Abstract
COMFORT behavior scale (Cb) has been applied in neonatal units to measure pain in newborns. This study aimed to analyze parameter’s scale testing if they differ in sensibility to pain. The scores were correlated to skin conductance activity (SCA). Thirty-six newborns were videotaped whilst heel prick. The images were analyzed in three intervals: before, during and after the pain event. Cb scale scores were compared to SCA variables: number of waves/sec and area under curves in three different time intervals after the pain event: 15, 30 and 180sec. All factors of Cb were sensitive to changes among periods during-before and after-during. Significant correlations values were found between Cb and number of waves ($r < 0.6$). Facial Tension was the gold standard response to pain meanwhile factors as Crying and Calmness can be considered poor indicators of pain. These results are discussed in terms of phenomenological approach and anxiety paradigm.

Keyword: COMFORT behavior scale, pain, neonates, skin conductance activity, anxiety.

Introduction
The evaluation and scaling of pain perception are fundamentally related to the clinical art dependent on patient's report, behavioral observation and physiological measures based on physical examination. Newborns follow these parameters except the ability to report what they perceive. Although the statement that newborns are able to perceive pain was controversial for many decades, nowadays there are enough evidence that they are capable of perceive and report pain both on their medical condition or clinical procedures performed as collection of blood, endotracheal suction, surgery or other invasive procedures (Harrison et al., 2006). Pain is defined by the International Association for the Study of Pain (IASP) as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Merskey H. Bogduk, 1994; IASP Task Force on Taxonomy, 1994, updated 2011). This definition has been often used in studies about pain despite theoretical models or kind of subject, but this worldwide use can’t prevent or hidden the truth of how difficult is to define pain, specially the pain perceived by non-verbal subjects. To assess pain in infants, behavioral and physiological parameters were designed to reduce the subjectivity linked to patient response and give more subsides for research in neonates who do not report the pain (Eriksson et al., 2008; Storm, 2008). Several pain scales have been introduced, either unidimensional or multidimensional which combines behavioral and physiological dimensions of pain (de Oliveira et al., 2010) such as COMFORT scale (Ambuel et al., 1992; van Dijk et al., 2005), Neonatal Infant Pain Scale (Lawrence et al., 1993), Neonatal Facial Coding System (Grunau & Craig, 1987) and Neonatal Pain, Agitation and Sedation Scale (Hummel et al., 2008, Hummel et al., 2010) among others.

Despite the crescent pool of validated pain scales for infants, the physiological parameters as heart rate (Pereira et al., 1999, Padhye et al., 2009, Jesus et al., 2011), blood pressure, oxygen saturation (Hummel & van Dijk, 2006, Jesus et al., 2011) have attended to assess pain and validate other instruments in newborns. Skin conductance activity (SCA) (Storm, 2000; Storm & Freming, 2002, Gjerstad et al., 2008) also has been used as a measure of pain specially in monitoring context of
infants under sedation or anesthetized (Eriksson et al., 2008; Storm, 2001; Hullett et al., 2009, Jesus et al., 2011; de Oliveira et al., 2012). This type of sweat is dependent on the response of the cerebral cortex through the activation of the sympathetic nervous system (SNS) on the sweat glands, and regardless of weather or cardio respiratory conditions (Storm, 2001; Harrison et al., 2006; Storm, 2008).

Previous study has already compared skin conductance to the scores of the COMFORT scale and COMFORT behavior scale. Gjerstad, Wagner, Henrichsen & Storm (2008) analyzed skin conductance fluctuations during endotracheal suctioning and they founded better correlation with the increase in the COMFORT scale score than the variation of heart rate and arterial blood pressure. Considering that the skin conductance is the fastest measurement system of all, giving pain perception measurement in short intervals as 15 seconds, one possible question raised from these results is whether some dimensions of the COMFORT behavior scale are as sensitive and fast in revealing infant’s pain perception. If it is so, it can be used as alert signals to clinical teams in emergency contexts or limited contexts for use pain scales or the skin conductance device, a common situation in ICU’s context. van Dijk adapted and modified this scale cutting off these physiological variables and created a COMFORT behaviour scale which uses only the behaviour and the phenomenological dimensions (van Dijk et al., 2005). This phenomenological dimension is linked to the behavioral one, and consists of at least two sub-dimensions, sensory-discriminative and affective-emotional (experience’s spontaneous cognitive/conative reactions to own pain experiences). According to Aydede et al., 2010 it means that “These reactions were conceived as forming conative propositional attitudes. In other words, the painfulness of pains was constituted by their power to immediately evoke in [one] the peremptory desire that the [pain] perception should cease”. The sensory-discriminative aspect of pain is representational: it represents tissue damage. To define the phenomenological aspect is very difficult, but it can be said that feeling pain involves perception although perception doesn't exhaust its nature: feeling pain is also an affective/emotional experience that can be explained in terms of the functional role of pain's sensory/representational content.

Taking into account the above mentioned aspects, this study aims to compare all COMFORT behavior scale’s dimensions and its behavioral indicators to the physiological measurement of pain by skin conductance to test the sensibility and specificity of each scale’s item. Hence, this study assessed whether each variable in the COMFORT behavior scale can be used independently as a measure predictor of pain in newborns. To assess each variable of COMFORT behavior scale we used the validated equipment for measuring pain in neonates, Skin Conductance Measurement System (SCMS®), as a comparative method of results analysis (Harrison, 2006) in three different time windows to verify the efficacy of each item of the scale. We hypothesized that the best correlations between behavioral and physiological indicators would reveal the most efficient responses of neonates to be used in future studies about acute pain in infants and the most effective response to be considered for clinical and research purposes.

Methods

Subjects

Were selected 36 newborns, 19 males and 17 females, with gestational age between 37 to 41 weeks (mean = 38.95 weeks; ± 1.35 weeks) with up to 48 hours of life at the Maternity of the University of Brasilia Hospital. These babies were subjected to routine procedure in the ICU such as daily assessment of glucose by heel prick. Parents of infants were consulted and informed about the purpose of the study by signing the consent form. Were excluded from the sample infants with postnatal age less than 24 hours, with Apgar score less than seven in the fifth minute of life with a diagnosis of intracranial hemorrhage in the third or fourth degree (Volpe 2008); with metabolic, respiratory, circulatory, congenital disorders; and has used drugs that interfere with the perception of pain (analgesics, sedatives or muscle relaxants), neonates whose mothers used opioid and/or its derivatives during pregnancy.

Procedure, Apparatus and COMFORT Behavior Scale
The infants’ responses were videotaped using a camcorder (DCR-SR 47, Sony), SCA was measured by the Skin Conductance Measurement System (SCMS®, Medstorm Innovation) through three established conductance variables: basal level of conductance peaks, number of waves per second (NWps) and area under the curve of waves (AUC). COMFORT behavior scale (Cb) was used to assess the following variables: muscle tone, facial expression, alertness, calmness/agitation, respiratory pattern and physical movement. Each variable has a range of five points, obtaining a total sum of six behavioral variables. Thus, one can obtain six as lower value reflecting the minimum degree of discomfort and a maximum of 30 points (van Djik et al., 2005).

To evaluate the behavioral response to noxious stimulus, the neonates were submitted to their daily routine heel prick for glucose monitoring. The exams were done early morning, at their bed and by the same examiner. The three electrodes of the equipment were attached and wrapped to the left foot 10 min before starting the observation period. The skin conductance measures were taken at three time intervals after the heel prick: 15, 30 and 180sec. All variables were analyzed in three periods "before" "during" and "after" the procedure. One trained observer assessed the movies and scored the infant’s behaviors by Cb. The SCA parameters were taken from the SCMS® software register system for three minutes.

Statistics

Each item’s score of Cb was compared between the periods "before", "during" and "after" the procedure by the paired-related sample when comparing the differences during-before. The Wilcoxon nonparametric-paired test was used to analyze the significant difference of the change in scores along the studied periods. To assess the global score of Cb, as well as their variables, were compared to SCA by the Spearman’s bivariate correlation. To verify if the clinical and demographic were related, it was used GLM two-way ANCOVA analyses. Analyses of agreement between Cb scores and subscores and skin conductance variables, all them calculated as difference between during-after pain periods, was made using Kendall's coefficient of concordance. Kolmogorov-Smirnov’s normality test was passed for all data sets (p > 0.05) and the Levene’s test of homogeneous variances was not significant for all analyses (p > 0.05). The data was stored on computer and analyzed using SPSS Package Version 17.0 and Minitab® 15.1.30.0.

Results

The sample variables had a mean gestational age of 38.9 weeks; 68.3% were delivered by cesarean section; 39% were large for gestational age; 41.5% small for date and 5.1% from diabetic mothers; 68% were breastfed one hour before the procedure. The paired-sample test of each variable of Cb showed significance for all variables both the period during–before and after–during (Table 1). All variables were statistically significance p < 0.001. According to the Spearman’s bivariate correlation (Table 2) between each variable of Cb and SCA considering NWps after the procedure (15sec, 30sec and 180sec) all of them were significant (p < 0.05) but showed from fair to moderate correlations (r < 0.6). Crying and calmness were the weakest factors to all time windows (Table 2). Only physical movement and facial expression showed a significant correlation between AUC 15sec and 30sec after the procedure, but all of them showed from fair to moderate correlations (r < 0.6). Global score of the Cb was compared with the SCA by Spearman’s Bivariate Correlation in each period of analysis. Were not found statistically significance between the score of the scale before and during the procedure (heel prick) with the NWps (15sec, 30sec, 180sec) and AUC (15sec, 30sec, 180sec). The Cb score after the heel prick was statistically significant (p <0.005) for the NWps (15sec, 30sec, 180sec), but the highest correlation was to NWps 180sec (r = 0.504, p <0.001).

### Table 1. Paired-samples test of each variable of Cb in the 37 neonates.

<table>
<thead>
<tr>
<th>Pair</th>
<th>During -before</th>
<th>After -during</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cb</td>
<td>-4.956**</td>
<td>-5.450**</td>
</tr>
<tr>
<td>Alertness</td>
<td>-4.057**</td>
<td>-3.849**</td>
</tr>
<tr>
<td>Calmness</td>
<td>-4.965**</td>
<td>-4.096**</td>
</tr>
<tr>
<td>Crying</td>
<td>-5.597**</td>
<td>-5.412**</td>
</tr>
</tbody>
</table>

**Note:** The *p* values and significance levels are indicated with **.
Table 2. Spearman’s Bivariate Correlation between each variable of Cb and SCA considering 15, 30 and 180 sec after the procedure (heel prick).

<table>
<thead>
<tr>
<th>Variables</th>
<th>15sec</th>
<th>30sec</th>
<th>180sec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cb and NWps</td>
<td>0.424**</td>
<td>0.383*</td>
<td>0.504**</td>
</tr>
<tr>
<td>Alertness and NWps</td>
<td>0.576**</td>
<td>0.468**</td>
<td>0.444**</td>
</tr>
<tr>
<td>Alertness and AUC</td>
<td>0.431**</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Calmness and NWps</td>
<td>0.449**</td>
<td>0.405**</td>
<td>0.333*</td>
</tr>
<tr>
<td>Crying and NWps</td>
<td>0.328*</td>
<td>0.348*</td>
<td>0.437**</td>
</tr>
<tr>
<td>Physical Movement and NWps</td>
<td>0.560**</td>
<td>0.533**</td>
<td>0.609**</td>
</tr>
<tr>
<td>Physical Movement and AUC</td>
<td>0.424**</td>
<td>0.314*</td>
<td>-</td>
</tr>
<tr>
<td>Muscle Tone and NW</td>
<td>0.383*</td>
<td>0.404**</td>
<td>0.413**</td>
</tr>
<tr>
<td>Facial Tension and NW</td>
<td>0.418**</td>
<td>0.391*</td>
<td>-</td>
</tr>
<tr>
<td>Facial Tension and AUC</td>
<td>0.327*</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Notes: * p < 0.05; ** p < 0.01
time interval more related to the pain event (15sec). Facial Tension seems to be the gold standard of this scale as it kept in high levels all over the behavioural observation time. Otherwise, factors as Crying and Calmness can be considered poor indicators of pain. Other factors as Muscle Tone, Physical Movement and Alertness only agreed with time interval of 180sec. Nevertheless, all agreements were only to NWps and all were only in a fair level of agreement, which was expected as the SCA is a highly fast way to measurement compared to behavioral scales.

The Cb should be evaluated in structured its three dimensions or components that comprise (Ambuel et al., 1992) physiological, phenomenological and behavioral. Analyzing under this theoretical approach, it is possible to assume that the SCMS® system, built to be sensitive not only to physiological dimension but also to the emotional one, and the facial tension factor of Cb are more related to the physiological level, while factors as alertness, physical movement and muscle tone are more related to the phenomenological dimension.

The phenomenological component of a behavioral scale, described as the personal account of pain, anxiety, among others, is the most difficult to assess in newborns since they are unable to speak. According to Ambuel et al (1992), anxiety can exist even in the absence of pain while the pain is related to an external noxious stimulus able to activate ascending cortical pathways for perception and interpretation of pain, and descending pathways to the development of a response (Anand et al., 2007). Associated with this mechanism, researchers assessed that these mechanisms are integrated with the sympathetic nervous system by changing the conductance of the skin due to the release of acetylcholine at postganglionic synapses of the muscarinic receptors of the sweat glands (Storm, 2008). According to the behavioral component, can be observed in this study that all the behavioral variables of the Cb when conducting an assessment using non-parametric pair before-during and during-after the procedure (heel prick) showed differences statistically significant but a weak correlation between SCA variables and the scale. Thus, it allows inferring that this variation in the score of each variable follows the variation of the scale of perception/response to pain by the newborn. Hence, the data also allow raising the hypothesis of responses like increase in physical movements, muscle tone and alertness is likely signals of anxiety than pain. To study this premise it could be suggested, in future studies, instead of considering the COMFORT’s entire interval of two minutes, to use varieties of observation behavior strategies as time sample, splitting the time window in smaller intervals searching for the decay of some responses and the raising of others. In that way it would be possible to define which responses are more related to the past painful event and which are related to fear of future pain.

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