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REVIEW

Emerging Clinical Technology: Application of Machine Learning to Chronic Pain Assessments Based on Emotional Body Maps

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Abstract

Depression and anxiety co-occur with chronic pain, and all three are thought to be caused by dysregulation of shared brain systems related to emotional processing associated with body sensations. Understanding the connection between emotional states, pain, and bodily sensations may help understand chronic pain conditions. We developed a mobile platform for measuring pain, emotions, and associated bodily feelings in chronic pain patients in their daily life conditions. Sixty-five chronic back pain patients reported the intensity of their pain, 11 emotional states, and the corresponding body locations. These variables were used to predict pain 2 weeks later. Applying machine learning, we developed two predictive models of future pain, emphasizing interpretability. One model excluded pain-related features as predictors of future pain, and the other included pain-related predictors. The best predictors of future pain were interactive effects of (a) body maps of fatigue with negative affect and (b) positive affect with past pain. Our findings emphasize the contribution of emotions, especially emotional experience felt in the body, to understanding chronic pain above and beyond the mere tracking of pain levels. The results may contribute to the generation of a novel artificial intelligence framework to help in the development of better diagnostic and therapeutic approaches to chronic pain.

Key Words Chronic pain · low back pain · interoception · bodily sensation map · emotions · pain assessment

Introduction

The USA is in the midst of dual epidemics of chronic pain and opioid abuse, with approximately 20% of the population in persistent pain, and over 40,000 lives lost each year to opioid misuse. Chronic back pain (CBP) is the most common pain disorder and one of the main reasons for prescribing opioids. It is, therefore, urgent to develop strategies to help reduce CBP without opioids.

A critical challenge in pain management emerges from the fact that pain cannot be directly measured. Although several multidimensional pain assessments have been proposed, the current gold standard for the assessment of pain is self-report, often assessed with a single-item visual analogue scale (VAS) or numeric pain scale (NPS) [1–3]. Yet, this one-dimensional pain estimate does not capture the multiple aspects of chronic pain and shows low consistency with patients' judgment about the severity of ongoing clinical pain and its effect on daily life [1]. Therefore, multidimensional measures of pain are needed to better inform pain management.

Recent research highlighted the significant role of psychological health for pain patients' wellbeing. Chronic pain is associated with vulnerability to life stressors, resulting in co-

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occurring depression, anxiety, and emotional disorders, which may, in turn, amplify pain [4–7]. Chronic pain patients also have impaired emotional awareness [8]. For example, alexithymia, a deficit in one's ability to identify emotions, is elevated in a range of disorders, particularly in central sensitization conditions such as lower back pain (LBP), fibromyalgia, and temporomandibular disorder [9].

Emotion can be defined as "a psychic and physical reaction subjectively experienced as strong feeling and physiologically involving changes that prepare the body for immediate vigorous action" [10]. The introspective emphasis on the "feeling" aspect of emotions has played a prominent role in the development of many theories of emotion. Multiple approaches attempting to conceptualize emotion processing agree that people have affective information about their current relationship with the world, at a sensory level, either by homeostatic feedback from the body or by neural representations of prior instances when an object or event predicted some allostatic change [11]. Classic [12] and more recent [11, 13] models of emotional processing propose that subjective emotional feelings are triggered by the perception of emotion-related body states, reflecting changes in the skeletomuscular, neuroendocrine, and autonomic nervous systems [14]. Such conscious feelings help individuals to voluntarily adapt their behavior to the challenges of the environment [15]. For example, fatigue, a response to stressors, can be managed by rest and sleep [16].

Recent research has shown that the bodily changes associated with different emotions are specific enough to serve as the basis for discrete emotional feelings, demonstrating that topographic body representation of emotions (or a bodily sensation map, BSM) is an important correlate of emotion that varies across emotion categories [17, 18]. Some physiological bases of this phenomenon have also been characterized. For example, recent studies have found that bidirectional brain–gut communication affects our emotions [19], and that these pathways may be useful for treating depression and anxiety [20].

Our body sensations affect emotional states. Persistent sensations, such as those experienced in the chronic pain state, may have a particularly high impact. Early detection of dysregulated emotions and their associated patterns of reference to body locations may be an important way of understanding mental illness and chronic pain conditions. Thus, assessments of pain, negative emotion, and positive emotion, together with their corresponding BSMs, may provide us with a better understanding of chronic pain conditions. Several studies have demonstrated spatial (i.e., body site) diversity of pain patterns in nonspecific CBP patients. One study found that only 39.4% have constant local pain, the rest reporting widespread pain, mostly constant in time [21]. The two subgroups differ in conditioned pain modulation [22], and widespread pain patients are at increased risk of death from cardiovascular causes [23].

It is, therefore, common to construct pain-focused BSMs, in which chronic pain patients indicate where the pain is in their body. Recent literature on embodied emotion has used BSMs to map the body locations in which emotions such as anger and fear are experienced in healthy populations. These maps of somatic referents of feelings (BSMs) are a rich source of potential information for understanding emotions in ways that go beyond the categories of words used and may provide new information about the emotional antecedents of chronic pain symptoms.

Smartphone-based ecological momentary assessments offer a simple and effective way of collecting patient data. As of 2020, 62% of the world population owned a mobile phone, which is an increase from 35% in 2011 [24]. We have developed a mobile platform for tracking pain patients' emotions, cliexa-EASE, which allows patients to self-report BSMs of emotional states, pain, stress and fatigue in a user-friendly and engaging way (Fig. 1). In the current study, we used cliexa-EASE to collect the data of 84 CBP patients and applied a machine learning (ML) approach to predict patients' pain levels in 2 weeks, based on the reported ratings of feeling and the corresponding BSM.

Methods

Participants

The study was conducted at the University of Colorado, Boulder, and approved by the University of Colorado Institutional Review Board. The data were collected as part of a randomized controlled trial testing two psychological treatments for chronic back pain (trial registered at clinicaltrials.gov, NCT #03294148). Treatment results from the trial are in preparation. The data presented here come from two baseline, pre-randomization (pre-treatment) study timepoints on a subset of participants who completed smartphone assessments.

Eighty-four LBP patients were recruited for the smartphone-based portion of the study. Patients were recruited from the community using electronic bulletin boards, advertisements on social media and in local newspapers, and physician referrals. Of these, 13% were excluded based on eligibility criteria, leaving 65 LBP patients whose data were used in the analysis. Assessment sessions included a battery of patient-reported outcomes, functional magnetic resonance imaging (fMRI), and a body mapping assessment. The body mapping assessment, described below, is the focus of this manuscript.

Inclusion criteria were age between 21 and 70 years and reported average back pain intensity of at least 4 on a scale of 1–10 over the past week, in keeping with inclusion criteria of previous CBP trials [25–27] and

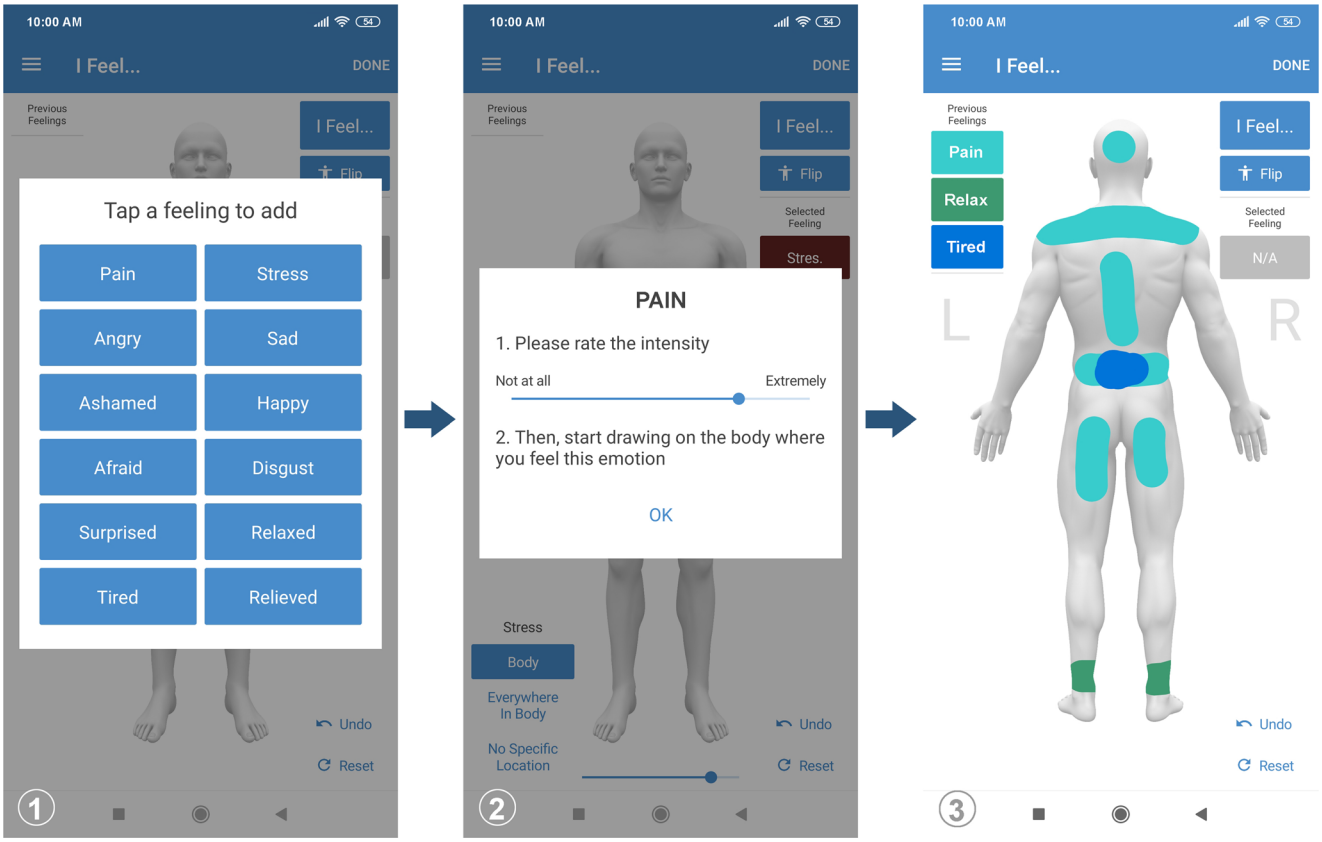

Fig. 1 Interface of the cliexa-EASE mobile platform. CBP participants reporting the following feelings and their corresponding spatial (body) locations: "tired," "ashamed," "afraid," "sad," "angry," "stress," "disgust," "surprise," "happy," "relieved," "relaxed," and "pain."

meeting the CBP definition established by a recent NIH task force, requiring a pain duration of at least 3 months, with back pain being an ongoing problem for at least half the days of the preceding 6 months [28]. Exclusion criteria were back pain associated with compensation or litigation issues within the past year, as determined by self-report; leg pain that is worse than back pain, indicating a greater likelihood of neuropathic pain; self-reported history of metastasizing cancers, to exclude cancer-related pain; self-reported diagnosis of an inflammatory disorder, to exclude inflammatory pain; unexplained, unintended weight loss of 20 lb or more in the preceding year; cauda equina syndrome, based on self-reported inability to control bowel or bladder function; self-reported diagnoses of schizophrenia, multiple personality disorder, or dissociative identity disorder; and self-reported use of intravenous drugs.

Of the participants included in the study, 82% were white, 9% black, 3% American Indian or Alaskan Native, 3% Asian or Pacific Islander, and 3% other; 42% were women, 75% had at least some college education, 60% had a full-time job, 57% were married, and 46% had 7 or more hours of exercise per week. The average age of participants was 43.23 years (SD = 15.68).

Procedure

First, CBP participants completed a study eligibility assessment session, reporting experienced feelings and their spatial (body) locations (Fig. 1). Patients reported the following feelings: "tired," "ashamed," "afraid," "sad," "angry," "stress," "disgust," "surprise," "happy," "relieved," "relaxed," and "pain." The feelings could be reported multiple times for different body locations, in the front and back sides of the body. Next, 2 weeks later, participants were asked to report their current level of pain. All participants provided written informed consent in accord with the Declaration of Helsinki and as approved by the Institutional Review Board.

Measures

We initiated the development of the mobile platform based on the wheel of emotions model suggested by Plutchik [29]. The development included an iterative process of an expert panel (T.D.W. and P.G.) and pilot study with LBP patients.

In the present study, LBP patients reported the feelings they experienced and the spatial (body) locations where they experienced them, using our mobile platform cliexa-EASE, developed by cliexa. The drawing tool was designed using scalable

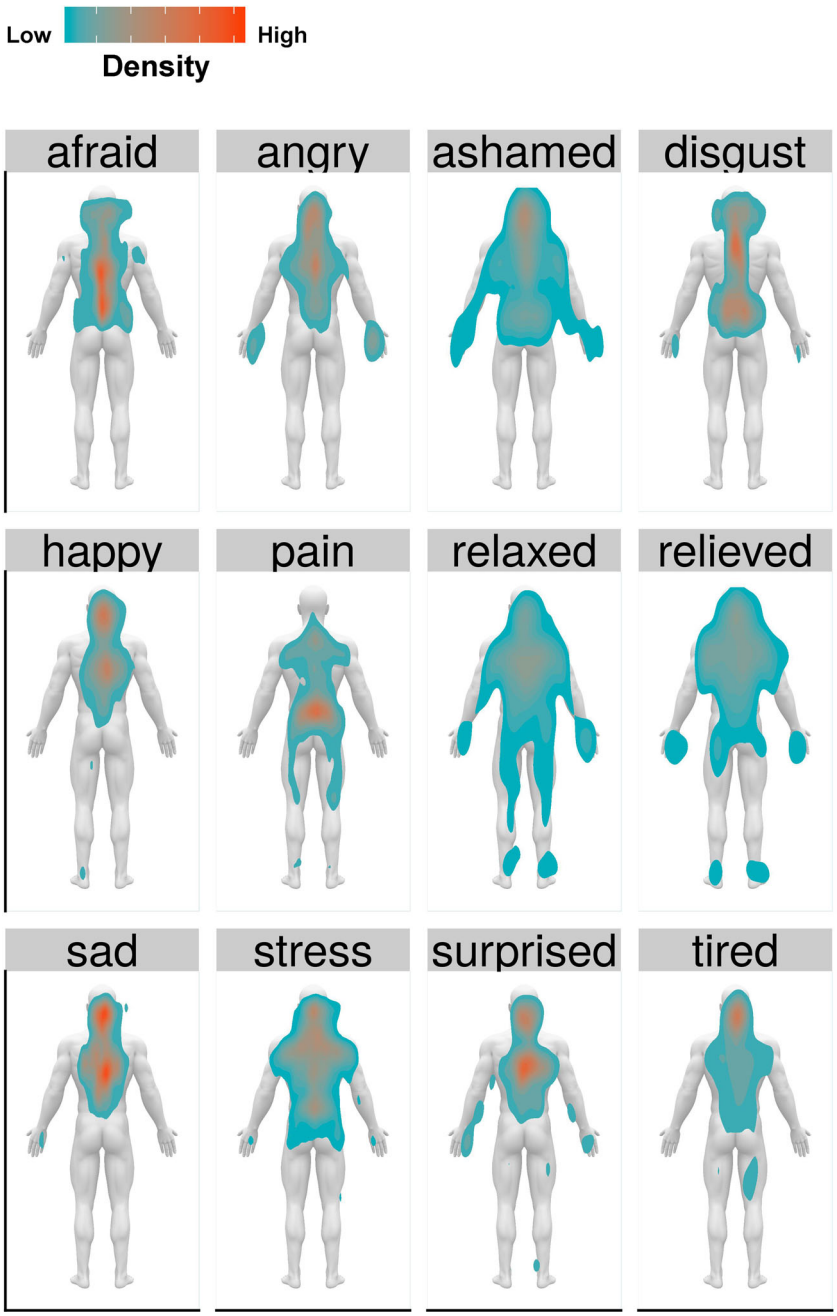

Fig. 2 Bodily sensation maps (BSMs) for pain and 11 feelings: tired, ashamed, afraid, sad, angry, stress, disgust, happy, relieved, relaxed, pain. The heatmap represents the density of the reported BSMs over the entire sample for LBP patients. Minimum densities are colored blue and maximum densities red

vector graphics (SVG) paths capable of creating complex shapes by combining multiple lines (Fig. 2). During a rating session, participants engaged in one or more rating episodes, which were defined as (1) selecting an emotion category, pain, or fatigue; (2) rating the overall intensity of the feeling on a visual analogue scale (VAS); and (3) drawing with the finger on a body map to report where the feeling was experienced in the body. Participants could complete as many rating episodes for the same or different categories as they liked during the session. For each BSM, they could draw on both the front and back of the body. Based on the BSMs, we calculated the areas covered by each drawing and the total length of the line path connecting the sequence of data points. Following the correlational patterns, we reduced the redundancy in the space of feeling representations. "Tired" was defined as a separate category, and all other negative feelings (ashamed, afraid, sad, angry, stress, disgust) were clustered together as "negative feelings." Positive feelings (happy, relieved, relaxed) were also clustered together, and pain was treated separately. For each category of feelings (happy, pain, negative, tired), we calculated the following features: minimum, maximum, mean, and standard deviation across all rating episodes in the cluster for (a) VAS feeling

ratings; (b) path length and area covered by the drawing. We also considered the overall number of reported feelings. All the features were standardized before the statistical analysis.

We also collected demographic information and used the four-item PROMIS depression questionnaire, with high reliability (Cronbach's alpha = 0.93) and strong convergent validity, to estimate depression comorbidity [30].

Statistical Analysis

We applied two analyses on the features extracted from the feeling ratings and the BSMs to assess patients' momentary pain levels 2 weeks later. In the first analysis, all the features based on the feeling-based ratings and BSMs (combining individual emotion categories as specified above), except pain-related features, were used to assess pain ratings 2 weeks later. The second analysis was similar, but this time, pain-related features were also included. We used an ML approach to develop models for pain assessment, applying a linear regression framework with leave-one-participant-out cross-validation (LOOCV) that outperforms *k*-fold cross-validation for small sample sizes [31]. Despite a current trend for more complicated ML models, their benefit is questionable in many cases, and at times, simple models perform as well as highly sophisticated ones but are more interpretable [32]. We tested all possible models with up to 2 main effects and one interaction term. For Model 1, main effects (possible features) included three categories (negative emotion, positive emotion, and fatigue) with 6 measures for each (minimum, maximum, mean, and SD of intensity ratings over rating episodes, BSM line length, and BSM area), for a total of 24 possible predictors. The space of possible models with one or two predictors was 171 possible models. For Model 2, four categories (the three above plus pain ratings) with the same features were included, for a total of 300 possible models. Because of the sample size restriction, we defined the search space for the model parameters only for the main effects and pairwise interactions between the defined features. We used the Bayesian Information Criterion for model selection and evaluation, choosing the best overall model in each category.

Results

Analysis Without the Pain-Related Features

Table 1 presents the final model for predicting patients' CBP levels 2 weeks later, based on feeling ratings and BSM-related features not related to pain. The final model included main effects of negative feelings and fatigue, and their interaction (statistics are shown in Table 1). Figure 3A shows the model fit, and Fig. 3C presents the interaction effect and length of "tired" line × maximum area covered by negative feelings about pain 2 weeks later ($B = 0.78$, 95% CI [0.29–1.28], $T(61) = 3.10$, $p = 0.003$, $R^2_{LOOCV} = 0.25$). When participants used long lines to describe tiredness in their bodies, the increased maximum area used to express their negative feelings was associated with higher pain levels 2 weeks later (simple effect at 1 SD above the mean: $B = 1.91$, 95% CI [1.05–2.75], $T(61) = 4.49$, $p < 0.001$). By contrast, when patients used shorter lines to describe tiredness in their bodies, the increased maximum area used to express their negative feelings was not related to their pain levels 2 weeks later (simple effect at 1 SD below the mean: $B = 0.33$, 95% CI [− 0.18 to 0.85], $T(61) = 1.30$, $p = 0.20$). Classifying predicted and observed values of pain intensity with a threshold of 4 (pain > 4), the model produced a predictive accuracy of 65% in discriminating between low and high levels of pain. In sum, pain was predicted by a combination of fatigue and negative emotion expressed in BSMs two weeks earlier.

Table 2 presents the second model for predicting patients' CBP levels 2 weeks later, using feeling intensity ratings, BSM features, and pain intensity ratings and BSMs. Figure 3B shows the model fit, and Fig. 3D presents the interaction between the minimum pain reported and the mean positive feeling ($B = -1.01$, 95% CI [− 1.63 to − 0.39], $T(61) = 3.18$, $p = 0.002$, $R^2_{LOOCV} = 0.35$). For participants who reported low mean positive feelings, the minimum reported pain level was associated with higher levels of pain 2 weeks later (simple effect 1 SD below the mean: $B = 2.00$, 95% CI [1.23–2.76], $T(61) = 5.21$, $p < 0.001$). By contrast, for participants who reported increased mean positive feelings, there was no

Table 1 Model 1, based on feelings excluding pain

Predictors	Pain 2 weeks later			
	Estimates	CI	*T*	*p*
(Intercept)	3.63	3.21–4.06	16.61	< 0.001
Max area of neg. feelings	1.12	0.64–1.60	4.59	< 0.001
Length of "tired" line	− 0.35	− 0.81 to 0.12	− 1.45	0.151
Max area of neg. feelings × length of "tired" line	0.78	0.29–1.28	3.10	0.003
R^2 training/R^2 LOOCV	0.276/0.249			

The model assesses pain 2 weeks later, based on the features extracted from LBP patients' reports on their feelings and associated body representations excluding pain

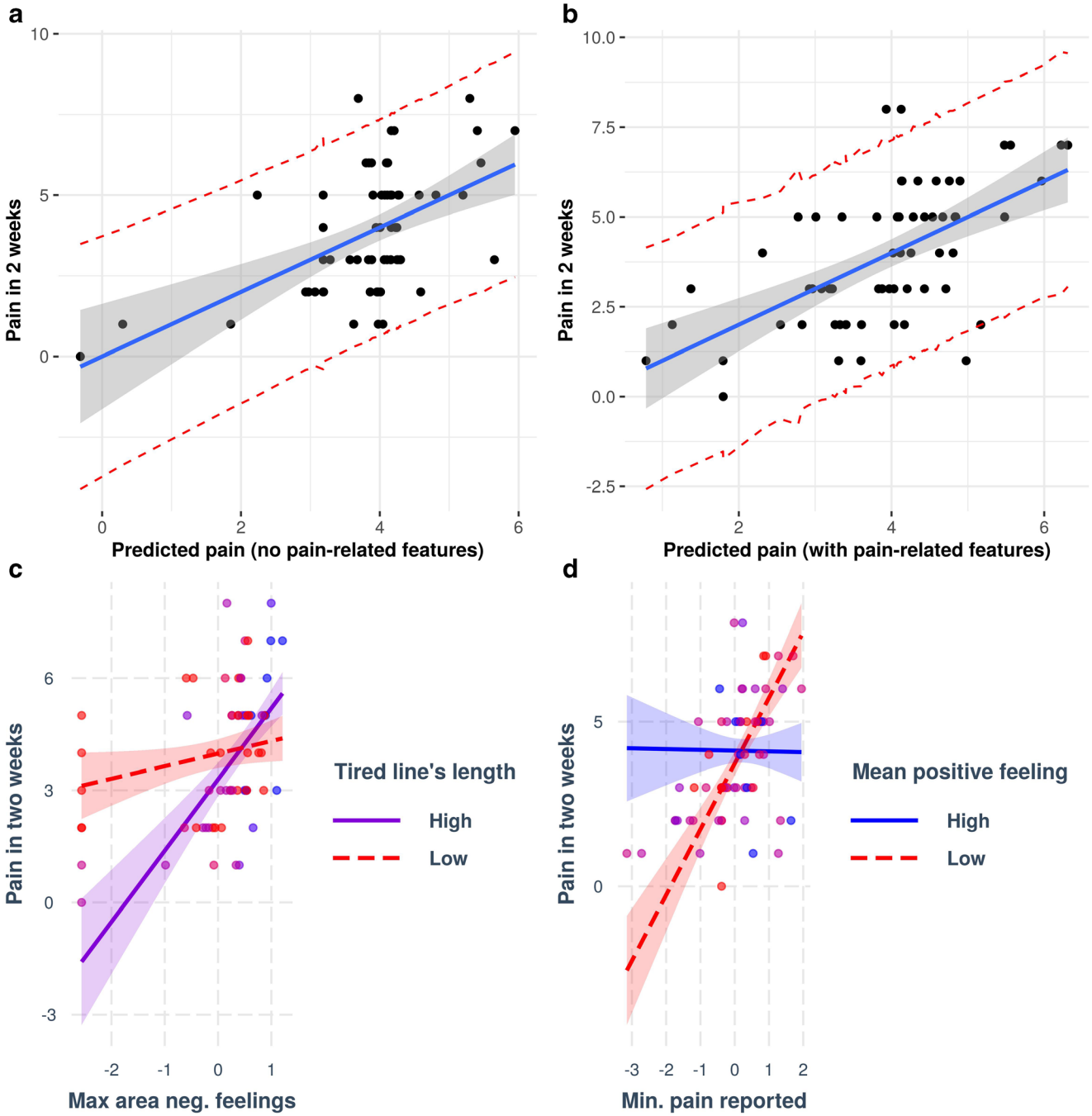

Fig. 3 Pain-predictive models. (A) Predictive feeling-based model without pain-related features for pain 2 weeks later. The filled area around the regression line and the dotted red lines represent confidence and prediction intervals, respectively. (B) Predictive feeling-based model including pain-related features for pain 2 weeks later. The filled area around the regression line and red dotted lines represent confidence and prediction intervals, respectively. (C) Interpretation of the predictive pain model excluding pain-related features (A). The figure presents the interaction effect between the maximum area covered by negative feelings and the total length of the line associated with the "tired" feeling. Low/high levels of the length of the "tired" feeling line are represented by 1 SD deviation below/above the average length of the line, respectively. For participants who used a long line to describe tiredness in their bodies, the increased maximum area used to express their negative feelings was associated with higher levels of pain 2 weeks later. For participants who used a shorter line to describe tiredness in their bodies, there was no relationship between the maximum area used to express their negative feelings and pain levels 2 weeks later. (D) Interpretation of the predictive pain model including pain-related features (B). The figure presents the interaction effect between the minimum pain reported and the mean positive feeling. Low/high levels of mean positive feelings are represented by 1 SD deviation below/above the average of positive feelings, respectively. For participants who reported low mean positive feelings, the minimum reported level of pain was associated with higher levels of pain 2 weeks later. For participants who reported increased mean positive feelings, there was no relationship between the minimum pain reported and levels of pain 2 weeks later.

Table 2 Model 2, based on feelings including pain

Predictors	Pain 2 weeks later			
	Estimates	CI	*T*	*p*
(Intercept)	3.92	3.55–4.30	20.29	< 0.001
Min. pain reported*	0.99	0.60–1.37	5.06	< 0.001
Mean positive feeling	0.20	− 0.21 to 0.60	0.95	0.348
Min. pain reported × mean positive feeling	− 1.01	− 1.63 to − 0.39	− 3.18	0.002
R^2 training/R^2 LOOCV	0.356/0.352			

The model assesses pain 2 weeks later, based on the features extracted from LBP patients' reports of their feelings and associated body representations including pain

*Minimum pain across several reported locations

relationship between the minimum pain reported and pain levels 2 weeks later ($B = -0.02$, 95% CI [− 0.75 to 0.70], $T(61) = -0.07$, $p = 0.95$). Classifying predicted and observed values of pain intensity with a threshold of 4 (pain > 4), the model produced a predictive accuracy of 72% in discriminating between low and high levels of pain. In sum, pain was predicted by a combination of low positive emotion and consistently high previous pain two weeks earlier.

Finally, we tested whether self-reported depression symptoms explain the findings in both models (including/excluding pain-related features) by adding depression to the reported models. Depression symptoms did not contribute to the first model, without pain-related features ($F(1, 60) = 1.09$, $p = 0.28$), or to the model that included pain-related features ($F(1, 60) = 1.91$, $p = 0.06$).

Discussion

Unidimensional pain intensity represents the primary outcome in most chronic pain conditions, and it is nearly universally assessed in chronic pain research. Clinical pain, however, is a complex experience that relies at least partially on emotional experience, and the correspondence between the subjective experience of pain and objective bodily damage varies. Although these two points are widely acknowledged by experts in pain research and practice, they are still not fully appreciated in more general practice settings, where pain is often treated as a purely sensory experience reflecting underlying tissue damage. As a result, wide gaps remain between our understanding of chronic pain and the ways in which many patients are assessed and treated.

In this study, we developed and validated a novel approach for tracking pain and emotional wellbeing in LBP patients, predicting future pain levels. We developed a mobile platform to record patients' feelings and their corresponding bodily expressions (BSMs). Our validation study showed a promising ability to predict LBP patients' levels of pain 2 weeks later, using two sets of predictive features: (a) BSMs and feeling ratings excluding pain-related features and (b) BSMs and feeling ratings including pain-related features.

Both models rely on the interaction effect between two features. According to the first model, increased bodily expression of negative feelings is associated with higher pain levels only for CBP patients who demonstrate increased fatigue ("tired") through their BSMs. Fatigue is a product of physical and mental overload, and it results in a reduction of our attention and stress resilience [33]. Consistent with this, chronic pain patients previously demonstrated a positive association between negative affect and pain levels in cases of low pain acceptance [34], low pain resilience [35], and cannabis use with high frequency [36]. Moreover, fatigue, negative affect, and pain have shared brain correlates [33]. Thus, it may be suggested that experienced fatigue serves as a gate for the brain representations of pain and negative affect, with high levels of fatigue opening the gate, after which the experienced negative affect results in more pain. Fatigue seems to play a key role in generalized chronic primary pain conditions such as fibromyalgia [37]; therefore, there is a strong association between the spatial extent of pain and fatigue.

The second model concerns the required conditions for the pain to be predictable by the minimum pain experienced in the past. According to the model, experienced positive affect (PA) moderates this effect, so that current pain is positively associated with the future level of pain only for patients with a low level of PA. A previous study including 2715 LBP patients showed that past pain predicts future pain [38]. Others confirmed this association [39, 40]. Here, we suggest a qualification of the initial model, emphasizing PA as a moderating factor in the association between past and future pain. PA may indeed serve as a resilience factor for patients with fibromyalgia [41] and other types of chronic pain [42, 43]. Others demonstrated a weaker relationship between pain and negative affect in patients with rheumatoid arthritis in the case of increased PA [44].

Perhaps at its most basic level in humans, the influence of evoked PA on evoked or clinical pain can be demonstrated in controlled experimental studies. Numerous studies have experimentally demonstrated the benefits of induced PA on acute pain,

with the general finding that PA inductions reduce pain sensitivity [45, 46]. Recent work using the nociceptive flexion reflex suggests that the effects of induced PA on pain may be spinally mediated [45, 47, 48]. Neuroimaging studies have demonstrated that increased PA on pain is associated with activity in the anterior cingulate cortex, bilateral insula, right secondary somatosensory cortex, and left orbital frontal cortex [49]. Together, these findings suggest that PA is integrated within a central pain modulatory network. As we show here, collecting the associated BSMs may also contribute to the accuracy of the models, suggesting that interoception plays a significant role.

Interoception, the sense of the internal state of the body, has received extensive attention in recent years [50]. Some fundamental questions concerning the mechanisms underlying the relation between emotion and interoception remain unclear, however. Interoceptive warning is connected primarily with homeostasis and threatened tissue damage, which is an important feature of subjective feelings such as pain [13]. Although previous research suggested that bodily sensations have a unique spatial representation [17] that is culturally universal [51] in healthy populations, we still lack basic understanding about bodily expressions of emotion in clinical populations, such as chronic pain patients.

The present study relies on data collected at two time points, but chronic pain often manifests as a continuous ebb and flow of periods of elevated, normal and attenuated pain. Thus, affective states are likely to be dynamically influenced by changes in environmental and physiological demands, as well as by random, unpredictable fluctuations. Chronic pain patients show an abnormal and maladaptive response to life stressors resulting in depression, anxiety and emotional disorders, which, in turn, may amplify pain and affect the patients' wellbeing [4–7]. Future studies should track fluctuations of emotional states and pain continuously to develop predictive pain models based on appropriate tracking tools, as, for example, ecological momentary assessments (EMAs).

Studies typically assess behaviors and emotions based on retrospective data collection tools or synthetic manipulations, an approach that misses the concrete situations that precipitate behavior changes. EMA assesses individuals' current experiences, behaviors, and moods as they occur in real time and in their real-world settings [52]. Previous studies have used EMA to research emotions in chronic pain patients. These studies, however, mostly (a) used small sample sizes, (b) focused on between-groups comparisons, (c) used cross-sectional analyses that do not consider temporal dynamics (e.g., lagged effects), and (d) did not investigate the spatial distribution of pain and emotion across body sites. It is increasingly appreciated that EMA is uniquely positioned to assess a patient's pain [53] and emotional experience [54] with high precision. EMA involves just-in-time tracking in participants' natural environments at multiple time points, with three main benefits: (a) momentary measurement decreases recall biases by capturing present pain and emotional experiences rather than pain beliefs or summary ratings based on memory; (b) the tracking takes place in the patients' natural environments and social contexts, increasing the ecological validity of the tool; and (c) data collection at multiple time points provides potentially fine-grained information about pain experiences [53]. Thus, investigating temporal lagged dynamics between emotions and developing a novel classification of chronic pain patients based on temporal and spatial fluctuations of emotions and pain with real-life data may improve our understanding of chronic pain phenomena.

EMA-based tracking tools, such as cliexa-EASE, used here, together with established predictive models may be translated into artificial intelligence systems. A monitoring platform may be established by combining clinical levels of research with continuous follow-up, computer vision approaches, and by deploying online machine learning techniques. Such a platform may serve as a just-in-time feedback tool for clinicians, providing in-depth multidimensional personalized understanding of chronic pain patients.

Such insights could accelerate further development of chronic pain models, resulting in more efficient treatment approaches. For example, a tool that delivers information about patients' experiences to clinicians, including feedback about the patients' status and health trajectories, can help personalize prevention and treatment. A similar tool may be used by patients for self-monitoring and self-insight. Such feedback may also have a therapeutic side effect, serving as mindfulness intervention. Indeed, recent studies have demonstrated the effectiveness of mind–body therapy that concentrates on body sensations for treating chronic pain [55–57].

The proposed direction is especially relevant today, when many patients and their clinicians try to find a way out of the opioid crisis. Current pain drugs are inadequate, and patients and physicians are often unaware of relationships between patterns of medication use and pain, fatigue, and emotional outcomes. This is particularly true for opioids, which do not effectively relieve pain for many individuals, but rather result in a vicious cycle of escalating drug use, increased pain due to opioid-induced hyperalgesia, and depression. Opioid use has negative effects on multiple cognitive functions [58], including memory, information processing, sleep quality (25% of opioid users), constipation (40%), loss of appetite (23%), sexual dysfunction (18%) [59], and emotional states [60], resulting in decreased wellbeing and life quality. There is a complex set of interactions between pain, medication use, and emotion [61–64], which varies with individual patients. If patients and physicians could see the relationships between medication use, pain, and emotion over time, it would be easier to identify the causes and triggers of negative outcomes and optimize treatment for individual patients. Based on this understanding, we could develop artificial intelligence technologies to support chronic pain patients and their clinicians on a large scale.

These results should be interpreted in light of several limitations. First, studies with larger samples are needed to make the present findings generalizable, in light of the machine learning approach we used. Second, the first and second visits were conducted at different times of day, without any control. It is possible that time of day affects the associations between emotional states and pain levels. Third, because of the correlated nature of some features, other models with reduced fit may be considered in addition to the models reported here. Finally, because our findings are not specific to LBP, the findings reported here may be generalizable to other chronic pain conditions, but non-LBP patients may vary on the association between feelings and future levels of pain.

In conclusion, using our mobile platform, we developed and validated a predictive model of future pain, emphasizing both the reliability and interpretability of the model. These findings increase our understanding of the role that feelings and their bodily reflections may play in chronic pain. Our findings may result in the creation of a novel artificial intelligence framework, which will help in the development of better therapeutic approaches to chronic pain, integrating psychological and traditional biomedical approaches.

Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

References

1. van Boekel RLM, Vissers KCP, van der Sande R, Bronkhorst E, Lerou JGC, Steegers MAH (2017) Moving beyond pain scores: Multidimensional pain assessment is essential for adequate pain management after surgery. PLoS One 12:e0177345
2. Melzack R (1975) The McGill Pain Questionnaire: major properties and scoring methods. Pain 1:277–299
3. Clark WC, Kuhl JP, Keohan ML, Knotkova H, Winer RT, Griswold GA (2003) Factor analysis validates the cluster structure of the dendrogram underlying the Multidimensional Affect and Pain Survey (MAPS) and challenges the a priori classification of the descriptors in the McGill Pain Questionnaire (MPQ). Pain 106: 357–363
4. Fishbain DA, Cutler R, Rosomoff HL, Rosomoff RS (1997) Chronic pain-associated depression: antecedent or consequence of chronic pain? A review. Clin J Pain 13:116–137
5. Bair MJ, Robinson RL, Katon W, Kroenke K (2003) Depression and pain comorbidity: a literature review. Arch Intern Med 163: 2433–2445
6. Tsang A, Von Korff M, Lee S, et al (2008) Common chronic pain conditions in developed and developing countries: gender and age differences and comorbidity with depression-anxiety disorders. J Pain 9:883–891
7. McWilliams LA, Cox BJ, Enns MW (2003) Mood and anxiety disorders associated with chronic pain: an examination in a nationally representative sample. Pain 106:127–133
8. Zunhammer M, Halski A, Eichhammer P, Busch V (2015) Theory of Mind and Emotional Awareness in Chronic Somatoform Pain Patients. PLoS One 10:e0140016
9. Lumley MA, Cohen JL, Borszcz GS, Cano A, Radcliffe AM, Porter LS, Schubiner H, Keefe FJ (2011) Pain and emotion: a biopsychosocial review of recent research. J Clin Psychol 67: 942–968
10. Merriam-Webster, Inc (1983) Webster's Ninth New Collegiate Dictionary. Merriam-Webster
11. Barrett LF, Mesquita B, Ochsner KN, Gross JJ (2007) The experience of emotion. Annu Rev Psychol 58:373–403
12. James W (1884) What is an emotion? Mind 9:188–205
13. Damasio A, Carvalho GB (2013) The nature of feelings: evolutionary and neurobiological origins. Nat Rev Neurosci 14:143–152
14. Levenson RW (2003) Blood, sweat, and fears: the autonomic architecture of emotion. Ann N Y Acad Sci 1000:348–366
15. Damasio AR (1998) The somatic marker hypothesis and the possible functions of the prefrontal cortex. The Prefrontal Cortex
16. Mengshoel AM (2010) Life strain-related tiredness and illness-related fatigue in individuals with ankylosing spondylitis. Arthritis Care Res 62:1272–1277
17. Nummenmaa L, Glerean E, Hari R, Hietanen JK (2014) Bodily maps of emotions. Proc Natl Acad Sci U S A 111:646–651
18. Nummenmaa L, Hari R, Hietanen JK, Glerean E (2018) Maps of subjective feelings. Proc Natl Acad Sci U S A. https://doi.org/10.1073/pnas.1807390115
19. Mayer EA (2011) Gut feelings: the emerging biology of gut–brain communication. Nat Rev Neurosci 12:453
20. Slyepchenko A, Carvalho AF, Cha DS, Kasper S, McIntyre RS (2014) Gut emotions - mechanisms of action of probiotics as novel therapeutic targets for depression and anxiety disorders. CNS Neurol Disord Drug Targets 13:1770–1786
21. Tesarz J, Gerhardt A, Hartmann M, Kohlmann T, Eich W (2016) The Course of the Spatial Extent of Pain in Nonspecific Chronic Back Pain: A Prospective Population-based Cohort Study With Clinical Evaluation. Clin J Pain 32:580–587
22. Gerhardt A, Eich W, Treede R-D, Tesarz J (2017) Conditioned pain modulation in patients with nonspecific chronic back pain with chronic local pain, chronic widespread pain, and fibromyalgia. Pain 158:430–439
23. Tesarz J, Eich W, Baumeister D, Kohlmann T, D'Agostino R, Schuster AK (2019) Widespread pain is a risk factor for cardiovascular mortality: results from the Framingham Heart Study. Eur Heart J 40:1609–1617
24. Ericsson AB (2015) Ericsson mobility report: On the pulse of the Networked Society. Ericsson, Sweden, Tech. Rep. EAB-14
25. Baliki MN, Petre B, Torbey S, Herrmann KM, Huang L, Schnitzer TJ, Fields HL, Apkarian AV (2012) Corticostriatal functional connectivity predicts transition to chronic back pain. Nat Neurosci 15: 1117–1119
26. Cherkin DC, Sherman KJ, Balderson BH, Cook AJ, Anderson ML, Hawkes RJ, Hansen KE, Turner JA (2016) Effect of Mindfulness-Based Stress Reduction vs Cognitive Behavioral Therapy or Usual Care on Back Pain and Functional Limitations in Adults With Chronic Low Back Pain: A Randomized Clinical Trial. JAMA 315:1240–1249
27. Seminowicz DA, Wideman TH, Naso L, et al (2011) Effective treatment of chronic low back pain in humans reverses abnormal brain anatomy and function. J Neurosci 31:7540–7550
28. Deyo RA, Dworkin SF, Amtmann D, et al (2014) Report of the NIH Task Force on research standards for chronic low back pain. J Pain 15:569–585
29. Plutchik R (1980) Chapter 1 - A GENERAL PSYCHOEVOLUTIONARY THEORY OF EMOTION. In: Plutchik R, Kellerman H (eds) Theories of Emotion. Academic Press, pp 3–33

30. Kroenke K, Yu Z, Wu J, Kean J, Monahan PO (2014) Operating characteristics of PROMIS four-item depression and anxiety scales in primary care patients with chronic pain. Pain Med 15:1892–1901
31. Wong T-T (2015) Performance evaluation of classification algorithms by k-fold and leave-one-out cross validation. Pattern Recognit 48:2839–2846
32. Christodoulou E, Ma J, Collins GS, Steyerberg EW, Verbakel JY, Van Calster B (2019) A systematic review shows no performance benefit of machine learning over logistic regression for clinical prediction models. J Clin Epidemiol 110:12–22
33. Boksem MAS, Meijman TF, Lorist MM (2005) Effects of mental fatigue on attention: an ERP study. Brain Res Cogn Brain Res 25: 107–116
34. Kratz AL, Davis MC, Zautra AJ (2007) Pain acceptance moderates the relation between pain and negative affect in female osteoarthritis and fibromyalgia patients. Ann Behav Med 33:291–301
35. Schütze R, Rees C, Preece M, Schütze M (2010) Low mindfulness predicts pain catastrophizing in a fear-avoidance model of chronic pain. Pain 148:120–127
36. Wilson M, Gogulski HY, Cuttler C, Bigand TL, Oluwoye O, Barbosa-Leiker C, Roberts MA (2018) Cannabis use moderates the relationship between pain and negative affect in adults with opioid use disorder. Addict Behav 77:225–231
37. Vincent A, Benzo RP, Whipple MO, McAllister SJ, Erwin PJ, Saligan LN (2013) Beyond pain in fibromyalgia: insights into the symptom of fatigue. Arthritis Res Ther 15:221
38. Papageorgiou AC, Croft PR, Thomas E, Ferry S, Jayson MI, Silman AJ (1996) Influence of previous pain experience on the episode incidence of low back pain: results from the South Manchester Back Pain Study. Pain 66:181–185
39. Rollman GB, Abdel-Shaheed J, Gillespie JM, Jones KS (2004) Does past pain influence current pain: biological and psychosocial models of sex differences. Eur J Pain 8:427–433
40. Gedney JJ, Logan H (2006) Pain related recall predicts future pain report. Pain 121:69–76
41. Zautra AJ, Johnson LM, Davis MC (2005) Positive affect as a source of resilience for women in chronic pain. J Consult Clin Psychol 73:212–220
42. Karoly P, Ruehlman LS (2006) Psychological "resilience" and its correlates in chronic pain: Findings from a national community sample. Pain 123:90
43. Sturgeon JA, Zautra AJ (2010) Resilience: a new paradigm for adaptation to chronic pain. Curr Pain Headache Rep 14:105–112
44. Strand EB, Zautra AJ, Thoresen M, Ødegård S, Uhlig T, Finset A (2006) Positive affect as a factor of resilience in the pain-negative affect relationship in patients with rheumatoid arthritis. J Psychosom Res 60:477–484
45. Rhudy LJ, Williams EA, McCabe MK, Russell LJ, Maynard JL (2008) Emotional control of nociceptive reactions (ECON): do affective valence and arousal play a role? Pain 136:250–261
46. de Wied M, Verbaten MN (2001) Affective pictures processing, attention, and pain tolerance. Pain 90:163–172
47. Rhudy JL, Williams AE, McCabe KM, Nguyen MATV, Rambo P (2005) Affective modulation of nociception at spinal and supraspinal levels. Psychophysiology 42:579–587
48. Rhudy JL, DelVentura JL, Terry EL, Bartley EJ, Olech E, Palit S, Kerr KL (2013) Emotional modulation of pain and spinal nociception in fibromyalgia. Pain 154:1045–1056
49. Kamping S, Bomba IC, Kanske P, Diesch E, Flor H (2013) Deficient modulation of pain by a positive emotional context in fibromyalgia patients. Pain 154:1846–1855
50. Schoeller F, Haar AJH, Jain A, Maes P (2019) Enhancing human emotions with interoceptive technologies. Phys Life Rev 31:310–319
51. Volynets S, Glerean E, Hietanen JK, Hari R, Nummenmaa L (2019) Bodily maps of emotions are culturally universal. Emotion. https://doi.org/10.1037/emo0000624
52. Shiffman S, Stone AA, Hufford MR (2008) Ecological momentary assessment. Annu Rev Clin Psychol 4:1–32
53. May M, Junghaenel DU, Ono M, Stone AA, Schneider S (2018) Ecological Momentary Assessment Methodology in Chronic Pain Research: A Systematic Review. J Pain 19:699–716
54. Andrewes HE, Hulbert C, Cotton SM, Betts J, Chanen AM (2017) An ecological momentary assessment investigation of complex and conflicting emotions in youth with borderline personality disorder. Psychiatry Res 252:102–110
55. Luskin FM, Newell KA, Griffith M, Holmes M, Telles S, DiNucci E, Marvasti FF, Hill M, Pelletier KR, Haskell WL (2000) A review of mind/body therapies in the treatment of musculoskeletal disorders with implications for the elderly. Altern Ther Health Med 6: 46–56
56. Morone NE, Greco CM (2007) Mind–Body Interventions for Chronic Pain in Older Adults: A Structured Review. Pain Med 8: 359–375
57. Hadhazy VA, Ezzo J, Creamer P, Berman BM (2000) Mind-body therapies for the treatment of fibromyalgia. A systematic review. J Rheumatol 27:2911–2918
58. Schiltenwolf M, Akbar M, Hug A, Pfüller U, Gantz S, Neubauer E, Flor H, Wang H (2014) Evidence of specific cognitive deficits in patients with chronic low back pain under long-term substitution treatment of opioids. Pain Physician 17:9–20
59. Brown RT, Zuelsdorff M, Fleming M (2006) Adverse effects and cognitive function among primary care patients taking opioids for chronic nonmalignant pain. J Opioid Manag 2:137–146
60. Hebb ALO, Poulin J-F, Roach SP, Zacharko RM, Drolet G (2005) Cholecystokinin and endogenous opioid peptides: interactive influence on pain, cognition, and emotion. Prog Neuropsychopharmacol Biol Psychiatry 29:1225–1238
61. Carter LE, McNeil DW, Vowles KE, Sorrell JT, Turk CL, Ries BJ, Hopko DR (2002) Effects of emotion on pain reports, tolerance and physiology. Pain Res Manag 7:21–30
62. Wiech K, Tracey I (2009) The influence of negative emotions on pain: behavioral effects and neural mechanisms. Neuroimage 47: 987–994
63. Hampton AJD, Hadjistavropoulos T, Gagnon MM, Williams J, Clark D (2015) The effects of emotion regulation strategies on the pain experience: a structured laboratory investigation. Pain 156: 868–879
64. Meagher MW, Arnau RC, Rhudy JL (2001) Pain and emotion: effects of affective picture modulation. Psychosom Med 63:79–90