Machine-based Multimodal Pain Assessment Tool for Infants: A Review

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Abstract

The current practice of assessing infants' pain depends on using subjective tools that fail to meet rigorous psychometric standards and requires continuous monitoring by health professionals. Therefore, pain may be misinterpreted or totally missed leading to misdiagnosis and over/under treatment. To address these shortcomings, the current practice can be augmented with a machine-based assessment tool that continuously monitors various pain cues and provides a consistent and minimally biased evaluation of pain. Several machine-based approaches have been proposed to assess infants' pain based on analysis of whether behavioral or physiological pain indicators (i.e., single modality). The aim of this review paper is to provide the reader with the current machine-based approaches in assessing infants' pain. It also proposes the development of a multimodal machine-based tool to assess infants’ pain.

1. Introduction

Pain is defined as the unpleasant sensory and emotional experience happened due to an actual or a potential tissue damage or injury [1]. Caregivers rely on pain to understand patients’ medical conditions and develop suitable treatments. Therefore, to
guarantee the best pain management, it is crucial to develop an optimal pain assessment tool. Several by-proxy (i.e., traditional) pain assessment tools have been developed to evaluate pain and estimate its intensity. The most popular assessment tool is the patient self-evaluation in which the patient provides a verbal description of his/her pain intensity. Another assessment tool to nonverbally communicate pain is the Visual Analog Scale “VAS”, which has faces or numbers for different levels of pain [2, 3].

Although the verbal and nonverbal self-evaluation of pain is the gold standard for assessing pain, they are not applicable for individuals with communicative/neurologic impairments (e.g., dementia) and infants. To evaluate pain in this population, other tools that observe specific signs of pain should be utilized. These tools scale the pain based on observation of various behavioral, physiological, and contextual indicators that are associated with pain [4-6]. Figure 1 summarizes as a tree diagram the pain indicators that are used in NICU to evaluate pain.

![Pain Indicators Tree Diagram](image)

Fig. 1. Tree diagram of the pain indicators

Assessing infants’ pain using the traditional indicators-based tools is difficult and has limitations due to several reasons:
1. Infants require continuous monitoring because they might experience pain when they are left non-attendant; this is especially true for infants with chronic pain. Continuous monitoring of infants' pain by caregivers is not applicable (i.e., it is hard and costly).

2. Pain is a subjective experience that depends on several idiosyncratic factors such as the observer's cognitive bias, gender, past pain experience, knowledge, culture, and background [7-10]. Rebecca and Kenneth [11] conducted a study to measure the differences in judgments of pain for different groups of observers. Particularly, Profile analysis was performed to measure the variations in the pain assessments of 123 caregivers (41 parents, 41 inpatient nurses, 41 pediatricians); Profile analysis is an alternative to ANOVA test but requires fewer assumptions. The study's results show that there are significant differences in judgments of infant pain among the three groups of caregivers. Parents provided the highest scores of pain (mean 6.70 at p<0.01) while the pediatricians provided the lowest scores of pain (mean 5.94 at p<0.01). Nurses provided pain scores (mean 6.50 at p<0.01) that are intermediate to and didn't differ significantly from either group. This finding highlights the role of the observer's bias; the parents' assessments were more sensitive than the nurses or pediatricians. Another study [12] demonstrated the relationship between the observer's experience and their judgment of infants' pain. According to the study, the greater the clinical experience of the observer, the more likely she/he is to underestimate the infant pain.

3. Some pain indicators (e.g., crying) can be associated with other conditions such as discomfort, hunger or stress [13].
Due to these reasons, caregivers may miss or misinterpret the infant’s pain experience leading to misdiagnosis and over/under treatment. Studies have shown that poor treatment of infant’s pain may cause permanent neuroanatomical changes and behavioral, developmental and learning disabilities [14, 15]. To alleviate these shortcomings, the current practice of assessing infants’ pain can be augmented with a machine-based assessment tool that monitors various pain indicators and provides a consistent, continuous, and minimally biased evaluation of pain. This tool can be used by caregivers in the Neonatal Intensive Care Unit (NICU). It can also be used in homes as pain-monitoring tool or in the developing countries where caregivers and resources are scarce.

In the past several years, there has been an increasing interest in the use of a machine for understanding human behavioral responses correspond to pain/distress based on analysis of facial expressions [16-33], body or head movements [34-37], and sound signals [38-50]. Several other studies have shown that machine-based systems can be used to detect and analyze physiological changes associated with pain such as pupil dilation [51-53], changes in skin color [53-56], an increase in heart rate [57-60], and changes in the cerebral hemodynamic of brain’s regions [61-64].

Despite the fact that several approaches are developed to assess pain on the basis of whether behavioral or physiological pain indicators, there is no literary evidence that provides a comprehensive review for these approaches. In this paper, we provide a review for the existing machine-based pain assessment approaches and discuss their limitations. However, rather than providing a detailed investigation of pain assessment approaches in general (i.e., pain assessment in adults, kids and infants), we narrowed our
domain and focused on infants’ pain assessment. To the best of our knowledge, this is the first paper that provides a literature review of existing methods for analyzing infants’ pain using signal processing and machine learning approaches. It also proposes the development of a machine-based multimodal pain assessment tool (MPAT) that dynamically measure pain in infants based on analysis of various behavioral and physiological pain indicators. Figure 2. depicts a general overview for the proposed multimodal pain assessment tool (MPAT).

The rest of the paper is structured as follows: Section 2 explores existing behavioral and physiological pain assessment approaches and discusses their limitations. Section 3 summarizes the current challenges of pain assessment and proposes future directions. Introduction to the machine-based multimodal pain assessment tool (MPAT) is presented in Section 4 followed by a discussion of the preliminary approach and implementation in Section 5. Finally, Section 5 concludes the paper.

![General Overview of MPAT](image)

Fig. 2. General Overview of MPAT. The dashed purple box indicates another option to generate the final pain score by combining all the inputs in one learning stage.
2. Literature Review

Machine-based pain assessment is a growing area of research due to the increasing demands for its applications, which include consistently and continuously evaluating pain in clinical practice and homes. Numerous machine-based approaches have been introduced to evaluate the infant pain and scale its intensity based on analysis of weather behavioral or physiological pain indicators. We grouped these approaches into two main categories: behavioral-based and physiological-based approaches. These approaches are further grouped into different subgroups, as it will be presented in the subsequences sections. A summary for existing machine-based approaches to assess infants’ pain is presented in Figure 3.

![Fig. 3. Summary for existing machine-based infant pain assessment approaches](image)

2.1. Behavioral-based Pain Assessment Approaches

Behavioral-based approaches observe and analyze behavioral signs of pain. These signs, which represent the patient’s reaction to a pain stimulus, include facial expressions, body movements (i.e., head, arms, and legs movements), and sounds (e.g., whimper and crying). Various methods have been proposed to evaluate pain in infants
based on analysis of behavioral pain indicator. Existing behavioral-based approaches to evaluate infants’ pain can be grouped into: approaches of facial expressions, inarticulate sounds, and body movements. We present each group and discuss its limitations next.

2.1.1. Facial Expressions of Pain

Infants often communicate pain by moving their facial muscles. The facial expression of pain is one of the most important behavioral indicators in people with verbal communication deficits and infants. Pain expression is defined as the distortions in facial muscles associated with a pain stimulus. It provides a reliable and accurate information about the infant’s pain condition [65, 66]. Facial distortions associated with pain in infants include prominent forehead, narrowed eyes, deepening of the nose, lip furrow, and an angular opening of the mouth [5, 66].

The automatic recognition of pain expression in infants involves three main stages: (1) Face detection and registration; (2) Features representation or extraction; and (3) Pain recognition. Face detection is a wide area of research that is little relevance to this study and, therefore, will not be discussed further. In feature representation stage, different approaches can be utilized to extract useful and representative features from a face image. These approaches can be divided into four categories:

- Image-based feature representation.
- Velocity-based feature representation.
- Model-based feature representation.
- Facial Action Coding System (FACS).

We present each of these categories next and discuss its limitations.
Image-based Feature Representation

Methods under this category utilize static images to extract global (aka. holistic) features. For example, image's pixel intensities can be extracted and used to form a feature vector. To reduce the dimensionality of this vector, a dimension reduction algorithm (e.g., PCA) could be applied.

The first work that investigates infants’ pain assessment based on analysis of pain expression is presented in [67]. This work introduced COPE dataset, which consists of 200 static images photographed under four pain stimuli: puncture of a heel lance, transport from one crib to another, air stimulus to the nose, and friction on the external lateral surface of the heel. These images were rotated, cropped, and reduced to 100X120 pixels. In the feature representation stage, the cropped images are converted to gray scale and centered within an ellipse. The ellipse's rows are then concatenated into a feature vector of 12,000 dimensions and PCA is applied to reduce this vector dimensionality. For classification, support vector machine (SVM), linear discriminant analysis (LDA), and principal component analysis (PCA) were used to classify the images as: pain/no-pain, pain/rest, pain/cry, pain/air-puff, and pain/friction. SVM yielded the highest accuracy and outperformed LDA and PCA in classifying pain versus no-pain (88.00%), pain versus rest (94.62%), pain versus cry (80.00%), pain versus air-puff (83.33%), and pain versus friction (93.00%). This work was extended in [29, 68] to include the neural network simultaneous optimization algorithm (NNSOA) along with LDA, PCA, and SVM in classifying infants’ facial expression as pain (i.e., heel lancing) or no-pain (i.e., other stressors). Moreover, leave-one-subject-out evaluation protocol, which is known to be more accurate and realistic in clinical setting, is applied to evaluate the classifiers'
performance. NNSOA achieves classification rate of 90.20%, which is the highest rate in comparison to SVM, PCA, and LDA; linear SVM achieves average classification rate of 82.35% and PCA and LDA achieve average classification rate of 80.39% and 76.96%, respectively.

Similarly, Golahmi [31] expanded the classification techniques in [29, 68] and developed a system to determine the intensity of the classified pain expression using a relevance vector machine (RVM) classification technique [69] and COPE dataset. RVM is a classifier that provides the posterior probabilities for the class memberships; it’s a Bayesian version of SVM. The classification accuracy of RVM with linear kernel was around 91%. This result proves the efficiency of using RVM and other probabilistic classifiers in assessing pain expression and estimating its intensity.

Another powerful image-based approach with less sensitivity to noise and illumination is the local binary pattern (LBP). LBP is a local texture operator to describe the image texture by comparing the gray value of a pixel x with the gray values of its neighbors within a predefined window of radius R. Nanni et al. [30, 70] proposed an algorithm to classify facial expression of pain using different local descriptors. The algorithm started by normalizing the static images of COPE dataset and divided them into NxN overlapping cells. Next, several local texture descriptors are used to extract the local features of the overlapping cells. Examples of these descriptors include local binary pattern (LBP), Local Ternary Patterns (LTP), and an Elongated Ternary Pattern (ELTP), which is a novel descriptor introduced in this work. Feature selection algorithm is performed then to choose the best subset of the overlapping cells and use them to form the feature vectors. For classification, ensemble of SVM classifiers (i.e., SVM classifier
for each of the selected cells) is applied. These classifiers are combined using the sum rule. The best classification accuracy was obtained by ELTP texture descriptor. Additional image-based approaches to assess pain expression can be found in [22, 25, 71].

The main limitation of the approaches discussed above is the use of 2D static images dataset (COPE) to classify infant’s pain expressions. Static images ignore the expression’s dynamic and temporal information and affect on the ability of understanding the pain expression and its evaluation over time. Hence, in order to develop an efficient pain assessment of infant’s pain expression, it’s important to consider the dynamic nature of the pain expression. Another limitation is that the presented approaches except [70] utilized holistic (i.e., global) features to form the feature vectors. Holistic-based approaches are known to perform poorly in the presence of occlusions and hence will fail in case of self-occlusion by the infant's hands or occlusion by external objects such as the medical tapes and the pacifier. Finally, COPE dataset has images of infants during acute pain, crying, and discomfort states. Studies have shown that untreated or poorly assessed chronic pain might cause neurodevelopmental disorders in infants [8-9]. To build an efficient pain assessment system, it is important to assess both acute and chronic pain.

**Velocity-based Feature Representation**

Approaches under this category estimate the motion vectors that describe the transformation of an object or a pixel from one video frame to another. Optical flow is a commonly used velocity-based method. It is defined as the estimated pixels' velocity flow over consecutive video frames [72]. It depends on the brightness conservation principle and provides a dense pixel-to-pixel correspondence.
The first work that utilized optical flow to classify infant's pain expression in video sequences is presented in [33, 73, 74]. The proposed approach depends on the optical strain, derived from the optical flow vectors, to detect a facial expression by measuring the facial tissues deformations (i.e., changes) caused by that expression. This approach is robust in that it can detect expressions including the pain expression without requiring training for a specific expression. It consists mainly of three stages: (1) detection of the infant’s face in a video sequence followed by preprocessing operations; (2) expression segmentation based on facial strain analysis; and (3) pain expression classification. In the face detection stage, the infant’s face is detected manually and then sixty-six facial points are extracted. These points are used to crop the exact face and divide it into four regions. This can handle the partial occlusion problem caused by the infant’s hands or a pacifier. Subsequently, the strain algorithm is employed to segment the pain expression by computing, in each frame, the strain values for the face's regions and sums these values together to generate the overall strain magnitude. Then, for detecting the expressions, a peak detector algorithm is applied to find the maximum strain magnitudes values and average them to generate a single strain value for each expression. Finally, these strain values are used to form the feature vectors and train k Nearest-Neighbor (KNN) and support vector machine (SVM) classifiers. The accuracy of classifying the segmented expressions as pain expression or no pain expression using KNN and SVM is 96% and 94%, respectively.

A noticeable limitation of this work is the manual detection for the infant’s face. As has been discussed in [33], existing face detection algorithms fail to detect the infant’s face because these algorithms are trained and built for adult faces. In addition, the utilized
dataset, which has video sequences of ten infants, were recorded under challenging conditions (e.g., low-light condition) and has strong out-of-plane head movements especially during the pain procedure. Other velocity-based approaches to detect and recognize pain expression are presented in [21, 24]. These approaches were built to analyze pain expression of adult patients, however.

**Model-based Feature Representation**

Model-based approaches work by finding the model’s parameters of a specific object that maximize the match between that model and the input object. A well-known model-based approach that uses the shape and appearance parameters to describe the model is called Active appearance Model (AAM) [75]. To fit AMM to an image of facial expression, the error between the representative model and the input image should be minimized (i.e., the non-linear optimization problem). The idea of using AMM to analyze facial expression of pain was first introduced in [17]. The proposed approach derives a set of features from AMM and uses them to detect pain expression in videos of adult patients with rotator cuff injury (i.e., shoulder pain). An extension of the work in [17] is presented in [26]. As in [17], the proposed approach employed AMM to extract the features for classification. However, it maintains the temporal information of the pain expression instead of compress it like in [17]. The results show that this modification yields a significant improvement in the performance.

In case of infants, Fotiadou et al. [76] discussed the use of AAM in the application of detecting infant pain expression in videos. AAM is applied, in each frame, to extract both the global motion and the inner features of the infant’s face. The system, which is evaluated in 15 videos for 8 infants, achieves 0.98 AUC in detecting the pain
expression using SVM classifier. The main limitation of the model-based approaches is that these approaches are not robust against occlusions. For example, the fitting algorithm of AAM tends to get stuck in local minima when important features are missing.

**FACS-based Feature Representation**

Facial Action Coding System (FACS) [77] is a comprehensive system for describing the movements of facial muscles for all observable facial expressions using a set of numeric codes. This set of codes, known as action unit (AUs), is the FACS's basic unit of measurement. Neonatal Facial Coding System (NFCS) is an extension of FACS designed specifically to observe infants’ facial muscles correspond to pain. Like FACS, NFCS uses a set of action units to measure the movements of seven facial movements: brow bulge, eye squeeze, nasal root wrinkles, prominent forehead, opening of the mouth, lips pursed, taut tongue, and chin quiver.

The vast majority of the methods in the field of automatic facial expressions recognition use FACS to detect and describe facial expressions. However, few of the existing methods handle the pain expression in infants. Sikka. et al. [18, 32] presented a FACS-based system to detect and describe children's facial expression of pain. The proposed algorithm was built from videos of 50 children, age ranges from 5 to 18 years old, recorded under both ongoing and transient pain conditions. It includes three main stages: (1) face detection; (2) extract pain-related features (i.e., AUs); (3) and classification of pain expression. CERT [78], stands for Computer Expression Recognition Toolbox, is used to detect the face and extract pain-related facial action units; a total of 14 AUs (e.g., AU4 brow lower, AU7 lid tighten, and AU27 mouth open) were selected to represent the pain expression. Next, different statistics such as the mean,
75th percentile, and 25th percentile for each of these AUs were computed and used to form the feature vectors. The binary classification of the pain expression achieves good-to-excellent accuracy with 0.84-0.94 AUC for both ongoing and transient pain. For estimating the pain level, CVML shows moderate-to-strong correlations (r = 0.65–0.86 within; r = 0.47–0.61 across subjects) for both pain conditions. The primary limitation of this work is the restricted light and motion condition. The algorithm requires moderate lighting and motion, which might be difficult to accomplish in clinical setting especially in case of infants in NICU. Infants tend to make strong and unpredictable motions when they are in pain.

As for adults, Bartlett et al. [27] investigated the use of FACS in discriminating real from fake facial expression of pain in video sequences. Twenty-six participants were videotaped in three experimental conditions: baseline, posed pain, and real pain. Immersing an arm in cold water induces the real pain condition. These videos were analyzed using CERT to detect the face and code each frame as a set of facial action units. A total of 20 action units (e.g., AU10 lip raise, AU15 lip corner depress, and AU7 lid tighten) were extracted from each video frame and used to represent two sets of descriptors: event descriptors and interval descriptors. The first set is used to describe the dynamics of facial movement events (i.e., AUs’ dynamics) while the other is used to describe the interval between events. These descriptors are used then to train SVM to discriminate real from faked pain. The accuracy of discriminating the real pain from the fake pain as measured by area under the ROC was 91%. It has been demonstrated that this accuracy is significantly better than the accuracy of the human observers.

Although FACS is a reliable and comprehensive system to analyze facial
expressions, it has a primary limitation. FACS-based approaches require human experts to manually label the action units in each video's frame. The cost of frame-by-frame manual labeling is exceedingly high. It has been found that a human expert needs around three hours to code one minute of a video sequence [16]. Therefore, it is important to automate the process of detecting action units (AUs) is each video’s frame. Automatic detection of facial action units is a new and challenging area of research that is little relevant to this literature review and thus wont be discussed further. The interested reader is referred to references [79-84] for more information about automatic detection of facial action units.

In summary, this section presented several pain expression recognition approaches and discussed their limitations. The current state of the art in detecting and analyzing the facial expression of pain can be grouped into four categories: image-based, velocity-based, model-based, and FACS-based. Next, we present the existing machine-based approaches that analyze infants’ crying sounds.

2.1.2. Infants’ Crying Sounds

Infants’ cry is a common sign of discomfort, anger, and pain. It conveys a lot of information that help caregivers to assess the infants' emotional state and react properly. Nevertheless, this traditional assessment of infants' crying is biased and depends totally on the observer's subjective judgment [11]. Therefore, developing a quantitative and minimally biased crying assessment system is suggested. Infant’s crying analysis involves two main stages: (1) signal processing stage, which includes preprocessing the signal and extracting representative features; and (2) the classification stage. Existing approaches of signal processing stage can be categorized into: (1) frequency-domain; (2)
cepstral-domain; and (3) time-domain approaches. We examine each of these categories and discuss its limitations in the next subsections.

**Frequency-domain Feature Representation**

Frequency-domain is a domain to analyze a signal with respect to frequency, rather than time. The frequency-domain shows how much of the signal lies within a specific range of frequencies. Fundamental frequency (F0) is a well-known frequency-domain feature that has been used to analyze infants’ crying sounds. It is defined as the lowest frequency of a periodic signal. It is worth to mention that pitch, which represents the brain’s perceptual estimation of the fundamental frequency, is used often to refer to the fundamental frequency.

Infants’ cries can be classified based on the fundamental frequency as either [85]: 1) phonated cries that have a smooth and harmonic structure with a fundamental frequency’s range of 400 to 500 Hz; 2) dysphonated cries that have less harmonic structure comparing to phonated cries; 3) hyperphonated cries with abrupt and extremely high pitch (up to 2000Hz) followed by a long period of no breathing. As stated in [85], hyperphonated cries appear to be associated with a painful stimulus.

Several approaches have been proposed to estimate the phonated and hyperphonated fundamental frequency of infants’ crying sounds. Lederman [86] estimated the fundamental frequency for infants’ cry using a simple inverse filtering tracking (SIFT) algorithm. The proposed algorithm was able to reliably estimate the fundamental frequency (F0) and overcome the problem of over/under-estimation. In order to evaluate the proposed algorithm, the fundamental frequency estimated using SIFT is compared to the real fundamental frequency estimated by the visual inspection of
the signal. The average error rate for phonated and hyperphonated cries were 3.75% and 6.10%, respectively. Similarly, Várallyay et al. [87] investigated the phonated and hyperphonated fundamental frequency’s characteristics of crying sounds for 37 infants with deafness/severe hear loss. Smoothed Spectrum Method (SSM) is proposed to detect the fundamental frequency and compared with other existing methods such as Local maximum value detection and cepstrum analysis. The results show that SSM is the most reliable in analyzing the phonated and hyperphonated cries comparing to the other two methods.

Different approaches were proposed to classify the infants’ state as pain or other stressors based on analysis of crying sounds in frequency domain. In [88], the fundamental frequency is used along with the first three formants (i.e., $F_0$, $F_1$, $F_2$, $F_3$) to build k-means clustering algorithm for determining the infant’s state (e.g., pain, hunger, fear); features of infants’ facial expression were also utilized. The correct classification rate for pain cries was 91%. Mima and Arakawa presented a method [43] that analyzes newborns' cries in frequency domain and classifies them as cries due hunger, sleepiness, or discomfort. The difference of the tendencies of the Fourier spectrum for the crying signals were extracted and used to build a rule-based system for classification. The overall accuracy of the proposed method was 85%. Other approaches that analyze infants’ crying sounds in frequency-domain can be found in [43, 89, 90].

**Cepstral-domain Feature Representation**

The cepstral-domain of a signal is generated by taking the inverse Fourier transform (IFT) of the logarithm of the spectrum of a specific signal. Mel frequency cepstral coefficients (MFCC), which are mathematical coefficients to represent a given
signal, are common and useful cepstral-domain features. They are used to extract useful and representative set of features (i.e., coefficients) from a voice signal and discard noise and non-useful features. It has been claimed that MFCC are the best features in analyzing infants’ crying sounds [91].

One of the first studies to analyze infants’ crying sounds using MFCC was introduced in [45]. The extracted features (i.e., 16 coefficients) are fed to a neural network as input and used to classify the sample sounds into pain, fear, or anger. The accuracy of applying this method on crying signals of 16 infants yields 90.4%. Barajas-Montiel et al. [83] discussed MFCC-based method to classify infants' cries as pain cries, hunger cries, and no-pain-no-hunger cries using fuzzy support vector machine (FSVM). FSVM is an extension to SVM that reduces the affect of outliers by assigning a fuzzy value or weight for each training point rather than assigning equal points as in SVM. The proposed method has two main stages. In the first stage, crying signals are cleaned, normalized, and divided into segments. Then, MFCC (i.e., 16 coefficients) are extracted for each segment and used to form the feature vectors. In the second stage, FSVM classifier is trained to distinguish pain cries, hunger cries, and no-pain-no-hunger cries; 10-fold cross validation technique is used to evaluate the classifier performance. The best classification score was about 97.82%. The accuracy of SVM classifier in similar experiment setting was about 97.79%, which shows an improvement by 0.03%.

Yousra and Sharrifah introduced an approach in [91] to classify infants’ cries as pain or no-pain. A set of 150 pain samples and 30 no-pain samples were recorded for newborns babies. The pain samples were recorded during the routine immunization procedure in NICU. No-pain samples were recorded during other emotional states (e.g.,
anger and hunger) that are not pain. These samples were segmented and used to extract two sets of features, namely, Mel Frequency Cepstral Coefficients (12 MFCC coefficients) and Linear Predication Cepstral Coefficients (16 LPCC coefficients). The extracted features are fed then to a neural network trained with the scaled conjugate gradient algorithm. The average accuracies of classifying infants’ cries as pain or no-pain were 68.5% and 76.2% for LPCC and MFCC respectively. This result suggests that MFCC outperforms LPCC in classifying infants’ cries as pain or no-pain.

Similarly, Vempada et al. [92] investigated the use of Mel-frequency Cepstral Coefficients (13 MFCC coefficients) along with other time-domain features for recognizing infants' crying sounds. A total of 120 hospitalized premature infants were recorded undergoing different emotional states, namely pain, hunger, or wet-diaper. The number of the crying clips collected for pain, hunger, and wet-diaper were 30, 60, and 30 respectively. The extracted features are used then to train SVM to classify an infant's cry as one of the three classes. Three sets of experiments were conducted. In the first experiment, MFCC features are used to train SVM; evaluating the trained classifier in testing set yielded 61% weighted accuracy. The time-domain features are used in the second experiment to build the classifier; the weighted accuracy of testing the classifier was approximately 57%. In the last experiment, a feature and score fusion of both cepstral and time domains were performed to classify the infants' cries as pain, hunger, or wet-diaper. The weighted accuracy using feature and score level fusion was observed to be around 74% and 81% respectively. The results of this study show that features of cepstral domain can yield better performance than time-domain features in similar application. They also show that the feature and score level fusion represent the best
practice for recognizing the types' of infants' cries.

For the purpose of analyzing crying sounds of normal and pathological infants, Lederman et al. [86, 93] introduced a cepstral-domain method to distinguish crying sounds of normal infants from crying sounds of infants with Respiratory Distress Syndrome. The method starts by segmenting the crying sounds into cry and silent segments based on energy thresholding. For each of the crying segments, MFCC (i.e., 16 coefficients) features are extracted to characterize crying sounds and form the feature vectors. The accuracy of classifying different types of crying using Continuous Density Hidden Markov Models (CD-HMM) was 63%; expert human's classification yields 47% accuracy. Another MFCC-based method introduced by the same author in [94] to distinguish normal infants and infants with Cleft-palate condition, which is gap between the two sides of the upper lip. MFCC coefficients along with energy are extracted and used to train Hidden Markov Model (HMM) classifier. The correct classification rate of the proposed approach was around 91%. Although this approach is developed to discriminate normal from pathological cry, it can be employed to classify pain from hunger cries, as claimed in the paper. Other cepstral-domain methods to analyze infants’ crying sounds are presented in [95-97].

**Time-domain Feature Representation**

Time-domain analysis is the analysis of a signal with respect to time (i.e., the variation of a signal’s amplitude over time). One of the most common time-domain methods to analyze sounds is known as Linear Prediction Coding (LPC). The main concept behind LPC is the use of a linear combination of the past time-domain samples to predict the current time-domain sample. LPC can also be applied in frequency-domain
and it is known as Frequency-domain linear Prediction (FDLP) [98].

Other time-domain features that have been used to analyze infants crying sounds are energy, amplitude and pause duration. The energy and pause duration are utilized in [92] to analyze infants’ crying sounds associated with pain, hunger, and wet-diaper states. Specifically, short-time energy (STE), which is the average of the squared values in a window, and pause duration within the crying segment are extracted and used to train SVM classifier. The average recognition rate of classifying infants crying into pain, hunger and wet-diaper using time-domain features is 57.41%. In order to improve the recognition rate, it has been suggested to combine STE and pause duration with cepstral-domain features such as MFCC. The recognition rate for combining features of time and cepstral domains is 74.07%. It is important to note that the low accuracy can be attributed to the fact that the dataset of this study is real-world data collected from 120 infants (age 12-40 weeks) in NICU environment. Another study that employs time-domain features to analyze infants’ crying sounds can be found in [99].

In summary, this section briefly describes the existing works that analyze infants’ crying sounds. We have grouped existing works based on the utilized features into: frequency-domain, cepstral-domain, and time-domain feature representation. It has been found that cepstral-domain features are better in classifying infants’ crying sounds than features of time or frequency domain [92, 96, 97]. Additionally, it has been shown that combining features of different domains (e.g., MFCC and LPC) is the best practice for analyzing infants’ crying sounds.

2.1.3. Body Movements Analysis

Infants tend to make specific body movements such as extension of the arms and
legs, finger splays, and head shaking when they experience pain. Also, It has been found that analyzing infants' pattern of movements can help in detecting different movement disorders [100]. Therefore, observing and analyzing infants’ body movements is necessary to guarantee a good pain estimation and early disease diagnosis. Because the current practice of observing infants’ body movements is subjective and requires continuous monitoring, developing an automated system to observe infants’ body movements is needed.

Several machine-based approaches were introduced to analyze infants' body movements for the purpose of diagnosing a specific disease. We are not aware of any work, except the work of this study, that analyzes infant’s’ body movements automatically for the purpose of assessing pain. Existing approaches to diagnose an infant disease based on analysis of body movements can be divided into: instrument-based approaches and velocity-based approaches. We provide a review for both categories and discuss their limitations below.

**Instrument-based Approaches**

Methods under this category employ specific devices to analyze infants’ body movements. Examples of these devices include reflective markers, accelerometers, and motion sensors. Meinecke [101] et al. proposed a method to predict the possibility of developing spasticity, which is a muscle control disorder, using kinematic biomechanical model. The model is applied to segment infants' body parts into hand, forearm, upper arm, head, trunk, thigh, lower leg and foot; and a marker is attached to each of these segments. To capture the motion of these markers, a 3d motion analysis system with a temporal resolution of 50 Hz and a high spatial precision was employed. For the
classification of infants' into "healthy" or "at-risk", a set of quantitative parameters, extracted from the motion data, is used with a multiple discriminant analysis (MDA) to build a prediction model. This model achieved an overall detection rate of 73%.

Similarly, Conover [102] introduced an accelerometer-based method to quantify infants' general movements for the purpose of diagnosing cerebral palsy disorder. Another instrument-based approach to analyze infants’ body movements is presented in [103]. Methods under this category require specific devices, which can be obtrusive, expensive, and non-friendly in clinical settings. Next, we present unobtrusive and more practical methods to analyze body motions in clinical environment.

**Motion-based Approaches**

Motion-based approaches measure the 2d displacement vector field of an object or pixel between consecutive video’s frames. Examples of well-known motion-based approaches are optical flow and motiongram. Optical-flow is a motion estimation technique that has been used by different studies to predict movement’s disorders such as Cerebral Palsy.

Rahmati et al. discussed in [104] an optical flow-based method to discriminate infants into healthy infants and infants with Cerebral Palsy. The presented method has three main stages: (1) motion segmentation using optical flow; (2) features extraction; and (3) SVM classification. Motion segmentation stage involves three steps. First, generating a dense trajectory field to track points of the infant’s body parts using optical flow. Second, a graph-cut optimization algorithm is applied to separate similar trajectories into different segments (e.g., head segment or left hand segment). The last step in the motion segmentation stage is to compute a single representative trajectory for
each body part. The generated trajectories are used to extract three types of features: correlation between trajectories, area out of standard deviation (STD) from moving-average, and periodicity. Correlation between trajectories measures the dependencies between the limbs motions; and STD and periodicity features measure the smoothness and the frequency in the movement pattern. To classify the infants as healthy or affected, the extracted features are combined to form a feature vector for each infant. The feature vectors of different infant are used then to train a support vector machine classifier. The average accuracy of evaluating the SVM on unseen dataset of infants yields 87%.

Another optical flow-based algorithm is proposed in [105] to predict infants with Cerebral Palsy. Similarly, optical-flow is used to generate motion trajectories, which are transferred to time dependent trajectory signals. These signals are analyzed further to extract three types of features: the wavelet coefficients, absolute motion distance, and relative frequency features. The wavelet coefficients measure the variety of infants' movements; the other two features measure the activity and the occurring frequencies in the movement patterns. Using relative frequency feature with SVM yields 93.7% average classification accuracy, which is the highest comparing to wavelet coefficients and absolute motion distance features. More optical flow-based approaches are discussed in [106-108].

Motiongram is a method to represent the motion image, which is an image with values of 0 (no-motion) and 1 (motion), over time by computing the average of each image motion. Adde et al. [109, 110] utilizes the motiongram to discriminate infants’ fidgety movements from non-fidgety movements. The algorithm started by computing the motion image for each video frame. These images are used then to generate the
motiongram and extract quantitative measures (i.e., features) such as quantity of motion and centroid of motion. Finally, logistic-regression model on fidgety versus non-fidgety as dependent variable was performed to investigate the association between the dependent and each of the independent variables. The results show a strong association between the quantitative features and the presence of fidgety movements. Another motiongram method to assess infants’ body movements is examined in [111].

To summarize, existing works to analyze infants' body movements are divided into: motion-based and instrument-based. These works focus on analyzing infants' body movements for the purpose of diagnosing a specific disorder. To date, we know of no work to assess infants' pain automatically based on body movements’ analysis.

2.2. Physiological-based Pain Assessment Approaches

Physiological pain indicators represent the body’s reactions to a pain stimulus. Examples of physiological indicators associated with pain include skin conductance, increased activity in specific regions of the brain, and increased heart/respiratory rate. Various machine-based approaches have been presented to assess pain based on analysis of physiological indicators [56, 61, 63, 112-114]. Most traditional pain scales that are used in the NICU take the vital signs readings into consideration when assessing pain. Also, recent studies [63, 115-117] have found a strong association between infants’ pain and changes in specific brain regions. In the following subsections, a review of existing methods to assess pain based on analysis of vital signs and brain dynamics is presented.

2.2.1. Vital Signs Analysis
Vital signs are defined as measurements of changing in the body basic functions. Caregivers to understand infant’s body condition and discover medical problems continuously monitor these signs. There are four main vital signs: the heart rate (HR), respiratory rate (RR), blood oxygen saturation (SpO2), and the blood pressure. Studies have shown that there is a high correlation between pain/discomfort and changes in vital signs (e.g., heart rate increasing) [118].

Lindh et al. [113] presented an approach to assess infants pain by frequency domain analysis of heart rate variability (HRV) during heel lancing procedure. Heart data were collected from 23 infants in four different events: baseline, sham heel prick, sharp heel prick, and heel squeezing event. Statistical and spectral analysis was carried on the data to extract the heart rate mean (HR\textsubscript{mean}), the variance ($P_{\text{tot}}$), and the power in low-frequency LF ($P_{\text{LF}}$) and high-frequency HF ($P_{\text{HF}}$); these values are used as independent variables for multivariate statistics to analyze the correlation between these variables and each of the four events. The results showed increasing in HR\textsubscript{mean} and decreasing in $P_{\text{HF}}$ associated with heel squeezing event (i.e., heel squeezing is concluded to be the most painful event during heel lancing).

In [119], the heart rate variability (HRV) was investigated for a group of infants (age > 34 gestational weeks) with chronic pain. EDIN scale (Échelle Douleur Inconfort Nouveau-Né, neonatal pain and discomfort scale) was used to score the pain and separate infants into two groups: (1) "Low EDIN," with EDIN score<5; and (2) "High EDIN," with EDIN score $\geq$5. To study the association between chronic pain and cardiovascular data, linear regression analysis was performed using the mean of heart rate (HR\textsubscript{mean}), respiratory rate (RR\textsubscript{mean}), blood oxygen saturation (SpO2\textsubscript{mean}), and High Frequency
Variability Index (HFVI). The results showed that chronic pain is associated with an increase in HR, slight decrease in RR, and significant decrease in HRV. It also showed that HFVI is able to predict the pain with a sensitivity of 90%, and a specificity of 75%.

In different domain, vital signs data have been used to detect and classify certain diseases using machine-learning methods such as neural network. The interested reader is referred to [59, 112, 114, 120].

2.2.2. Brain Regions Analysis

Recent studies [115-117] found that pain causes hemodynamic changes in specific cortical regions of the brain in premature and term infants. Additionally, it has been claimed that measurements of the brain activity may provide the most accurate pain indicators in infants [115]. There exist various brain imaging instruments to measure the brain region activity. Examples of these instruments include functional magnetic resonance imaging (fMRI) and near infrared spectroscopy (NIRS). fMRI produces an activation map that shows which parts of the brain are involved in an emotional event (i.e., pain). NIRS is similar to fMRI but it’s cheaper, safer, and more practical. NIRS uses works by measuring changes in the near infrared light that correspond to changes in blood flow using probes; these probes are small in size and attached to the head.

Machine learning has been used in conjunction with neuroimaging techniques to assess pain. Marquand et al. [121] presented a machine-based approach that used fMRI for pain assessment. fMRI data were extracted from set of subjects during different events of pain and used to train SVM. The result of evaluating the trained SVM on the same set of subjects yields 91.67% best classification accuracy. Using the same set of subjects for training and testing generates an overfitted classifier that will perform poorly
on new subjects. To overcome overfitting problem, Brown et al. [61] extended the work by Marquand and presented a SVM model trained on one set of individuals, and used to accurately classify pain in different set of individuals. The model yields 86.6% average accuracy.

In case of infants, Ranger et al. [63] discussed a pain assessment approach to assess infants' pain based on analysis of brain regions. NIRS signals for 40 infants were recorded during chest tube removal following cardiac surgery. Specifically, the cerebral deoxygenated hemoglobin concentrations (HbH) readings were recorded in three periods: baseline (T0), removal of dressing (T1), and removal of chest tube (T2). To verify associations between NIRS signal and pain stimulus, univariate linear regression was performed on the extracted HbH measurements. The results showed a significant increase in HbH during pain (i.e., the difference of HbH measurement between the baseline (T0) and pain (T2) was significant).

To summarize, different studies have shown a strong association between brain’s regions activity and pain stimulus. Few machine-based approaches have investigated this association for the purpose of assessing infants’ pain. Generally, using machine-based methods to study the impact of pain stimulus in NIRS is a recent area of research that requires more investigations. In this study, we propose an automated approach to analyze the association between these readings and pain in infants.

3. Current Limitations and Future Directions
The automated assessment of pain has several limitations that affect on its progress. First, majority of existing approaches were built using a non-realistic data collected in a laboratory environment. We believe these approaches may completely fail or perform poorly if they are applied to a more-realistic clinical data due to several reasons. For example, severe pose, occlusion, and illumination are common in a clinical setting. The second limitation is the noticeable lack of infants’ data that is needed for analysis. At the time of writing this paper, we are unaware of any accessible dataset that is collected for the purpose of assessing pain in infants, except COPE dataset [67]. COPE dataset has images for twenty-six infants recorded in five emotional conditions, which are rest, cry, air stimulus, friction, and pain. However, this dataset is not suitable for analyzing pain dynamically since it consists of static images that ignore the emotional dynamic and its evolution over time. Also, COPE dataset has data for a single pain indicator (i.e., facial expressions) and thus it is not sufficient to develop an automated multimodal assessment of pain.

In case of adult patients, Lucey et al. [122] collected a dataset for 129 participants with acute shoulder pain. This database, which is known as UNBC-McMaster Shoulder Pain Expression Archive, has video sequences recorded during a series of movements to test the affected and unaffected areas of a shoulder. The ground truth of this dataset consists of FACS codes, self-evaluations, and observer evaluation. Although this dataset addressed the need for a temporal, realistic and well-annotated data, it is designed specifically to assess pain based on facial expression analysis (i.e., single modal). Another dataset that has multiple behavioral indicators of pain is introduced in [123]. The dataset is part of the Emotion and Pain project [123], which aims to develop a set of
methods for automatically recognizing audiovisual signals related to pain in video sequences. Given the variation in pain experiences between adults and infants, similar data are needed for infants to develop an automated and reliable pain assessment. In this paper, we presented MPAT dataset, which is a novel dataset collected by our research team to assess pain in infants in clinical setting. The dataset has video and audio signals of infants recorded prior to and during several pain procedures. It also has readings for different physiological pain indicators such as heart rate. More description of the dataset is presented in Section 5.

Another main limitation is the single modality (e.g., facial expression) of existing approaches in assessing pain. Studies [13, 124] have shown that pain causes behavioral and physiological changes and have suggested considering several indicator to guarantee the best pain assessment. Additionally, it has been reported that some infants have limited ability to behaviorally express pain due to specific disorders (e.g., Moebius syndrome and paralysis) or physical exertion, (e.g., exhaustion) [125]. Therefore, it is important to consider both behavioral and physiological pain indicators for assessment. It is also important to incorporate contextual information (e.g., gender and presence of the mother) with other pain indicators to refine the assessment process as demonstrated in [20]. We believe that developing a continuous, context-sensitive, and multimodal system may provide the best practice to assess infants’ pain.

A fourth limitation of the automated approaches for pain assessment is that the majority of the existing approaches focus on assessing pain during acute painful procedures. It has been found that infants' behavioral and physiological responses to acute pain are different than chronic pain. Therefore, monitoring and analyzing different
types of pain is essential for an efficient and reliable assessment.

4. Multimodal Pain Assessment Tool (MPAT)

The vast majority of the machine-based pain assessment approaches discussed above utilized a single pain indicator for assessment (i.e., single modality). Notwithstanding that several studies have demonstrated the relationship between isolated behavioral and physiologic changes and infant pain, to our knowledge no work has developed a tool that allows for the automated integration of both behavioral and physiological indicators (i.e., multimodal). In this paper, we propose a machine-based multimodal pain assessment tool (MPAT) that automatically measures and assesses pain in infants based on analysis of several behavioral and physiological pain indicators. Specifically, we propose a tool to classify the infant’s pain state by analyzing infants’ facial expressions, body movements, crying sounds, vital signs, and brain's dynamic readings. The benefits such a tool might provide include:

1. Continues and minimally biased assessment of pain.
2. Pain assessment comparable to the traditional assessment in NICU (i.e., the traditional “by-proxy” pain assessment tools utilize both behavioral and physiological pain indictors).
3. Fault-tolerant multimodal system (i.e., MPAT has tolerance to the failure of recording a specific pain indicator).

We believe once this novel and diagnostic tool is developed, it will improve the assessment of pain in infants, and help guide treatment. A general overview of MPAT is depicted in Figure 2 above.

6. Conclusion and Future Works
This paper provides a survey on the current state of art in assessing infants' pain and proposes a multimodal pain assessment tool (MPAT). The first part of the paper focuses on the current approaches for pain assessment. We divide these approaches based on the utilized pain indicators into behavioral-based and physiological-based approaches. We then explore each of these categories and discuss their methods and limitations. The main limitations of the current approaches in assessing infants’ pain include:

1. The vast majority of existing approaches are built using non-realistic data collected in a laboratory environment.
2. In general, there is a noticeable lack of data for analysis especially in case of infants.
3. Existing approaches focus on acute pain and ignore chronic pain. They also ignore the contextual information (e.g., presence of the infant's parents) when assessing pain.
4. Most existing approaches utilize a single indicator to analyze infants' pain. To develop an efficient pain assessment approach, combining various indicators (i.e., multimodal) is needed.

The second part of the paper proposes a machine-based multimodal pain assessment tool (MPAT) that integrates both behavioral (e.g., face, voice, body) and physiological pain (e.g., vital signs and NIRS data) cues for assessment. Then, the paper demonstrates the benefits of utilizing a multimodal system for assessment of infants’ pain.
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