Integrating Anticipatory and Physiological Factors to Predict Injection Pain Intensity

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***Abstract*—Pain from subcutaneous injections remains a significant barrier to patient adherence, influenced by sensory, psychological, and physiological factors. This study integrates anticipatory factors, including fear of needles, sleep quality, and stress levels, with physiological data such as skin conductance (SC) and electrodermal activity (EDA), to predict pain intensity during injections. By analyzing temporal physiological patterns and mental states, we developed models to assess inter-subject variability in pain responses and identified injection parameters that minimize pain. The findings highlight the importance of multimodal approaches incorporating autonomic reactivity and mental states, paving the way for a comprehensive pain prediction framework. This research underscores the need for personalized strategies in optimizing medical procedures, ultimately improving patient outcomes.**

***Index Terms*—pain prediction, subcutaneous injection, anticipatory psychological factors, multimodal pain assessment, EDA, SC, ANS**

I. Introduction

Subcutaneous injections tend to be a painful experience, especially when done on a daily basis like for insulin, heparin, human growth hormone, and interferons. Pain in injection has been shown to be related to injection volume,[1] flow rate, injectate viscosity,[2] and needle gauge.[3] There are efforts by pharmaceutical companies attempting to minimize this pain experienced to improve patient adherence for these injections.[4] However, pain is inherently subjective with sensory, emotional, cognitive, and social components,[5] which make it difficult to holistically consider and interpret. Specifically, the Visual Analog Scale (VAS) is the most commonly used pain intensity scale for clinical trials[6]; however, these pain score methods are limited in consideration of the participant's alertness and cooperation in addition to excluding certain populations with impairments limiting proper communication surrounding the pain intensity.

Research integrating self-reported VAS scores with physiological signals has been leveraged to attempt to better understand inter-subject variability in pain scores.[7] The processing of nociceptive information is involved in activating the autonomic nervous system (ANS), primarily triggering the sympathetic nervous system (SNS) to induce physiological responses like increased heart rate[8] or sweating.[9] However, the correlation of these autonomic responses with self-reported pain is moderately low[10]; this suggests that inter-subject variability may be primarily due to individual differences in autonomic activity independent of stimulus activity. Thus, complementing pain scores with autonomic arousal data has allowed for the development of personalized pain recognition models[11] as well as efforts to cluster patients based on pain profiles.[12]

Insights reveal that individuals perceiving injections as threatening experience higher pain sensitivity,[13] disrupted sleep patterns exacerbate pain responses,[14] and heightened anticipatory stress before painful procedures amplifies pain perception.[15] However, the integration of additional mental factors like fear of needles, sleep quality, and stress level with more anticipatory physiological data in multimodal frameworks of physiological and pain score data has yet to be done. Thus, in this work we investigate the potential of anticipatory-related data for improved, personalized pain recognition in subjects receiving subcutaneous injections of different methodologies like dose volumes, flow rates, needle gauges and injectate viscosity. Initially, we will identify the optimal parameters for minimizing overall injection pain. Next, we will develop a person-independent model that predicts pain intensity. Then, we will compare this model with a personalized model that considers subject-specific differences in autonomic reactivity. These models will be further returned after training/validation on external datasets. More comprehensive physiological and general questionnaire data can underscore a patient's potential tolerance to pain to potentially improve the understanding of inter-subject differences. With these considerations, more personalized approaches can be taken to optimize ideal injection methods for patients.

II. Background

This paper dives into the existing work of subjective pain measurement using HCI and aims to propose a comprehensive framework of metrics incorporating both physiological and mental factors in deducing subjective pain level building on the theories. It lies in the overlap between machine learning and pain prediction, personalized pain level, and multimodal framework forming.

Subjective pain measurement has long been studied and finessed. So it's important to define what has been done

and what we can do building on it. Existing studies have been well-established in pain prediction using single modal or multimodal inputs and machine learning/ neural network. There have been established metrics for multimodal pain measurement, including physiological signals, self-reported and movement metrics. And existing literature has been focusing on personalized pain level, automation, and continuous measurement.

Impact of Injection Fear on Pain

Lim et al. (2020) has shown that individuals who perceive injections as threatening exhibit higher pain sensitivity. In addition, Young et al. (2012) demonstrated how individual differences in pain sensitivity are linked to genetic and neurobiological variability such as differences in the expression of pain-related neurotransmitters and receptors. This aligns with variable autonomic nervous system responses despite the same pain stimulus. This is complemented by different injection parameters also affecting pain response. Zijlstra et al. (2017) showed how injection speeds and lower viscosity fluids can significantly reduce perceived pain.

Sleep Effect on Pain

Sleep's effect on pain perception is highly cited. Staffe et al. (2020) demonstrated how individuals exhibit heightened nociceptive sensitivity and slower pain recovery. Kourbanova et al. (2022) found that poor sleep exacerbates pain perception through its impact on stress hormones and autonomic nervous system regulation. In addition, Yin et al. (2024) found how sleep deprivation led to hyperalgesic responses, where individuals exhibit increased sensitivity to painful stimuli; this is due to the disruption of normal sleep patterns, which impairs the body's ability to modulate pain effectively.

Stress Effect on Pain

Overall and anticipatory stress has also been shown to affect pain intensity. Xu et al. (2024) shows how heightened stress and anxiety before painful procedures activate regions (amygdala and prefrontal cortex) linked to emotional regulation and pain amplification. Additionally, Vachon-Presseau et al. (2013) demonstrates that acute stress alters pain perception through increased levels of cortisol and other stress-related neuropeptides, which sensitize pain pathways. Lastly, Michalska et al. (2020) shows how heightened anticipatory stress leads to increased pain sensitivity during injections, in which fear of needles strongly correlates with higher self-reported pain scores.

Multimodal framework

Across the literature, pain measurement has an established framework encompassing biological: nociceptive, receptive; physiological: skin conductance like EDA, cardiovascular, metabolic, brain activity, etc.; behavioral: facial and body movement.

For example, Lucey et al. (2011) introduced the UNBC-McMaster Shoulder Pain Expression Archive Database as a benchmark dataset for pain recognition, including videos, self-reports, and FACS-coded facial expressions for training and evaluating machine learning models.

Studies such as Lopez-Martinez & Picard (2017) and Lopez-Martinez et al. (2018) indicate that combining multiple modalities (e.g., facial expressions, physiological signals, brain signals) offers better pain recognition accuracy than single-modality approaches.

Several studies emphasize the need for multimodal approaches to pain assessment, combining facial expressions, physiological signals (e.g., EDA, PPG, ECG), and behavioral measures.

Rojas et al. (2023) introduced multimodal approaches integrating physiological signals like EDA and PPG enhance the detection of acute pain. EDA is identified as the most reliable signal for non-invasive pain assessment. Hammal et al. (2017) offer a review of multimodal pain assessment techniques, emphasizing facial expressions and contextual analysis. The study identifies gaps in real-world validation of automated systems. Sequentially, Hammal et al. (2023) offer a systematic review synthesizing neurophysiological sensing methods for acute pain assessment, highlighting the integration of EDA, ECG, and EEG for enhanced pain measurement.

EDA emerges as a key physiological signal for pain detection in multiple papers, such as Pouromran et al. (2021) and Kong et al. (2021). EDA, which reflects sympathetic nervous system activity, is shown to be highly sensitive to pain, providing a reliable and objective measure of pain intensity. This makes EDA particularly useful for real-time and ambulatory pain detection. Pouromran et al. (2021) evaluated the effectiveness of various physiological signals and machine learning models for pain intensity estimation. Electrodermal activity is found to be the most informative signal for wearable pain monitoring systems. Kong et al. (2021). proposed a real-time pain detection system combining wearable EDA sensors with smartphone applications, achieving 81.5% accuracy. The system is practical for ambulatory pain monitoring.

ML/NN, continuous pain measurement and intersection with clinical practice

Many papers, particularly Lopez-Martinez et al. (2017), Liu et al. (2017), and Lopez-Martinez & Picard (2019), employ neural networks (especially recurrent models) to model pain dynamics. Across the literature, Recurrent Neural Networks are utilized for temporal patterns and Multitask Neural Networks are used for regularization between different features.

RNNs, in particular, are suitable for capturing temporal patterns in pain data, e.g., facial data that are temporally correlated, enabling continuous pain intensity estimation rather than static or binary predictions. This dynamic modeling is essential for clinical applications where real-time pain monitoring is critical. Lopez-Martinez et al. (2017) used a bidirectional LSTM-RNN to estimate the Prkachin and Solomon Pain Intensity (PSPI) scores for each frame. The PSPI scores are fed into a Hidden Conditional Random Field (HCRF) model for sequence-level VAS estimation, augmented by the Individual Facial Expressiveness Score (I-FES) for personalization. Liu et al. (2017), alternatively, used DeepFaceLIFT, a two-stage hierarchical learning model for automatic and personalized VAS estimation, which invloves: 1, a weakly supervised NN

predicting frame-level VAS scores; and 2, a Gaussian Process (GP) regression model with an RBF-ARD kernel estimating sequence-level VAS scores using summary statistics of frame-level predictions. Multitask NN is used here to learn from OPI and VAS simultaneously and prevent overfitting to a single task, as opposed to integrating OPI and VAS into a single IFES score in the previous paper.

Lopez-Martinez & Picard (2017) proposed a multi-task NN with hard parameter sharing to simultaneously learn personalized pain responses for multiple subjects, where the shared layer captures general pain-related patterns across all subjects using skin conductance (SC) and electrocardiogram (ECG) features, and the subject-specific layers are task specific and tailored to each subject to account for inter-subject variability in pain responses. This laid the groundwork in applying Multitask NN in multimodal pain prediction, especially in accounting for demographic differences. MT-NN is often applied with clustering to reduce overfitting. Lopez-Martinez et al. (2017) grouped participants into clusters (profiles) based on similar physiological and behavioral pain responses by constructing a similarity graph using radial basis function (RBF) kernels on normalized feature vectors and applying spectral clustering. Then the MT-NN is used to predict pain levels (P1-P4) using the clusters as tasks, where each task is personalized for a specific profile.

Multiple Kernel Learning is often used with MT-NN for channel-specific modeling and feature combination. Lopez-Martinez et al. (2018) employed a Multi-task Multiple Kernel Learning (MT-MKL) algorithm to establish an objective and automated system for pain detection by utilizing functional near-infrared spectroscopy (fNIRS) brain signals. Task is assigned using spectral clustering, corresponding to a group of sessions sharing similar pain response patterns. Multiple kernels are used to model fNIRS data, allowing the model to: 1, learn task-specific patterns; 2, identify the importance of individual fNIRS channels. This approach models fNIRS data channel-wise, combining information across channels for accurate pain classification.

Wearables for pain detection

Several studies, including Kong et al. (2021) and Ji et al. (2023), explore real-time pain detection systems that use wearable devices and smartphones. These systems offer practical solutions for continuous pain monitoring outside of clinical settings, providing timely feedback to patients and caregivers.

Personalized Pain Measurement

Several studies (e.g., Lopez-Martinez et al. (2017), Liu et al. (2017), and Lopez-Martinez & Picard (2017)) emphasize the importance of personalization in pain detection. Pain is highly subjective, with significant variability in how individuals express and experience pain. Personalizing models based on individual characteristics, such as facial expressiveness or physiological response profiles, greatly improves the accuracy of pain intensity estimation.

Research such as Adams et al. (2017) and Felipe et al. (2021) explores how personalized informatics systems can support chronic pain self-management. These studies highlight the need for tailored interfaces that allow individuals to accurately log their pain experiences, facilitating better self-management and communication with healthcare providers.

Automation

Advances in machine learning and artificial intelligence have driven the development of automated pain recognition systems. Papers like Prkachin & Hammal (2021) review the progress in this field, noting that while current methods show promise, challenges such as the need for better datasets and more robust models remain.

The introduction of Embodied Conversational Agents (ECAs) by Murali et al. (2023) highlights how interactive, narrative-based systems can improve pain assessment by simulating face-to-face conversations.

III. Dataset, Methods and Experiments

A. Dataset

This randomized, crossover, single-center study was done in 21 healthy participants. Overall, the participants were 50% female, between 18-60 years of age, and with a body mass index (BMI) between 18 and 32 kg/m2 to exclude obesity conditions. Exclusion criteria included conditions that could interfere with the delivery of the injectate or interpretation of assessments or significantly impair pain perception; susceptibility to bleeding; clinically significant skin allergies or active dermatological disorders; sensitivity to injectate ingredients; and pain medications (non-steroidal anti-inflammatory drugs within 5 days before study day, steroids within 7 days before study day, and antihistamines or analgesics within 48h prior to injection).

The interventions included injectate temperature (cold vs. room temperature), volume, viscosity, and flow rate. Arm 1 (6 participants) were given saline injections and arm 2 (15 participants) were given a viscous placebo buffer that contained sodium carboxymethyl cellulose (Na-CMC). Note, arm 1 did not have varied viscosities while arm 2 did not have varied injectate temperature. Participants received five 1-2 mL subcutaneous injections over 10-60 seconds in different quadrants of the abdomen. Each injection was separated by around 30 minutes to eliminate the carry-over effect of the previous injection. Each participant completed a total of three of these sessions on non-consecutive days led by a nurse using a subcutaneous injection set, butterfly/cannula set, and infusion pump. The participants reported their VAS scores immediately after the injection, 5 after the injection, and 25 minutes after the injection. Any adverse administration site reactions and swelling was noted. A pre-study mock session consisting of a single injection was done to familiarize the participants with the protocol.

Data collection from the FlexComp Infiniti System collected heart rate variability (HRV) from 1-lead electrocardiogram (ECG) and electrodermal activity (EDA) from bilateral finger skin conductance (SC) during the injection procedures. For the anticipatory physiological data, Empatica E4's were placed bilaterally on the ventral part of both wrists from the night before the experiment session. The wearable was also kept on

during the entire injection session to collect EDA from SC, skin temperature, HRV from photoplethysmography (PPG), and acceleration. Additional anticipatory questionnaires were completed indicating the fear of needles, sleep quality, and stress level.

B. Three-Dimensional Model

Dimension 1: Participants: Each participant represents a unique pain tolerance profile.

- Includes participant-level characteristics that remain constant over sessions, including:
  - Baseline Mental Factors:
    - Fear of needles (e.g., score from a pre-questionnaire).
    - Demographic factors (age, gender, etc.).
  - Baseline Physiological Signals:
    - Resting heart rate, baseline ECG variability, etc.

Dimension 2: Sessions: Reflects session-specific variations due to contextual factors.

- Session-Specific Mental Factors:
  - Acute stress (measured before the session).
  - Sleep quality prior to the session.
- Pain Metrics for the Session:
  - Initial pain intensity.
  - Peak intensity.
  - Average intensity.
  - Pain reduction.
  - Rate of reduction.
  - VAS scores at the three time points (immediate, 5 min, 25 min).
- Captures variability in participants' responses to injections across sessions.

Dimension 3: Physiological Signals:

- Seven physiological signals (e.g., ECG, PPG, skin conductance, etc.).
- Temporal signal dynamics can be included to model their relationship with subjective pain over time:
  - Immediate response.
  - 5-minute delayed response.
  - Sustained (25 minutes).

The Model

Central hypothesis: Subjective pain (VAS scores) can be predicted by a combination of mental factors (both baseline and session-specific) and physiological signals, capturing variability across participants and sessions.

Key elements of the model:

- Participant-Level Features (1st Dimension):
  - Baseline mental and physiological characteristics.
  - Represent individual differences in pain tolerance.
- Session-Level Features (2nd Dimension):
  - Contextual variations that modify pain response for the same participant across sessions.
- Signal-Level Features (3rd Dimension):
  - Continuous physiological signals recorded during and after injection, serving as objective predictors of subjective pain.

C. Formula-Based Pain Prediction

$$P_t = w_m M + w_p P + \epsilon_t$$

- Where:
  - P_t: Predicted pain score at time t (i.e., 0, 5, 25 minutes).
  - M: Weighted sum of mental factors.
  - P: Weighted sum of physiological factors.
  - w_m: Weight for mental factors.
  - w_p: Weight for physiological factors.
  - ϵ_t: Time-dependent adjustment term (captures how pain evolves over time).

Breaking down M and P:

$$M = \alpha_1(\text{Stress}) + \alpha_2(\text{Sleep Quality}) + \alpha_3(\text{Fear of Needles})$$

$$P = \beta_1(\text{ECG}) + \beta_2(\text{PPG}) + \beta_3(\text{Skin Conductance})$$

Time-dependent adjustment:

$$\epsilon_t = \gamma_1 e^{-\lambda t} + \gamma_2 t$$

- Where:
  - $e^{-\lambda t}$: Exponential decay factor to capture pain reduction over time.
  - γ_1, γ_2: Coefficients for time effects, calibrated based on observed VAS patterns.

D. Combining the 3-Dimensional Model with the Prediction Formula

General Formula:

$$w_m[M_{ij} + M_i] + w_p P_{ijt} + \gamma_1 e^{-\lambda t} + \gamma_2 t$$

- Where:
  - P_{ijt}: Predicted pain score for participant i, session j, and time t (e.g., 0, 5, or 25 minutes).
  - M_{ij}: Session-specific mental factors (e.g., acute stress, sleep quality) for participant i in session j.
  - M_i: Baseline participant-level mental factors (e.g., fear of needles, trait anxiety) for participant i.
  - P_{ijt}: Physiological signals for participant i, session j, at time t.

Integration:

- Base level - Participant-level features:
  - Participant-specific baseline features (e.g., fear of needles, baseline HR) as constants.
- Mid level - Session-level features:
  - Including session-specific factors such as stress level and sleep quality for each session.
- Top level - Physiological signal features:

  - PCA-reduced key features by physiological data recorded during each session.

Weights:

- Higher for session-level factors to capture variability between sessions.
- Lower weights for participant-level mental factors.

E. Random Effects Model

Given the small sample size of four participants and the multidimensionality of the data (i.e., multiple sessions, time points, and physiological signals), a random effects model is well-suited to address the hierarchical structure of the data. This approach allows for:

- Participant-level variability: Participants exhibit individual differences in pain tolerance, which are not fully explained by the measured physiological signals or mental factors.
- Session-level variability: Pain responses can vary across sessions for the same participant due to differences in mental states (e.g., acute stress or sleep quality).
- Time-point variability: Pain intensity evolves over time (immediate, 5 min, 25 min), which requires modeling these temporal dynamics.

The model incorporates fixed effects to estimate the contribution of key predictors (e.g., electrodermal activity [EDA] and electrocardiogram [ECG]) while accounting for random effects at the participant, session, and time levels. This hierarchical structure ensures that the model captures both individual and group-level patterns in the data.

Model Description

The VAS pain score (VAS_{ijt}) is modeled as:

$$VAS_{ijt} = \beta_0 + \beta_1 \cdot EDA_{ijt} + \beta_2 \cdot ECG_{ijt} + u_i + v_{ij} + w_{ijt} + \epsilon_{ijt}$$

Explanation of Terms:

- Dependent Variable (VAS_{ijt}):
  - The Visual Analog Scale (VAS) score for participant i, session j, and time point t.
- Fixed Effects:
  - β_0: Intercept, representing the baseline VAS score when $EDA = 0$ and $ECG = 0$.
  - β_1: Coefficient for EDA, representing the contribution of electrodermal activity to the pain score.
  - β_2: Coefficient for ECG, representing the contribution of electrocardiogram data to the pain score.
- Random Effects:
  - $u_i \sim N(0, \sigma_u^2)$: Participant-level random effect, capturing variability in pain tolerance between participants.
  - $v_{ij} \sim N(0, \sigma_v^2)$: Session-level random effect, accounting for differences across sessions for the same participant.
  - $w_{ijt} \sim N(0, \sigma_w^2)$: Time-point random effect, modeling variability across time points within sessions.
  - $\epsilon_{ijt} \sim N(0, \sigma^2)$: Residual error, representing unexplained variability in pain scores.

Model Implementation

The random effects model will be implemented using Python's `statsmodels` package. The dataset included:

- 4 Participants: Each with 3 sessions and 3 time points (immediate, 5 min, 25 min).
- Physiological Signals: EDA and ECG recorded for each time point.
- VAS Scores: Collected immediately after, 5 minutes after, and 25 minutes after injection.

The model is specified as:

$$VAS_{ijt} \sim \beta_0 + \beta_1 \cdot EDA_{ijt} + \beta_2 \cdot ECG_{ijt} + u_i + v_{ij} + w_{ijt} + \epsilon_{ijt}$$

where:

- EDA_{ijt} and ECG_{ijt} are included as predictors.
- Random effects are nested at the participant, session, and time-point levels.

Model Advantages

The random effects model was chosen for its ability to:

- Handle small sample sizes by leveraging both fixed and random effects, the model maximizes the utility of the available data.
- Incorporate hierarchical structure by accounting for nested data (participants $\rightarrow$ sessions $\rightarrow$ time points) without violating statistical assumptions.
- Estimate individual contributions by providing insights into how individual participants and sessions contribute to the overall variability in pain responses.

IV. Results

Figure 1 highlights the influence of needle stress on electrodermal activity (EDA) and pain reactivity by comparing two subjects. Subject 7, who reported closing their eyes during needle administration, shows more pronounced peaks in both SC_C and SC_D, indicative of stronger sympathetic responses. This suggests heightened autonomic reactivity, potentially due to increased anticipatory stress or fear associated with the injection process. Conversely, Subject 12, who did not report similar needle stress, exhibits less pronounced responses, indicating lower sympathetic activation.

Figure 2 illustrates the effect of sleep on EDA and pain reactivity by comparing responses across different instances of Subject 3. The larger and more prolonged responses in Instance 3 (Graph 2) suggest heightened sensitivity or stress due to self-reported poor sleep before this session. The SC_C and SC_D responses show increased peak amplitudes and delayed recovery, reflecting hyperalgesic responses.

Figure 3 examines the effect of overall stress on EDA and pain reactivity for Subject 7 across different instances. In Instance 2, Subject 7 reported "almost never" finding it hard to cope, and this corresponds to lower peaks in SC_C and SC_D. In contrast, during Instance 3, where the subject reported increased stress ("fairly often"), the EDA signals show higher peak amplitudes and prolonged responses, indicating elevated autonomic reactivity.

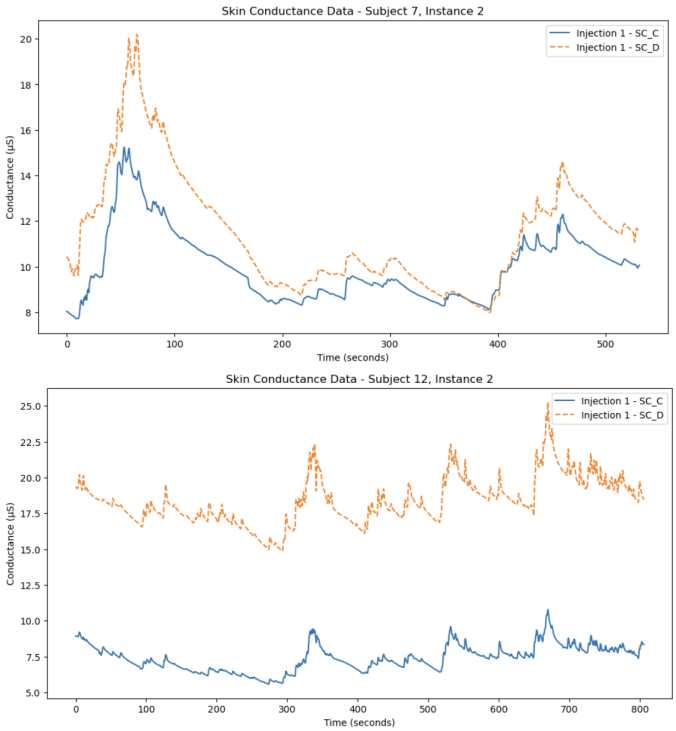

Fig. 1. Effect of Needle Stress on EDA/Pain Reactivity

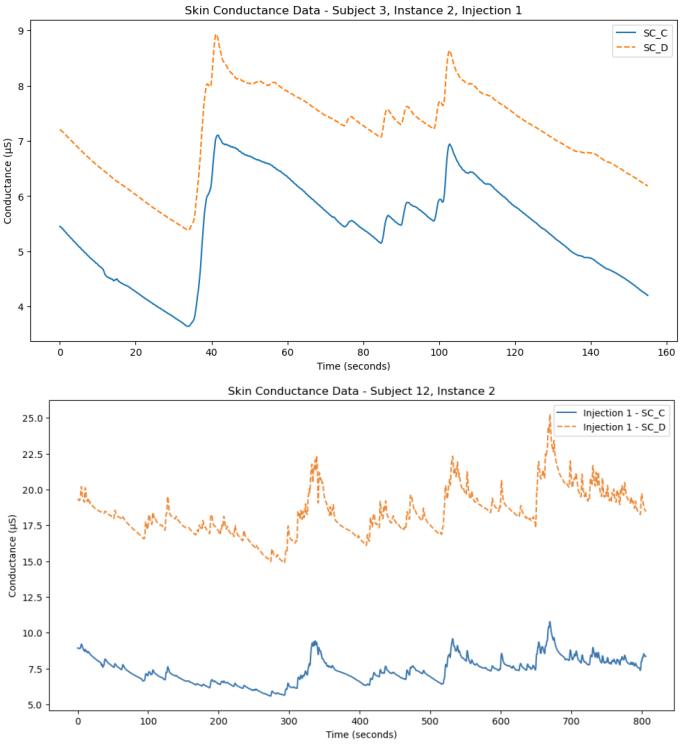

Fig. 2. Effect of Stress on EDA/Pain Reactivity

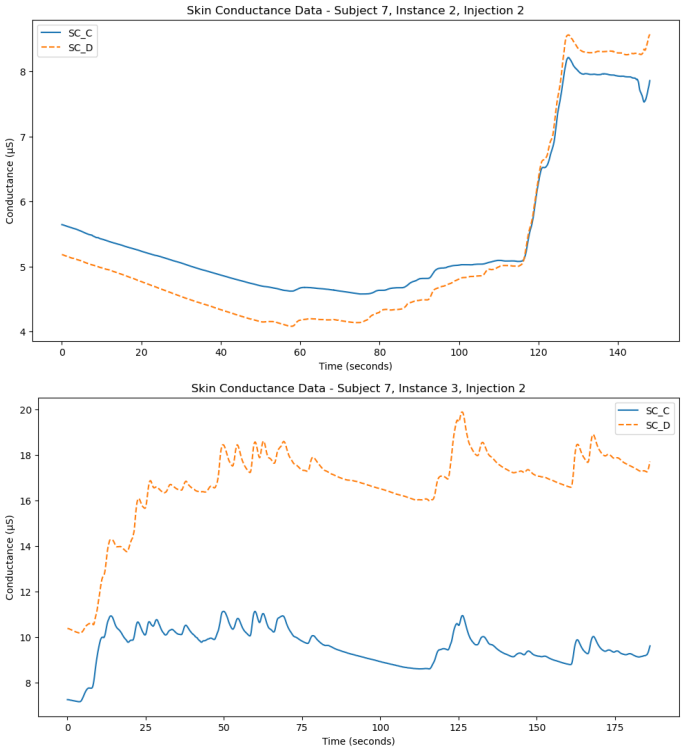

Fig. 3. Effect of Sleep on EDA/Pain Reactivity

V. Discussion

The observed effects on pain sensitivity due to fear of needles, sleep deprivation, and stress align closely with findings in the literature, further validating the importance of integrating anticipatory and psychological factors with physiological metrics for a more comprehensive understanding of pain perception. The results from this study highlight the critical role of autonomic reactivity, as demonstrated through skin conductance (SC) responses, in mediating the relationship between psychological states and pain intensity. Specifically, our findings confirm that fear of needles significantly heightens pain sensitivity, sleep deprivation exacerbates pain perception through impaired autonomic regulation, and anticipatory stress amplifies pain intensity via increased sympathetic activation. These insights underscore the interplay between psychological and physiological domains in shaping pain experiences.

To advance the goal of developing a predictive model for pain intensity, future research must integrate additional physiological metrics, including heart rate (HR), blood volume pulse (BVP), and pain scores, alongside SC/EDA data. This 3-D approach will enable the construction of a more holistic and person-independent model, allowing us to capture the complexity of pain responses and the dynamic interactions between mental and physiological states.

Our findings also highlight the potential of leveraging pre-injection physiological data, such as SC and HR patterns recorded the night before, to anticipate pain reactivity during injections. Sleep quality appears to influence baseline physio-

logical states and modulate subsequent pain responses, making it a valuable predictor in pain modeling. Incorporating such temporal data into predictive frameworks could enhance the precision of pain predictions and identify individuals at higher risk for heightened pain sensitivity.

Furthermore, exploring how prediction methods trained on injection-related pain stimuli translate to other pain modalities (e.g., thermal or mechanical pain) could offer new insights into the generalizability of pain models. Databases like BioVid provide opportunity for model fine-tuning and cross-comparison, enabling the validation of pain prediction methods across diverse stimuli and contexts. Such work could reveal common markers of pain perception while identifying stimulus-specific variations.

Although this study primarily focused on SC responses, future work should delve deeper into understanding individual differences in autonomic reactivity by accounting for baseline physiological signals and session-specific mental states. This approach would enable us to identify the most variable and influential factors driving inter-subject variability in pain responses. Additionally, exploring how injection parameters, such as volume, viscosity, flow rate, and needle gauge, interact with psychological factors to modulate pain intensity will provide actionable insights into optimizing medical procedures.

In conclusion, our findings lay the groundwork for developing a comprehensive, multi-modal framework for pain prediction and management. By integrating diverse physiological and psychological metrics, future research can achieve a more holistic understanding of pain, ultimately enabling the identification of optimal conditions to minimize pain intensity and improve patient outcomes across a variety of contexts.

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