Behavioral Inhibition and Behavioral Activation are Related to Habituation of Nociceptive Flexion Reflex, but Not Pain Ratings

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Abstract: Habituation (ie, decreases in responding) and sensitization (ie, increases in responding) after prolonged or repeated exposures to a fixed stimulus have been identified as important in adaptation to repeated or prolonged noxious stimulation. Determinants of habituation or sensitization are poorly understood, and experimental investigation of habituation of pain ratings have generally relied on pain reports and statistical techniques that average responses across a group of participants. Using a cross-sectional design, the current study used multilevel growth curve analyses to examine changes in the nociceptive flexion reflex (NFR), a spinal nociceptive withdrawal reflex, and pain ratings in response to 12 repeated, constant intensity, noxious electrocutaneous stimuli. Unconditional growth curve models indicated that, on average, participants evidenced habituation of the NFR and sensitization of pain ratings. However, a substantial subgroup of participants exhibited the opposite pattern of change. In conditional models, behavioral inhibition, $\beta = .10$, $P = .003$, and behavioral activation, $\beta = -.07$, $P = .07$, independently interacted with the growth curve to predict changes in NFR, but not pain ratings, across the 12 stimuli. These findings provide preliminary experimental support for Jensen and colleagues’ 2-factor model of pain experience and implicate a role for approach and avoidance motivations in descending modulation of NFR.

Perspective: Using repeated NFR stimulation, this study showed that most participants exhibited NFR habituation and pain sensitization; however, a substantial subgroup showed an opposite pattern of pain habituation (25.0%) and NFR sensitization (31.4%). Further, NFR habituation was moderated by individual differences in behavioral activation and behavioral inhibition.

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Key words: Pain, NFR, habituation, sensitization, behavioral inhibition, behavioral activation.
pain catastrophizing was shown to be negatively associated with habituation to repeated suprathreshold heat stimuli. In the second, resilience and purpose in life were positively related to increases in heat pain thresholds over multiple assessments. These findings point to a role for psychosocial factors and suggest that pain-related vulnerability and pain-related resilience may have opposite effects on habituation.

One impediment to a direct interpretation of psychological influences on habituation versus sensitization to noxious stimuli is the fact that most studies rely on subjective pain ratings. In a notable exception, Rhudy and colleagues examined habituation of the nociceptive flexion reflex (NFR), a withdrawal response elicited by noxious electrocutaneous stimulation of the sural nerve, and showed that NFR responses decreased throughout a testing session whereas electrocutaneous pain ratings increased. These findings indicate that spinal and supraspinal responses (ie, NFR and pain ratings, respectively) can show different patterns of habituation and sensitization to the same stimulus. Further, these findings also suggest that psychological factors may have a differential influence on adaptation to nociception and adaptation to pain, because it has been repeatedly shown that pain catastrophizing is positively related to electrocutaneous pain ratings but unrelated to NFR activity.

Recently, Jensen and colleagues put forward a new conceptualization of chronic pain on the basis of the application of Gray's systems of behavioral inhibition and behavioral activation. The behavioral inhibition and activation systems are theorized to be distinct and largely independent neurophysiological systems determined by genetics and learning history, and involved in avoidance and approach motivations, respectively. As outlined by Jensen and colleagues, the dimensions of behavioral inhibition and behavioral activation broadly align with current theories regarding the role of psychosocial vulnerability and resilience in pain. Consistent with this notion, as well as the studies discussed previously, it is possible that behavioral inhibition and behavioral activation are associated with adaptation to noxious stimuli. To date, however, tendencies toward behavioral inhibition and behavioral activation have remained unexamined in studies of pain habituation and they have not been applied in studies of spinal nociception. Accordingly, the aims of the current study were twofold. First, we collected concurrent measures of electrocutaneous pain ratings and NFR activity to determine the proportion of individuals who habituate or sensitize in each domain. We expected to replicate previous evidence indicating that most individuals evidence pain sensitization and NFR habituation. However, we also anticipated a substantial subgroup would evidence the opposite pattern. Second, we examined self-reported tendencies toward behavioral inhibition and activation as potential correlates of individual differences in patterns of habituation and sensitization to pain as well as NFR responses. We hypothesized that behavioral inhibition would be related to attenuated habituation and behavioral activation would predict enhanced habituation of NFR and pain responses.

**Methods**

This was a secondary analysis of data from a parent study that examined the effects of placebo analgesia manipulations on pain and NFR. The current results are novel and do not overlap with the report of the main findings from the parent study. In the parent study, participants were randomly assigned to receive 1 of 4 experimental manipulations that involved receiving a sham (“painless”) cream. However, the data reported here were collected in identical conditions before the manipulations were administered, so data were pooled across groups for the current analyses.

**Participants**

Participants were primarily recruited from the community (via fliers, newspaper advertisements, and/or e-mail announcements), although 4 were recruited from a psychology subject pool. Those recruited from the community received a $100 honorarium for completion of the study, whereas those from the psychology subject pool received course credit. Participants were excluded for: younger than 18 years old, health conditions that could interfere with pain testing (neurological, cardiovascular, and/or circulatory problems), currently pregnant, recent psychological trauma, hearing impairments, use of medications that could interfere with testing (ie, analgesics, antidepressants, anxiolytics, stimulants), use of narcotic analgesics for 2 weeks before the experiment, use of non-narcotic analgesics (eg, nonsteroidal anti-inflammatory drug, acetaminophen) 24 hours before the experiment, body mass index (BMI) > 35 (because of potential difficulties obtaining an NFR in individuals with high adiposity), or current chronic pain diagnosis. A stratified random sampling approach was taken to promote equal gender and racial/ethnic distributions across the experimental groups. Participants were included in the current study as long as they completed the required pain/NFR testing and questionnaires, regardless of whether they completed the parent study (3 later dropped out). As such, 142 participants contributed pain ratings for analysis (140 of these contributed NFR data). The average age was 34.11 years (SD = 12.64), average BMI was 24.80 (SD = 4.06), average years of education was 15.20 years (SD = 3.10), and average household income was $41,600 (SD = $73,167). Most participants were white (80%), non-Hispanic (95%), currently employed (66%), and single (56%). There were roughly equal numbers of men (51%) and women (49%). All participants provided written and verbal informed consent and were told that they could discontinue participation at any time.

**Apparatus and Signal Acquisition**

Electric stimulus presentation, questionnaires, self-report ratings, and physiological data collection were...
all controlled by a PC with dual monitor capacity, A/D board (PCI-6036E; National Instruments, Austin, TX), and LabVIEW software v2010 (National Instruments). One computer monitor was used by the experimenter to monitor physiological signals, and the other monitor was used by the participant to complete questionnaires and to make ratings of electric stimuli. Testing was completed in a sound-attenuated and electrically-shielded testing room. Participants were monitored from an adjacent control room via a video camera connected to a flat panel television. Participants wore sound-attenuating headphones (TDH-49; Telephonics, Farmingdale, NY) that allowed them to hear the experimenter’s instructions and they could speak to the experimenter via the microphone on the video camera. A mechanical physical scale with attached height rod (Detecto, Webb City, MO) was used to assess weight and height for the calculation of BMI.

Electric stimuli to assess pain and NFR were generated by a Digitimer stimulator (D55; Hertfordshire, England) and delivered using a bipolar surface stimulating electrode (Nicolet, Madison, WI; 30-mm interelectrode distance) attached to the left leg over the retromalleolar pathway of the sural nerve (impedance ≤2 kΩ). The computer controlled the timing and intensity of the stimulations, and the maximum stimulation intensity was set at 50 mA to ensure safety. Each electric stimulus was a train of five 1-ms square wave pulses delivered at 250 Hz. Biceps femoris electromyography (EMG) to assess NFR was recorded from 2 active Ag-AgCl electrodes (F-E9-40-5; Grass Technologies, West Warwick, RI) placed 10 cm superior to the popliteal fossa. The signal was amplified (10,000 × ) and bandpass filtered (10–300 Hz) online by a Grass Model 15LT amplifier (with AC Module 15A54) and sampled at 1,000 Hz. A ground electrode was placed over the lateral epicondyle of the femur. Before NFR electrodes were applied, the skin was cleaned with alcohol and exfoliated using an abrasive paste (Nuprep; Weaver and Company, Aurora, CO) to reduce impedances <5 kΩ.

Questionnaires
Demographic Characteristics
A custom-built demographic and health status questionnaire was used to obtain background information and health problems to assess inclusion/exclusion criteria.

Pain Ratings
To assess pain intensity in response to suprathreshold electric pain stimuli, participants used a vertically oriented, computer-presented visual analog scale (VAS) with the following anchors: “no pain sensation” and “the most intense pain sensation imaginable.” Participants used a computer mouse to slide an indicator along the scale to make ratings and pressed the mouse button to submit the rating that returned the scale to 0 before the next rating. The computer converted the scale to values between 0 and 100, with higher values representing greater pain intensity.

Behavioral Inhibition and Behavioral Activation Scale
The Behavioral Inhibition Scale (BIS)/Behavioral Activation Scale (BAS) is comprised of 24 items used to assess underlying behavioral motivation systems. The behavioral inhibition system serves to initiate avoidance of aversive situations, whereas the behavioral activation system motivates one toward seeking appetitive stimuli. There are 3 BAS-related subscales including drive, fun-seeking, and reward responsiveness, whereas there is only 1 BIS subscale. Items are on a Likert-scale ranging from 1 (very true for me) to 4 (very false for me) and responses were averaged to create individual subscale total scores. The BIS/BAS scales have been shown to demonstrate good reliability and convergent and discriminant validity.

Determination of Suprathreshold Test Stimulation Intensity
Suprathreshold electric stimulations were individually calibrated to each participant to ensure that: 1) the stimulations were above NFR threshold so NFRs could be reliably evoked, and 2) the stimulations were at least moderately painful (≥40 on the VAS). Average pain rating for the first stimulus in the series was 41.7 (SD = 24.8). NFR threshold was assessed using 3 ascending-descending staircases of electric stimuli. The first ascending staircase started at 0 mA and increased in 2 mA steps until an NFR was detected. NFR was said to occur when the mean rectified biceps femoris EMG response in the 90 to 150 ms poststimulus interval exceeded the mean rectified biceps femoris EMG activity during the 60-ms prestimulus baseline interval by at least 1.4 times the baseline SD. After an NFR was detected, the stimulus intensity was decreased in 1 mA steps until an NFR was no longer detected. The second and third ascending-descending staircases used 1-mA steps. The interval between electric stimulations varied randomly between 8 and 12 seconds to reduce predictability and reflex habituation (during this procedure). After each stimulus, participants rated their pain sensation using the VAS. The stimulus intensity (mA) of the 2 peaks and 2 troughs of the last 2 ascending-descending staircases were averaged and used to define NFR threshold. In the event that NFR threshold stimuli did not produce a rating ≥40 on the VAS, stimulations were increased in steps of 2 mA until a rating ≥40 was obtained (ie, PAIN40). The suprathreshold stimulation intensity used during subsequent testing of habituation was set at 120% of NFR threshold or 120% PAIN40, whichever was higher.

Assessing Changes in NFR Magnitude
Changes in NFR magnitude were used to assess changes in spinal nociception in response to constant intensity suprathreshold stimulations. NFR magnitudes were calculated from a d-score: $d = (\text{mean rectified}$
EMG during 90- to 150-ms poststimulus interval minus mean rectified EMG during 60-ms prestimulus interval)/(average of baseline interval SD and 90- to 150-ms interval SD). This scoring method was used because it is normally distributed and is positively correlated with pain ratings.27,29 Individual NFRs were excluded from analysis if the baseline EMG exceeded 3 μV, indicating excessive muscle tension before the stimulation (3.1%). This resulted in exclusion of NFR data for 2 participants.

Procedures

Interested participants were administered a brief phone screen to provide an overview of the study and to administer a cursory assessment of inclusion/exclusion criteria. Potentially eligible participants were then invited to attend a laboratory session during which informed consent was obtained and then a comprehensive assessment of inclusion/exclusion criteria was conducted. Afterward, participants were provided instructions on the VAS for rating pain, instrumented for NFR recording, and then seated in a comfortable reclining chair that kept their knee angle at approximately 160° (PC-6 Perfect Chair, Human Touch, Long Beach, CA).

Participants were told that they were participating in a study to examine the effects of a strong pain-relieving cream on physiological reactions to painful stimuli. At study entry, participants were randomized to 1 of 4 groups. Some were told they were assigned to a control condition that does not receive the pain-relieving cream, whereas others were told the painkilling cream would be applied once or twice at some point. Participants then completed startle testing (data not reported), followed by NFR threshold assessment and PAIN40 (if necessary) to determine the suprathreshold stimulus intensity to use during testing.

The rest of the experiment was divided up into 2 identical assessment periods separated by a 30-minute break. Each assessment period included a pretest, application of a sham cream, and then a post-test. Each pretest and post-test involved the delivery of 12 electric stimulations with a randomly determined interstimulus interval (14–24 seconds). Data for the present study were all collected during the pretest of assessment 1 before the sham cream was applied and before any procedures diverged on the basis of the assigned group. All electric stimulations were delivered at the same intensity, on the basis of the participant’s NFR threshold or PAIN40. The BIS/BAS was administered during the 30-minute break. The study was conducted in the Department of Psychology at the University of Tulsa, and all procedures were approved by the ethics review board at the University of Tulsa.

Data Analysis

Two separate unconditional growth curve models were constructed to examine changes in NFR responses and pain ratings. For each model, random intercepts, random slopes, and fixed effects for 3 potential growth curves (linear, logarithmic, and quadratic) were examined to determine which provided the best fit to the data on the basis of Aikake information Criteria (AIC). AIC provides a relative estimate of the amount of information lost when a given model is used to represent the observed data.1,2 To that end, lower AIC values indicate superior model fit. Model selection guidelines suggest that ΔAIC >3 represents meaningful change, whereas change >10 is strongly meaningful.7,19 An unstructured covariance matrix was used to examine random effects. Random intercept and random slope terms were included in all models to control for variability and rate of change in the dependent variable, respectively. After determination of the best fitting growth curve, random intercept and slope coefficients were extracted from each individual to analyze intergroup variability in rate and direction of change. Next, 2 separate conditional growth curve models tested the influence of time-invariant covariates (ie, behavioral inhibition and behavioral activation) on change in NFR and pain ratings in response to repeated stimulation. Electrocutaneous stimulus intensity (in mA) and participant sex were entered into each of the models as control variables. Post hoc tests of simple slopes were conducted to follow-up on significant interactions. All analyses were conducted using the “MIXED” procedure in SPSS version 22 (IBM Corp, Armonk, NY); random effect coefficients were extracted using the “PROC MIXED” procedure in SAS version 9.4 (SAS Institute Inc, Cary, NC).

Results

Changes in NFR and Pain Ratings

Results of unconditional growth curve analysis of change in NFR magnitude in response to repeated noxious electrotactaneous stimulation indicated that the logarithmic growth curve (AIC = 2,262.32) provided a better fit to the data than either quadratic (AIC = 2,280.78,) or linear (AIC = 2,281.96) models. On average, NFR responses habituated across the 12 stimulations, b = −.50, P < .01. Variance estimates of the random intercept and slope indicated that the intercept (Wald Z = 6.85, P < .001) as well as slope (Wald Z = 3.84, P < .001) of change in NFR varied significantly across individuals. In the unconditional model, the random slope tended toward negative covariance with the random intercept parameter (Wald Z = −1.75, P = .1), indicating that slopes were more negative if the NFR to the first stimulus (ie, intercept) is larger. Random slope coefficients for each individual, which ranged from −.35 to .31, were then extracted from the model. An example of the extensive variability in intercept and slope is depicted in Fig 1.

Results of unconditional growth curve analysis of change in pain ratings in response to repeated noxious electrotactaneous stimulation indicated that logarithmic growth curve (AIC = 12,175.36) provided a better fit to the data than either the quadratic (AIC = 12,275.07) or linear (AIC = 12,289.84) models. On average, pain responses sensitized across the 12 stimulations, b = 3.95, P < .001. Variance estimates for the random intercept
(Wald Z = 8.08, \( P < .001 \)) and the random slope (Wald Z = 7.6, \( P < .001 \)) were significant, indicating both had significant variation. Furthermore, the random intercept was negatively associated with the random slope, Wald Z = −3.14, \( P < .01 \), indicating that there was a greater sensitization when an individual’s pain ratings to the first stimulus (ie, intercept) was lower. Individual random slope coefficients were then extracted from the unconditional model. As with NFR responses, the range of random slope coefficients for pain rating changes, from −25.2 to 27.74, indicated large intergroup variability. This variability is depicted in Fig 2.

The proportion of individuals who habituated and sensitized in each response modality is described in Table 1. With respect to repeated NFR responses, 68.6% of participants evidenced habituation (ie, coefficients...
Behavioral activation and behavioral inhibition interacted with the growth curve to predict changes in NFR magnitude over time. Fig 3 illustrates the interaction for behavioral inhibition, with low behavioral inhibition scores related to habituation whereas high behavioral inhibition scores were not, b = .10, P < .01, but not when behavioral inhibition was fixed at 1 SD above the mean, b = .03, P = .38. Regarding control variables, neither stimulus intensity nor sex interacted with the growth curve, both Ps > .05. Stimulus intensity, however, was positively associated with average NFR magnitude, b = .018, P < .001. Together, behavioral inhibition and behavioral activation accounted for 17.8% of the random variance in the growth curve predicting change in NFR magnitude.

Table 1. Proportion of Sample Showing Habitation and Sensitization of NFR and Pain (N = 140)

<table>
<thead>
<tr>
<th></th>
<th>Pain Habitation</th>
<th>Pain Sensitization</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>NFR habituation</td>
<td>16.4% (23)</td>
<td>52.2% (73)</td>
<td>68.6% (96)</td>
</tr>
<tr>
<td>NFR sensitization</td>
<td>8.6% (12)</td>
<td>22.8% (32)</td>
<td>31.4% (44)</td>
</tr>
<tr>
<td>Total</td>
<td>25% (35)</td>
<td>75% (105)</td>
<td></td>
</tr>
</tbody>
</table>

Role of Behavioral Inhibition and Behavioral Activation

Conditional growth curve analyses were conducted to examine the influence of behavioral inhibition and behavioral activation on changes in NFR and pain ratings in response to repeated stimulation. The addition of behavioral inhibition and behavioral activation, as well as control variables, significantly improved the fit of the model (ΔAIC >10). As shown in Table 2, behavioral inhibition as well as behavioral activation independently interacted with the growth curve to predict changes in NFR magnitude over time. Fig 3 shows the interaction for behavioral activation, with high behavioral activation scores being marginally associated with greater NFR habituation compared with low behavioral activation scores, b = -.074, P = .07. Post hoc tests of simple slopes indicated significant habituation when behavioral activation is fixed at 1 SD above the mean, b = -.06, P = .05, but not when behavioral activation is fixed at 1 SD below the mean, b = .005, P = .86. To further examine this finding, BAS subscales were entered individually into the model in place of the composite behavioral activation score. In these models, the Fun subscale, b = -.06, P = .05, and the Reward Responsivity subscale, b = -.12, P = .002, were related to enhanced habituation of NFR; however, the Drive subscale was unrelated to changes in NFR (b = .01, P = .68). All subscales were unrelated to average NFR magnitude (ie, intercepts), all Ps > .1. Fig 4 illustrates the interaction for behavioral inhibition, with low behavioral inhibition scores related to habituation whereas high behavioral inhibition scores were not, b = .10, P < .01, but not when behavioral inhibition was fixed at 1 SD above the mean, b = .03, P = .38. Regarding control variables, neither stimulus intensity nor sex interacted with the growth curve, both Ps > .05. Stimulus intensity, however, was positively associated with average NFR magnitude, b = .018, P < .001. Together, behavioral inhibition and behavioral activation accounted for 17.8% of the random variance in the growth curve predicting change in NFR magnitude.

Together, the addition of behavioral inhibition, behavioral activation, sex, and stimulus intensity did not improve the fit of the model predicting pain ratings (ΔAIC <1). As detailed in Table 3, neither behavioral inhibition nor behavioral activation was related to change in pain ratings. Furthermore, neither stimulus intensity nor sex was significantly related to the growth curve. Stimulus intensity was negatively associated with average pain ratings, b = -.62, P < .001. Additionally, behavioral inhibition was marginally associated with higher average pain ratings, b = 5.74, P = .09. As with the composite BAS, BAS subscales were unrelated to either average pain ratings or change in pain ratings (all Ps > .10). Together, behavioral inhibition and behavioral activation accounted for 2.7% of the random variance in the growth curve predicting change in pain ratings.

Table 2. Tests of Fixed Effects for the Conditional Growth Curve Model Predicting Change in NFR Magnitude (N = 140)

<table>
<thead>
<tr>
<th>Fixed Effect</th>
<th>Estimate</th>
<th>Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1.52*</td>
<td>.08</td>
</tr>
<tr>
<td>Growth curve</td>
<td>-.03</td>
<td>.03</td>
</tr>
<tr>
<td>Sex*</td>
<td>.10</td>
<td>.11</td>
</tr>
<tr>
<td>Stimulus intensity</td>
<td>.02*</td>
<td>3E-2</td>
</tr>
<tr>
<td>Behavioral inhibition</td>
<td>-.07</td>
<td>.10</td>
</tr>
<tr>
<td>Behavioral activation</td>
<td>.12</td>
<td>.13</td>
</tr>
<tr>
<td>Sex × Growth curve</td>
<td>-.04</td>
<td>.03</td>
</tr>
<tr>
<td>Stimulus intensity × Growth curve</td>
<td>5E-4</td>
<td>1E-2</td>
</tr>
<tr>
<td>Behavioral inhibition × Growth curve</td>
<td>.10</td>
<td>.03</td>
</tr>
<tr>
<td>Behavioral activation × Growth curve</td>
<td>-.07</td>
<td>.04</td>
</tr>
</tbody>
</table>

*P < .001, 2-tailed.
*P < .05, 2-tailed.
*Male is the reference category.

Influence of Parent Study Characteristics on NFR and Pain Ratings

Because the current report is focused on baseline data from a larger study, characteristics of the parent study were examined to determine if the nature and events of the parent study were related to pain ratings and/or NFR. A between-groups variable was created for experimental condition (control, conditioning, placebo, placebo and conditioning). This variable was included in the conditional models predicting pain ratings and NFR. In the presence of BIS, BAS, sex, and stimulus intensity, experimental group was unrelated to average NFR magnitude, F = 1.91, P = .13; change in NFR magnitude, F = 1.14, P = .33; average pain ratings, F = 1.46, P = .23; or change in pain ratings, F = .01, P = .99. Data were
also reanalyzed after removing participants who later dropped out of the study (n = 3), and after removing individuals who were recruited through the undergraduate student participant pool (n = 4). Results of the study were unchanged in both cases.

Discussion

The current study sought to examine patterns of adaptation, in nociceptive reflexes as well as pain ratings, to repeated noxious electrocutaneous stimuli. Participants received a series of 12 electrocutaneous stimuli designed to elicit the NFR and moderate pain. The first aim of the study was to model changes in nociceptive reflexes and pain ratings across the 12 stimuli. To accomplish this aim, separate unconditional growth curve models were constructed to examine the pattern of change. For NFR and pain ratings, responses changed in a logarithmic fashion. Whereas the best fitting adaptation curve was the same for pain ratings and NFR, the direction of the curve was different. That is, on average, NFR responses habituated across the 12 stimuli, whereas pain ratings sensitized. This is consistent with the previous studies that have examined habituation of NFR and pain, both of which identified a dissociation between NFR and pain ratings.6,25

In addition to modeling change in pain ratings and NFR magnitude, we sought to examine interindividual variability in habituation of pain and NFR. Previous investigations of habituation and sensitization of pain ratings have indicated that group averages may obscure a proportion of the sample that evidence patterns of adaptation that differ from the group.3,12,35 This was shown to be the case for the current sample as well, with random slopes significantly improving model fit. To determine the proportion of the sample that evidenced habituation and sensitization of NFR and pain, random slope coefficients were examined. Although on average the sample showed habituation of NFR, examination of the random slope coefficients indicated that nearly one-third of the sample showed sensitization of NFR. With respect to pain, whereas the group average pain ratings increased

![Figure 3](Image.png) Change in NFR magnitude in response to repeated stimuli as a function of behavioral activation. High and low values on the BAS scale were fixed at 1 SD above the mean (high BAS) and 1 SD below the mean (low BAS). Post hoc tests of simple slopes indicated significant NFR habituation for high BAS but not low BAS.

![Figure 4](Image.png) Change in NFR magnitude in response to repeated stimuli as a function of behavioral inhibition. High and low values on the BIS scale were fixed at 1 SD above the mean (high BIS) and 1 SD below the mean (low BIS). Post hoc tests of simple slopes indicated significant habituation for low BIS but not high BIS.
across the 12 stimulations, approximately one-quarter of participants showed habituation. Further, there was no significant relationship between the likelihood of exhibiting NFR and pain habituation or sensitization, suggesting a dissociation between these adaptive processes. Clearly, future research is needed to better understand the factors that contribute to individual variability in pain and nociceptive adaptation.

As an initial test of potential psychological influences on adaptation to noxious stimuli, in the present study conditional growth curve modeling was used to determine if random variability in NFR and pain responses over time was related to self-reported behavioral inhibition and activation. Controlling for participant sex and individual differences in stimulation intensity, behavioral inhibition was shown to be negatively associated with habituation of NFR, whereas behavioral activation was positively associated with habituation of NFR. That is, individuals with higher behavioral inhibition scores had attenuated NFR habituation whereas those with higher behavioral activation scores scale had enhanced habituation. In contrast, neither behavioral inhibition nor behavioral activation were significantly related to the observed changes in pain ratings.

These findings provide support for 2 elements of the 2-factor model of chronic pain recently proposed by Jensen and colleagues. According to this model, behavioral inhibition and associated emotions, cognitions, and behaviors (eg, anxiety, catastrophizing, avoidance) are associated with maladaptive pain responses, whereas behavioral activation and associated emotions, cognitions, and behaviors (eg, joy, optimism, approach) are related to adaptive pain responding. The relationships among behavioral inhibition, behavioral activation, and habituation observed in the current study are consistent with this model, because habituation is generally considered to be an adaptive response to repeated or prolonged noxious stimulation. Individuals high in behavioral inhibition evidenced attenuation of this adaptive response, whereas those high in behavioral activation showed enhancement of habituation. Moreover, the enhanced habituation associated with behavioral activation was driven by scores on the Reward Responsivity and Fun subscales of the BAS scale.

A second component of the 2-factor model supported by the current study involves the automaticity of behavioral inhibition and behavioral activation systems. Behavioral inhibition and behavioral activation networks are held to reflect automatic motivational processes, acting outside of conscious control. It follows that the subconscious processes underlying avoidance and approach behavior would exert influence on the organization of subconscious nociceptive reflexes. Indeed, the effects noted in the current study appear to be consistent with the underlying motivations reflected by these neurophysiological systems. The behavioral inhibition system may potentiate avoidance behavior through descending modulation of nociceptive input in the spinal cord. Likewise, the behavioral activation system may dampen this nociceptive input to facilitate approach toward rewarding stimuli. This was confirmed by subscale tests, which indicated that reward-based facets of behavioral activation (ie, Reward Responsivity, Fun) drive the relationship between behavioral activation and habituation of NFR.

Interestingly, and contrary to our hypotheses and the 2-factor model, behavioral inhibition and behavioral activation were unrelated to changes in pain, although behavioral inhibition was marginally associated with higher average pain ratings. It may be the case that nociceptive changes governed by these automatic systems precede changes in conscious pain perception. As such, the relationships among behavioral inhibition, behavioral activation, and pain may be more readily apparent with more extended exposure to nociceptive input.

The results of the current study implicate the behavioral inhibition and activation systems in the descending modulation of nociceptive information in healthy individuals. However, the mechanisms of this action remain unclear. It may be the case that separate facilitatory and inhibitory neural networks independently modulate nociception. Behavioral inhibition and behavioral activation have previously been independently linked to activity of fear/anxiety and reward neural circuitry, respectively. These networks have each been implicated in descending modulation of pain in humans and nociceptive behavior in animals.

Although the present study has a number of important strengths, including a relatively large sample and concomitant assessment of nociceptive and pain responses, a couple of limitations are also worthy of note. First, because we analyzed existing data and the parent study was not designed to examine the potential influence of number and duration of applied stimuli, additional research is needed to examine changes in nociception and pain over longer intervals. Furthermore, we tested a variety of characteristics of the parent study (eg, sample makeup, experimental group) and found they were unrelated to habituation. Second, because
the sample included only healthy individuals it is not clear if the present findings will generalize to patient populations, and particularly to individuals with chronic or recurrent pain. Because approach and avoidance mechanisms may change with repeated exposure, future studies are needed to examine potential dynamic changes in pain and nociceptive habituation and sensitization in individuals with and without clinical pain.

Conclusions

In sum, most participants in this study showed habituation of NFR and sensitization of pain ratings; however, a sizeable proportion of the sample evidenced patterns of adaptation opposite from the group averages. Explaining this variability may be critical to identifying those at risk for negative pain-related outcomes. Behavioral inhibition and behavioral activation tendencies moderated the slope of adaptation for the NFR, but not pain. Thus, findings from the current study suggest that individual differences in approach and avoidance motivations are related to descending modulation of nociception in the spinal cord. Broadly, these findings support the contribution of these basic neurophysiological systems in shaping individual differences in pain experience.

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