 2015), and are more likely to score higher on items related to introversion, sensitivity, and emotional vulnerability (Conrad, 2013). However, Borchgrevink et al. (1997) studied the neck sprain patients with a long recovery period and found that the patients did not differ from each other on any of the Millon Clinical Multiaxial Inventory scales at intake or 6-month follow-up, and this finding was interpreted as evidence against the role of personality factors in the development of chronic pain and as indicative of a more indirect etiology. Although it is a common sense that pain is flexible and varies depending on the psychological state, the cause-and-effect relationship between psychological traits and chronic pain is still widely under debate.

TABLE 1. The recent finding of the specific personality types related to chronic pain

Author(s)	Year	Findings
Condin, Leppert, Ekselius, et al.	2013	Boys and girls with a Type D personality or the "distressed personality" characterized by negative affectivity and social inhibition had an approximately 2-fold increased odds of

		musculoskeletal pain and 5-fold increased odds of psychosomatic symptoms. There was a strong association between Type D personality and both psychosomatic symptoms and musculoskeletal pain where adolescents with a type D personality reported more symptoms.
Esteban, Ortuba, Izquierdo, et al.	2012	High scores in the depression, anxiety, and emotional instability scales primarily characterized by a neuroticism-related personality profile are found in neck pain patients.
Gustin, Burke, Peck, et al.	2015	Irrespective of type, chronic pain may be associated with Cluster C personality disorders characterized by significantly higher scores in Harm Avoidance and significantly lower scores in Self-Directedness.
Holley, Law, Zhou, et al.	2013	Chronic pain and depressive symptoms were significantly associated over time in adolescents, changes in pain intensity are predictive of subsequent depressive symptoms, but changes in depressive symptoms had less impact on subsequent pain in youth.
Mongini, Rota, Evangelista, et al.	2009	A specific personality profile characterized by a heavy emotional burden may increase the affective dimension of chronic pain with respect to a depressive profile, a converse profile, or a normal profile, independent of sex, age, and pain level and type.
Tavallaii, Kargar, Farzanegan, et al.	2010	Patients with a high score in hysteria and hypochondriasis trait had intense pain according to VAS.
Montoro and del Paso	2015	Patients with Fibromyalgia syndrome exhibited higher levels of neuroticism and psychoticism but not extroversion, neuroticism may only play a minor role in clinical manifestations of Fibromyalgia syndrome, and extraversion appears to exert a protective influence in Fibromyalgia syndrome, as it is associated with better health outcomes in several domains
van Middendorp, Kool, van Beugen, et al.	2016	Type D personality was present in 56.5% of patients with fibromyalgia, which exceeds prevalence estimates in general, cardiovascular, and chronic pain populations. Negative affectivity alone and combined with social inhibition was associated with worse mental and, more limited, physical health.

1.8.2 Psychological traits and experimental pain thresholds

Many studies have investigated the association between pain and psychological traits, but it remains unclear whether an individual's psychological profile contributes to the particular pain experience, or if previous pain experience influences a specific psychological profile (Tillisch, 2009). Translational studies of experimental pain models have tried to solve this problem in a standardized healthy population measuring the psychological tests as well as basic physiology of experimental pain. It may be possible to find an association between psychological traits and experimental pain.

Table 2 presents the recent researches regarding the influence of psychological traits on experimental pain induced by four mainly pain stimulation methods. Parts of these studies identified the association between pain catastrophizing and the experience of experimental

pain. Pain catastrophizing can be defined as the tendency to focus on pain and negatively evaluate one's ability to deal with pain, which is considered as a trigger for the development of acute to chronic pain and also has an essential influence on acute pain (Edwards, 2006; Swinkels-Meewisse, 2006). Not surprisingly, pain catastrophizing is determined by the psychological traits of individuals and a link between personality and pain catastrophizing has been acquired (Edwards, 2006; Helsen and Goubert, 2013; Schrooten, Karsdorp, and Vlaeyen, 2013). The rest of the studies focused on the influence of personality traits, anxiety, or depression on the experimental pain, but several contradictory findings were reported. A critical systematic review conducted by Hansen et al. (2015) explored the association between psychological variables and pain in experimental pain models, and with a strict excluding criterion, twenty-nine studies which investigated 45 different psychological tests and 27 different types of pain models were included into the qualitative analysis. A total of 16 studies indicated that psychological variables might predict the level of pain, seven studies found divergent results, and six studies found no significant relationship between psychological traits and experimental pain. As a result, the conclusion made by Hansen et al. (2015) is that psychological variables may have a predictive association with experimental pain, but firm conclusions are not possible, due to extensive heterogeneity in pain models and psychological tests.

TABLE 2. The recent findings of the relationships between psychological traits and different experimental pain models

Pain model	Psychological test method	Findings
Heat pain models		
Breimhorst et al. 2012	NEO-FFI, CSQ, and PCS	No significant correlation between pain intensity and unpleasantness and psychological variables.
Edwards et al. 2006	Situation-specific PCS	No significant difference in heat pain threshold and pain tolerance when comparing high and low catastrophizers. High catastrophizers had higher ratings of suprathreshold thermal pain stimuli and more significant increases in pain across repeated stimuli.
Quiton et al. 2008	Trait anxiety inventory, Trait-positive and Trait-negative affect scale, BDI, Kohn reactivity scale, Insomnia questionnaire, CSQ	No significant correlation between psychological variables and individual variability sensitivity.
Helsen et al., 2013	PCS, FPQ, IUS, IRI, PANAS	Pain catastrophizing moderated the relationship between stimulus type and pain unpleasantness and pain intensity, IUS, trait FPQ, and IRI were associated with enhanced pain intensity. Participants with higher intolerance of uncertainty, trait fear of pain, or fantasy reported more pain unpleasantness and higher pain intensity.
Granot et al. 2006	STAI, PCS	A significant correlation between the absolute difference in pain scores of tonic heat stimulation and pain catastrophizing. A significant correlation

		between trait anxiety and absolute difference in pain ratings following repetitive-phasic stimuli, and tonic heat stimulation. A significant correlation between state anxiety and absolute difference in pain ratings and percent change in pain ratings.
Cameron, 2011	Minnesota Multiphasic Personality Inventory (MMPI)	A significant negative relationship between hysteria and pain threshold and a positive relationship between gender inversion and pain threshold.
Electrical pain models and the nociceptive flexion reflex		
Schrooten et al. 2013	PCS	Higher levels of catastrophizing were associated with shorter electrocutaneous stimulus duration.
Lin et al. 2013	PCS, BDI, Modified Dental Anxiety Scale, Revised Dental Belief Survey	A significant correlation between increased pain ratings modulated by unpredictability and pain catastrophizing score.
Ruscheweyh et al. 2013	PCS, Catastrophizing self-statement task	No significant correlations between Pain catastrophizing assessed before the pain stimulus and pain thresholds, nociceptive flexion reflex, or temporal summation of pain. Pain ratings and nociceptive flexion reflex were significantly reversibly increased by catastrophizing self-statements task. Temporal summation ratios of pain perception were not affected by catastrophizing self-statements.
Terry et al. 2012	The Anxiety Sensitivity Index-Revised	Anxiety sensitivity was positively correlated with affective pain ratings and temporal summation of pain.
Cold pressor models		
Hanssen et al., 2013	PCS	Pain intensity was significantly lower in the induced optimism group compared to the control group. Regression analyses demonstrated that situational catastrophizing is a strong predictor of reported pain intensity.
Goodin et al. 2011	BDI, Standard and situation specific PCS	Standard catastrophizing was significantly correlated with pain intensity. Situation-specific catastrophizing was significantly correlated with reports of pain intensity, unpleasantness, and pain tolerance.
Forsythe et al., 2011	PCS, The Pain Appraisal Inventory	Univariate tests indicated that pain catastrophizing was positively associated with pain intensity and pain unpleasantness. Univariate tests indicated that threat/harm appraisals were inversely related to tolerance time, and that challenge appraisals were positively related to tolerance time.
Muscle injury models		
Lee et al. 2013	Eysenck Personality Questionnaire-Revised, PANAS, STAI, FPQ, PCS, Anxiety Sensitivity Index, Somatosensory	The high negative emotionality subgroup reported significantly higher local pain intensity compared with the low negative emotionality subgroup. The highest negative emotionality subgroup reported the greatest local pain and hyperalgesia relative to either

	Amplification Scale, Whiteley index	the high fear only or low negative emotionality subgroups. Referred pain incidence was 2.2 times more likely to occur in the high negative emotionality subgroup compared to the low negative emotionality subgroup.
Akhter et al, 2014	PCS, Mcgill questionnaire, DASS	Pain intensity, unpleasantness, perceived area, and pain rating were significantly higher in high PCS during HS vs. low PCS. High catastrophizers also had slower jaw movements than low catastrophizers during HS-infusion.
Parr et al., 2012	Fear of Pain Questionnaire, PCS, Tampa Scale of Kinesiophobia	Fear of pain was a significant predictor of pain prior to pain induction, and pain catastrophizing was a significant predictor of pain intensity after pain induction.

Abbreviations: DAS, Dysfunctional Attitude Scale; NEO-FFI, Neuroticism-Extraversion-Openness Five-Factor Inventory; CSQ, Coping Strategies Questionnaire; PCS, Pain Catastrophizing Scale; BDI, Becks Depression Inventory; STAI, State-Trait Anxiety Inventory; IUS, Intolerance of uncertainty; IRI, Interpersonal reactivity index; PANAS, Positive and Negative Affect Schedule; FPQ, Fear of Pain Questionnaire.

Compared with the study of chronic pain, experimental pain study conducted in the healthy population may obtain objectivity in a replicable environment; however, the analysis of the association between psychological traits and experimental pain performance is still a humongous challenge and current literature does not yet present a clear picture. As suggested by Tillisch (2009), standardized pain models, carefully precise evaluation of methodology, careful processing and interpretation of data, and application to large healthy samples are necessary for the advance of this research area.

1.8.3 Psychological traits and objective experience of experimental pain

The research on facial expressions of pain have been got more and more attention, and a general agreement has been made that facial activities during pain is not unspecific grimacing but conveys pain-specific information, which may be crucial for survival by signaling the experience to others, and it is characterized by substantial inter-individual differences (Williams, 2002; Hadjistavropoulos et al., 2011; Karmann, Lautenbacher and Kunz, 2015). Among the variables influencing the facial expression of pain, psychopathology plays an important role (Davies et al., 2016). However, only a few studies have researched the facial expressions of experimental pain in patients with mental disorders. A study conducted by Lautenbacher et al. (2017) found that one of the key facial responses of pain (contraction of the eyebrows) was significantly increased in patients with major depression disorder, besides; a recent review concluded that facial emotional expressivity decreased in individuals with different non-psychotic disorders (Davies et al., 2016). For healthy people, to date, less is known about whether personality traits are responsible for regulating the degree of facial experimental pain expression, as only a 2015 study found that self-evaluated impulse control does not have a significant relationship with the degree of facial pain expressiveness in healthy participants (Karmann, Lautenbacher, and Kunz, 2015).

1.9 Research questions and hypotheses

The first objective of this study was to investigate the relationships between sex and experimental heat pain experience, which include the influence of sex on pain thresholds, biopotentials, and facial expression of pain. Except for the sex difference in pain thresholds, previous studies with traditional measurement tools either did not find sex-related facial pain expression or did not explore the sex difference in biopotentials of pain. Thus, the present study systematically explores the sex difference in the objective experience of pain with the employ of several biopotential measurements and automatic facial expression assessment.

Hypothesis 1a: females should be more sensitive to heat pain.

Hypothesis 1b: the facial EMG activities of females will be stronger than males during the pain thresholds.

Hypothesis 1c: the facial expression change of females will be larger than males in pain.

The second goal of this study was to explore the influence of age on experimental pain experience. As studies of the sex difference in pain, little is known about the age-related change in the objective experience of pain. Based on the previous studies and the influence of aging on physical function, it may exist age-related change in pain.

Hypothesis 2a: older people will have a higher pain threshold compared with their young counterparts.

Hypothesis 2b: the biopotentials of pain may decrease with aging.

Hypothesis 2c: the young will present more facial expressiveness during pain than the elderly.

The third aim of the present study was to find the influence of psychological traits on the experience of experimental pain. Many psychological traits such as personality, behavioral activation and inhibition systems, emotion regulation strategies, and self-reported psychological symptom tendencies, are measured.

Hypothesis 3a: the psychological traits will influence the pain thresholds in the experimental setting.

Hypothesis 3b: the psychological traits may explain some individual variances of biopotentials of pain.

Hypothesis 3c: the psychological traits will be related to the facial expression of experimental pain.

CHAPTER 2

MATERIAL AND METHODS

This chapter describes the experiment procedure, which includes the pain induction method, the measurements, and the extraction of biopotentials, the measurements, and the extraction of facial expressions, and the acquisition of psychological traits from four questionnaires.

2.1 Participants

A total of 96 participants were recruited for the experiment, and all the samples were equally divided into three age groups: age group 1 (18-35 years), age group 2 (36-50 years), and age group 3 (51-65 years), and with a balanced gender distribution. Recruitment was performed through notices posted at the University of Ulm for age group 1 and through advertisement in local newspapers for age groups 2 and 3. The study was conducted in accordance with the ethical guidelines set out in the WMA Declaration of Helsinki (ethical committee approval was granted: 196/10-UBB/bal). The study was approved according to the ethics committee of the University of Ulm (Helmholtzstrasse 20, 89081 Ulm, Germany). All participants provided written informed consent to participate in this study before the experiment and received monetary compensation of 70 Euro.

Exclusion criteria: Before the experiment, the case history of each applicant was assessed in order to identify persons who met the exclusion criteria. Only healthy subjects were recruited. Pre-existing neurological conditions, chronic pain, cardiovascular diseases, regular use of pain medication, and use of pain medication immediately before the experiment were applied as exclusion criteria.

2.2 Pain induction method

For pain induction, a tonic heat stimulation elicited by a MEDOC PATHWAY thermode (see Figure 1) was used at the beginning of the experiment. A tonic heat stimulation method has several advantages, which include that it resembles clinical pain more precisely than experimental phasic pain in the areas of pain quality, temporal pattern, and underlying physiologic mechanisms, and it is helpful to study facial expression changes during pain condition with changeable stimulus intensity, and it causes least possible differences in the subjective experience (Handwerker and Kobal, 1993; Lautenbacher, Roscher and Strian, 1995).

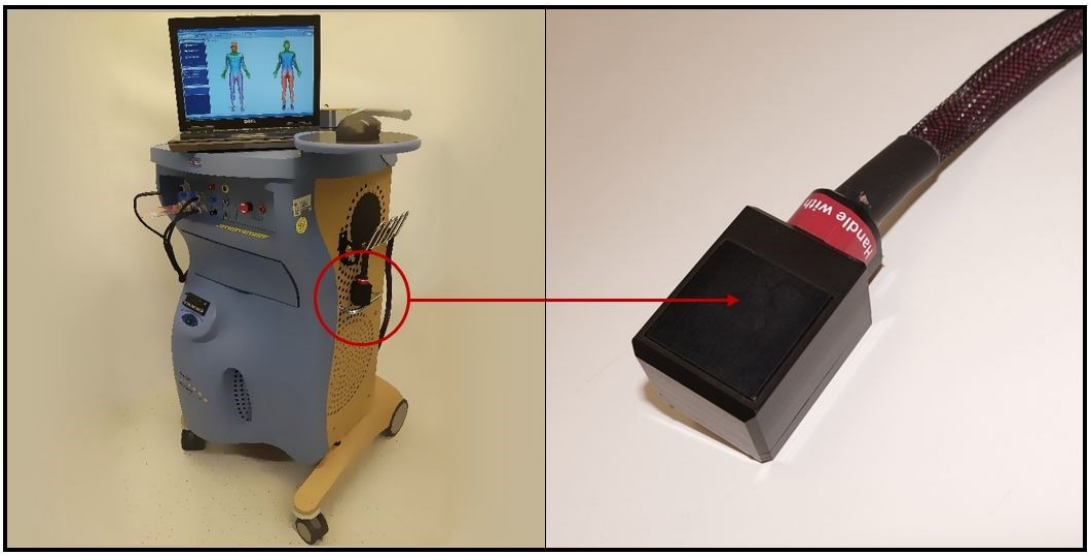

Figure 1: MEDOC PATHWAY thermode with its thermode head (right) (Reprinted with permission from Gruss, 2015).

During the induction, all the participants sat in a steel chair with a computer mouse held in the left hand, and the thermode was attached to their right arms (see Figure 2). This technology can provide a controllable quantified pain level and can prevent skin burns. The heating temperature is not allowed to above 50.5°C.

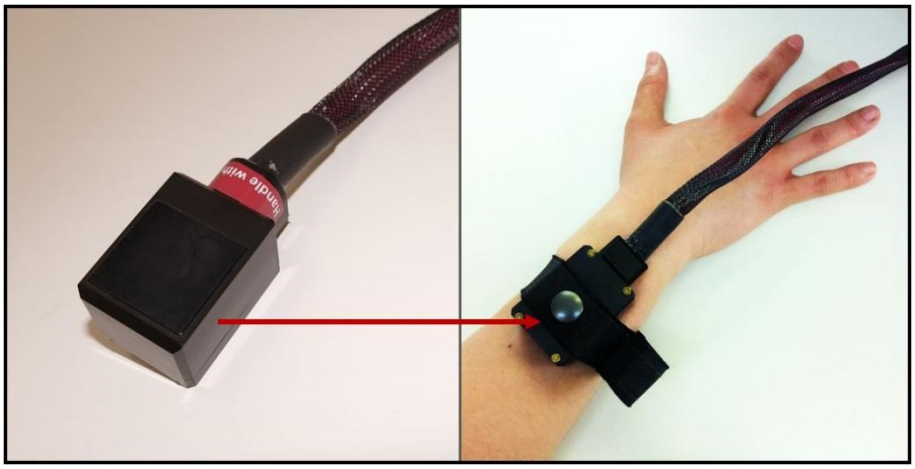

Figure 2: Attaching the thermode head on the right forearm of participants (Reprinted with permission from Gruss, 2015).

The baseline temperature (no pain) was 32°C and the ramp rate is 1°C /s with a negligible interstimulus interval. The heating temperature which can cause a feeling of warm sensation was defined as the detection while participants were instructed to press a button. For the measurement of pain threshold (P_1), participants were told as follows: "Please press the stop button immediately when you experience a burning, stinging, piercing or pulling sensation

in addition to the feeling of heat." For the measurement of pain tolerance threshold (P_4), the following instruction was given: "Please press the stop button immediately when you can no longer tolerate the heat, taking into account the burning, stinging, piercing or pulling sensation." Furthermore, for each participant, two other intermediate pain thresholds (P_2 and P_3) were calculated according to this formula:

$$P2 = P1 + \frac{P4 - P1}{3} \quad \text{und} \quad P3 = P1 + 2 * (\frac{P4 - P1}{3})$$

The four pain levels (P1-P4) were programmed into the thermode software, and each participant was stimulated randomly with these four pain thresholds. Each pain threshold was induced 20 times. The duration of the pain stimuli was maintained for 4 s independent of the pain intensity, while the pauses between stimuli were randomized between 8 and 12 s.

2.3 Measurements of pain parameters

To assess pain experience objectively, biopotentials of psychophysiological changes and facial expression changes of each participant were measured during experimental pain stimulation.

2.3.1 Measurements of biopotentials

The acquisition of the psychophysiological data in this experiment was carried out by a NeXus-32 amplifier from the Dutch company Mind Media (www.mindmedia.info). Electromyography (EMG), electrocardiogram (ECG), electrodermal activity (EDA) were measured continuously over the whole experimental pain stimulation (Walter et al., 2013). Moreover, the Biotrace software was applied, which allows a visual representation of the signals with the verification of the functionality and quality of the used electrodes, and offers a variety of options for uncomplicated recording, processing, and analysis of signals (see Figure 3).

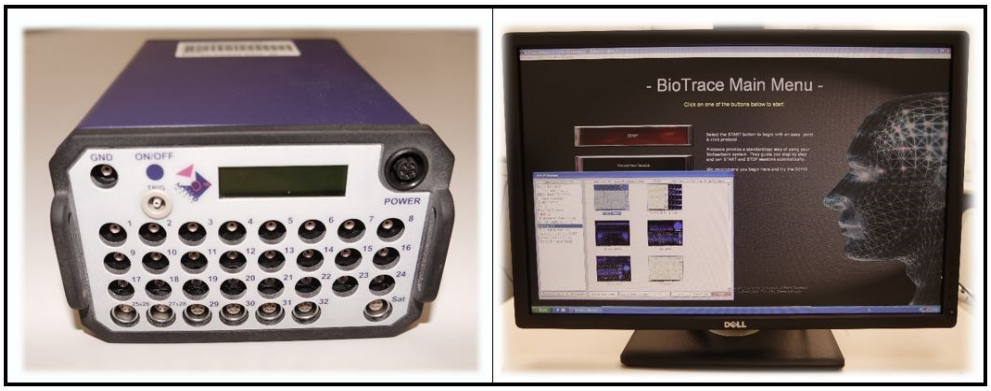

Figure 3: NeXus-32 amplifier with related Software BioTrace+ (right) (Reprinted with permission from Gruss, 2015).

For the measurements of EMG, 2-channel NeXus-EXG-Sensors were applied to record the zygomatic major, corrugator supercilii, and trapezius (see Figure 4). Electrical muscle activity is considered as an indicator of general psychophysiological arousal, as an increased muscle tone is associated with an increasing activity of the sympathetic nervous system, while a decrease in somatomotor activity represents excitation of the parasympathetic nervous system. Two electrodes were attached on the corrugator supercilii and two on the zygomatic major, which are both considered as the facial muscles. The former draws the brow downward and medialward to form a frown, while the latter elevates the corners of the mouth superiorly and posteriorly, and both are expected to be active during the pain experiment (Walter, 2013). Another two electrodes were attached on the right trapezius, which extends from the occipital bone to the lower thoracic vertebrae and laterally to the spine of the scapula. The activity of the trapezius is an indicator of a high-stress level and also to be expected during pain stimulation (Johnson et al., 1994; Gruss et al., 2015).

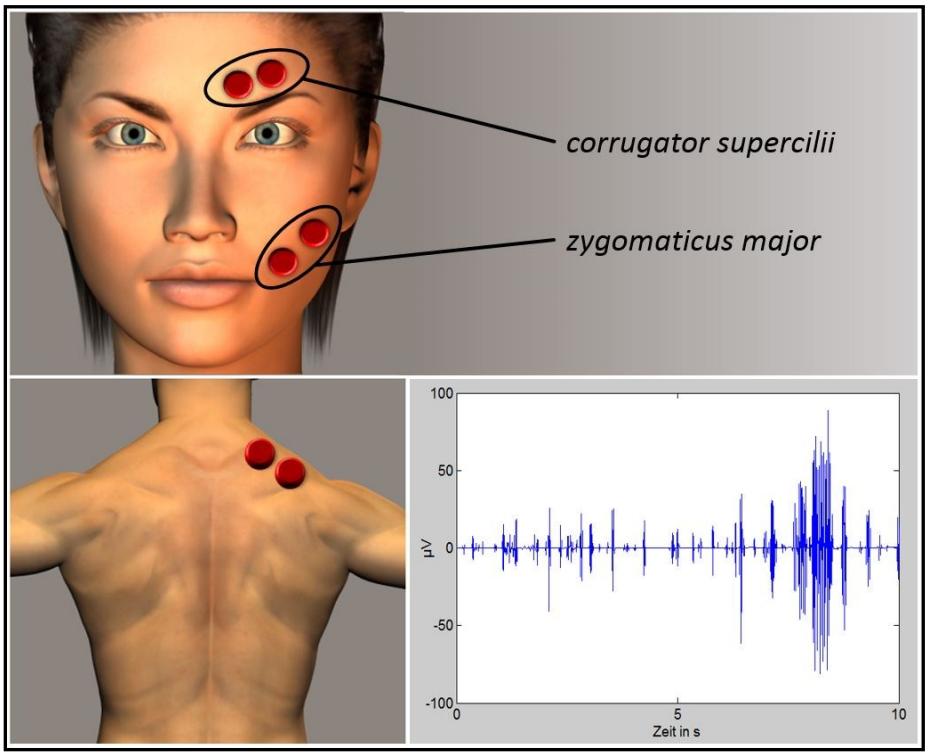

Figure 4: Graphical EMG demonstration. *Above*: electrode placement of facial EMGs; *left below*: electrode placement of the neck EMG; *right below*: Typical EMG signal. EMG = electromyography, µV = microvolts, s = second (Reprinted with permission from Gruss, 2015).

For the measurements of EDA, two Ag/AgCl electrodes connected to the NeXus-GSR-Sensors were positioned on the index and ring fingers of the left hand of the participants (see Figure 5). The EDA is very sensitive to the increased sweat secretion with an increased electrical skin conductance. As the sweat glands are innervated exclusively sympathetically (without the influence of the parasympathetic nervous system), so the EDA is thought to be a good indicator of the "inner" tension of a person (Chapman et al., 2001). The skin conductance is measured in microsiemens (µS), as a slow biopotential, which can be

observed with a rapid increase within 1-3 s after the onset of a stress stimulus and this kind of low voltage change can be recorded by two finger electrodes.

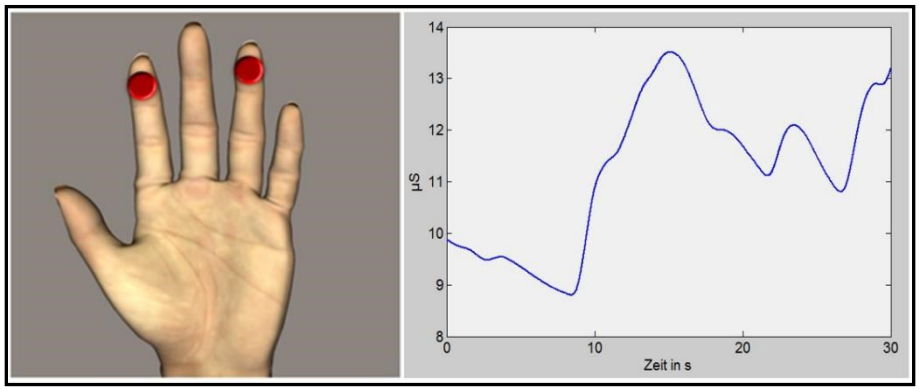

Figure 5: Graphical EDA demonstration. *Left*: Placement of electrodes for recording the EDA; *Right*: Typical EDA raw signal. µS = microsiemens, s = second (Reprinted with permission from Gruss, 2015).

For the measurements of ECG, 2 electrodes connected to the NeXus EXG-sensor were used for recording the ECG, one of which was placed on the right side of the upper body just below the collarbone, the other of which was attached on the last third rib of the left side (Figure 6). Common ECG features include heart rate, interbeat interval, and HRV, the last one of which represents the oscillation of the interval between consecutive heartbeats and is considered as an indication of mental effort and stress in adults (Kim and Andre, 2008).

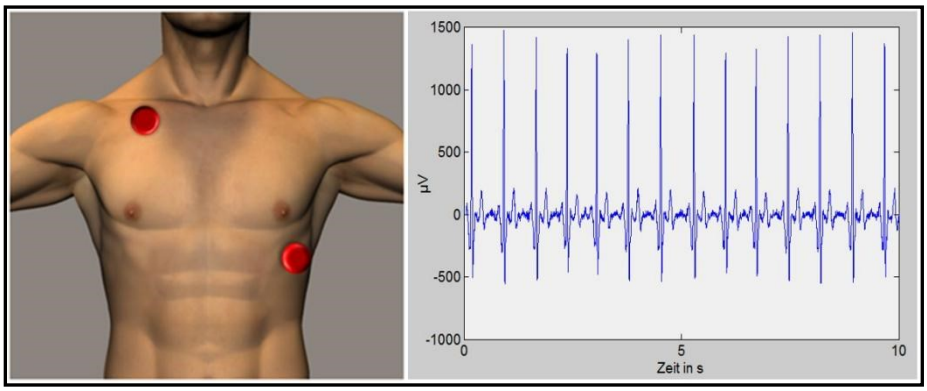

Figure 6: Graphical ECG demonstration. *Left*: Placement of electrodes for recording the ECG; *Right*: Typical ECG raw signal. µV = microvolts, s = second (Reprinted with permission from Gruss, 2015).

2.3.2 Measurements of facial expression changes

For facial expressions recording, three AVT Pike F145C cameras were applied with a frame rate of 25 Hz and a resolution of 1388 x 1038 colored pixels. One camera was positioned directly in front of the participant, and the other two were placed at both sides in case the participant turned his/her head 45°to the left or right. Moreover, a Kinect Sensor fixed above the frontal Pike camera was employed to record depth maps (640 x 480 pixels, ca. 30 Hz), color images (1280 x 1024 pixels, ca. 10 Hz). The Kinect also provided the associated timestamps. The Pike and Kinect video streams were synchronized with the biopotential biofeedback (see Figure 7).

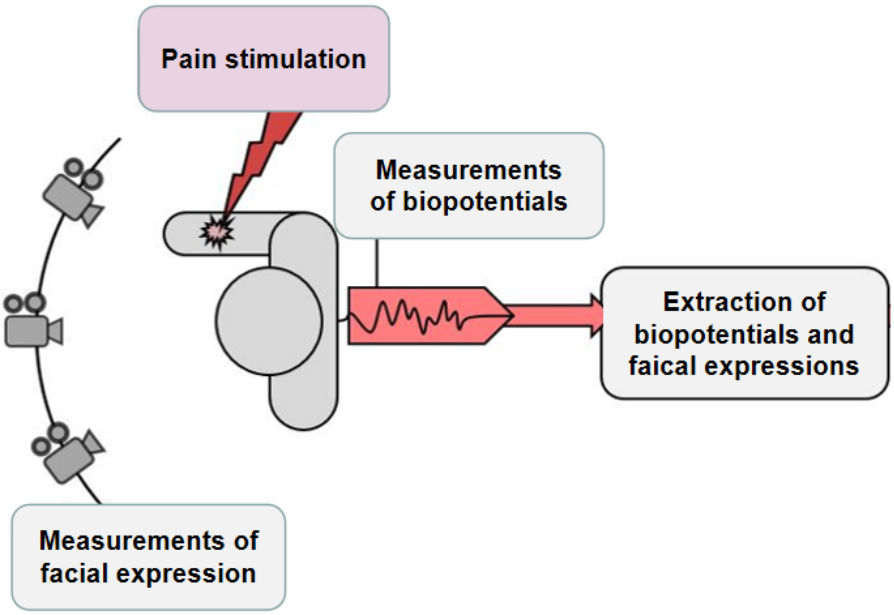

Figure 7: Measurements and extraction of pain parameters.

2.4 Extractions of pain parameters

2.4.1 Extraction of biopotentials

According to Gruss et al. (2015), the biopotentials preprocessing includes the following steps:
1. Visualize all biopotentials to check the intensity of the noise and activity concerning pain stimulation.
2. Apply a Butterworth filter to the EMG (20-250 Hz) and ECG (0.1-250 Hz) signals.
3. Applied an additional filter using the Empirical Mode Decomposition technique for the EMG.
4. Quantified the pain level caused by the heat stimulus during the "pain window" (5.5 s) and the baseline level during the "non-pain window" (see Figure 8).
5. Detected bursts of EMG activity using the Hilbert Spectrum.

The feature extraction followed the procedure developed in the emotion lab of Ulm University (Gruss et al. 2015). The following biopotential features were extracted: 1.amplitude (Σ= 40), 2. frequency (Σ= 24), 3. stationarity (Σ= 24), 4. entropy (Σ= 20), 5. linearity (Σ= 8), 6. variability (Σ= 19), 7. similarity (Σ= 24). The total number of features (Σ= 159) were normalized by z-transformation for each individual (Gruss et al. 2015). The dataset of the study is available at https://www-e.uni-magdeburg. de/biovid/. It includes the raw and preprocessed signals, as well as the extracted features.

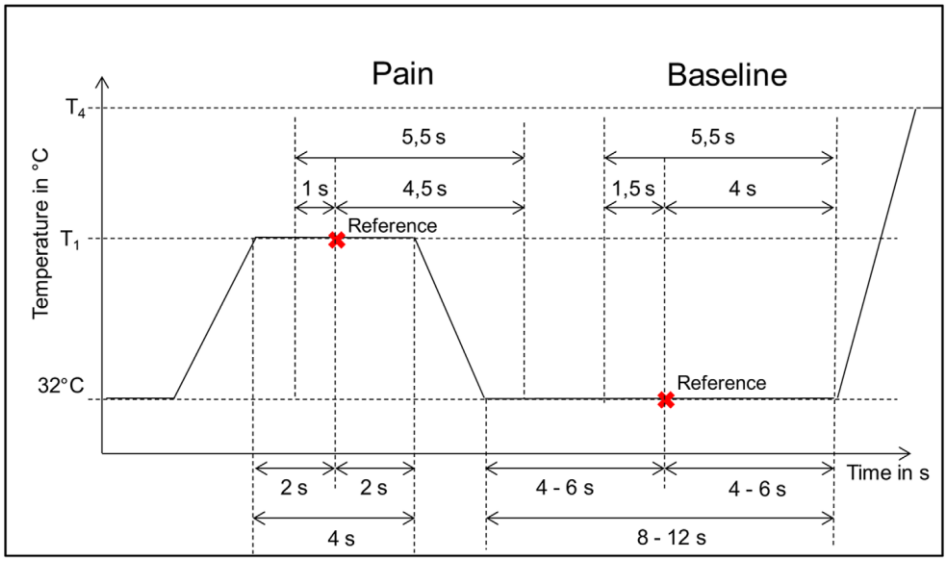

Figure 8: Graphical description of pain quantification (s = seconds, T1 = temperature of pain threshold, T4 = temperature of pain tolerance threshold.

2.4.2 Extraction of facial expression data

With the BioVid Heat Pain database (Walter et al., 2013), Werner et al. (2017) conducted the extraction of facial expression features. The landmarks of the face (see Figure 9a) were detected and tracked automatically with the application of the publicly available state-of-the-art software IntraFace and the Haar-like feature detector during a time window. Besides, a variant of the Iterative Closet Point algorithm was utilized to obtain the 3D position and 3D orientation (see Figure 9b). Based on the 3D landmarks, a set of facial expression features were obtained to represent pain associated facial actions containing lowering of the brows, tightening of the lid, closing of the eyes, raising of the cheeks and the upper lip, wrinkling of the nose, and stretching and opening of the mouth. These 3D distance features were calculated by the distance between brows and eyes, brows and mouth, eyes and mouth, as well as the width and height of the mouth and so on (see Figure 9c), and the 3D gradient features measuring the texture of the facial changes were calculated by the mean gradient magnitude of these regions (see Figure 9d) (Werner et al., 2014; 2017).

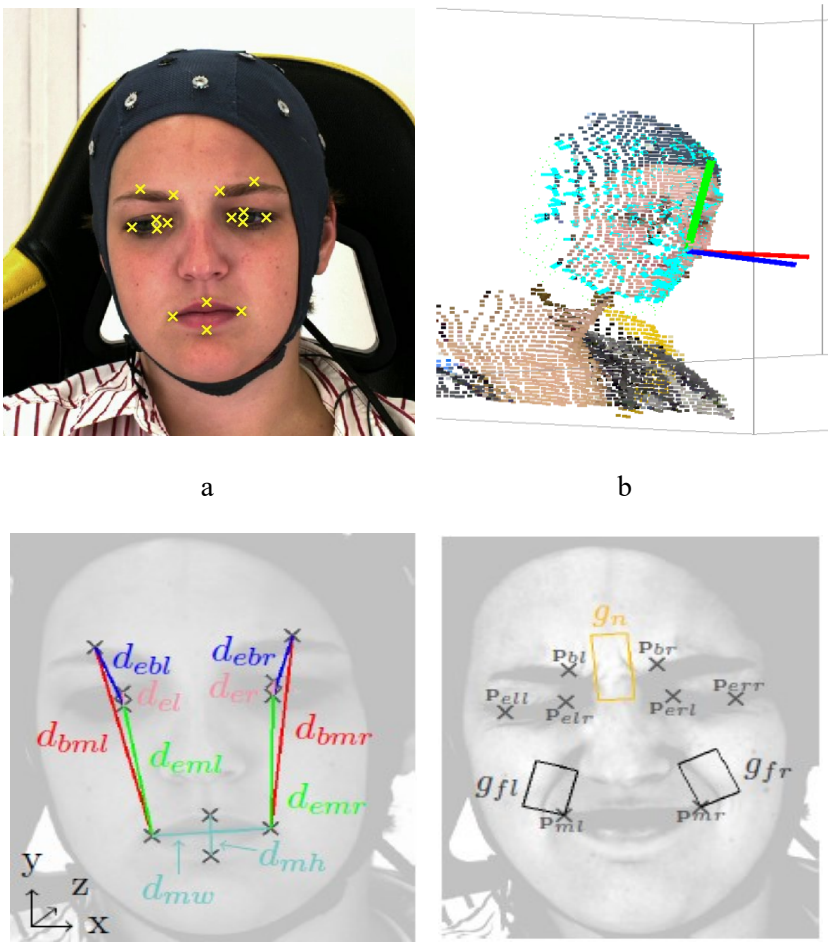

Figure 9: Facial landmarks and facial expression features. a: Used subset of the IntraFace landmarks; b: Measured 3D point cloud (from Kinect); c: 3D distance features; d: Gradient feature regions with anchor points. (Photo reprinted with the consent of the person depicted)

The descriptions of the facial expression features are presented in Table 3, for each of these features, Werner et al. (2017) considered the corresponding time series obtained from all frames during a time window length of 5.5 seconds. In each time window, each feature was automatically calculated 138 times, as each level of the pain stimulations was randomly repeated 20 times in this experiment, therefore, for each pain level each feature was automatically calculated 2760 times.

TABLE 3. Description of 3D facial expression features.

Facial expression feature	Description
$d_{bml/r}$	Left/Right brow/mouth closeness
$d_{eml/r}$	Left/Right eye/mouth closeness
$d_{ebl/r}$	Left/Right eye/brow closeness
d_{mw}	Mouth width
d_{mh}	Mouth height
$d_{el/r}$	Left/Right eye closeness
$g_{fl/r}$	Left/Right nasolabial folds
g_{n}	Nasal wrinkles
$d_{bml/r}$	Left/Right brow/mouth closeness

With the utilization of the Random Forest conditional variable importance, Werner et al. (2017) analyze the importance of the feature signals. The most important feature signal is the brow-to-mouth closeness $d_{bml/r}$, which is persuasive, as this signal describes two important pain-related facial actions at once: lowering of the brows and raising of the cheeks. The eye-to-brow closeness $d_{ebl/r}$, which measures the lowering of the brows, has the second importance. However, the eye-to-mouth closeness $d_{eml/r}$ is considered unimportant, probably because it does not add much information as the two features of brow-to-mouth and eye-to-brow have already been applied, and it can degrade the feature quality when the participate blinks. The nasal wrinkling g_n is the most useful texture-based measure with a high contribution. The deepening of the nasolabial folds $g_{fl/r}$ is rated lower, which is probably a result of out-of-plane rotations that disturb this measure (occlusion by nose and overlap with background) observed by Werner et al., (2017). Mouth width d_{mw} and mouth height d_{mh} have a moderate rating, which is in accordance with the previous results that facial actions like lip pulling, lip stretching, and mouth opening can also be observed during pain (Prkachin, 1992; Craig, Prkachin and Grunau, 2011), but these two features get less consistently than other facial actions. Eye closure $d_{el/r}$ gets a low rating, which indicates that eye closure is less specific to pain than other pain-related facial actions, which is in line with the observations

that some participates often close their eyes during no-pain experimental conditions (Werner et al., 2017).

Furthermore, compared with the recent relevant literature about the assessment of facial expression of pain using FACS (Prkachin, 2009; Craig, Prkachin and Grunau, 2011; Kunz and Lautenbacher, 2014), a total of nine facial expression features were elected to assess to the facial expression of pain. The table below describes the features with their corresponding Action Units. The 3D distances between the landmarks of the face were measured with a unit of "mm", while the measurement of nasal wrinkling g_n depended on the Pixel intensity without a physical unit.

TABLE 4. Descriptions of the chosen 3D facial expression features.

Facial expression features	Description	Action Unit with description
$d_{bml/r}$	Left/Right brow/mouth closeness	4+12 (Brow lower+Lip corner pull)
$d_{ebl/r}$	Left/Right eye/brow closeness	4 (Brow lower)
d_{mw}	Mouth width	20 (Horizontal mouth stretch)
d_{mh}	Mouth height	25+26+27 (Mouth open)
$d_{el/r}$	Left/Right eye closeness	6+7 (narrowed eyes)
g_n	Nasal wrinkles	9+10 (Nose wrinkle+uppper lip raiser)

In order to better represent the changes of participants' facial expressions during different pain levels, change of each facial expression features (C) was calculated, which equals facial expression feature during pain minus facial expression feature during Baseline: C = d(P) - d(B), for example, to obtain the change of left brow-to-mouth closeness d_{bml} during pain threshold (P_1): $C_{bml}(P_1) = d_{bml}(P_1) - d_{bml}(B)$. Besides, a new variable "Facial change" (FC) was defined as "the sum of changes of facial expression features except for the change of nasal wrinkling", which was used to describe the total distance change of participants' facial expressions.

2.5 Measurements of psychological traits

Before the pain stimulation experiment, each participant's psychological traits were tested by four questionnaires, which comprise the Neo Five-Factor Inventory (Neo-FFI), the

Behavioral Inhibition System/Behavioral Activation System scales (BIS/BAS), the Emotion Regulation Questionnaire (ERQ), and the Symptom Checklist-90-Revised (SCL-90-R).

Neo-FFI is a standardized personality inventory for measuring Five-Factor personality traits. It includes scales of neuroticism, extraversion, openness, agreeableness, and conscientiousness (McCrae and Costa, 1987). Neuroticism describes the degree to which an individual typically experiences negative affects, including sadness, anger, embarrassment, and guilt. Extroversion describes the degree to which an individual is characterized by socialization, assertiveness, activity, and positive emotionality. Openness to experience refers to imagination, curiosity, aesthetic responsiveness, and intellectual independence. Agreeableness describes cooperativeness, altruism, empathy, and straightforwardness. Conscientiousness describes planfulness, organization, self-discipline, and dutifulness (McCrae and Costa, 1987). Neo-FFI contains 60 items with 12 items per trait and takes 10 to 15 minutes to complete (McCrae and Costa, 2004). The Five-Factor model of personality has become one of the dominant theories in personality psychology research, and Neo-FFI has been proved to be a reliable, valid, and useful instrument during a decade of application in different contexts and cultures (McCrae and Costa, 1987, 2004).

BIS/BAS scales are used to assess the individual difference in the sensitivity in the behavioral inhibition system (BIS) and the behavioral approach system (BAS), which comprises a total of 24 items with 4 fillers (individual difference). According to Gray's two motivational systems underlying behavior and affect, the aversive motivational system is called BIS which is sensitive to signals of punishment, non-reward, and novelty and inhibits behavior that may lead to negative or painful outcomes, and it is also responsible for the experience of negative feelings such as fear, anxiety, frustration, and sadness in response to these cues; BAS controls the appetitive motivation, which is sensitive to signals of reward, non-punishment, and escape from punishment, and is responsible for the experience of positive feelings such as hope, elation, and happiness (Gray, 1990). In these scales, seven items measure BIS, and BAS is divided into three subscales, namely Drive, Fun-seeking, and Reward responsiveness measured by the remaining thirteen items.

ERQ is a 10-item scale designed to assess individuals' tendency to regulate their emotions with two emotion regulation strategies: cognitive reappraisal and expressive suppression (Gross and John, 2003), which is one of the first instruments for the investigation of emotion regulation processes with good reliability and validity (Abler and Kessler, 2009). Cognitive reappraisal is a form of cognitive change that involves construing a potentially emotion-eliciting situation in a way that changes its emotional impact, and expressive suppression is a form of response modulation that involves inhibiting ongoing emotion-expressive behavior (Gross and John, 2003).

SCL-90-R is a widely-used 90-item self-report symptom inventory for measuring psychological symptoms and psychological distress invented by Leonard R. Derogatis in the late 1970s (Hardt, Gerbershagen and Franke, 2000). It consists of nine symptom subscales which are labeled as Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism, respectively. In addition, it also measures three global scores which are referred to as the

Global Severity Index (GSI), the Positive Symptom Distress Index (PSDI), and the Positive Symptom Total (PST). As one of the most widely used questionnaire in clinical practice and research, SCL-90-R is considered as a useful tool for measuring psychological status, measuring the change in outcome studies, or screening for mental disorders, which has shown impressive reliability and validity in Germany (Schmitz et al., 2000). Furthermore, it is often usefully included in the evaluation of chronic pain patients (Hardt, Gerbershagen, and Franke, 2000).

2.6 The strategy of analysis

The following elaborates the analysis method: firstly, all the experimental variables including psychological traits, pain thresholds, biopotentials, and facial expression changes, were tested whether they are normally distributed; second, to analyze the sex difference in thresholds, biopotentials, and facial changes during pain, T-test was employed; third, to test the age difference in pain experience, Kruskal-Wallis H Test and correlation analysis were employed; finally, to examine the influence of psychological traits on pain experience, correlation analysis, and regression analysis were used.

CHAPTER 3

RESULTS

This chapter of results includes three parts: (1) The influence of sex, age, and psychological traits on experimental pain threshold and tolerance; (2) The influence of sex, age, and psychological traits on psychophysiological responding under experimental pain stimulation of different intensity; (3) The influence of sex, age and psychological traits on facial expressions of experimental pain.

3.1 The influence of sex, age, and psychological traits on experimental pain thresholds

3.1.1 The influence of sex and age on experimental pain thresholds

Two participants were excluded from the analysis because of the missing of the measurements of pain threshold and tolerance, and the rest 94 participants were included in the analysis. The sex and age information of all the participants is described in Table 5.

TABLE 5. Description of the sex and age information of the sample (m = males, f = females, M = mean, SD = standard deviation, mean and standard deviation in years).

Age group	94 Participants		2 Excluded participants	
	m (n = 47)	f (n = 47)	m	f
1 (18-35 years)	18 (M = 24.72; SD = 3.01)	17 (M = 23.94; SD = 2.30)	0	0
2 (36-50 years)	14 (M = 42.57; SD = 4.69)	16 (M = 42.06; SD = 4.28)	1 (38 years)	0
3 (51-65 years)	15 (M = 58.87; SD = 4.84)	14 (M = 58.57; SD = 5.03)	0	1 (62 years)

In terms of comparing the sex difference in pain thresholds, Mann-Whitney T test was employed. Table 6 represents the average temperature for pain threshold (M = 46.47°C, SD = 2.57°C) and pain tolerance (M = 49.79°C, SD = 1.67°C), and describes the pain thresholds in the sex groups. There was a nearly significant difference between males (M = 46.88°C, SD = 2.46°C) and females (M = 46.03°C, SD = 2.58°C) for pain threshold ($p = .073$), and a significant difference was found between males (M = 50.21°C, SD = 0.61°C) and females (M = 49.35°C, SD = 2.19°C) for pain tolerance threshold ($p < .001$).

TABLE 6. Description and comparison result of pain thresholds in sex groups (P1 = pain threshold, P4 = pain tolerance threshold, m = males, f = females, M = mean, SD = standard deviation).

Pain level	All	Gender groups		Mann-Whitney T test	
		m	f	Z	p
P1 (°C)	M = 46.45 SD = 2.54	M = 46.88 SD = 2.46	M = 46.03 SD = 2.58	-1.794	.073
P4 (°C)	M = 49.78 SD = 1.66	M = 50.21 SD = 0.61	M = 49.35 SD = 2.19	-3.353	.001

With regard to the comparison among age groups, the Kruskal-Wallis H Test was used for pain thresholds. Table 7 describes the pain thresholds and the comparison results in the age groups. A significant difference was found among age groups for pain threshold (Age group 1: M = 45.96°C, SD = 1.95°C; Age group 2: M = 46.37°C, SD = 2.95°C; Age group 3: M = 47.13°C, SD = 2.65°C), and the post hoc tests indicated a significant difference only between the 18-35 and 51-65 groups ($p < .01$). No significant difference was found among age groups for pain tolerance threshold (Age group 1: M = 49.72°C, SD = 1.04°C; Age group 2: M = 49.86°C, SD = 2.01°C; Age group 3: M = 49.78°C, SD = 1.90°C).

TABLE 7. Description and comparison result of pain thresholds in age groups (P1 = pain threshold, P4 = pain tolerance threshold).

Pain level	Age group			Kruskal-Wallis H Test	
	1 (18-35 years)	2 (36-50 years)	3 (51-65 years)	Chi-Square	p
P1 (°C)	M = 45.96 SD = 1.95	M = 46.37 SD = 2.95	M = 47.13 SD = 2.65	8.765	.012
P4 (°C)	M = 49.72 SD = 1.04	M = 49.86 SD = 2.01	M = 49.78 SD = 1.90	5.070	.079

The correlation analysis was also conducted to compare age and pain thresholds. The results shown in Table 8 represent that age reports positive significant relationships both with pain threshold ($r = 0.301$, $p \leq 0.01$) and with pain tolerance threshold ($r = 0.243$, $p \leq 0.05$).

TABLE 8. Results of correlation analysis between age and pain thresholds.

	Pain threshold		Pain tolerance threshold	
	Correlation	**Sig. (2-tailed)**	**Correlation**	**Sig. (2-tailed)**
Age	0.301**	0.003	0.243*	0.018

Note: *: $p < 0.05$; **: $p < 0.01$

3.1.2 The influence of psychological traits on experimental pain thresholds

Four participants were excluded from the analysis because of the missing of their psychological traits data and the rest 92 participants' results were valid and included in the analysis. The gender and age information of the participants is described in Table 9.

TABLE 9. Description of the sample with valid psychological data. (m = males, f = females, M = mean, SD = standard deviation, mean and standard deviation in years).

Age group	92 Participants		4 Excluded participants	
	m (n = 46)	**f (n = 46)**	**m**	**f**
1 (18-35 years)	18 (M = 24.72; SD = 3.01)	17 (M = 23.94; SD = 2.30)	0	0
2 (36-50 years)	13 (M = 42.15; SD = 4.90)	15 (M = 42.20; SD = 4.40)	1 (38 years)	1 (36 years)
3 (51-65 years)	15 (M = 58.87; SD = 4.84)	14 (M = 58.57; SD = 5.03)	1 (54 years)	1 (62 years)

92 participants' psychological traits measured by four questionnaires of Neo-FFI, BIS/BAS, ERQ, and SCL-90-R are represented below, which include a total of 24 variables. The results of the test of normality indicate that, besides variables of the personality traits and emotion regulation strategies, the rest of the psychological traits are not normally distributed (see Table 10).

TABLE 10. Description and test of normality of 24 psychological traits. (M = mean, SD = standard deviation, SCL-90-R_GSI = Global Severity Index; SCL-90-R_PST = Positive Symptom Total; SCL-90-R_PSDI = Positive Symptom Distress Index)

Psychological traits	Descriptive statistics				Kolmogorov-Smirnov Test of normality		
	Min	**Max**	**M**	**SD**	**Statistic**	**df**	**Sig.**

NEO_Neuroticism	.25	3.00	1.58	.69	.066	92	.200
NEO_Extraversion	.83	3.67	2.39	.54	.069	92	.200
NEO_Openness	1.58	3.75	2.64	.51	.086	92	.089
NEO_Agreeableness	1.25	3.75	2.62	.46	.084	92	.109
NEO_Conscientiousness	1.00	4.00	2.87	.55	.090	92	.061
BAS_Total	2.31	4.00	3.13	.38	.077	92	.200
BAS_Drive	2.00	4.00	3.03	.52	.125	92	.001
BAS_Fun Seeking	1.50	4.00	2.96	.53	.123	92	.002
BAS_Reward Responsiveness	2.20	4.00	3.35	.41	.128	92	.001
BIS_Total	1.71	3.86	2.79	.47	.104	92	.015
ERQ_Cognitive Reappraisal	1.00	7.00	4.53	1.21	.069	92	.200
ERQ_Expressive Suppression	1.00	7.00	3.45	1.29	.052	92	.200
BAS_Total	2.31	4.00	3.13	.38	.077	92	.200
SCL-90-R_Somatization	1.00	3.83	1.33	.41	.210	92	.000
SCL-90-R_ Obsessive-Compulsive	1.00	2.90	1.52	.45	.151	92	.000
SCL-90-R_ Interpersonal Sensitivity	1.00	2.33	1.39	.36	.179	92	.000
SCL-90-R_Depression	1.00	2.69	1.44	.44	.218	92	.000
SCL-90-R_Anxiety	1.00	2.80	1.30	.35	.198	92	.000

SCL-90-R_Anger-Hostility	1.00	2.50	1.27	.32	.205	92	.000
SCL-90-R_ Phobic Anxiety	1.00	2.43	1.12	.24	.322	92	.000
SCL-90-R_ Paranoid Ideation	1.00	3.17	1.40	.44	.204	92	.000
SCL-90-R_Psychoticism	1.00	2.50	1.19	.27	.258	92	.000
SCL-90-R_GSI	1.01	2.54	1.35	.29	.142	92	.000
SCL-90-R_PST	1.00	55.00	22.98	15.09	.113	92	.006
SCL-90-R_PSDI	2.00	3.67	2.27	.34	.205	92	.000

Correlation analysis was conducted to show the influence of psychological traits on pain thresholds (see Table 11). The personality traits measured by NEO-FFI do not report any significant relationship with pain thresholds. Among the behavioral scales, BIS is negatively related to pain threshold ($r = -.225$, $p < 0.05$), as well as to pain tolerance threshold ($r = -.227$, $p < 0.05$). The subscales of ERQ did not show any significant relationship with pain thresholds. Some subscales of SCL-90-R indicate several negative relationships with pain threshold (Somatization, $r = -.278$, $p < 0.01$; Obsessive Compulsive, $r = -.206$, $p<0.05$; Phobic Anxiety, $r = -.286$, $p < 0.01$; Psychoticism, $r = -.226$, $p<0.05$; Global Severity Index, $r = -.253$, $p < 0.05$ and Positive Symptom Distress Index, $r = -.301$, $p < 0.01$); Somatization ($r = -.257$, $p < 0.05$) and Phobic Anxiety ($r = -.316$, $p < 0.01$) were negatively related to pain tolerance threshold.

TABLE 11. Correlation analysis results between psychological traits and pain thresholds. (SCL-90-R_GSI = Global Severity Index; SCL-90-R_PST = Positive Symptom Total; SCL-90-R_PSDI = Positive Symptom Distress Index)

Psychological traits	**Pain threshold**		**Pain tolerance threshold**	
	r	**p**	**r**	**p**
NEO_Neuroticism	-.163	.121	-.092	.383
NEO_Extraversion	-.041	.696	-.101	.336
NEO_Openness	.113	.282	-.051	.632

NEO_Agreeableness	.115	.139	.030	.773
NEO_Conscientiousness	.156	.275	.087	.409
BAS_Total	-.056	.597	.009	.932
BAS_Drive	-.031	.767	.081	.443
BAS_Fun Seeking	-.056	.593	-.026	.807
BAS_Reward Responsiveness	-.043	.683	-.035	.744
BIS_Total	-.225*	.031	-.123	.245
ERQ_Cognitive Reappraisal	.147	.163	.149	.157
ERQ_Expressive Suppression	-.104	.323	-.084	.424
BAS_Total	-.278**	.007	-.257*	.014
SCL-90-R_Somatization	-.206*	.049	-.120	.253
SCL-90-R_ Obsessive-Compulsive	-.134	.203	-.110	.298
SCL-90-R_ Interpersonal Sensitivity	-.095	.369	-.135	.198
SCL-90-R_Depression	-.175	.095	-.139	.186
SCL-90-R_Anxiety	-.206*	.049	-.048	.650
SCL-90-R_Anger-Hostility	-.286**	.006	-.316**	.002
SCL-90-R_ Phobic Anxiety	-.063	.548	-.106	.316
SCL-90-R_ Paranoid Ideation	-.226*	.031	-.121	.249

SCL-90-R_Psychoticism	-.253*	.015	-.204	.051
SCL-90-R_GSI	-.186	.076	-.167	.111
SCL-90-R_PST	-.301**	.004	-.194	.065
SCL-90-R_PSDI	-.163	.121	-.092	.383

Note: * $p < 0.05$; ** $p < 0.01$

Due to the above results that psychological traits are partly correlated with pain thresholds, a linear regression analysis was applied to study the influence of psychological traits on pain thresholds further. As it is represented in Table 12, among the total of 24 psychological variables, only two subscales of SCL-90-R can significantly predict pain thresholds. For pain threshold, "Positive Symptom Distress Index" can significantly predict 8% of the total variance ($T(90) = -3.00$, $p = 0.004$); and for pain tolerance threshold, "Phobic Anxiety" can significantly predict 9% of the total variance ($T(90) = -3.16$, $p = 0.002$). Obviously, the linear regression results indicate that all the 24 psychological traits have a low influence on both pain threshold and tolerance threshold during experimental heat stimulations.

TABLE 12. Regression models for the pain thresholds explained by psychological traits. (SCL-90-R_PSDI = Positive Symptom Distress Index)

	Predictors	**B**	**SE B**	**Beta**	**R^2**
Pain threshold	Model				
	SCL-90-R_PSDI	-2.31	0.77	-0.30**	0.08
Pain tolerance threshold	Model				
	SCL-90-R_Phobic Anxiety	-2.25	0.71	-0.32**	0.09

Note: ** $p<0.01$

3.2 The influence of sex, age, and psychological traits on biopotentials of pain

Because of the poor quality of biopotential measures three participants' experimental raw data were excluded from the analysis of this part. The sex and age information of the rest 93 participants is described in Table 13.

TABLE 13. Description of the sample with valid biopotential data. (m = males, f = females, M = mean, SD = standard deviation, mean and standard deviation in years).

Age group	93 Participants		3 Excluded participants	
	m (n = 46)	f (n = 47)	m	f
1 (18-35 years)	18 (M = 24.72; SD = 3.01)	17 (M = 23.94; SD = 2.30)	0	0
2 (36-50 years)	15 (M = 42.27; SD = 4.92)	16 (M = 42.06; SD = 4.28)	0	0
3 (51-65 years)	13 (M = 59.08; SD = 4.46)	14 (M = 58.57; SD = 5.03)	2 (M = 57.50; SD = 9.19)	1 (62 years)

The current study employs seven features to describe the biopotential performance of contact heat pain. Table 14 presents the description of the analysis variables of the biopotentials of experimental pain.

TABLE 14. Description of the seven biopotential variables (EDA = Electrodermal activity, EMGtrap = Electromyography of trapezius, EMGcorr = Electromyography of corrugator supercilii, EMGzyg = Electromyography of zygomaticus major, ECG = Electroencephalography).

Feature name	Category	Description
EMG_{zyg}_peak	amplitude	Peak
EMG_{corr}_peak	amplitude	Peak
EMG_{trap}_peak	amplitude	Peak
EDA_peak	amplitude	Peak
ECG_meanRR	variability	the mean of the inter-beat intervals
ECG_rmssd	variability	the root mean square of the successive differences $\sqrt{\frac{1}{N-1}(\sum_{i-1}^{N-1}(RR_i - RR_{i-1})^2)}$
ECG_slopeRR	variability	the slope of the linear regression of the inter-beat intervals in its time series

3.2.1 The influence of sex and age on biopotentials of pain

Independent Samples T-test was employed to analyze the sex difference in biopotentials of pain during five different stimulation levels. The results indicate that there is no significant sex difference in the biopotential performance of pain, besides one nearly significant difference ($p = .051$) in EMG_{zyg} during pain threshold stimulation with higher peak activity of zygomaticus major in males (see the table in Appendix 1).

Regarding the comparison of biopotential performance among age groups, ANOVA was used (see Table 15). Significant differences were found among age groups for biopotential performance during pain threshold levels. Post Hoc Tests show that, at pain threshold level, age group 2 has a higher meanRR of ECG than age group 1 (age group 1 : M = 0.23, SD = 0.24; age group 2 : M = 0.10, SD = 0.23, $p \leq .05$), age group 3 has a higher meanRR of ECG than age group 1 (age group 1 : M = 0.23, SD = 0.24; age group 3 : M = 0.05, SD = 0.24, $p \leq .01$), age group 2 has a higher rmssd of ECG than age group 1 (age group 1 : M = 0.22, SD = 0.23; age group 2 : M = 0.09, SD = 0.24, $p \leq .05$), age group 3 has a higher rmssd of ECG than age group 1 (age group 1 : M = 0.22, SD = 0.23; age group 3 : M = 0.04, SD = 0.22, $p \leq .01$).

At pain tolerance threshold level, age group 1 has a higher peak activity of EMG_{zyg} than age group 3 (age group 1 : M = 1.05, SD = 0.74; age group 3 : M = 0.33, SD = 0.67, $p \leq .01$), age group 1 has a higher peak activity of EMG_{zyg} than age group 2 (age group 1 : M = 1.05, SD = 0.74; age group 2 : M = 0.67, SD = 0.72, $p \leq .05$), and age group 1 has a higher peak activity of EMG_{corr} than age group 3 (age group 1 : M = 1.24, SD = 0.70; age group 3 : M = 0.60, SD = 0.79, $p \leq .01$), age group 1 has a higher peak activity of EMG_{corr} than age group 2 (age group 1 : M = 1.24, SD = 0.70; age group 2 : M = 0.85, SD = 0.77, $p \leq .05$), age group 1 has a higher peak activity of EMG_{trap} than age group 3 (age group 1 : M = 0.56, SD = 0.55; age group 3 : M = 0.22, SD = 0.55, $p \leq .05$), age group 1 has a higher peak activity of EMG_{trap} than age group 2 (age group 1 : M = 0.56, SD = 0.55; age group 2 : M = 0.21, SD = 0.48, $p \leq .01$), and age group 1 has a higher peak of EDA than age group 3 (age group 1 : M = 0.43, SD = 0.45; age group 3 : M = 0.08, SD = 0.45, $p \leq .01$), age group 1 has a higher peak of EDA than age group 2 (age group 1 : M = 0.43, SD = 0.45; age group 2 : M = 0.15, SD = 0.43, $p \leq .05$), age group 3 has a higher slopeRR of ECG than age group 1 (age group 1: M = -0.57, SD = 0.39; age group 3 : M = -0.16, SD = 0.45, $p \leq .01$), age group 2 has a higher slopeRR of ECG than age group 1 (age group 1 : M = -0.57, SD = 0.39; age group 2 : M = -0.25, SD = 0.65, $p \leq .05$).

TABLE 15. Description and comparison of the biopotential performance of three age groups during pain stimulation. (M = mean, SD = standard deviation).

Biopotentials	Age group 1		Age group 2		Age group 3		ANOVA	
	M	SD	M	SD	M	SD	F	p
Baseline								

EMG_{zyg}_peak	-0.237	0.215	-0.208	0.238	-0.144	0.242	1.260	0.289
EMG_{corr}_peak	-0.302	0.233	-0.238	0.274	-0.198	0.288	1.246	0.292
EMG_{trap}_peak	-0.147	0.175	-0.087	0.187	-0.046	0.295	1.669	0.194
EDA_peak	-0.254	0.286	-0.176	0.369	-0.050	0.311	3.046	0.052
ECG_meanRR	0.127	0.260	0.179	0.300	0.135	0.292	0.318	0.729
ECG_rmssd	0.140	0.257	0.173	0.292	0.148	0.287	0.131	0.877
ECG_slopeRR	0.097	0.217	0.062	0.254	0.004	0.321	0.964	0.385
Pain threshold level								
EMG_{zyg}_peak	-0.215	0.261	-0.119	0.283	-0.122	0.258	1.378	0.257
EMG_{corr}_peak	-0.194	0.257	-0.160	0.274	-0.155	0.287	0.202	0.817
EMG_{trap}_peak	-0.179	0.220	-0.104	0.197	-0.103	0.286	1.134	0.326
EDA_peak	-0.176	0.258	-0.145	0.330	-0.030	0.290	2.044	0.136
ECG_meanRR	0.230	0.236	0.102	0.231	0.051	0.236	4.917	0.009
ECG_rmssd	0.221	0.231	0.095	0.239	0.041	0.224	5.031	0.008
ECG_slopeRR	0.140	0.271	0.132	0.252	0.130	0.242	0.013	0.987
Pain tolerance threshold level								
EMG_{zyg}_peak	1.052	0.740	0.666	0.723	0.332	0.668	7.851	0.001
EMG_{corr}_peak	1.242	0.702	0.852	0.773	0.600	0.786	5.824	0.004
EMG_{trap}_peak	0.563	0.545	0.214	0.479	0.218	0.553	4.758	0.011
EDA_peak	0.427	0.449	0.148	0.427	0.079	0.445	5.639	0.005
ECG_meanRR	-0.413	0.413	-0.243	0.448	-0.252	0.450	1.577	0.212
ECG_rmssd	-0.403	0.415	-0.244	0.444	-0.254	0.448	1.369	0.259
ECG_slopeRR	-0.566	0.395	-0.249	0.655	-0.159	0.446	5.653	0.005

3.2.2 The influence of psychological traits on biopotentials of pain

To explore the influence of psychological traits on the 7 biopotential features during experimental heat pain stimulations, a correlation analysis was conducted with a Bonferroni-corrected significance level of $p < 0.007$. The results indicate that only BIS total is correlated significantly with the peak activity of EMG_{zyg} during the pain threshold level (see Table 16); and only one factor of SCL-90-R, namely Hostility, is found to positively associate with the EMG activities of the zygomaticus major and corrugator supercilii during pain tolerance level (see Table 17).

TABLE 16. Correlation analysis results between psychological traits and biopotential features during the pain threshold. (SCL-90-R_GSI = Global Severity Index; SCL-90-R_PST = Positive Symptom Total; SCL-90-R_PSDI = Positive Symptom Distress Index)

Psychological traits	EMG_{zyg}_peak	EMG_{corr}_peak	EMG_{trap}_peak	EDA_peak	ECG_meanRR	ECG_rmssd	ECG_slopeRR
NEO_Neuroticism	-0.225	-0.153	-0.017	-0.017	0.000	0.004	0.225
NEO_Extraversion	0.117	0.080	0.063	0.118	0.062	0.059	-0.023
NEO_Openness	0.037	-0.043	-0.122	0.064	0.021	0.029	0.087
NEO_Agreeableness	-0.087	-0.183	-0.113	0.058	0.160	0.160	0.050
NEO_Conscientiousness	0.070	0.069	-0.020	0.006	0.123	0.109	0.024
BAS_Total	0.034	0.102	0.024	0.220	0.022	0.030	0.087
BAS_Drive	-0.002	0.022	-0.046	0.099	0.154	0.149	0.064
BAS_Fun Seeking	0.058	0.090	0.175	0.243	-0.097	-0.083	0.135
BAS_Reward Responsiveness	0.022	0.124	-0.080	0.168	-0.004	0.008	0.001
BIS_Total	-0.305*	-0.182	-0.036	-0.018	0.028	0.022	0.166
ERQ_Cognitive Reappraisal	-0.018	-0.105	-0.068	-0.140	0.101	0.106	-0.064

ERQ_Expressive Suppression	0.207	0.185	0.113	0.049	-0.237	-0.240	-0.198
SCL-90-R_Somatization	-0.090	-0.138	-0.012	0.136	-0.146	-0.156	0.165
SCL-90-R_ Obsessive-Compulsive	-0.169	-0.148	0.024	0.134	-0.072	-0.070	0.170
SCL-90-R_ Interpersonal Sensitivity	-0.026	-0.003	0.001	-0.005	-0.116	-0.091	0.064
SCL-90-R_Depression	-0.137	-0.215	0.023	0.064	-0.023	-0.016	0.163
SCL-90-R_Anxiety	-0.167	-0.094	-0.115	0.086	0.016	0.021	0.142
SCL-90-R_Anger-Hostility	-0.227	-0.248	-0.029	-0.009	-0.061	-0.058	0.089
SCL-90-R_ Phobic Anxiety	-0.088	-0.068	-0.029	0.088	-0.155	-0.158	0.164
SCL-90-R_ Paranoid Ideation	0.088	0.079	0.091	0.128	-0.193	-0.184	-0.026
SCL-90-R_Psychoticism	-0.128	0.015	-0.065	0.009	-0.100	-0.087	0.060
SCL-90-R_GSI	-0.139	-0.128	-0.017	0.098	-0.111	-0.103	0.148
SCL-90-R_PST	-0.174	-0.178	-0.039	0.077	-0.110	-0.106	0.144
SCL-90-R_PSDI	-0.096	0.008	0.003	0.065	0.041	0.049	0.096

Note: * $p<0.007$

TABLE 17. Correlation analysis results between psychological traits and biopotentials at the pain tolerance level. (SCL-90-R_GSI = Global Severity Index; SCL-90-R_PST = Positive Symptom Total; SCL-90-R_PSDI = Positive Symptom Distress Index)

Psychological traits	EMG_{zyg}_peak	EMG_{corr}_peak	EMG_{trap}_peak	EDA_peak	ECG_meanRR	ECG_rmssd	ECG_slopeRR
NEO_Neuroticism	0.195	0.154	-0.010	0.034	-0.047	-0.038	0.021
NEO_Extraversion	0.014	0.054	-0.043	0.039	-0.008	-0.014	-0.096

NEO_Openness	-0.051	0.107	0.009	0.107	0.024	0.029	-0.020
NEO_Agreeableness	0.055	0.079	0.255	0.040	-0.084	-0.079	-0.157
NEO_Conscientiousness	-0.139	-0.089	0.041	-0.049	0.007	0.006	-0.041
BAS_Total	-0.011	0.049	-0.068	-0.008	0.018	0.017	0.059
BAS_Drive	-0.001	0.142	0.044	0.040	-0.071	-0.071	-0.065
BAS_Fun Seeking	0.016	-0.019	-0.195	-0.020	0.030	0.031	0.109
BAS_Reward Responsiveness	-0.041	-0.006	-0.001	-0.038	0.082	0.080	0.092
BIS_Total	0.196	0.082	-0.042	0.065	-0.094	-0.089	0.036
ERQ_Cognitive Reappraisal	0.118	0.207	0.058	0.221	-0.062	-0.054	-0.230
ERQ_Expressive Suppression	-0.164	-0.146	-0.158	-0.026	0.186	0.183	0.235
SCL-90-R_Somatization	0.034	0.091	-0.094	-0.060	0.070	0.083	0.051
SCL-90-R_ Obsessive-Compulsive	0.151	0.175	-0.039	-0.075	-0.016	-0.009	-0.050
SCL-90-R_ Interpersonal Sensitivity	0.069	0.062	-0.069	-0.045	0.017	0.021	0.077
SCL-90-R_Depression	0.145	0.203	-0.004	-0.020	0.013	0.027	-0.036
SCL-90-R_Anxiety	0.147	0.203	-0.005	0.042	-0.021	-0.002	-0.068
SCL-90-R_Anger-Hostility	0.364*	0.291*	0.053	-0.086	-0.102	-0.100	-0.171
SCL-90-R_ Phobic Anxiety	0.119	0.087	-0.114	-0.042	0.064	0.070	-0.058
SCL-90-R_ Paranoid Ideation	-0.094	-0.078	-0.192	-0.183	0.195	0.189	0.172

SCL-90-R_Psychoticism	0.059	0.022	-0.022	0.003	0.006	0.018	0.093
SCL-90-R_GSI	0.136	0.154	-0.069	-0.074	0.040	0.051	0.011
SCL-90-R_PST	0.164	0.183	-0.049	-0.061	0.013	0.026	-0.008
SCL-90-R_PSDI	0.111	0.103	-0.059	-0.065	0.002	0.010	-0.046

Note: * p<0.007

To further explore the effect of psychological traits on the two facial EMG activities during pain threshold and tolerance, a linear regression analysis was applied. Table 14 presents the Regression Models for the two facial EMG activities explained by the psychological traits. At the level of pain threshold, the "BIS Total and ERQ_ Expressive Suppression" can significantly predict 11.9% of the total variance of the activity of EMG_{zyg}; and "SCL-90-R_Anger-Hostility" can significantly predict 5.1% of the total variance of the peak activity EMG_{corr}; at the level of pain tolerance threshold, the "SCL-90-R_Anger-Hostility SCL-90-R_Paranoid_ideation" can significantly predict 18.3% of the total variance of the peak activity EMG_{zyg}; "SCL-90-R_Anger-Hostility, SCL-90-R_Paranoid Ideation, and ERQ_Cognitive Reappraisal" can significantly predict 15.1% of the total variance of the peak activity EMG_{corr}. The linear regression results indicate that only a limited number of psychological traits have a low influence on the facial muscle response to experimental heat pain.

TABLE 18. Regression models for the facial EMG activities explained by the psychological traits.

	Predictors	**B**	**SE B**	**Beta**	**R^2**
Pain threshold level					
EMG_{zyg}_peak	Model				
	BIS_Total	-0.177	0.057	-0.310**	0.119
	ERQ_Expressive Suppression	0.045	0.021	0.215*	
EMG_{corr}_peak	Model				

	SCL90R_Ange-Hostility	-0.208	0.087	-0.248*	0.051
Pain tolerance threshold level					
EMG_{zyg}_peak	Model				
	SCL90R_Anger-Hostility	1.137	0.249	0.479**	0.183
	SCL90R_Paranoid Ideation	-0.497	0.181	-0.287**	
EMG_{corr}_peak	Model				
	SCL90R_Anger-Hostility	0.950	0.263	0.385**	0.151
	SCL90R_Paranoid Ideation	-0.482	0.194	-0.267*	
	ERQ_Cognitive Reappraisal	0.149	0.065	0.226	

*: p<0.05; **: p<0.01

3.3 The influence of sex, age, and psychological traits on facial expressions of pain

3.3.1 The influence of sex and age on facial expressions of pain

Because of the missing psychological traits data of several participants and technical problems during facial expression recording, a total of 11 participants' experimental raw data was excluded from the analysis of this part. The sex and age information of the remaining 85 participants is described in Table 19.

TABLE 19. Description of the sample with valid facial expression data. (m = males, f = females, M = mean, SD = standard deviation, mean and standard deviation in years).

Age group	**85 Participants**		**11 Excluded participants**	
	m (n = 43)	**f (n = 42)**	**m**	**f**
1	15	15	3	2
(18-35 years)	(M = 24.46; SD = 2.80)	(M = 24; SD = 2.27)	(M = 26; SD = 4.36)	(M = 23.5; SD = 3.54)

2 **(36-50 years)**	13 (M = 42.15; SD = 4.90)	14 (M = 42.20; SD = 4.40)	1 (38 years)	2 (M = 34.8; SD = 1.54)
3 **(51-65 years)**	15 (M = 58.87; SD = 4.84)	13 (M = 58.08; SD = 4.87)	1 (54 years)	2 (M = 61.6; SD = 1.21)

The following table describes the total facial changes of the six facial features and the changes of nasal wrinkling during pain threshold levels. For comparing the sex difference in facial expressions of pain, the Independent Samples T-test was employed (see Table 20). During the two levels of pain stimulation, no significant sex difference was found for facial distance change. With respect to nasal wrinkling, there was a significant difference between men (M = 0.55, SD = 0.61) and women (M = 1.23, SD = 1.95) at pain tolerance threshold level ($p < .05$). The results indicate that females perform more obvious nasal wrinkling at the pain tolerance level than males.

TABLE 20. Description and comparison of sex difference in facial expression changes during pain. (m = males, f = females, M = mean, SD = standard deviation, FDC = facial distance change, g_n = nasal wrinkles).

	All	**m**	**f**	**Independent Samples Test**	
				t	**p**
Pain threshold level					
FDC	M = 1.80, SD = 2.05	M = 2.00, SD = 2.50	M = 1.58, SD = 1.47	0.094	0. 350
g_n	M = 0.18, SD = 0.36	M = 0.15, SD = 0.17	M = 0.22, SD = 0.48	-1.588	0.116
Pain tolerance threshold level					
FDC	M = 6.66, SD = 7.08	M = 6.52, SD = 7.86	M = 6.81, SD = 6.27	-0.194	0.847
g_n	M = 0.89, SD = 1.47	M = 0.55, SD = 0.61	M = 1.23, SD = 1.95	-2.170	0.035

In order to compare the age groups, an ANOVA was calculated (see Table 21). No significant difference was found among age groups for facial distance change in threshold levels, but Multiple Comparisons indicated that there was a significant difference between the age group 1 and group 3 (Age group 1: M = 8.92, SD = 6.35; Age group 3: M = 5.09, SD = 8.78) during pain tolerance level ($p < .005$). The result shows that young participants

perform more facial expressions during pain tolerance stimulation than senior participants. As for nasal wrinkling, no significant difference was found among age groups.

TABLE 21. Description and comparison of age difference in facial expression changes during pain (m = males, f = females, M = mean, SD = standard deviation, FDC = facial distance change, g_n = nasal wrinkles).

	Age group 1	Age group 2	Age group 3	ANOVA	
				F	p
Pain threshold level					
FDC	M = 1.73, SD = 2.14	M = 1.86, SD = 1.54	M = 1.81, SD = 2.43	0. 027	0. 974
g_n	M = 0.17, SD = 0.16	M = 0.28, SD = 0.58	M = 0.11, SD = 0.15	1.638	0. 201
Pain tolerance threshold level					
FDC	M = 8.92, SD = 6.35	M = 5.78, SD = 5.24	M = 5.09, SD = 8.78	2.502	0. 088
g_n	M = 0.89, SD = 1.51	M = 0.90, SD = 1.02	M = 0.86, SD = 1.81	0. 005	0. 995

3.3.2 The influence of psychological traits on facial expressions of pain

Correlation analysis was conducted to analyze the influence of psychological traits on facial distance changes and nasal wrinkling during two pain levels, and the results were described (see the table in Appendix 2). Only during the pain tolerance level, subscales of ERQ and SCL-90-R indicate positive relationships with facial distance change (Cognitive reappraisal, $r = .23$, $p<0.05$; Anger-Hostility, $r = .25$, $p<0.05$). Concerning nasal wrinkling, two subscales of SCL-90-R show positive relationships with it only during pain tolerance stimulation (Anxiety, $r = .26$, $p<0.05$; Phobic Anxiety, $r = .28$, $p<0.05$).

It is indicated that several subscales of the questionnaires show significant relationships with the facial distance changes and nasal wrinkling during pain stimulations, and a linear regression analysis was applied to further study the influence of psychological traits on facial expressions of pain. As it is represented in Table 22, at the level of pain tolerance stimulation, "SCL-90-R_Anger-Hostility, SCL-90-R_Paranoid Ideation, and ERQ_ Cognitive Reappraisal" can significantly predict 15% of the total variance ($T (81) = 6.02$, $p = 0.001$) of facial distance change; and NEO_Neuroticism and NEO_Agreeableness" can significantly predict 8% of the total variance ($T (82) = 4.84$, $p = 0.01$) of nasal wrinkling.

The linear regression results indicate that all 24 psychological traits have a low influence on facial expressions during experimental heat pain.

TABLE 22. Regression models for the facial expressions of pain explained by psychological traits at pain tolerance threshold level (FDC = facial distance change, g_n = nasal wrinkles).

	Predictors	B	SE B	Beta	R^2
FDC	Model				
	SCL-90-R_Hostility	7.672	2.390	0.351**	0.151
	SCL-90-R_ Paranoid Ideation	-4.781	1.752	-0.302**	
	ERQ_ Cognitive Reappraisal	1.454	0.582	0.263*	
g_n	Model				
	NEO_Neuroticism	0.587	0.239	0.260*	0.080
	NEO_Agreeableness	0.802	0.342	0.251*	

*: $p<0.05$; **: $p<0.01$

CHAPTER 4

DISCUSSION

The results of the present study demonstrate that women are more sensitive to experimental heat pain with lower pain tolerance and more obvious nasal wrinkling, which support Hypothesis 1a and 1c; while Hypothesis 1b cannot be proved, as women only show a nearly significant difference of zygomaticus major activity during pain threshold level. Regarding the influence of age on pain experience, Hypothesis 2a, 2b, and 2c are all supported, as the elderly present higher pain threshold, decreased biopotential activities, and fewer facial expressions during heat pain compared with the young. Moreover, the findings of this research can partly support Hypothesis 3a, 3b, and 3c, as several psychological traits can partly predict the performance of pain, which will be described in detail below. The discussions of the results of this study include three parts, each of which discusses the influence of sex, age, and psychological traits on the experimental pain performance, respectively.

4.1 The influence of sex on pain experience

4.1.1 The influence of sex on pain thresholds

The average temperature of the pain stimulation thresholds (threshold: M = 46.47°C, SD = 2.57°C; tolerance threshold: M = 49.79°C, SD = 1.67°C) is in line with the former investigations (Fillingim et al., 2005; Treister et al., 2012). Regarding the sex difference in pain thresholds, the results of the study indicate that females are more sensitive to experimental heat pain than males with a significant difference in pain tolerance and a nearly significant difference in pain threshold, which are consistent with previous studies (Wise et al., 2002; Fillingim et al., 2005; Treister et al., 2012).

It is well established that sex differences exist in the clinical pain population, as pain is reported more frequently by women (Fillingim et al., 2009; Mogil, 2012; Bartley and Fillingim, 2013). In the area of experimental pain study, numerous studies have been conducted to confirm the sex difference in pain sensitivity. However, there is still an argument about whether sex has a consistent and robust influence on pain sensitivity. An important review including 122 pain studies from 1998 to 2008 analyzed sex differences in the perception of laboratory-induced thermal, pressure, ischemic, muscle, electrical, chemical, and visceral pain in healthy subjects, which failed to find a clear and consistent pattern of sex differences in human pain sensitivity. Specifically, females and males have no threshold differences for cold and ischemic pain, but there is strong evidence that females tolerate less thermal and pressure pain than males (Racine et al., 2012a). In contrast, previous qualitative and quantitative reviews have indicated that women are more sensitive to multiple experimental pain modalities than men (Riley et al., 1998; Fillingim et al., 2009; Mogil, 2012; Bartley and Fillingim, 2013). In response to the review of Racine et al. (2012a), Mogil (2012) conducted a re-analysis of the relevant data and argued that the conclusion of

Racine et al. (2012a) was too conservative. Sex differences absolutely exist in experimental pain sensitivity across modalities, the size, and the importance of which is still debatable (Mogil, 2012). To explain the variability in effect size across studies, several influence factors have been identified. For example, insufficient statistical power in many studies can account for the lack of sex difference, as the samples with a large size in the review of Racine et al. (2012a) always present significant sex differences in pain sensitivity. Several biological factors can influence the magnitude of the sex difference in pain perception, such as sex hormones, immune system, and genetics et al. (Hashmi and Davis, 2014; Sorge and Totsch, 2017). Some demographic factors, such as race and age, could potentially interact with sex to magnify or attenuate pain sensitivity (Fillingim, 2017). Furthermore, gender and other characteristics of the experimenter can influence sex differences in pain perception (Fillingim, 2017). Finally, psychological and sociocultural factors, such as emotional states, pain coping strategies, and gender roles, can modulate pain differently in the sexes (Mogil, 2012; Bartley and Fillingim, 2013; Hashmi and Davis, 2014; Fillingim, 2017). Based on the previous reviews, certainly, this study supports the conclusion that females consistently are more sensitive to experimental pain than males across stimulus modalities.

4.1.2 The influence of sex on biopotentials of pain

Regarding the biopotentials of pain, the present study shows that the biopotentials of ECG and EDA fail to support a sex difference in experimental pain. HRV is an index of the capacity of the autonomic nervous systems to regulate and habituate stressors (Thayer et al., 2012). Greater HRV predicts an adaptable nervous system, while impairments in HRV have been proposed as an independent risk factor for increased cardiac mortality and morbidity (Koenig et al., 2016; Tracy et al., 2016). HRV which is an index of baroreflex activity may be more suitable to study autonomic reactions to nociceptive stimulation (Koenig et al., 2014), as it plays a key role in regulating and inhibiting autonomic reactivity (Tracy et al., 2018).

Most of the previous research in this area focused on the role of resting HRV during experimental pain, the main conclusion of which represents that the frequency domain changes of HRV can describe a decrease in parasympathetic activity and an increase in sympathetic-baroreflex activity (Koenig et al., 2014). As regarding the sex difference in resting HRV, a recent meta-analysis presented that in healthy human subjects, the female possesses a greater variability in parasympathetic regulation, while the male shows a relative dominance of sympathetic activity (Koenig and Thayer, 2016), which can be explained by the influence of estrogen on the autonomic systems (Nahman-Averbuch et al., 2016).

However, the current study neither finds a sex difference in baseline HRV nor supports a significant sex difference in HRV during experimental heat pain. The former finding of this study can be supported by the previous study that showed a lack of sex difference in resting HRV (Tracy et al., 2018), which concluded that there may exist small sex differences in resting HRV and a small sample size cannot present significant sex differences, as the meta-analysis including a large sample size ($n > 6000$) found significant sex differences (Koenig and Thayer, 2016). Given that there exist sex differences in resting HRV and the sample size of the current study is not large enough, the latter finding of no sex difference in HRV during

pain should be considered carefully, and further research is needed, as sex difference in HRV during pain is rarely explored.

The experience of pain is correlated with the activation of the sympathetic nervous system. The consequence of the activation includes an increased activity of sweat glands, which can be measured by EDA (Loggia, Juneau, and Bushnell, 2011; Jänig, 2012). The present result is consistent with the previous review which was not successful to support that sex difference in experimental pain can be accounted for EDA with all the reviewed studies except one found no significant results within sexes (Racine et al., 2012b). Besides, Breimhorst et al. (2012) also reported that females and males did not differ in EDA during heat pain stimulation after a careful transformation and calculation of individual variability in EDA. Although it is a common belief that men perform a greater sympathetic activity than women, the present result does not find a significant sex difference in EAD during heat pain. Several reasons may explain the inconsistency. First, the females are more susceptible to negative stimuli such as pain (Breimhorst et al., 2011), while the males present a greater sympathetic activity during pain, thence the two effects may cancel each other out, resulting in a hard sex difference during pain. Second, the sample sizes of all the reviewed studies (Racine et al., 2012b) and the research conducted by Breimhorst et al. (2012) are less than 70 subjects, therefore, a larger sample should be a consideration in the future study. Third, Brown and Macefield (2014) reported sex differences in the sympathetic neural responses to emotionally-charged images using intraneural microelectrodes, while the measurement of skin sweat release could not discern sex differences, which implies different measuring tools can present inconsistent results. Finally, there may exist other autonomic parameters that can present the sex differences in EAD during pain.

Comparing the sex performance of EMG activity, males show a higher amplitude of zygomaticus major than females with a near significance ($p = .051$) only during the level of pain threshold stimulation. The current study is the first study that aims to explore whether there is a sex-related difference in EMG performance during experimental heat pain. According to the research of sex influence on EMG activity during emotion elicitations, the result of the current study is a little surprising. There were many studies presented that females reported relatively higher EMG activity while viewing emotion-provoking pictures compared to males, specifically, with a stronger performance of zygomatic major while watching pleasant pictures and with a stronger performance of corrugator supercilii while viewing unpleasant pictures (Schwartz, Brown and Ahern, 1980; Dimberg and Lundquist, 1990; Lundqvist, 1995; Huang and Hu, 2009). During the emotion experiments, all participates are exposed to the same emotion elicitation materials; however, in the present study each subject endured individual heat stimulation to induce experimental pain, and generally, females endured slightly lower heat stimuli than males. Consequently, the difference in the inducing stimuli between women and men may explain no sex difference in the EMG activity during pain while there exists a sex difference during an emotional response. Besides, the current study measures the EMG performance during four levels of experimental pain, therefore, a nearly significant difference of the amplitude of zygomaticus major between females and males only during the pain threshold level is not sufficiently credible to support a sex-related difference in facial EMG of pain. As there exists no previous

study exploring the sex difference in EMG performance during experimental heat pain, more research is needed.

4.1.3 The influence of sex on facial expressions of pain

Both verbal and nonverbal methods are important for the study of pain communication. Regarding the research of sex influence on pain experience, the nonverbal measurements of pain are much less studied than the verbal reports of pain (Keogh, 2014). The facial expression of pain has been considered to be the most significant nonverbal performance of pain experience (Prkachin, 1992; Williams, 2002), which may be a promising direction to study the sex difference in pain, as most of the studies relied on verbal reports of pain (Riley et al., 1998; Keogh, 2014). The facial expressions can be easily observed, and are especially useful to evaluate pain for infants, young children, older people with dementia, or others having difficulties in verbal reporting (Craig et al., 2010; Prkachin, 2009). Besides, the facial expression of pain is an innate quality and is available from the earliest stage of life (Reissland, Francis, and Mason, 2013). Nevertheless, to date, several studies were conducted with no significant sex differences in facial expression of pain (Craig, 1991; Kunz, 2006; Racine et al., 2012). In terms of facial expressions of pain, one finding of the present study is no sex differences in the six facial distance changes, which is consistent with the previous study which used FACS to analyze the facial expressions of healthy participants during experimental heat pain (Kunz, 2006). Taking together the six facial features, the facial distance change of males is larger than that of females, which could be explained by the anatomical differences within sexes. However, an exciting finding of this study is that females show more obvious nasal wrinkling during pain tolerance level and a nearly significant ($P = 0.07$) nasal wrinkling difference during higher level pain (P3). This finding is the first report describing sex differences in partly facial expressions of pain with a carefully examining method using an autonomic pain recognition system. As a unique facial characteristic of disgust, wrinkling the nose can reduce the volume of the nasal cavities and decrease the air inhale, which can protect the human being from smelly or dangerous odors (Chapman and Anderson, 2012). At the pain tolerance level, the heat stimuli may be thought as a disgust resource, therefore, the sex difference of nasal wrinkling during pain can be supported by the previous disgust reviews, which conclude that females are more disgust sensitive than males (Fleischman, 2014; Al-Shawaf, Lewis, and Buss, 2018). Based on the hypotheses explaining the sex-related dissimilarity of disgust and the evolutionary perspective, several reasons may explain why women performance more obvious nasal wrinkling during pain tolerance level. The first potential explanation is that women should be more facially sensitive to pain because of the protecting and teaching role for their offspring, as the obviously facial expression of pain may convey alarm for the descendants and serve to seek help from others (Williams, 2002; Al-Shawaf, Lewis, and Buss, 2018). Secondly, males with a lower facial expression of pain may result from selective pressures related to hunting and warfare (Hashmi and Davis, 2014; Williams, 2002). Finally, social factors such as stereotypical beliefs can shape women with more facial responses during pain (Keogh, 2014).

Compared with the current finding, several previous studies did not report sex difference in nasal wrinkling during pain in adults (Prkachin, 1992; Kunz, 2006; Simon et al., 2008). This inconsistency could be explained by the application of different measuring methods, as the above three research employed the FACS which depended on manually coding of action units with potential subjective bias (Craig, Prkachin and Grunau, 2011; Bartlett et al., 2014), while the present study uses an automatic pain recognition method to encode the Pixel change for measuring nasal wrinkling. Experimentally induced emotion research highlights sex differences in the encoding and decoding of facial expressions of emotions, and females generate more facial expressions of emotion and are better at recognizing emotions in the face (Kring and Gordon, 1998; Keogh, 2014; Thompson and Voyer, 2014). The current finding may support the expectation that females should be facially more expressive than males during experimental pain. Despite this interesting finding, there is a dearth of study exploring the sex differences in facial expressions of pain. FACS has been proved to be effective in the measurement of facial expressions of pain and has been used extensively in both clinical area and experimental research. However, it has several shortcomings, which include too time-consuming for training and coding, and potential subjective bias, and ignoring subtle or invisible changes of the face (Craig, Prkachin and Grunau, 2011; Bartlett et al., 2014; Dawes et al., 2018). Therefore, based on the application of FACS, automatic measurements of facial AUs during pain may provide innovation and objectivity for future pain research.

4.2 The influence of age on pain experience

4.2.1 The influence of age on pain thresholds

Regarding the difference in pain threshold and tolerance among the three age groups, only elderly participants perform a higher pain threshold than their young counterparts. Correlation analysis indicates that age is positively related to heat pain threshold and tolerance. The present results are consistent with the results of an important systematic-review and meta-analysis of age influence on pain thresholds, which firmly reported that pain threshold increases with age by a large effect size especially when pain is elicited by heat stimulation while pain tolerance does not (Lautenbacher et al., 2017). Consistent with previous researches, the elderly in this study show a significant increase in pain threshold and no significant change of pain tolerance, which indicates pain range decrease with age (Lautenbacher, 2012; Lautenbacher et al., 2017). Heat stimuli activate various sub-types of cutaneous heat-nociceptors, most of which are located in the superficial tissue (Olesen et al., 2012). When heat contact is employed to stimulate the elderly participants, the C-fibers can mediate the pain experience, as age seems to dull the exteroceptive pain function (Lautenbacher, 2012; Lautenbacher et al., 2017). Besides, changes of autonomic function, and altered neuronal physiology and function, can result in pain modulatory imbalance in the elderly (Fillingim, 2017; Lautenbacher, 2012). Moreover, special psychosocial factors in older people, such as the decrease of cognitive function, poor sleep quality, and lack of social support can make pain more sensitive (Racine et al., 2012). In conclusion, firm evidence supports that the elderly show less sensitivity to lower pan intensities, and the

biopsychosocial model should be taken into consideration to explain the age-related pain changes.

4.2.2 The influence of age on biopotentials of pain

The comparison results of biopotentials of pain among age groups present that, at the pain threshold level, both the middle age group and the older group show significantly lower ECG_meanRR and ECG_rmssd compared with the young group (negative correlation); while at the level of pain tolerance, both the middle age group and the older group present lower performance in EMG_{zyg}_peak, EM_{Gcorr}_peak, EMG_{trap}_peak and EDA_peak, and higher performance in ECG_slopeRR compared with the young group. There is no group difference in biopotentials at the levels of pain 2 and pain 3. These findings are the first result exploring the influence of age on the Biopotential performance of healthy participants during experimental heat pain. In respect of HRV, recent studies are more and more highlighting its indices as bio-markers of the capacity of the autonomic nervous systems and its appropriate role when investigating the autonomic ability to nociceptive stimulation (Koenig et al., 2016; Thayer et al., 2012; Tracy et al., 2016). The age difference of HRV activity in experimental pain may be explained partly by a relative decrease of sympathetic activity with an increase in age (Abhishekhet al., 2013; Holzman and Bridgett, 2017), and partly by a decline of somatosensory functions (warmth, cold, touch, vibration) with age (Lautenbacher et al., 2017).

4.2.3 The influence of age on the facial expression of pain

With regard to the facially expressive difference among the three age groups, the result shows that young participants perform larger facial distance changes during the pain tolerance stage than senior participants, and no age difference was found for nasal wrinkling. Pain is potently associated with age, as pain prevalence increases among the elderly (Gibson and Farrell, 2004). The facial expression has been proved to be a valid predictor of pain for the senior individuals (Hadjistavropoulos et al., 2011), whereas there is a short of study examining the age effect on the facial expression of experimental pain. Kunz et al. conducted the first study to explore the impact of age on the facial expression of pain using FACS, which found that age did not have a significant influence on the facial expression of pain during pressure stimulation and electrical stimulation (Kunz et al., 2008). The present study indicates that young participants are more facially expressive than the elderly, which is not in accordance with the previous study. Kunz et al. (2008) compared the age differences just during threshold and suprathreshold stimulations without the pain tolerance stimulation; however, the present study compares four levels of heat pain stimulations among three age groups with only a significant age difference during pain tolerance level using a differently objective automatic method, and specifically, only the younger group (age group 1) significantly present more facial expression than the older group (age group 3).

This present study is the first time that age differences in facial expression of pain have been examined with a new automatic assessment, the result of which may partly support the traditional belief that older people have been believed to show less frequent and less intense facial expression of emotion (Kunz et al., 2008). Furthermore, when comparing the age differences with self-evaluation measures of behavioral expression of pain, the elderly

participants have rated themselves as being more stoic than their young counterparts (Yong, 2006), which could be consistent with the present finding. It exists the traditional stereotype that aging is related to a decline of facial expression of pain, as older age is associated with a deterioration of physical conditions that may affect pain experience and pain processing, however, no objective studies have supported this assumption. The current tentative finding could partly help to remove this discrepancy by supporting the age-related decline in facial expressivity of experimental pain, nevertheless, this is a need for further research aiming to explore age-related pain expressivity with other pain stimulations, as different stimulation methods and different facial expressive assessments may reach an inconsistent conclusion about the age-related differences in facial expression of pain (Kunz et al., 2008).

4.3 The influence of psychological traits on experimental pain experience

The major aim of this study was to explore whether psychological traits have a significant influence on experimental heat pain thresholds and to what extent can psychological variables predict the pain thresholds. Previous studies on experimental pain have represented inconsistent findings, which have mostly focused on specific traits such as personality traits, positive and negative state-traits, and specific causes of pain such as pain catastrophizing (Cameron, 2011; Hansen, Horjales-Araujo, and Dahl, 2015; Helsen, Goubert, Vlaeyen, 2013; Edwards et al., 2006; Schrooten, Karsdorp, and Vlaeyen, 2013; Breimhorst et al., 2012). This study comprehensively investigated the association between experimental pain and psychological traits which include personality traits, emotional regulation strategies, behavioral motivational systems, and self-report psychological symptoms in the healthy population.

4.3.1 The influence of psychological traits on pain threshold and tolerance

In the present study, the correlation analysis between psychological traits and pain thresholds shows that among the total four questionnaires only the subscales of BIS/BAS and SCL-90-R show significant influences on pain thresholds. Regarding the results, neither neuroticism nor extroversion was significantly related to the experimental heat pain thresholds, which support the hypothesis 1a, and this finding is in line with the results of the previous experimental studies in healthy participants (Coen et al., 2011; Harkins, Price, and Braith, 1989; Vassend, Røysamb, and Nielsen, 2013; Ruffle et al., 2015). Former investigations indicate neuroticism is not related to nociceptive processing of sensory mechanisms such as pain thresholds or scores, instead, the cognitive and emotional aspects of pain processing, such as suffering/unpleasantness and affective disturbance, have a direct influence on pain, and neuroticism just performs an influence on pain-related fear during vigilance to pain (Coen et al., 2011; Edwards et al, 2006; Schmidt, Hooten, Carlson, 2011). However, Coen et al. (2011) studied the influence of neuroticism on the brain activity during pain, and suggested that higher neuroticism is associated with the decreased activity of brain regions including the parahippocampus, insula, thalamus, and anterior cingulate cortex, which are responsible for emotional and cognitive appraisal during pain; besides, a recent study showed that extraversion is associated with brain processing during experimental pain and

pain anticipation, but extraversion does not have a direct influence on pain thresholds or rating (Ruffle et al., 2015). The inconsistencies between the influence of personality on experimental heat pain thresholds and its effect on the brain activity of pain could be explained by the weak and unstable association between heat pain thresholds and personality (Vassend, Røysamb, and Nielsen, 2013). Based on the results of the present study and previous findings, it can be concluded that both neuroticism and extraversion are related to the brain activity of pain processing, but neither have a direct significant influence on the experimental heat pain thresholds in the healthy population.

The current results indicate that reduced pain threshold and higher BIS are related ($r = -.225$, $p < 0.05$), and a negative relationship between pain tolerance with BIS is found ($r = -.227$, $p < 0.05$), which can be partly supported by the research results which conducted by Streff et al. with a negative correlation between total BIS score and experimental pain tolerance (Streff et al., 2010). An investigation on the influence of BIS/BAS on chronic patients found that BIS showed a significant association with both pain intensity and headache frequency and BAS was not significantly related to pain intensity (Jensen, Tan, and Chua, 2015). The association between BIS and pain thresholds could be explained by a stronger behavioral avoidance producing a more intense pain experience. According to Gray's theory of brain function and behavior, BIS may be activated in the presence of signs of punishment, non-reward, novel stimuli, or unconditioned fear stimuli (Gray, 1990; Corr, 2013). The present results may identify the biological factors that influence the perception of pain, and indicate that individuals with high BIS may be sensitive to pain with lower pain intensities.

Following the biopsychosocial model, there is a substantial growth of research exploring the mutual influence among pain and emotions. To be specific, much neurobiological research, psychological research, and social research have presented that pain and emotions share many inextricable links, and emotions are considered to be integral to the conceptualization, assessment, and treatment of experimental and clinical pain (Lumley et al., 2011). Unexpectedly, the previous results describe that self-report emotion regulation strategies do not relate to pain thresholds. Little research reported the correlation between self-reported emotion suppression and cognitive reappraisal and experimental pain. Hampton et al. (2015) compared the different influence of instructed emotion regulation strategies and self-reported suppression and reappraisal on the thermal pain task, which found that the former methods led to reductions in nonverbal and verbal index of pain, but the latter questionnaire measured tendencies of participants showed no correlation with pain responses. In conclusion, the influence of self-reported emotion regulation characters on pain may be subtle and future research should employ more objective assessment tools and more careful experimental design.

As a single-factor instrument, the nine subscales of SCL-90-R do represent only one common factor, which entirely describes general psychological discomfort representing the individual degree of distress caused by the total of psychological symptoms (Hardt, Gerbershagen, and Franke, 2000; Schmidt, Hooten, and Carlson, 2011). Regarding the Global severity index of SCL-90-R, hypothesis 1c is supported by the results, as the GSI shows a significantly negative relationship with the pain threshold. It indicates that the participant who has a higher score of GSI shows a lower pain threshold. The finding that

higher GSI is predictive of higher pain sensitivity is not surprising given the previous studies exploring the influence of psychological distress on pain perception in chronic pain patients (Klauenberg et al., 2004; Schmidt, Hooten, and Carlson, 2011; Davies et al., 2016). In these studies, pain patients usually show higher GSI with psychological symptoms. As mostly used in chronic pain studies, SCL-90-R has been rarely used in the studies of experimental pain in the healthy population. In the present study, some subscales of SCL-90-R, such as Somatization, Obsessive-compulsive, Hostility, Phobic Anxiety, and Psychoticism, present negative relationships with pain threshold, besides, Somatization and Phobic anxiety are negative related to pain tolerance. These findings are consistent with the previous studies which used the Psychological questionnaires exploring the influence of anxiety, fear, and somatization on experimental pain (Hansen, Horjales-Araujo, and Dahl, 2015; Helsen, Goubert, and Vlaeyen, 2013; Lautenbacher et al., 2017).

Considering the regression results, only SCL-90-R_PSDI and SCL-90-R_PA can predict pain threshold and pain tolerance with limited prediction rates. This part concludes that in the healthy population psychological variables have a low influence on experimental heat pain thresholds.

4.3.2 The influence of psychological traits on biopotentials of experimental pain

The biopotential activities could assess the objective experience of pain (Ben-Israel et al., 2013; Cowen et al., 2015; Gruss et al., 2015; Treister et al., 2012), and undoubtedly, psychological traits have an influence on the experimental pain responses, and the assessment, diagnosis, and management of clinical pain (Conrad et al., 2013; Hansen, Horjales-Araujo, and Dahl, 2015; Mongini et al., 2009; Tunks, Crook, and Weir, 2008), however, the association between the psychological traits and the biopotentials of pain have not been directly studied. To better explain the pain experience measured by the biopotentials, the present study is the first one to explore the relationship between self-reported psychological traits and the biopotential performance during experimental heat pain.

It is revealed that (see Table 16), only BIS is negatively correlated to the EMG activity of zygomaticus major during the pain threshold level. This finding can be partly supported by the previous emotion study, which described that BIS was significantly related to facial EMG responses for all the negative pictures (Balconi, Falbo, and Conte, 2012). Each subscale of BAS and BAS total do not relate to the biopotentials of pain, the explanation of which could be that BAS seems to be more responsive to positive stimuli while pain is experienced as a negative threat with a low valence and high arousal (Carver and White, 1994; Hadjistavropoulos et al., 2011; Craig, 2018). On the contrary, as the aversive motivational system, BIS serves to alert participant to the possible danger and promotes a withdrawal behavioral response during pain, which support the explanation that high BIS may induce a greater sensitivity for experimental pain that generates a low facial EMG activity (Balconi, Falbo, and Conte, 2012; Carver and White, 1994).

During the pain tolerance level, the results present that the higher SCL-90-R_Hostility predicts both lower activity of zygomaticus major and corrugator supercilii (see Table 16), which is the first finding showing the influence of psychological symptom tendencies on facial EMG during experimental pain. Characterized as aggressive behavior and angry

attitude, hostility has been linked to many health outcomes, such as pain (Crombez et al., 2009; Graham et al., 2006; Hardt, Gerbershagen, and Franke, 2000). The positive effect of hostility on facial EMG during experimental pain could be partly supported by the facial EMG studies about emotion, which indicated that negative affective stimuli can increase EMG amplitude of corrugator supercilii, while EMG amplitude of zygomaticus major cannot discriminate negative and neutral emotions (Larsen, Norris, and Cacioppo, 2003; Tan et al., 2012). Furthermore, as the EMG features of both corrugator supercilii and zygomaticus major could help to recognize experimental pain (Gruss et al., 2015), hostile related psychological traits may predict the facial EMG activities during experimental pain.

Surprisingly, it seems that personality does not significantly influence the biopotentials of pain, one explanation of which could be the high significance level of the Bonferroni correction ($p < 0.007$). Besides, in the current study neuroticism is significantly related to BIS and all self-reported symptom subscales, another explanation could be that neuroticism may have an indirect influence on facial EMG. Based on the Regression Models (see Table 17), it could conclude that several psychological traits could explain part of the individual variance of facial EMG during pain, which should be taken into consideration when researchers want to better understand the facial EMG of pain and mean to improve the classification accuracy of pain autonomic recognition.

4.3.3 The influence of psychological traits on the facial expression of pain

The experience of pain is often represented by changes in facial expression, which is specific and can be distinguished from other facial expressions (Hadjistavropoulos et al., 2011; Kunz and Lautenbacher, 2014). Evidence of pain that is available from facial expression has been the subject of considerable scientific investigation. Facial Action Coding System (FACS) has been used in most of the studies, which has been criticized for time-consuming, lack of objectivity, and disability to represent temporal sequences (Hadjistavropoulos et al., 2011; Bartlett et al., 2014; Craig, 2018). Taking those shortcomings into account, the present study used automatic recognition systems to analyze the facial expression of pain, which can record and encode dynamic facial pain expressions.

The facial expression of pain plays a crucial role in pain communication and pain diagnostics, which is influenced by many factors consisting of cognitive, affective, behavioral, and motivational factors; biological processing systems; and the cultural, interpersonal, and situational contexts (Hadjistavropoulos et al., 2011). Compared with the research highlighting the area of brain processing and social contexts such as sympathetic attention or help reinforcement, to date, systematic study of the impact of the psychological traits on the facial expression of pain has received little attention (Hadjistavropoulos et al., 2011; Karmann et al., 2014; Karmann, Lautenbacher, and Kunz, 2015; Keogh, 2014; Kunz et al., 2011; Williams, 2002). To bridge the gap between facial expression and psychological traits, another aim of the present study is to explore the influence of psychological traits on the facial expressions of experimental pain.

In the research area of face and personality, the previous studies mostly focus on the study of the relationship between facial symmetry and personality, whereas a consistent conclusion cannot be reached (Racine et al., 2012). The result of the negative association between facial

distance change and agreeableness is partly consistent with the result of the study conducted by Fink et al. (2005) which found a negative relationship between facial symmetry and openness and agreeableness. According to evolutionary psychologists, facial symmetry relates to health, while asymmetrical faces were rated as being more neurotic, less agreeable, and less conscientious (Craig et al., 1991; Racine et al., 2012). As a hurt stimulus, heat pain can be considered as a threat jeopardizing human health, so the personality traits may partly predict the facial expression of pain.

Regarding the facial distance change during experimental heat pain, the correlation analysis results show that higher agreeableness is related to smaller facial distance change in low-level heat pain (P2), and higher scores of cognitive reappraisal and hostility are positively associated with a larger facial expression change in the tolerance level of pain (P4). As for nasal wrinkling, during low-level heat pain (P2) higher psychoticism relates to a slighter nasal wrinkling, and higher scores of obsessive-compulsive and hostility show a more obvious nasal wrinkling in high-level heat pain (P3), besides, during pain tolerance level (P4) higher scores of anxiety and Phobic anxiety are related to a more obvious nasal wrinkling. The results indicate that only limited psychological variables are related to the facial distance change and nasal wrinkling during pain. As a positive character, agreeableness contrasts traits such as kindness, trust, and warmth with such traits as hostility, selfishness, and distrust (McCrae and Costa, 2004), which may provide some information for facial pain expression. Unexpectedly, neuroticism and extroversion do not present influence on the facial distance change during pain. Until now it has been no report about the effect of personality on facial change during experimental pain, further research is needed to better understand this tentative result.

BIS/BAS systems concern behavioral regulation and have got much attention in the studies of emotions and relevant behaviors. BAS is conceptualized as a motivational system, which is sensitive to reward and non-punishment, responding strongly to positive approach-related emotions. Not surprisingly, it is understandable that the present study does not find any relationship between facial changes of pain with BAS (Carver and White, 1994; Gray, 1990). On the contrary, BIS is considered as an attentional system that is sensitive to signals of punishment and non-reward, with promoting the inhibition processing of behavioral withdraw (Carver and White, 1994; Gray, 1990). The result does not indicate a significant relationship between self-report BIS and the degree of facial pain expression, which is consistent with a 2015 study that evaluated the role of inhibitory mechanisms in the regulation of facial expressiveness during pain (Karmann, Lautenbacher, and Kunz, 2015). The reasons to explain the result can be: firstly, the completion of the self-report BIS/BAS scales needs the participants' explicit thinking and conscious processing while the facial changes were assessed by automatic implicit method (Balconi, Falbo, and Conte, 2012); secondly, as each participant received four levels of heat pain which were repeatedly applied 20 times, the participants are no longer sensitive to the punishment-like stimuli without a subjective inhibition; the last but not the least, no association exists.

The regulation of negative emotions is important and necessary in daily life. Gross and John (2003) have identified a process model of emotion regulation including two strategies named reappraisal and suppression respectively. Reappraisal decreases negative emotional

experience and expression but increases positive emotional experience and expression, however, suppression decreases not only negative but also positive emotional experience with less impact on the former and more impact on the latter (Gross and John, 2003). The present results indicate that a higher score of cognitive reappraisal can predict a larger facial distance change during pain tolerance, to be specific, the correlation analysis shows that cognitive reappraisal is negative related to the eye/brow closeness measuring the lowering of the brows, which is a crucial facial expression of pain. This finding is partly consistent with the results of a 2015 study that reappraisal and suppression can reduce both verbal reports and facial expressions of pain (Hampton et al., 2015). The study does not find any association between expressive suppression and facial changes of pain, the reason for which could be that it seems much easier for the participant to reappraise than to suppress in an expected pain experiment with the absence of social pressure. All in all, the present result may support the function of reappraisal on the inhibition of emotional expressiveness of pain.

In terms of SCL-90-R, a higher score of hostility predicts a larger facial distance change during pain tolerance, specifically, which predicts a smaller brow mouth closeness in both parts of the face. No study has explored the correlation between facial expressions and self-reported psychological symptoms. The current results indicate that several negative symptoms may are related to facial distance change and nasal wrinkling, especially, the positive influence of several anxiety-related factors such as obsessive-compulsive, anxiety, and hostility, are obvious.

The linear regression results show that, only at pain tolerance level, “SCL-90-R_Hostility, SCL-90-R_Paranoid ideation, and ERQ_Cognitive reappraisal” can explain 15% of the total variance of facial distance change, and “NEO_Neuroticism and NEO_Agreeablenes” can predict 8% of the total variance of nasal wrinkling (see Table 18). Obviously, the linear regression results indicate that all 24 psychological traits have a low influence on facial expressions during a heat experimental pain. Associations between facial appearance and personality attributes could depend on a number of possible mechanisms. The tolerance pain is the least controllable stimuli among the four pain stimuli by the subjects, so the pain behaviors of the tolerance pain can be considered as the strongest and truest evidence to study. Past studies showed that healthy people can regulate their facial expressions of pain in accordance with social display rules. For instance, healthy subjects showed more facial expressions of pain with the accompany of their partner, conversely presented facially express less pain in the presence of a stranger (Hadjistavropoulos et al., 2011; Lautenbacher et al., 2017). In other words, social display rules influence healthy individuals cognitively and emotionally on the actually expressed facial pain (Hadjistavropoulos et al., 2011; Karmann, Lautenbacher, and Kunz, 2015). With this in mind, in the current study, the subjects were introduced to perform the experiment along with the absence of the experimenter and others. Accordingly, compared to the previous studies, the present study used a different more objective method especially measuring the specific facial distance changes during pain stimulations, which is the first one to explore the influence of the personality traits on facial expressions of experimental pain. The present facial expression study can partly support Williams’ general point that facial expressions of pain have a non-operant, evolutionary origin (Hadjistavropoulos et al., 2011; Williams, 2002), but these

results, of course, require further investigation before one can make any warranted interpretation.

4.4 Limitations and future directions

Individual differences are a core characteristic of the experience of pain and have been a vital topic in the area of pain research for many years. The current study tried to identify the factors contributing to individual differences in pain, which explored the influence of sex, age, and psychological traits on experimental heat pain experience, especially focusing on their influence on the objective measurements of pain thresholds. In this chapter, some limitations of this study should be discussed first.

To begin, as a subjective and personal phenomenon, pain is a complicated experience and always results from the dynamic interaction between biological, psychological, and social factors (Melzack, 1988; Duncan, 2000). As a result, the experience of pain is hard to quantify and the precise measurement of pain is difficult. Based on the pain threshold and pain tolerance threshold, the current study employed the measurements of biopotentials and facial expressions of pain, but the entire presentation of pain experience may still be unreachable.

Second, except for sex and age, other demographic characteristics of the participants were not controlled in this investigation, for example, the education level and the past pain experience of the participant may influence the pain experience. Besides, the participants were enrolled through notices posted at the university campus and through advertisement in local newspapers, so the voluntary sample possibly shared some kind of tendency of pain experience which could be potentially biasing to the results and influence the interpretation of the results.

Thirdly, there were some limitations on the data acquisitions of the pain parameters and their interpretations, as the outcome variables may not fully and clearly present the details and construct of good and poor outcomes. According to Gruss et al. (2015), the biopotential features of pain experience were extracted based on a mathematical procedure developed in the emotion lab of Ulm University, which included amplitude, frequency, stationarity, entropy, linearity, variability, and similarity, however, only EMG_{zyg}_peak, EMG_{corr}_peak, EMG_{trap}_peak, EDA_peak which described the amplitude, and ECG_meanRR, ECG_rmssd, and ECG_slopeRR which represented the variability of ECG, were included in the analysis, as the rest features were calculated for automated pain recognition and without precise interpretation for pain experience. For the data extraction of facial expression features of pain, two variables were invented to describe the facial expression change of participants. The first one was calculated by the 3D distance between brows and eyes, brows and mouth, eyes and mouth, as well as the width and height of the mouth, and the second one measured the texture of the nasal wrinkles calculated by the mean gradient magnitude of the encoding facial regions (Werner et al., 2017). Due to the different calculation methods, the two facial expression features cannot be combined into one variable that describes the changes in the face, which brings difficulty in the interpretation of facial expression changes during pain stimulations.

Although the limitations above are available, the present research has important implications for studies on understanding the individual differences in pain experience and improving the accuracy of automated pain recognition in a clinical condition. The recommendations for the further research can be made based on the limitations.

Firstly, as pain is an integrative phenomenon, careful experimental design and precise measurement are needed, furthermore, the gender role of the experimenters should be considered and explored.

Secondly, the education level, the past pain experience, and the current situation of individuals should be taken into consideration in the pain experiment. Besides, when conducting the enrollment, the experimenter should recruit the participants with different backgrounds from more than one channel and should consider enrolling passive participants who possibly tend to avoid experimental pain, especially for the purpose of clinical application.

Thirdly, when investigating the individual differences in experimental pain experience, many previous studies have compared the scoring of pain, pain thresholds, or facial expressions of pain based on FACS, which can hardly describe the experience of pain precisely and consistently. Along with the advancement of technology, more and more researchers attach great importance to the automated recognition of pain, in which the objective assessment of pain plays an important role such as biopotentials of pain and automated facial measurement of pain (Bartlett et al., 2014; Gruss et al., 2015; Werner et al., 2017; Xiong and De la Torre, 2013). Automated pain recognition based on the objective measurements of pain will be more and more important and promising, and the influence of individual differences on pain recognition performance will be deemed as an attractive topic. In addition, the objective variables should be well calculated and be of appropriate interpretation meaning, taking the current study for example, it is better to combine the facial distance change with nasal wrinkling.

The ultimate aim of the present dissertation is to help to advance and improve the automated recognition accuracy of pain. Given the findings of this study, a deeper investigation into the individual differences in automated pain recognition would be interesting. It will be beneficial to consider the influence of sex, age, and psychological traits on pain experience, as ultimately the goal is to help the medical professionals to better understand patients' pain and to better recognize their pain through objective measurement, especially when the patients are infants, young children, older people with dementia, or others having difficulties in verbal reporting.

CHAPTER 5

SUMMARY

The purpose of the present dissertation was to explore the potential influence of individual differences including sex, age, and psychological traits on experimental heat pain experience. As pain is a very personal and subjective phenomenon, the comparison of individual differences in pain experience is less objective and this problem lasts for centuries. However, with the rise of pain measuring via biopotentials and automatic systems for facial recognition, it is possible to investigate the influence of individual characteristics on experimental pain experience more objectively.

For assessing the psychological traits of participants, four questionnaires were selected, including the Neo Five-Factor Inventory (Neo-FFI), the Behavioral Inhibition System/Behavioral Activation System scales (BIS/BAS), the Emotion Regulation Questionnaire (ERQ), and the Symptom Checklist-90-Revised (SCL-90-R). Regarding experimental pain elicitation, a tonic heat stimulation method was used. For pain measurement, biopotentials including electromyography (EMG), electrocardiogram (ECG), and electrodermal activity (EDA) were recorded during pain stimulations, besides, automatic recording of facial expressions of pain was applied.

After extraction of biopotentials data, seven features were employed to describe the biopotential performance of pain, with three describing the variability of Electroencephalography, and four presenting the peak of EDA, the peak activity of EMG of trapezius, EMG of corrugator supercilia, and EMG of zygomaticus major, respectively. A set of facial expression features were acquired to describe pain-related facial actions including lowering of the brows, tightening of the lid, closing of the eyes, raising of the cheeks and the upper lip, wrinkling of the nose, and stretching and opening of the mouth, based on the 3D landmarks obtained by the Iterative Closet Point algorithm. As a result, the variable “facial distance change” (FDC) representing the total facial changes of the facial features except for the change of nasal wrinkling and the variable “nasal wrinkling” (g_n) representing the change of nasal wrinkling were calculated to describe the facial expressions of pain.

From the perspective of the method, the present study is the first study that investigated the individual differences in objective pain experience by measuring biopotentials and facial expressions during experimental heat pain stimulations, which is a noteworthy contribution to future pain research.

With respect to the results, several remarkable findings were obtained in this study. Considering the influence of sex, the female is more sensitive to experimental heat pain with lower pain tolerance and behaves more obvious nasal wrinkling during pain tolerance stimulation. Regarding the age groups, the elderly are less sensitive to experimental pain with higher pain thresholds, besides, they present decreased biopotential activities and fewer facial expressions during heat pain thresholds compared with their young counterparts. Moreover, several psychological traits can partly predict pain experience. With respect to

pain thresholds, the correlation results indicate that individuals with high Behavioral Inhibition System may be sensitive to pain with lower pain intensities, and Somatization, Obsessive-compulsive, Hostility, Phobic Anxiety, and Psychoticism are associated with pain tolerance negatively, and the regression model indicates only Positive Symptom Distress Index and Phobic Anxiety can predict pain threshold and pain tolerance with a low influence. Considering biopotentials of pain, the correlation results show that only BIS has a negative relationship with the EMG activity of zygomaticus major during the pain threshold level and Hostility can predict both lower activity of zygomaticus major and corrugator supercilii at the level of pain tolerance, and the regression results indicate that several psychological traits could explain part of the individual variance of facial EMG during pain. In terms of facial expressions of pain, only limited psychological variables are associated with the facial distance change and nasal wrinkling during pain, and the regression results present that only at pain tolerance level Hostility, Paranoid ideation, and Cognitive reappraisal can explain 15% of the total variance of facial distance change and Neuroticism and Agreeableness can predict 8% of the total variance of nasal wrinkling.

In conclusion, although there exist several limitations in this study, the findings that several factors can influence the objective measurements of experimental pain are insightful and advantageous for the better advancement and improvement of the automated recognition accuracy of pain both under the experimental or clinical condition.

CHAPTER 6

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APPENDIX

APPENDIX I Description and results of sex difference in biopotential performance (m = males, f =females, M = mean, SD = standard deviation).

Biopotentials	m		f		t	p
	M	SD	M	SD		
Baseline						
EMG_{zyg}_peak	-0.208	0.241	-0.194	0.224	-0.282	0.779
EMG_{corr}_peak	-0.261	0.261	-0.241	0.270	-0.367	0.715
EMG_{trap}_peak	-0.107	0.207	-0.089	0.236	-0.383	0.703
EDA_peak	-0.175	0.331	-0.162	0.332	-0.189	0.850
ECG_meanRR	0.101	0.295	0.192	0.262	-1.574	0.119
ECG_rmssd	0.104	0.289	0.203	0.254	-1.766	0.081
ECG_slopeRR	0.074	0.266	0.043	0.262	0.579	0.564
Pain threshold level						
EMG_{zyg}_peak	-0.101	0.330	-0.210	0.179	1.997	0.051
EMG_{corr}_peak	-0.139	0.279	-0.202	0.259	1.130	0.261
EMG_{trap}_peak	-0.100	0.238	-0.163	0.230	1.313	0.193
EDA_peak	-0.139	0.277	-0.109	0.315	-0.485	0.629
ECG_meanRR	0.117	0.249	0.153	0.240	-0.716	0.476
ECG_rmssd	0.110	0.250	0.143	0.234	-0.657	0.513
ECG_slopeRR	0.086	0.269	0.181	0.231	-1.823	0.072
Pain tolerance threshold level						
EMG_{zyg}_peak	0.714	0.802	0.715	0.737	-0.010	0.992
EMG_{corr}_peak	0.946	0.764	0.904	0.821	0.255	0.799
EMG_{trap}_peak	0.276	0.515	0.415	0.575	-1.229	0.222
EDA_peak	0.272	0.509	0.195	0.414	0.807	0.422
ECG_meanRR	-0.331	0.404	-0.288	0.473	-0.473	0.637
ECG_rmssd	-0.326	0.397	-0.287	0.475	-0.428	0.670
ECG_slopeRR	-0.392	0.513	-0.294	0.555	-0.886	0.378

APPENDIX 2: The results of correlation analysis between psychological traits and facial expression change during pain stimulations (FDC = facial distance change, P1 = pain threshold level, P2 = pain tolerance threshold level, g_n = nasal wrinkles).

Psychological Traits	FDC(P1)	FDC(P2)	g_n(P1)	g_n(P2)
NEO_Neuroticism	0.022	-0.061	0.023	0.2011
NEO_Extraversion	-0.082	0.141	-0.043	0.140
NEO_Openness	-0.041	-0.013	0.142	0.201
NEO_Agreeableness	-0.161	-0.242*	-0.054	0.073
NEO_Conscientiousness	-0.062	-0.058	0.063	-0.112
BAS_Total	-0.162	0.019	0.063	0.042
BAS_Drive	-0.101	0.043	0.061	0.002
BAS_Fun Seeking	-0.189	0.141	0.123	0.062
BAS_Reward Responsiveness	-0.081	-0.142	0.043	0.051
BIS_Total	0.013	-0.121	-0.083	0.042
ERQ_Cognitive Reappraisal	0.014	0.113	0.181	0.202
ERQ_Expressive Suppression	0.012	-0.001	-0.013	-0.051
SCL-90-R_Somatization	-0.061	0.027	0.128	0.202
SCL-90-R_ Obsessive-Compulsive	-0.062	-0.122	-0.040	0.191
SCL-90-R_ Interpersonal Sensitivity	0.104	-0.051	-0.189	-0.012

SCL-90-R_Depression	0.051	-0.103	-0.011	0.162
SCL-90-R_Anxiety	-0.050	-0.112	0.143	0.256
SCL-90-R_Anger-Hostility	0.032	-0.031	0.030	0.152
SCL-90-R_ Phobic Anxiety	0.033	0.040	0.081	0.281*
SCL-90-R_ Paranoid Ideation	0.012	-0.051	-0.122	0.057
SCL-90-R_Psychoticism	-0.014	-0.052	-0.031	0.068
SCL-90-R_Global Severity Index	0.002	-0.091	-0.062	0.149
SCL-90-R_Positive Symptom Total	-0.014	-.0113	-0.047	0.162
SCL-90-R_Positive Symptom Distress Index	-0.051	-0.058	0.011	0.161

Note: * $p<0.05$

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CURRICULUM VITAE

CV was removed for data privacy protection reasons.