Experimental Assessment of Affective Processing in Fibromyalgia

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Abstract: Fibromyalgia syndrome (FMS) is a chronic pain disorder associated with widespread musculoskeletal pain, tenderness, and fatigue. Additionally, correlational research suggests negative affect (eg, depression, anxiety) and deficits in positive affect may contribute to FMS symptomatology. However, well-controlled, experimental research is necessary to ascertain whether patients with FMS have problems in affective processing. The present study used a well-validated picture-viewing paradigm to evoke emotional responses in 17 patients with FMS and 17 sex- and age-matched healthy control participants. Each participant viewed pleasant (erotica), neutral, and unpleasant (attack related) pictures, and abrupt white noises were delivered during two-thirds of the pictures to evoke startle eyeblinks. Appetitive and defensive responding was assessed from subjective (valence/pleasure and arousal ratings) and physiological (corrugator EMG, heart rate, skin-conductance response, startle-reflex modulation) reactions to pictures. Results suggested FMS was associated with greater defensive activation (displeasure, subjective arousal, corrugator EMG) to the unpleasant, threat-related pictures, but not deficits in appetitive activation to erotic pictures. Although preliminary, these data suggest individuals with FMS have deficits in affective processing, but this dysregulation may be limited to defensive activation. Implications for treatment and future research are discussed.

Perspective: Fibromyalgia is a debilitating disease associated with affective distress. Results from the present study suggest that FMS is associated with enhanced defensive activation to nonpainful threat-related stimuli, but not deficits in appetitive reactions to erotic stimuli. These findings have implications for the treatment and study of FMS.

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Key words: Fibromyalgia, emotional pictures, startle, skin conductance, facial electromyogram, heart rate.

Fibromyalgia syndrome (FMS) is an idiopathic disorder typified by generalized hyperalgesia and enhanced sensitivity to non-noxious stimuli.\textsuperscript{19,25} Though pervasive musculoskeletal pain and tenderness are central features, FMS is commonly associated with a myriad of symptoms (eg, fatigue, cognitive impairment) and coexisting medical illnesses (eg, irritable bowel, migraine) that make its pathogenesis difficult to discern.\textsuperscript{47}

FMS also carries significant psychological burden. For example, persons with FMS are at greater risk of psychiatric disorders such as depression and anxiety,\textsuperscript{17} and a dysfunction of the sympathetic response system has been noted.\textsuperscript{38} Given the prominence of psychological-emotional factors in FMS, deficits in affective processing could play a role in exacerbation and maintenance of symptoms. Consistent with this possibility, correlational research has suggested affect may contribute to FMS pain.\textsuperscript{48,52,58}

Affective experience is believed to emanate from evolutionarily old and centrally-mediated motivation systems. The defensive system is activated by threatening stimuli and associated with the subjective experience of negative affect, whereas the appetitive system is activated by rewarding stimuli and associated with the subjective experience of positive affect. Research suggests defensive activation enhances pain/nociception, whereas appetitive activation inhibits pain/nociception.\textsuperscript{81,42,44} Thus, pain could be enhanced in persons with a greater propensity for defensive activation, and/or in those with deficits in appetitive activation. Unfortunately, there is a paucity of experimental research on affective processing in FMS.

Affective processing can be studied by assessing reactions to standardized emotionally-charged stimuli. Perhaps the most widely used stimuli are the International...
Affective Picture System (IAPS), a normed set of 900+ pictures that engage cortico-limbic circuits and evoke reliable physiological-emotional responses in healthy participants. The IAPS, with its diverse picture contents and normative ratings, provides experimental control over the degree of appetitive/defensive activation induced.

Valence refers to the subjective pleasantness vs unpleasantness evoked by a stimulus, and is thought to reflect appetitive or defensive system activation, respectively. Valence can be assessed from subjective report, but physiological indices such as corrugator electromyogram (EMG), heart rate (HR), and startle magnitude can also be used to assess appetitive/defensive activation. Corrugator is a facial muscle (frowning) used to assess defensive activation and correlates negatively with valence/pleasure ratings. Emotional pictures evoke an initial HR deceleration (indicative of orienting) followed by a relative acceleration. The accelerative component is used to assess appetitive activation and correlates positively with valence/pleasure ratings. Startle is an interspecies reflex to an abrupt, unexpected stimulus and serves as a protective mechanism against threat. In humans, startle magnitude is quantified from the eyeblink (via orbicularis oculi EMG), which is increased during unpleasant picture viewing and decreased during pleasant picture viewing. Thus, startle modulation can be used to index defensive or appetitive activation.

Arousal refers to the level of metabolic activation evoked by a stimulus, and is believed to reflect the degree/level of motivation system activation. Arousal/activity can be measured by subjective report and skin conductance (SC; sympathetic activity). The more emotionally intense a stimulus is (ie, motivational salience), the more subjective arousal and SC it generates.

The Present Study

This study assessed physiological (corrugator EMG, SC, HR, startle reflex) and subjective (valence, arousal) reactions to IAPS stimuli in 17 participants with FMS and 17 age- and sex-matched healthy control participants. Pleasant, neutral, and unpleasant pictures were presented in random order and acoustic startle probes (noise bursts) were delivered during pictures. Evidence suggests FMS is associated with increased negative affect, decreased positive affect and a hypoactive sympathetic response. Thus, we predicted FMS patients would react with greater defensive activation to unpleasant stimuli and inhibited appetitive activation to pleasant stimuli. Portions of this paper were presented at the 2008 American Pain Society national meeting.

Methods

Participants

Table 1 presents demographic as well as other clinical variables for FMS and healthy control (HC) participants. Participants were recruited from the community by email distribution. FMS participants were included only if they met 1990 American College of Rheumatology (ACR) diagnostic criteria for FMS. Participants were excluded for cardiovascular, neurological, and/or circulatory problems; diagnoses of rheumatoid arthritis, Raynaud’s disease, hypothyroidism, ankylosing spondylitis, systemic lupus erythematosus, osteoarthritis, vasculitis, Lyme disease, Epstein-Barr virus, spinal stenosis, or cervical myelopathy; any chronic pain condition not related to FMS (eg, back pain, irritable bowel, migraines); recent use of analgesic medication and/or muscular means of radio/newspaper advertisement, flyers, and email distribution. FMS participants were included only if they met 1990 American College of Rheumatology (ACR) diagnostic criteria for FMS. Participants were excluded for cardiovascular, neurological, and/or circulatory problems; diagnoses of rheumatoid arthritis, Raynaud’s disease, hypothyroidism, ankylosing spondylitis, systemic lupus erythematosus, osteoarthritis, vasculitis, Lyme disease, Epstein-Barr virus, spinal stenosis, or cervical myelopathy; any chronic pain condition not related to FMS.
relaxants; narcotic analgesics used within 2 weeks of participation; current anxiolytic medication use; recent psychological trauma (as defined by DSM-IV-TR); or specific phobia of snakes or spiders due to picture viewing. Of 18 FMS patients recruited, 1 was excluded due to equipment problems; thus, 17 were included in the present study. Of these 17 participants, most were female (94.1%), white non-Hispanic (88.2%), married (64.7%), and employed full-time (41.2%). Average years of education was 15.2 yrs (SD = 2.14) and average age of FMS participants was 48.59 yrs (SD = 13.03).

Age- and sex-matched HC participants were recruited from the community. The same exclusion criteria listed above pertained to HC participants; however, they were also excluded if they met ACR tender-point criteria for FMS. Of the 17 HC participants, most were female (94.1%), white non-Hispanic (94.1%), single (41.2%), and employed full-time (64.7%). Average years of education was 16.18 yrs (SD = 2.74) and average age of HC participants was 43 yrs (SD = 13.11). All participants provided their written and verbal consent for participation and were provided a $20 gift card as an honorarium upon completion of the study.

**International Affective Picture System (IAPS) Picture Stimuli**

Attack (unpleasant), neutral, and erotic (pleasant) contents from the International Affective Picture System (IAPS) were used because they have been previously shown to elicit the most robust modulation of physiological and pain responses. Pictures were each presented for 6 seconds, with an 11- to 22-second inter-trial interval (ITI). The sequence of pictures was random within and between participants, with the limitation that not more than 2 pictures from the same content were presented consecutively. Mean normative valence and arousal ratings and image numbers for the contents are as follows: attack (valence: \( M = 3 \); arousal: \( M = 6.35 \); Image numbers: 1052, 1111, 1205, 1301, 1525, 1932, 3500, 6230, 6242, 6250, 6550, 6560), neutral (valence: \( M = 4.93 \); arousal: \( M = 2.53 \); Image numbers: 5531, 7000, 7004, 7010, 7025, 7030, 7040, 7080, 7090, 7150, 7175, 7225), and erotic (valence: \( M = 6.66 \); arousal: \( M = 6.1 \); Image numbers: 4606, 4607, 4608, 4611, 4623, 4651, 4653, 4666, 4669, 4670, 4690, 4810).

**Apparatus**

A PC equipped with dual monitors, A/D board (PCI-6036E; National Instruments, Austin, TX), and LabVIEW software controlled all data acquisition, as well as picture stimuli and questionnaire administration. All picture stimuli and questionnaires were presented by a 17” flat panel monitor positioned 5 meter from participants. Monitoring of physiological signals and experimental timing was conducted by an experimenter from an adjacent control room by use of an additional 17” flat panel monitor. In order to communicate with participants, all subjects wore sound-attenuating headphones throughout the experimental session, and the experimental chamber was equipped with a video camera to allow for participant observation. Acoustic startle-noise bursts were delivered by a Coulbourn Instruments (Allentown, PA) audio signal generator (Part number A12-33), amplified by a 40 W amplifier (Radio Shack, Part #32-2054), and presented over TDH-49 Telephonics (Farmingdale, NY) headphones. All psychophysiological signals were collected and filtered by a Grass Instruments (West Warwick, RI) Model 15LT Bipolar Amplifier with Quad AC (15A54) and Dual DC (15A12) modules, and a Grass Instruments adaptor (Model SCA1) measured skin conductance response.

**Questionnaires**

**Center for Epidemiological Studies-Depression Scale (CES-D)**

The CES-D is a 20-item self-report questionnaire assessing depressive symptomatology. Items on the CES-D are based on a 4-point Likert scale, and respondents indicated the degree to which they experienced the specific situation or symptom over the past week. The possible range of scores is 0 to 60 and a cut-off score of 19 or above was used to detect the presence of depressive symptomatology. The CES-D has good internal consistency and test-retest reliability, as well as construct validity. The CES-D was used to determine whether there were group differences in depressive symptoms that might contribute to differences in affective processing.

**Fibromyalgia Impact Questionnaire (FIQ)**

The FIQ is a 10-item self-report measure developed to assess fibromyalgia patient health status over the past week. The first item contains 11 questions that pertain to physical functioning. Items on the FIQ are rated on either a 4-point Likert scale or a 0 to 10 Visual Analogue Scale (VAS). The possible range of scores on the FIQ is 0 to 100, with FMS patients scoring around 50 on average, and scores over 70 indicating patients severely impacted by FMS. Adequate construct validity and test-retest reliability has been indicated for the FIQ. Instructions were altered slightly for the current study to refer to pain in general rather than only fibromyalgia pain (ie, by removing the word fibromyalgia) so items could pertain to both HC and FMS participants. The question from the FIQ that asked, “Over the past week, how bad has your pain been?” was used as a measure of pain severity to determine if pain severity contributed to the study findings. Responses ranged from 0 (no pain) to 10 (very severe pain).

**Toronto Alexithymia Scale-26 (TAS-26)**

The 26-item TAS is a self-report measure developed to assess 3 dimensions of the alexithymia construct, including difficulty identifying feelings, difficulty describing feelings, as well as externally-oriented thinking. Items are rated on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). The TAS-26 has demonstrated adequate internal consistency, as well as good test-retest reliability and construct validity. For the present study, a total scale score ranging from 0 to 130 was
used to assess alexithymia. The TAS was used to determine whether there were group differences in alexithymia that could contribute to differences in affective processing.

**Affective Reaction Outcomes**

**Subjective ratings: Self-Assessment Manikin (SAM)**

The SAM is a questionnaire consisting of 2 sets of 5 pictographs measuring affective valence (unpleasant-pleasant) and arousal (calm-excited). The SAM has been shown to have good validity, with correlations between SAM valence and arousal ratings and the multi-item Semantic Differential scale being $r = .96$ and $r = .95$, respectively. Further, SAM ratings have been shown to be reliable, with coefficients for valence and arousal being $r = .94$ and $r = .94$, respectively. A computerized version of the SAM was utilized for participant rating of picture stimuli. Participants responded by moving an indicator on or between any of the 5 pictographs that best represented their emotional valence or arousal, and then submitted their answer by computer mouse. A rating between 1 and 9 was produced for each dimension (higher scores = greater pleasure or arousal).

**Corrugator EMG**

Corrugator-muscle activity is associated with pulling the inner portion of the eyebrow down into a frown; thus, corrugator EMG has been shown to be inversely correlated with pleasure (valence) ratings. Corrugator EMG was used as a physiological measure of defensive activation and measured by 2 Ag/AgCl electrodes filled with conductive gel (EC60; Grass Instruments) affixed over the left corrugator Supercilius muscle. Raw signals from corrugator EMG were amplified 20,000, and frequencies below 30 Hz and above 1000 Hz were band-pass filtered.

**Heart Rate (HR)**

The heart rate waveform during emotional picture-viewing follows a triphasic shape, with an initial decelerative component followed by a relative accelerative component. HR acceleration has been shown to correlate positively with affective valence such that more pleasurable stimuli evoke greater acceleration. Thus, for the present study, electrocardiogram (ECG) was measured, converted to HR, and used as a physiological measure of appetitive activation. To measure ECG, 2 Ag-AgCl electrodes were filled with conductive gel (EC60; Grass Instruments) and placed on the left and right forearms. ECG was converted offline to HR in beats-per-minute in half-second bins from interbeat intervals. Each bin was then converted to a change score by subtracting the average BPM in the 1 second prior to picture-onset. HR acceleration was defined as the maximum increase in the 3 to 6 second postpicture interval.

**Acoustic Startle Reflex**

Numerous studies have shown the startle reflex varies linearly with affective valence, such that reflexes are larger when evoked during unpleasant pictures and smaller when evoked during pleasant pictures. Therefore, startle magnitude was used as a physiological measure of defensive and appetitive activation. To elicit startle, a 50-ms burst of white noise was delivered over Telephonics headphones. The first 7 participants received noises that were 95-dB(A), while the remaining 27 participants received noises that were 105-dB(A) (to be consistent with another study underway). Consistent with a larger parametric study that found startle modulation was unaffected by systematic variation in probe intensity (80 dB vs 105 dB), preliminary analyses on our data found that probe intensity was not a significant main effect, nor did it interact with other variables (eg, picture content). Therefore, data were collapsed across probe intensity in the reported analyses. Startle probes were randomly delivered during two-thirds of picture stimuli (equally dispersed among attack, neutral, and erotic picture contents), 3 to 5 seconds after picture onset. Probes were also elicited during one-third of interpicture intervals (intertrial interval, ITI) 11 to 22 seconds after interval onset. Startle-eyeblink magnitude was measured by affixing 2 Ag-AgCl electrodes over the left orbicularis oculi muscle according to published guidelines. Eyeblink magnitude was scored offline by subtracting the mean EMG of the 60 ms prior to startle-probe onset from the maximum rectified and integrated (8 ms time constant) EMG response in the 21 to 120 ms following startle-probe onset. Trials that did not have a visible eyeblink were given a score of zero and reported ($N = 3.4\%$). Trials with unstable baseline activity due to movement artifact or eyeblinks were rejected ($N = .5\%$). Startle-eyeblink magnitude was standardized within individuals by converting to z-scores, as is convention in the literature; however, similar results were obtained with unstandardized scores.

**Skin Conductance Response (SCR)**

SCR was used as a physiological measure of motivational-system activation. SCR was measured from 2 electrodes filled with isotonic paste (EC33; Grass Instruments) affixed to the volar surface of the index and middle fingers of the nondominant hand after the participant’s skin had been washed and dried. Each 11 second-recording trial was initially averaged by .5-second epochs; the mean activity in the 1-second prepicture interval was then subtracted from each .5-second postpicture epoch. SCR was defined as the maximum skin-conductance change that occurred 1 to 4 seconds after picture onset.

**Procedure**

All procedures were approved by The University of Tulsa ethics review board. A brief health-status interview was conducted via phone with participants prior to study participation. Potentially eligible participants were then instructed to refrain from using any narcotic analgesics 2 weeks prior to participation, as well as any over-the-counter or prescription analgesics 24 hours before study participation. At the testing session, all participants provided verbal and written informed consent. A
demographic/health status questionnaire was administered to assess inclusion/exclusion criteria. If eligible, participants were instructed on the use of the SAM for rating of affective stimuli. Following SAM training, a tender-point examination was conducted on all participants to determine if they met ACR criteria for FMS.46 Tender-point examination was performed by exerting 4 kg of force, at 1 kg of pressure per second, on each of 18 sites by use of a pressure algometer, and having participants indicate if the procedure elicited pain on the area. A positive FMS diagnosis is associated with pain on at least 11 of 18 tender-point sites. After tender-point examination, skin was degreased with alcohol and prepared with NuPrep gel to attain impedances below 5 KΩ. Physiological sensors were then attached with self-adhering collars. After sensors were affixed to the skin, participants received 3 acoustic-startle probes to calibrate orbicularis oculi EMG amplification, followed by 10 habituation trials. Emotional pictures were then presented by computer screen and startle probes were elicited during two-thirds of the pictures. After each picture, participants rated their affective valence and arousal by use of the SAM.7 After completion of the experimental session, participants were debriefed and provided with a $20 gift card as compensation.

Data Analysis

All analyses were conducted using the MIXED procedure within SPSS 14.0 (SPSS, Inc, Chicago, IL). 3 (Picture Content) x 2 (Group) mixed models ANOVAs were used for all analyses. Main effects and simple effects of Group were conducted with 2-tailed Fisher’s LSD tests. Cohen’s d was used as the effect size for mean comparisons. Cohen provides guidelines for interpreting d (small = .2, medium = .5, large = .8).9

Hypotheses

It was predicted that participants with FMS would react with greater defensive activation to unpleasant stimuli (greater subjective displeasure, greater corrugator EMG, greater startle facilitation) and inhibited appetitive activation to pleasant stimuli (less subjective pleasure, less HR acceleration, less startle inhibition). It was expected that subjective arousal would be enhanced in response to unpleasant stimuli (greater defensive activation) and inhibited in response to pleasant stimuli (inhibited appetitive activation); however, evidence of sympathetic dysfunction in FMS38 suggests that SCR (a measure of sympathetic activation) will be muted in FMS regardless of stimulus valence.

Results

Table 1 presents background information for both groups of participants. Means, standard deviations, and Cohen’s d effect sizes for subjective and physiological responses to affective picture stimuli are presented in Table 2.

Preliminary Analyses (Table 1)

To determine whether there were group differences on background variables, independent samples t-tests or chi-squared analyses were conducted on continuous-like or nominal variables, respectively (Table 1). Analyses did not find any significant group differences in demographic variables including age, gender, ethnicity, years of education, marital status, or employment status (all ps > .27). However, FMS participants had a higher tender-point count, were more likely to use antidepressant medication, and had more pain-related problems (FIQ scores). Given that antidepressant medication and/or pain severity could influence responses to emotional stimuli regardless of diagnostic status, preliminary analyses were conducted that entered them as predictors/covariates in the models. These variables were not significant covariates, and their addition to the models did not influence the conclusions. Thus, they were dropped for parsimony.
FMS participants reported more depressive symptoms and alexithymia traits, although these differences just eluded significance at \( P < .05 \). Nonetheless, depressive symptoms\(^1\),\(^4\) and alexithymia traits\(^5\) may influence affective responding; therefore, to ensure that any group differences in affective responding were not due to depression or alexithymia, these variables were controlled for by entering the CES-D and TAS-26 total scores as predictors/covariates in all analyses. However, depression and alexithymia were not significant covariates in any of the models (ps > .44 and ps > .13, respectively); therefore, they were dropped from the final models for parsimony. Additionally, mild depression was coded as present (CES-D \( \geq 19 \)) or absent (CES-D < 19) and entered as a predictor/covariate. One control participant and 7 FMS participants had CES-D scores \( \geq 19 \) or absent (CES-D < 19) and entered as a predictor/covariate. One control participant and 7 FMS participants had CES-D scores 19 or greater. However, this variable was also nonsignificant in all models (ps > .44)

**Subjective Valence (Table 2)**

The main effect of Picture Content for valence ratings was significant \([F(2, 1190) = 545.06, P < .001]\). Attack pictures were rated as more unpleasant than neutral \((P < .001, d = 1.75)\) and erotic pictures \((P < .001, d = 1.73)\), and erotic pictures were rated as more pleasant than neutral \((P = .048, d = .13)\). The Picture Content \( \times \) Group interaction was also significant \([F(2, 1190) = 28.34, P < .001]\). Simple effects tests of Group found that FMS participants rated attack pictures as more unpleasant than HC \((P = .002, d = .53)\) and erotic pictures as more pleasant than HC \((P = .03, d = .36)\). However, there were no significant differences between groups for neutral pictures \((P = .96, d = .01)\). The main effect of Group was nonsignificant \([F(1, 34) = .14, P = .72]\).

**Physiological Measures of Valence (Table 2)**

**Corrugator EMG**

The main effect of Picture Content was significant for corrugator EMG \([F(2, 1190) = 8.97, P < .001]\). Corrugator EMG was larger during attack pictures than neutral \((P < .001, d = .25)\) and erotic pictures \((P = .006, d = .18)\). There were no significant differences between erotic and neutral pictures \((P = .16, d = .11)\). The Picture Content \( \times \) Group interaction was also significant \([F(2, 1190) = 9.22, P < .001]\). Simple effects of Group indicated FMS participants had higher corrugator EMG during attack pictures \((P = .015, d = .26)\), and decreased corrugator EMG during erotic pictures \((P = .044, d = .35)\). There were no significant differences between groups for neutral pictures \((P = .66, d = .06)\).

**HR Acceleration**

The main effect of Picture Content was significant \([F(2, 1186) = 4.53, P = .011]\). Compared to neutral pictures, attack \((P = .055, d = .12)\) and erotic \((P = .003, d = .20)\) pictures led to lower HR acceleration, but were not different from one another \((P = .30, d = .07)\). However, diagnostic groups did not differ from one another as indicated by the nonsignificant main effect of Group \([F(1, 34) = 1.49, P = .23]\) and nonsignificant Picture Content \( \times \) Group interaction \([F(2, 1186) = .69, P = .50]\).

**Startle Eyeblink Magnitude**

There was a significant main effect of Picture Content for startle-eyeblink magnitude \([F(2, 809) = 45.71, P < .001]\). Relative to neutral pictures, startle-eyeblink magnitude was larger during attack pictures \((P < .001, d = .29)\) and smaller during erotic pictures \((P < .001, d = .55)\), which were different from one another \((P < .001, d = .81)\). There was no significant Picture Content \( \times \) Group interaction for startle eyeblink magnitude.

**Subjective Arousal (Table 2)**

The main effect of Picture Content was significant for arousal ratings \([F(2, 1190) = 511.22, P < .001]\). Compared to neutral pictures, erotic \((P < .001, d = 1.17)\) and attack \((P < .001, d = 1.79)\) pictures elicited more arousal, and attack was more arousing than erotica \((P < .001, d = .58)\). The Picture Content \( \times \) Group interaction was also significant \([F(2, 1190) = 22.95, P < .001]\). However, simple effects tests of Group found that FMS and HC participants did not differ on ratings of attack \((P = .12, d = .32)\), neutral \((P = .10, d = .44)\), or erotic pictures \((P = .38, d = .18)\). The main effect of Group was not significant \([F(1, 34) = .07, P = .79]\).

**Physiological Arousal: SCR (Table 2)**

Means for the main effect of Picture Content were in the predicted direction; nevertheless, the main effect of Picture Content was not significant \([F(2, 1190) = 2.08, P = .125]\). The main effect of Group \([F(2, 34) = .21, P = .65]\) and the Picture Content \( \times \) Group interaction \([F(2, 1190) = 1.43, P = .241]\) were also nonsignificant.

**Discussion**

Results suggested hypotheses were partially supported. Relative to controls, participants with FMS demonstrated increased defensive activation in reaction to attack-related pictures, as evidenced by larger corrugator EMG responses and lower valence ratings (greater displeasure). Our observation of enhanced defensive reactivity indicates individuals with FMS may attend more readily to aversive cues that signal potential threat. This pattern of defensive responsivity could suggest deficits in central-motivation circuitry that may ultimately be a marker for development and/or maintenance of FMS.

In further support for the hypothesis that FMS is associated with increased defensive reactivity, Montoya et al\(^3\) found that persons with FMS had abnormal somatosensory processing in reaction to nonnoxious somatic stimulation (assessed by cortical-evoked potentials), abnormalities that were enhanced by unpleasant pictures. Although that study did not assess subjective and physiological reactions to pictures,\(^3\) a study by Arnold et al\(^2\) assessed subjective reactions to unpleasant pictures but failed to find group differences. However, that study used unpleasant pictures depicting grieving, death,
accidents, and mutilated bodies. While the contents in their study are clearly unpleasant and evoke defensive/avoidance motivation, they may simultaneously evoke approach dispositions (empathy, motivation to help). By contrast, the attack pictures used in the current study have been shown to evoke a more pure defensive/avoidance motivation. Thus, the discrepancy between the present study and Arnold et al may have been due to this difference.

Interestingly, we did not find group differences in startle modulation. Indeed, both groups showed startle potentiation when they viewed threatening pictures and startle inhibition when they viewed erotic pictures. Research in animals and humans suggests the amygdala and periaqueductal gray (PAG) are involved with threat-potentiated startle, while human research suggests other structures (eg, hippocampus, medial prefrontal cortex) are associated with subjective report and facial displays of emotion. Thus, FMS could be associated with a disruption of the hippocampus and/ or medial prefrontal cortex, but not the amygdala-PAG circuit given that we observed group differences in corrugator and subjective valence, but not startle. If true, this could have clinical implications given the importance of the amygdala and PAG in nociception regulation. Alternatively, the lack of startle-group differences may stem from an inability of picture viewing to strongly engage modulation systems that are dysfunctional in FMS. For this reason, other startle modulation paradigms (eg, conditioned fear) should be explored.

Alternatively, the reason that group differences were found for corrugator EMG and subjective report, but not other physiological responses, may stem from the fact that corrugator activity and subjective reports are easier to modulate voluntarily than HR, SCR, or startle magnitude. Thus, FMS-related reactivity in corrugator and subjective report may reflect a greater tendency to communicate negative affect to others (ie, report bias). This tendency could contribute to augmented symptom and pain reporting in FMS, but cannot fully explain FMS-related symptomatology because studies using objective neurophysiologic measures have found enhanced spinal and supraspinal nociception in FMS.

The present study suggests appetitive activation was not disrupted in FMS. Compared to controls, erotica elicited higher pleasure ratings and lower corrugator activity in the FMS group. Additionally, startle was significantly inhibited in both groups by erotica. Moreover, when the FMS group’s pleasure/valence ratings of erotica ($M = 6.2$) are compared to normative ratings from healthy women ($M = 6.18$), they are statistically equivalent ($z$-score = .008, $P = .95$). Together, these findings appear inconsistent with research suggesting FMS is associated with deficits in positive affect. However, prior studies have focused on fluctuations in subjective positive affect assessed retrospectively (eg, past few hours/days), rather than immediate physiological-emotional reactions to specific events. Given the greater tendency for FMS patients to experience negative affect, retrospective measures of subjective experience may not accurately capture the full extent of appetitive activation, because negative affect can impair memory for pleasurable experiences. Therefore, FMS patients may not have deficits in appetitive activation, but perhaps the subjective experiences are short-lived or harder to recall because of the greater tendency to experience negative emotions. Alternatively, our failure to find impaired appetitive responding in FMS patients may reflect our use of erotic images. Erotica is known to elicit less appetitive motivation in female participants; therefore, our data may suffer from a floor effect.

HR acceleration was not significantly modulated by picture valence in either group. While this could represent an abnormality of appetitive activation in both groups, it is likely due to picture choice. In a study of multiple picture contents, Bradley and colleagues found erotica elicited the least HR acceleration of all pleasant contents. In the present study, erotica-evoked HR acceleration ($1.53$ bpm) was similar in magnitude to that noted in the Bradley et al study ($1.67$ bpm), which was relatively smaller than HR acceleration to other pleasant contents in their study ($= 3.14$ bpm). Therefore, HR may not have been sensitive enough to detect group differences.

**Implications and Future Directions**

This study provides preliminary evidence that FMS is associated with enhanced appetitive activation, but not deficits in appetitive activation. This implies interventions for FMS should train patients to regulate responses to threatening stimuli. This would reduce negative affect and could also improve pain, because defensive activation augments pain and nociception. It also appears to be important to get FMS patients to focus on increasing exposure to appetitive stimuli. This would increase positive affect and could also improve pain, because appetitive activation can reduce pain and nociception. Thus, a comprehensive approach to regulating emotional experience may prove successful in managing FMS-related symptoms.

While speculative, it is possible that enhanced defensive activation in FMS reflects a sensitization of central circuits responsible for processing threat-related information, that, in turn, enhances sensory input. This is consistent with imaging data that suggests FMS is associated with enhanced supraspinal processing during noxious stimulation, and that brain regions associated with cognitive-emotional factors (eg, affect, attention) contribute to the enhanced supraspinal processing. If true, heightened defensive activation may serve as an initiating/maintaining factor for FMS, and the current procedures might identify persons at risk. However, given the cross-sectional design, it is unclear whether enhanced defensive activation is a predisposing factor of FMS, a consequence of FMS, or a result of some third unmeasured factor that promotes FMS symptomatology and heightened defensive activation. Prospective, longitudinal studies are needed to answer this question.

Our laboratory and others have shown that emotional picture viewing provides a reliable method
of engaging supraspinal modulation of nociceptive processes. Importantly, we find the nociceptive flexion reflex, a measure of spinal nociception, is inhibited by pleasant (erotic) pictures and facilitated by unpleasant (attack-related) pictures. Thus, we have argued the picture-viewing paradigm is a reliable tool for assessing supraspinal modulation of spinal nociceptive input. Desmeules et al have found that FMS is associated with lowered nociceptive flexion reflex threshold, implying enhanced spinal nociception. Therefore, future research is needed to determine if differences in affective processing contribute to enhanced spinal nociception in FMS. A current study is underway that examines this issue.

**Study Limitations**

This study had several strengths, including a well-validated methodology for affect-evocation, strict inclusion/exclusion criteria for FMS, assessment of reactions to both pleasant and unpleasant stimuli, and the measurement of physiological as well as subjective responses. However, in addition to those limitations previously noted, a few others should be mentioned.

To minimize confounding factors, potential FMS participants were excluded for several frequently occurring comorbid conditions (eg, irritable bowel, migraine), as well as medications used to control fibromyalgia symptoms (eg, analgesics). These stringent inclusion/exclusion criteria improve the internal validity of our study and are consistent with criteria used in other research on FMS pain processing. Our FMS participants reported more pain-related difficulties than controls (FIQ scores), more painful tender-points, and greater antidepressant use. Nonetheless, we cannot rule out the possibility that Type II errors occurred. To aid the interpretation of our data, we report Cohen's $d$ effect sizes for all FMS vs HC comparisons in Table 2. Importantly, most nonsignificant findings (except for arousal ratings) were associated with small effect sizes (Cohen's $d < .20$).

To summarize, these preliminary experimental data suggest FMS is associated with enhanced defensive activation, but not deficits in appetitive activation. If replicated, these findings suggest interventions should help persons with FMS to regulate defensive responding to threat and increase exposure to appetitive stimuli. Doing so, could have implications for reducing FMS-related pain.

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