Emotional modulation of autonomic responses to painful trigeminal stimulation☆

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A R T I C L E   I N F O
Article history:
Received 8 August 2008
Received in revised form 13 October 2008
Accepted 13 October 2008
Available online 30 October 2008

Keywords:
Heart rate
Skin conductance
Pain
Emotion
Electrodermal stimulation
Trigeminal system

A B S T R A C T
Dysregulation of supraspinal pain modulation may contribute to chronic pain, including head/face pain. Our laboratory has shown that emotional picture-viewing reliably modulates subjective and physiological pain responses to noxious extracranial (sural nerve) stimulation, suggesting this is a valid method of studying supraspinal modulation. However, to study head/face pain, it is important to determine whether responses evoked by trigeminal stimulation are also modulated. In the present study (34 healthy participants), emotionally-charged pictures (unpleasant, neutral, pleasant) were presented during which painful trigeminal stimulations were delivered during and in between pictures. Autonomic responses to each shock (pain-evoked HR acceleration, pain-evoked skin conductance response [SCR]) were recorded. Consistent with research on extracranial pain, autonomic responses were larger during unpleasant pictures and smaller during pleasant pictures, with linear trends explaining 23% of the variance in pain-evoked HR and 35% of the variance in pain-evoked SCR (p < .05). Implications for studying cranial pain are discussed.

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1. Introduction

Pain is a dynamic experience that is significantly influenced by endogenous modulatory (facilitatory and inhibitory) mechanisms—some of which are mediated by supraspinal centers. These supraspinal circuits help maintain a pain “balance” under normal conditions (Crown et al., 2004; Mayer et al., 2006). However, if dysregulated (e.g., hypoxic inhibition or hyperactive facilitation), chronic pain may result. Consistent with this notion, some research has established a link between dysregulation of these modulatory circuits and chronic pain conditions (Edwards et al., 2003; Gebhart, 2004), including headache disorders (Goadsby, 1997; Knight and Goadsby, 2001; Sandrini et al., 2006; Weiller et al., 1995).

One important supraspinal circuit involves the periaqueductal gray (PAG) and rostral ventromedial medulla (RVM) (Goadsby, 1997; Knight and Goadsby, 2001; Weiller et al., 1995). This circuit is involved in cognitive and affective modulation of pain via input from the amygdala, hypothalamus, and anterior cingulate cortex (Bingel et al., 2006; Fields and Basbaum, 1999). For example, stimulation of the amygdala, an area involved in emotion (Phan et al., 2002; Reiman et al., 1997), leads to PAG-dependent modulation of nociception (Helmstetter et al., 1998), suggesting emotion can influence pain via the PAG-RVM circuit (Rhudy and Meagher, 2001a). To assess the ability of emotional stimuli to activate supraspinal modulation (presumably via the PAG-RVM circuit), recent studies have utilized a procedure called emotional controls of nociception (ECON; Rhudy et al., 2005a, 2006, 2008). This procedure involves the presentation of emotionally-charged picture stimuli known to activate the amygdala (Garavan et al., 2001; Garrett and Maddock, 2006; Pissiota et al., 2003). When noxious stimuli are delivered to the sural nerve of the ankle during the presentation of these pictures, subjective pain and concomitant nociceptive (pain-related) reflexes are reliably modulated. Pleasant pictures (eroticca) inhibit pain and nociceptive reflexes whereas unpleasant pictures (threat scenes) enhance them (Rhudy et al., 2005a, 2006, 2008).

An extension of these studies found autonomic responses to noxious sural nerve stimulation were similarly modulated. Pain-evoked skin conductance response (SCR) and heart rate (HR) acceleration were smaller during pleasant pictures than during unpleasant (Rhudy et al., 2007). This finding contrasts the typical pattern of emotional modulation of picture-evoked HR acceleration and SCR (Bradley et al., 2001; Lang et al., 1993). Picture-evoked HR acceleration is greatest during pleasant pictures and smallest during unpleasant pictures, whereas picture-evoked SCR is greater for pleasant and unpleasant pictures relative to neutral. Thus, given that emotional modulation of pain-evoked HR and SCR show the same valence trend as startle and pain (Bradley et al., 2001; Rhudy et al., 2005b), pain-evoked HR acceleration and SCR may index defensive responding.

In our previous ECON studies, nociceptive input was generated from extracranial stimulation (sural nerve of the ankle). To determine the contribution of ECON to the modulation of head pain and related...
disorders, it is necessary to study pain processing within the trigeminal system. Indeed, this could have important implications, given the putative involvement of supraspinal modulatory circuits in headache disorders (Goadsby, 1997; Knight and Goadsby, 2001; Weiller et al., 1995).

To address this issue, a recent study used the ECON paradigm to assess modulation of trigeminal pain and nociception (Williams and Rhudy, in press). Using stimulating parameters developed by others to elicit nociceptive-specific blinks (Kaube et al., 2000), painful electric shocks were delivered to the supraorbital branch of the trigeminal nerve on the forehead to evoke subjective pain and nociceptive blinks (Williams and Rhudy, in press). Consistent with prior findings, results indicated pain and nociceptive blinks were facilitated during unpleasant pictures and inhibited during pleasant pictures, with the valence linear trend explaining 51% of the variance in pain and 25% of the variance in nociceptive blinks (Williams and Rhudy, in press).

The autonomic nervous system and its supraspinal controls have been implicated in the initiation and maintenance of headaches (via abnormalities in the hypothalamic generator), and autonomic symptoms are common among some types of headaches (e.g., cluster headache, migraine) (May, 2006; Obermann et al., 2007). Therefore, it seems natural to extend the ECON paradigm to study modulation of autonomic responses to painful stimulation of the trigeminal nerve. Doing so would provide a means of comprehensively assessing modulation of trigeminal nociceptive reactivity (i.e., pain ratings, nociceptive blinks, HR reactions, SCR).

Data for the present study were collected during a recent experiment examining emotional modulation of trigeminal pain and nociceptive blinks in 34 healthy participants (Williams and Rhudy, in press). In that study, 24 emotionally-charged pictures (unpleasant, neutral, pleasant) were presented during which stimulations set at 150% pain threshold were delivered to the supraorbital branch of the trigeminal nerve. For the present study, pain-evoked HR acceleration and pain-evoked SCR were calculated following each stimulation to determine if emotional picture-viewing modulated autonomic responses to painful stimulations. It was predicted that pleasant pictures would inhibit pain-evoked HR acceleration and SCR, whereas unpleasant pictures would facilitate pain-evoked HR and SCR. Additionally, exploratory analyses examined the strength of the relationships between autonomic responses and pain ratings during emotional modulation to determine whether autonomic measures provide unique information about nociceptive responding above and beyond pain report. Although these data were collected during a prior study (Williams and Rhudy, in press), the results of these nociceptive outcomes have not been published elsewhere.

2. Method

2.1. Participants

Participants were recruited from the Tulsa community and The University of Tulsa psychology subject pool. The 36 participants were primarily female (66.7%), White-non Hispanic (77.8%); single (83.3%), employed (66.7%), with an average age of 21.22 years (SD = 2.27). Participants were excluded for: <18 years of age, a self-reported history of cardiac, neurological, or neuromuscular disorders; chronic pain, recent psychological trauma (as defined by the DSM-IV), use of OTC or narcotic pain medication within the last 24 h, or use of antidepressant, hypertensive, or anxiolytic medications. Participants provided informed consent after being fully informed of the details of the study and being told they could withdraw from the study at any time. One participant withdrew, and one participant was excluded from analyses due to equipment failure, leaving 34 participants with completed data. Participants were provided a $20.00 gift card to a local retailer (13 participants) or course credit (23 participants) for their participation.

2.2. Apparatus, stimulus & signal parameters, & electrode application

A computer running LabVIEW software (National Instruments, Austin, TX) equipped with dual monitors and A/D board (National Instruments, PCI-6036E) was used to control all stimuli, questionnaire presentation, and data acquisition, as well as offline data reduction. One 17” flat panel monitor was used by the experimenter to monitor physiological signals and experimental timing. Another 17” flat panel monitor (positioned approximately 5 m from the participant) presented picture stimuli and questionnaires. Sound attenuating headphones and a video camera allowed the experimenter to communicate with and monitor the participant from an adjacent room.

Electrical stimulations to the left supraorbital nerve (10 mm superior to the supraorbital foramen) were delivered by a Grass Instruments stimulator (Model S88, West Warwick, RI), stimulus isolation unit (Model SIU8T), constant current unit (Model CCU1), and a custom built concentric stimulating electrode. The concentric stimulating electrode had a .5 mm central cathode with an external ring anode (10 mm inner and 30 mm outer diameter) (Kaube et al., 2000). The smaller cathode and smaller distance between the cathode and anode, relative to normal electrode applications, utilizes lower current to selectively activate superficial nociceptors to the exclusion of deeper non-nociceptive A-fibers (Kaube et al., 2000). The onset/offset of the stimulator was controlled by computer, and a computer-controlled voltage regulator varied the current to the participant.

Psychophysiological signals were sampled at 1000 Hz and collected/filtered using a Grass Instruments Model 15LT Bipolar Amplifier with Quad AC (15A54) and Dual DC (15A12) modules. All recording electrodes were Ag/AgCl. To prepare the skin for the application of electrocardiogram (ECG) electrodes, orbicularis oculi EMG electrodes, stimulating electrodes, and the reference electrode, first the skin was degreased with alcohol, slightly abraded using NuPrep gel to achieve impedances below 5 KΩ, and then conductive gel (EC90, Grass Instruments) was used to fill the electrodes. A common reference electrode was placed on the mastoid process behind the left ear. To record ECG, electrodes were placed on each forearm. SCR was measured with an adaptor (Grass, Model SCA1) and two Ag/AgCl electrodes filled with isotonic paste (EC33, Grass Instruments) applied to the medial digit of the volar surface of the right index and middle fingers. Prior to SCR electrode application, participants washed and dried their hands (Venables and Christie, 1980). To measure nociceptive blinks, EMG electrodes were attached over the left orbicularis oculi muscle (data presented elsewhere) (Williams and Rhudy, in press).

2.3. Emotional picture stimuli

Digital pictures from the International Affective Picture System were used to induce emotion (CSEA, 1999; Lang et al., 1999). Pictures had varying content with eight pleasant (couples in erotic poses), eight neutral (household objects, mushrooms), and eight unpleasant (human and animal attack scenes) pictures. These contents were chosen because they have been shown to elicit reliable emotional modulation of pain and nociception (Rhudy et al., 2005b, 2007, 2008). Mean normative valence and arousal ratings (as assessed with the SAM, see below) and picture numbers for the pictures used in this study are as follows: attack (Valence: M = 2.90, Arousal: M = 6.88, Numbers: 1050, 1120, 1300, 1930, 3530, 6260, 6350, 6510), neutral (Valence: M = 5.11, Arousal: M = 2.68, Numbers: 5500, 5510, 5520, 5530, 7010, 7030, 7040, 7080), erotica (Valence: M = 6.82, Arousal: M = 6.18, Numbers: 4653, 4664, 4676, 4680, 4690, 4694, 4695, 4800) (Lang et al., 1999). Pictures were presented on a 17” computer monitor in a dimly lit room. The order of presentation was randomized across participants with the limitation that not more than two pictures of similar valence were shown consecutively.
2.4. Pain rating scale

Participants rated each electrical stimulation on a vertically oriented numerical rating scale presented by the computer (France et al., 2002; Rhudy et al., 2005a). Bottom-to-top, the scale was labeled: 0 (no sensation), 1 (just noticeable), 25 (uncomfortable), 50 (painful), 75 (very painful), and 100 (maximum tolerable). Participants responded by moving an indicator along the scale and submitting their answers by computer mouse. Emotional modulation of pain ratings are reported elsewhere (Williams and Rhudy, in press). For the purposes of the present experiment, the 0 to 100 unit ratings were used to determine pain threshold and to assess the relationship between autonomic responses and pain during emotional modulation.

2.5. Self assessment manikin

After each picture, affective valence (pleasure) and arousal were rated using a computer-presented version of the Self-Assessment Manikin (SAM) to assess emotional reactions to each picture (Bradley and Lang, 1994). This scale includes two sets of pictographs (valence & arousal) consisting of 5 pictures each. Ratings are made on computer by placing an indicator on or between any of the pictures. This results in ratings between 1 and 9 for valence (unhappy to happy) and arousal (calm to excited).

2.6. Procedure

All procedures were approved by The University of Tulsa institutional review board. Informed consent was obtained following provision of information about the experiment. A brief health screen and interview was used to assess health status and determine eligibility. If eligible, the participant was familiarized with rating scales (Self Assessment Manikin, pain rating scale), instrumented, and seated comfortably in a reclining chair. All ratings were made using a computer mouse positioned on a lap desk. Participants were instructed that there were 2 phases to the experiment. Pain threshold was assessed during Phase 1 by sending several electric stimulations to the trigeminal nerve. Throughout this phase, a pain rating scale and pain threshold were used to determine pain threshold and to assess the relationship between autonomic responses and pain during emotional modulation.

2.7. Data reduction and analyses

ECG was converted offline to beats per minute (BPM) in half second intervals by determining the interbeat interval in milliseconds and inspected for errors. Pain-evoked HR acceleration was calculated by determining the maximum increase in heart rate in BPM from baseline (1 s before shock onset) during the 6 s after shock presentation (Bradley et al., 2001; Rhudy et al., 2007). Pain-evoked SCR was calculated by subtracting baseline skin conductance level (mean of 1 s before shock onset) from the peak skin conductance response 1–4 s after shock presentation (Bradley et al., 2001; Rhudy et al., 2007; Venables and Christie, 1980). To be consistent with prior studies of emotional modulation of pain-evoked reactions (Rhudy et al., 2007, 2008), pain-evoked HR acceleration and SCR were standardized within-individuals by converting to z-scores and then averaged by picture valence (unpleasant, neutral, pleasant). Although not reported, results of analyses for unstandardized variables were similar to those reported for standardized variables (authors can be contacted for results). Means and standard errors for unstandardized variables are presented for comparison (Table 1).

Repeated measures ANOVAs were conducted on each dependent variable, with picture valence (unpleasant, neutral, pleasant) as the within-subject independent variable. Levels of the picture valence independent variable were entered along the continuum of affective valence (i.e., unpleasant, neutral, pleasant), thus, linear (+1, 0, –1) and quadratic (+1, –1, +1) trend analyses were used to test valence and arousal effects, respectively. Additionally, one-tailed Fisher’s LSD tests were used for a priori mean contrasts for autonomic responses. Order of DNIC and ECON procedures, and participant gender were initially included as between-subjects variables, however, all effects were nonsignificant (ps > .05) and thus dropped from final models. Partial eta-squared ($\eta^2$) and Cohen’s d effect sizes are reported. Cohen (1977) provides guidelines for interpreting $\eta^2$ (small = .01, medium = .06, large = .14) and d (small = .2, medium = .5, large = .8).

2.8. Hypotheses

Significant linear trends were expected for pain-evoked HR acceleration and SCR. Pain-evoked autonomic responses were

<table>
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<th>Table 1</th>
<th>Unstandardized means and standard errors for autonomic outcomes</th>
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<td>Autonomic responses</td>
<td>Picture content</td>
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<tr>
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<tr>
<td>Pain-evoked SCR (µS)</td>
<td>0.69</td>
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<td>Pain-evoked HR acceleration (BPM)</td>
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Note. M = mean, SEM = standard error of the mean, SCR = skin conductance response, µS = microSiemens, HR = heart rate, BPM = beats per minute.
predicted to be smaller during pleasant compared to unpleasant pictures, with neutral pictures in between (Rhudy et al., 2005a, 2006, 2007, 2008).

3. Results

3.1. Preliminary analyses

Repeated measures ANOVAs were conducted to determine if there were significant effects of picture valence for pre-shock baselines used to calculate SCR and HR acceleration. The main effect of picture valence was not significant for skin conductance baselines \([F(2, 66) = .49, p = .62, \eta^2 = .02]\) or HR baselines \([F(2, 66) = 1.87, p = .16, \eta^2 = .05]\). Thus, picture valence did not significantly alter pre-shock baselines.\(^1\)

3.2. Manipulation checks—self-reported emotion ratings

Manipulation checks (pleasure/valence, arousal) suggest subjective emotion was reliably manipulated. The main effect of picture valence was significant for valence/pleasure ratings \([F(2, 66) = 69.03, p < .001, \eta^2 = .68]\) with the linear trend explaining the greatest variance in pleasure ratings \((p < .001, \eta^2 = .76)\). Erotic pictures \((M = 6.01, SD = 1.39)\) elicited greater subjective pleasure compared to neutral \((M = 4.66, SD = .88; p < .001, d = 1.16)\), and attack pictures \((M = 2.94, SD = 1.12)\) elicited less pleasure compared to neutral \((p < .001, d = 1.71)\). The main effect of picture valence was significant for arousal ratings \([F(2, 66) = 62.47, p < .001, \eta^2 = .65]\) with the quadratic trend explaining the greatest variance in arousal \((p < .001, \eta^2 = .74)\). Compared to neutral pictures \((M = 2.76, SD = 1.43)\), attack \((M = 5.86, SD = 1.33)\) and erotic pictures \((M = 5.27, SD = 1.63)\) elicited greater subjective arousal \((p < .001, d = 1.64)\), and attack pictures elicited slightly more subjective arousal than erotic pictures \((p < .02, d = .38)\).

3.3. Pain-evoked autonomic responses

As predicted, autonomic responses were reliably modulated by picture-viewing (see Fig. 1 for standardized data and Table 1 for unstandardized data). The main effect of picture valence was significant for pain-evoked HR acceleration \([F(2, 66) = 5.30, p < .01, \eta^2 = .14]\) and pain-evoked SCR \([F(2, 66) = 9.18, p < .001, \eta^2 = .22]\). The linear trends \((p < .01)\), but not the quadratic trends \((p > .05)\), were significant for both dependent variables. The linear trend explained 23% of the variance in HR acceleration \((\eta^2 = .23)\) and 35% in SCR \((\eta^2 = .35)\). Pain-evoked HR acceleration was smaller during pleasant pictures compared to unpleasant pictures \((p < .01, d = .54)\) and neutral pictures \((p = .04, d = .94)\). Pain-evoked SCR was greater during unpleasant compared to neutral pictures \((p = .02, d = .68)\) and smaller during pleasant compared to neutral \((p = .03, d = .61)\) and unpleasant pictures \((p < .001, d = 1.26)\).

3.4. Exploratory analyses: relationships between pain-evoked ANS responses and pain ratings

To determine the strength of the relationships between pain ratings and pain-evoked SCR and HR acceleration, multilevel analyses were conducted in SPSS 14.0.2 using the MIXED procedure with maximum likelihood estimation. Initially, an intercept only model was constructed with pain ratings as the dependent variable, and then single predictor models were created (with pain-evoked SCR or pain-evoked HR as a fixed effect predictor) and compared to the intercept only model. The single predictor models suggested SCR was not a significant predictor \((p = .64)\) of pain ratings, did not improve model fit \((\Delta \chi^2 = .20, p > .05)\), and explained less than 2% of the variance \((\eta^2 = .01)\). By contrast, HR was a significant predictor of pain ratings \((p = .036)\), improved model fit \((\Delta \chi^2 = 4.42, p < .05)\), and explained 6% of the variance \((\eta^2 = .06)\). Therefore, HR but not SCR was significantly related to pain ratings during emotional modulation, but neither response shared large proportions of variance with pain ratings.

4. Discussion

This experiment examined the influence of emotional picture-viewing on autonomic responses (pain-evoked HR and SCR) to painful electric stimulation of the trigeminal nerve. Manipulation checks revealed that pictures influenced self-reported emotion as expected: pleasant pictures increased pleasure and arousal, whereas unpleasant pictures increased displeasure (decreased pleasure) and arousal. Pre-shock baseline recordings of skin conductance and HR were not influenced by picture valence, suggesting these data were appropriate for calculating change scores for SCR and HR acceleration. As predicted, picture-viewing modulated HR and SCR in parallel. Linear trends explained 23% of the variance in HR acceleration and 35% of the variance in SCR, suggesting valence modulation. HR acceleration and SCR were smaller during pleasant pictures compared to neutral and unpleasant pictures. In addition, pain-evoked SCR was larger during unpleasant pictures compared to neutral. The fact that unpleasant pictures did not lead to significant facilitation of pain-evoked HR acceleration may indicate a ceiling effect of HR. Although we cannot determine if this is the case from the current study, this finding is consistent with our previous study of emotional modulation of pain-evoked HR (Rhudy et al., 2007).

\(^1\) To confirm that baseline differences did not influence the interpretation of autonomic response data, analyses of autonomic outcomes were also analyzed using SPSS 14.0.2 MIXED procedure which provides a means of covarying baseline values for autonomic responses by individual trials. These analyses produced the same conclusions reported here; but because the MIXED procedure does not allow linear and quadratic trends to be assessed, we chose to report the results from the GLM procedure.
Previous research has demonstrated the modulatory effect of emotional controls of nociception (ECON) on pain report (Rhudy et al., 2005a, 2006, 2008), nociceptive reflexes (Rhudy et al., 2005a, 2006, 2008), and autonomic responses to extracranial (sural nerve) stimulation (Rhudy et al., 2007, 2008). In addition, the present results parallel our results for nociceptive blink reflexes and pain-evoked by noxious trigeminal nerve stimulation (Williams and Rhudy, in press). Across all of these previous studies, the pattern of modulation suggested a valence linear trend. The present study is in line with these prior reports, but is the first to extend the findings to autonomic responses to noxious trigeminal stimulation. Thus, autonomic responses may serve as another physiological measure of trigeminal nociceptive processes. Moreover, exploratory analyses suggested that pain-evoked SCR and HR shared little variance with pain report during the ECON picture-viewing. Indeed, only HR was a significant predictor of subjective pain. While it is unclear at this time why HR but not SCR would correlate with pain, perhaps pain-evoked changes in HR are more salient than SCR, thus influencing subjective evaluation. Regardless of the mechanism, these data suggests that, despite inter-individual emotional modulation patterns for HR and SCR that are similar to pain and nociceptive blinks, autonomic responses to painful trigeminal stimulation provide unique information about nociceptive responding. When combined with our previous studies, it appears that supraspinal modulation via ECON exerts a widespread, reliable effect across multiple response systems (subjective, autonomic, motoric) and multiple nociceptive systems (sural, trigeminal).

4.1. Relations to previous studies of emotion and pain/nociception

Reviews of the literature suggest a valence-by-arousal interaction best characterizes the influence of emotion on pain in healthy individuals (Rhudy and Meagher, 2000, 2001a; Rhudy and Williams, 2005). Positive valenced emotions including experimentally-induced positive mood (Akins et al., 1983; Bruelhe et al., 1993; Cogan et al., 1987; Weisenberg et al., 1998; Zelman et al., 1991; Zillman et al., 1996), sexual excitation (Komisaruk and Whipple, 1986; Meagher et al., 2001; Rhudy et al., 2008), and relaxation (Cogan et al., 1987; Westcott and Horan, 1977) consistently lead to reduced pain/nociception. However, the degree of inhibition is determined by the intensity of the emotional state (as assessed by arousal level), with more intense positive emotions (i.e., sexual excitement) eliciting the greatest inhibition (Komisaruk and Whipple, 1986; Rhudy et al., 2008).

In contrast, emotional intensity/arousal determines the direction of modulation evoked by negative valenced emotions in healthy participants. Negative emotions with low-to-moderate intensity/arousal (e.g., anxiety) lead to enhanced pain/nociception (e.g., Haslam, 1966; Rhudy and Meagher, 2000; Schumacher and Velden, 1984; Weisenberg et al., 1984), whereas negative emotions with high intensity/arousal (e.g., fear, intense stress) lead to decreased pain/nociception (e.g., Janssen and Arntz, 2001; Pitman et al., 1990; Rhudy and Meagher, 2000, 2001b, 2003; Rhudy et al., 2004). Although arousal was manipulated in the present study, pictures would not be expected to inhibit pain/nociception because unpleasant pictures do not represent a threat significant enough to evoke intense negative emotions in healthy participants. Therefore, the ECON paradigm is useful for studying positive emotion-induced inhibition and negative emotion-induced facilitation, but not negative emotion-induced inhibition.

4.2. Implications for the study of head and craniofacial pain

The results of the present study suggest autonomic responses to trigeminal stimulation are viable outcomes to use within the ECON paradigm. Indeed, autonomic responses can be used in conjunction with self-reported pain and nociceptive blink reflexes to provide a comprehensive assessment of responding to trigeminal nociceptive input. Evidence is currently equivocal whether autonomic system function contributes to head pain disorders (Feuerstein et al., 1982; Kroner-Herwig et al., 1993; Leistad et al., 2007; May, 2006; Obermann et al., 2007; Rubin et al., 1985). Nonetheless, assessing supraspinal modulation of autonomic reactivity to trigeminal stimulation in persons with head and craniofacial disorders could provide insight into their pathophysiology.

There is a strong connection between some head pain disorders and affective disturbance (McWilliams et al., 2004; Nicholson et al., 2007). Therefore, it is plausible to hypothesize that dysregulation of emotion circuitry (e.g., amygdala) could alter the manner in which emotion regulates pain. Dysregulation could lead to a decrease in pain inhibition (disinhibition), an increase in pain facilitation, or both; but with the net result being enhanced pain. Consistent with this hypothesis, persons with headache disorders experience greater stress responses (De Benedittis and Lorenzetti, 1992; Wacogne et al., 2003) and negative affect (Nicholson et al., 2007), recover more slowly from stress (Stroons et al., 1999), and report that emotion/stress is one of the most frequent triggers for headaches (Karli et al., 2005). Therefore, the ECON procedure could be used to determine whether there is a dysregulation of emotional modulation in disorders of the trigeminal system. A current study is underway to examine this issue.

A putative circuit involving the anterior cingulate cortex, hypothalamus, amygdala, periaqueductal gray, and rostral ventromedial medulla may mediate emotional modulation of pain and nociception (Bingel et al., 2006; Fields and Basbaum, 1999; Rhudy and Meagher, 2001a); however, additional mechanisms may contribute to the modulation of autonomic responses. For example, peripheral activity in the autonomic branches may influence HR (parasympathetic & sympathetic) and SCR (sympathetic) to the exclusion of central pain pathways. Thus, future research is needed to determine under what conditions the modulation of autonomic responses diverges from the modulation of other response systems, and to determine whether individual differences in autonomic function (e.g., heart rate variability) moderates emotional modulation of autonomic responses (Ruiz-Padial et al., 2003).

4.3. Pain-evoked autonomic responses versus picture-evoked autonomic responses

Emotional pictures modulate autonomic responses differently when a shock stimulus is not presented. In the absence of shock, picture-evoked SCR is larger during pleasant and unpleasant pictures relative to neutral pictures (Bradley et al., 2001). In contrast, picture-evoked HR acceleration is larger during pleasant pictures and smaller during unpleasant pictures (Bradley et al., 2001). Thus, in the absence of shocks, picture-evoked SCR correlates with subjective arousal and picture-evoked HR acceleration correlates with subjective pleasure/arousal intensity (Bradley et al., 2001). Neither of these patterns is consistent with our observation that a valence linear trend (pleasant < neutral < unpleasant) explains emotional modulation of pain-evoked HR and SCR. The reason for this divergence is that we are assessing autonomic responses to a threatening stimulus (noxious trigeminal stimulation) during picture-viewing. Thus, SCR and HR acceleration are responses to defensive activation, and motivational priming theory predicts that defensive responses are facilitated by stimuli that prime the defensive system (unpleasant picture-viewing) and inhibited by stimuli that prime the appetitive system (pleasant picture-viewing) (Lang et al., 1999; Lang, 1995). Thus, the emotional modulation of pain-evoked autonomic responses is consistent with motivational priming theory.

5. Conclusions

In summary, the present study suggests emotion modulates autonomic responses to painful trigeminal nerve stimulation. Future research can utilize this paradigm to assess emotional modulation of autonomic responses to trigeminal pain in persons with headache disorders.