

Abstract (249 words)

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KEY WORDS: Pain, Infants, Mother, Immunization

Predicting Maternal and Behavioral Measures of Infant Pain:
The Relative Contribution of Maternal Factors

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Abstract

The Sociocommunication Model of Infant Pain (Craig and Pillai Riddell, 2003) theorizes that maternal variables influence the pained infant and that the pained infant reciprocally influences maternal responses to the infant. The current analysis examines the relative predictive utility of maternal behavioral and psychosocial variables for both maternal judgments of her infant's pain and behavioral measures of infant pain, after infant factors have been controlled. A convenience sample of 75 mother-infant dyads was videotaped during a routine immunization in a pediatrician's office. Mothers were interviewed on the telephone, within two weeks, to complete a series of questionnaires. Infants were between the ages of 5 and 20 months. Infant pain was measured directly after the immunization using subjective maternal judgments. In addition, both maternal soothing behaviors and infant pain behaviors post-immunization were measured using objective coding systems. During the telephone interview, mothers were asked to recall infant pain levels for the day after the immunization and were also assessed for level of acculturative stress, perceived social support, general relationship style, feelings towards her infant and endorsed psychopathology. Regression analyses suggested that the role of maternal behavioral and psychosocial variables was highly dependent on the infant pain measure being predicted. These results imply that given the dependence of infants on their primary caregivers, quite often mothers, it is important to understand the dynamic influence of infants' behavior on maternal judgments of infants' pain and maternal psychosocial variables on infants' expression of pain.

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Predicting Maternal and Behavioral Measures of Infant Pain: The Relative Contribution of Maternal Factors

1. Introduction

Understanding the infant in pain necessitates a fundamental comprehension of the context in which the infant experiences pain. Minimal research attention has focused on the psychosocial context where an infant experiences pain (i.e., the caregiver-infant dyad) (Pillai Riddell & Chambers, in press).

Craig and Pillai Riddell (2003) modified the Sociocommunication Model of Infant Pain (Craig, Lilley, & Gilbert, 1996) to conceptualize the individual, familial, community, and cultural influences on infant pain. This model describes infant pain as a process of dynamic interaction between child and caregiver and delineates four stages of the infant pain event (infant pain experience, infant pain expression, caregiver assessment of pain, caregiver management of pain). Furthermore, by means of feedback loops, the model suggests that caregiver factors (e.g., acculturation, family and friend support, maternal mental health family) influence infant pain experience and expression, above and beyond the more direct infant factors (such as infant age, or irritability). Consistent with this premise, the infant development literature has also long promulgated that the most significant context of the young infant is the primary caregiver (Bowlby, 1969; Winnicott, 1960) with the primary caregiver of the infant most often being the mother (Crockenberg & Leerkes, 2001). **Moreover, while not focused on the pained individual**

but rather the observer/caregiver, a complimentary model on empathy (Goubert et al, 2005) also would concur that caregivers of individuals in pain are influenced by both “bottom-up influences” (e.g., behavior of the infant in pain) and “top-down influences” (e.g., caregiver background). However, despite these research-driven theories, no research to date has examined the relative contributions of infant factors and maternal factors when predicting behavioral measures of infant pain or maternal judgments of infant pain.

Measuring the impact of the maternal context on infant pain presents a unique challenge because although self-report is considered the gold standard of pain assessment (Agency for Health Care Policy and Research, 1994), this measure is not attainable from pre-verbal infants. Accordingly, we have argued elsewhere that a caregiver, with in-depth knowledge of the infant, would provide the best assessment of an infant’s pain (Pillai Riddell and Stevens, in press), particularly if pain is repeated or persistent.

However, when studying the impact of maternal behavioral and psychosocial variables on infant pain, there are distinct advantages to using an objective infant pain measure that does not rely on the maternal report. **Therefore, in order to explore the role different measurements of infant pain may play, the current study chose to include measures with varying levels of objectivity.**

For the current study, three validated and reliable measures of infant pain were utilized and compared: **one subjective** (maternal judgment of infant pain) **and two objective** (a composite behavior measure and a discrete facial action measure) measures. Using an infant immunization pain paradigm, the purpose of this study was to evaluate a tenet of the Sociocommunication Model of Infant Pain; namely, that maternal contexts

(i.e., cultural, community, familial and individual) are related to infant pain measures, after infant variables (i.e., infant age, infant behavioral reactivity) are controlled.

2. Methods

2.1 Study Population

With a retention rate of 86% (See Figure 1), a convenience sample of 75 mother-infant dyads were videotaped during a routine immunization session (Prevnar, Pentacel, Meningococcal C, Measles/Mumps/Rubella [MMR], Varicella, Hepatitis B) at the pediatrician's office and interviewed (mothers), over the phone, within two weeks of the clinic visit. Infants who: were between 5 and 20 months of age, had no suspected developmental delays or impairment, no chronic illnesses, and had never been admitted to a neonatal intensive care unit were eligible to participate in the study. Infant caregivers were the mother of the infant brought into pediatrician's office (only 1 eligible dyad was excluded due to the caregiver being a father), able to speak and read English and available for both phases of the study to meet the inclusion criteria. Infants were equally split between the genders (female = 37; male =38). Independent t-tests using a family-wise error rate of 10% were run to determine if gender differences existed on any of the infant pain measures. No significant differences were found and all analyses proceeded with the total sample.

2.2 Procedure

The protocol was approved by Research Ethics Boards at both the participating university and associated tertiary level pediatric hospital. After agreeing to speak with a researcher about the study, mothers were approached by the research assistant who explained the study and then asked them to sign informed consent forms. They were also

asked to schedule a telephone interview appointment within 2 weeks of the immunization session (two weeks was often required to start and complete interviews due to re-scheduling necessitated by competing demands on mother, such as baby crying during initially scheduled time; see below). Mothers were given a copy of all questionnaires in a sealed envelope and instructed not to open the envelope until the telephone interview. Videotaping lasted from 1 minute prior to immunization up to 3 minutes after the last immunization injection. All infant and mother behaviors were coded from this footage (see below for exact epochs). After the immunization, mothers were asked to provide a pain rating for her infant's pain on a numeric rating scale. After the immunization appointment, mothers completed a 40-minute psychosocial questionnaire interview with trained research assistants on the phone. Due to the length of the battery of measures, mothers were encouraged to schedule two telephone appointments to complete the interview. Four mothers (5%) asked for a second appointment to complete the phone interview. All mothers who began a phone battery, completed the battery within 2-weeks of the appointment. Except for the maternal pain judgment in the clinic, all maternal variables were obtained during the phone interview. Four senior undergraduate students were trained to administer the phone battery after completing three hours of at-home preparation (approximately), attending a 3-hour workshop run by RPR, and successfully administering the entire battery to RPR.

2.3 Measures

Three different measures that varied in level of objectivity were utilized for measuring infant pain in the clinic directly after the immunization: a maternal judgment of her infant's pain (Numeric Rating Scale [NRS]; Jensen, Karoly et al, 1989), an

objective micro-coding system for infant facial pain expression (Neonatal Facial Coding System; Grunau & Craig, 1987), and an objective composite measure of behavioral pain reactivity (Modified Behavior Pain Scale; Taddio, Nulman et al., 1995). In addition, maternal recall of infant pain on the day after immunization was obtained using the mother's NRS judgment during the telephone interview.

Furthermore, as maternal variables are hypothesized by the Sociocommunication Model to influence infant pain even after infant variables such as pain expressivity are controlled (Craig & Pillai Riddell, 2003), maternal variables that could be used to predict the infant pain measures (after relevant infant variables were controlled for) were selected. These maternal measures included maternal behaviors post-immunization (Measure of Adult and Infant Soothing and Distress; Cohen, Bernard, et al 2005) and maternal questionnaires that could sample contexts hypothesized to influence infant pain assessment and management such as culture (Vancouver Index of Acculturation; Ryder, Alden & Paulhus, 2000), community and familial functioning (Multidimensional Scale of Perceived Social Support [Zimet, Dahlem, Zimet & Farley, 1988]; Relationship Scales Questionnaire [Griffin & Bartholomew, 1994]; Maternal Postnatal Attachment Scale [Condon & Corkindale, 1998]), and personal/individual (Brief Symptom Inventory [maternal mental health], Derogatis, 1993). All maternal questionnaires were administered during the phone interview.

2.3.1 Subjective and Objective Measures of the Infant

Mother Judgment of Infant Pain (Numeric Rating Scale, Jensen, Karoly et al., 1989) Mothers were asked to rate their infant's immunization pain using a 0 to 10 scale where 0 was anchored with "No pain at all" and 10 was anchored with "The Worst Pain

Possible”. The NRS has been shown to be a valid and reliable measure of pain intensity with strong levels of clinical feasibility and utility (Jensen & Karoly, 2001). **Moreover, use of an individualized NRS has been shown to have preliminary feasibility and validity with non-verbal cognitively-impaired children (Solodiuk & Curley, 2003).** Two maternal pain judgments were requested: one directly after the immunization (NRS-Day 0) and one for the day after the immunization (NRS-Day 1). **For the Day 1 pain rating,** mother was asked during the phone interview (**among the other maternal questionnaires**), **“Please estimate the worst pain your child experienced the DAY AFTER his/her immunization injection at the pediatrician’s office” (i.e., pain rating for Day 1 was based on mother’s recall of infant pain for the day after immunization).**

Pain Facial Reactivity (Neonatal Facial Action Coding Scale [NFCS]; Grunau & Craig, 1987). NFCS is a well-validated multidimensional behavioral measure of pain in infants (Stevens, Pillai Riddell et al, in press), adapted from the Facial Action Coding System (Ekman & Friesen, 1978). Discrete facial actions were coded as present (1) or absent (0) for each of five consecutive 2-second epochs occurring directly after the final immunization stick (**10 seconds total**). Trained NFCS coders who were blinded to study hypotheses were utilized (Kappa reliability = .91). Based on previous studies (Craig, Whitfield et al, 1993; Oberlander, Grunau, et al, 2000; Pillai Riddell 2004), 7 indicators (brow bulge, eye squeeze, naso-labial furrow, open lips, vertical stretch mouth, horizontal stretch mouth, taut tongue) were utilized to create a facial pain reactivity score. The score was obtained by summing these seven facial actions over the five-2 second epochs **directly after the immunization**. Scores ranged from 0 to 35 with higher scores indicative of greater facial pain reactivity.

The use of 2-second epochs for very fine-grained behaviors was especially problematic because of obstructions in the video angle due mainly to infant movement. Accordingly, only missing data for NFCS was handled as follows. In order to avoid simple deletion of these subjects (and the resultant bias this would cause in the results due to the systematic deletion of infants whose faces did not stay faced outwards towards the camera during the whole 10-seconds post-immunization), a system was used that allowed coders to make conservative judgments about missing facial actions. Video footage that included missing data was reviewed by a blinded coder to determine why the data was missing (e.g., infant turned away from camera) and whether other infant behavioral pain indicators (i.e., cry and body movement) stayed constant. The assumption was made that if cry and body movement stayed constant, this strongly suggested that the infants' facial expression remained constant for the 10-seconds immediately following the last needle stick (no assumptions were being made past the initial 10-seconds post-immunization). Thus, if a) facial data were available for a portion of the 10 second period (at least 60%); b) cry and body movement data were available and remained constant during the 10-second period and; c) there were no other reasons suggesting a coder should not reasonably infer that an infant's missing facial action remained constant, the preceding value for the missing facial actions were used (constancy value). If no preceding value was available, the next adjacent facial action value was used as a constancy value. Across discrete facial actions, approximately 21% (range 18% to 23%) of data units were replaced with a constancy value. In some cases, constancy of infant facial expression could not be assumed (e.g., when infant cry and body movement suggested that infant facial expression did not stay constant during the

period of time within which data was missing). Facial action data for which constancy could not be assumed were treated as regular missing values (akin to the other behavioural coding measures) and replaced with imputed means (See Statistics and Limitations section).

Composite Measure of Pain Reactivity and Pre-Needle Irritability (Modified Behavior Pain Scale [MBPS]; Taddio, Nulman et al, 1995). This multimodal pain measure identified the intensity of infant's facial expression (0-3 scale), cry (0-4 scale), and body movements (0-3 scale) for fifteen seconds after the last immunization needle was administered. This scale also obtains baseline measurement on all 3 behaviors for 10 seconds prior to the application of a painful stimulus. The baseline measurement was used as a measure of infant irritability directly prior to the immunization. For both baseline and post-immunization measurements, a score (0 to 3 or 4) is given by a coder for each of the three behaviors that represents the most significant example of that particular behavior during the epoch (10 or 15 seconds). Scores are summed across the three behaviors to provide a 0-10 point score for both baseline and post-immunization. Moderate to high concurrent and construct validity and item-total and inter-rater reliability have been demonstrated within the immunization context. Trained coders were blinded to the study hypotheses. Inter-rater reliability was excellent (Intraclass correlation for baseline = .98; for post-needle pain score = .95).

2.3.2 Measure of Maternal Behavior

Maternal Soothing Behaviors (The Measure of Adult and Infant Soothing and Distress (MAISD); Cohen, Bernard et al., 2005). The MAISD builds on the Child Adult Medical Procedure Interaction Scale–Revised (Blount, Cohen et al, 1997) as a valid and

reliable measure for the infant immunization context. For the current analysis, the presence of 8 discrete mother behaviors were measured (i.e., distraction, rocking, physical comforting, offer food, offer toy, offer to nurse/breastfeed, offer pacifier, verbal reassurance) for the period beginning directly after the final immunization needle. Each behavior was coded as present or absent **during** each 5-second epoch **after the final needle was removed**. To control for different lengths of video footage, an index score was created whereby the total number of epochs a behavior was present was divided by the total number of epochs filmed (**Mean number of 5-second epochs coded was 20.03 with a standard deviation of 7.46**).

2.3.3 Measure of Maternal Cultural Context

Acculturation (Vancouver Index of Acculturation [VIA]; Ryder, Alden & Paulhus, 2000). This 20-item instrument was designed to provide separate measures of an individual's identification with both mainstream North American and Heritage cultures. There are two subscales (Mainstream [North American] culture and Heritage culture). On each subscale, high scores are indicative of stronger identification with either North American or their self-reported Heritage culture. This measure has high internal consistency and strong convergent validity with generational status, identification with western culture, time lived in North America, time educated in North America. Acculturation is seen as a more valid and predictive construct than traditional measures of ethnicity and race (**American Psychological Association**, 2003). As these dimensions can be used as an indicator of cultural stress (e.g., low identification with mainstream culture and very high identification of heritage culture), it is being administered as a

broad indicator of maternal cultural stress with each subscale being analyzed as a separate independent variable.

2.3.4. Measures of Maternal Familial and Community Context

Presence of Perceived Social Support (Multidimensional Scale of Perceived Social Support [MSPSS]; Zimet, Dahlem, Zimet & Farley, 1988). This is a well-validated measure comprised of 12 items across three subscales. Each subscale focuses on an individual's feeling of being supported by a different traditional network: family, friends, and a significant other. In addition to strong factorial validity, the MSPSS has good internal and test-retest reliability and moderate convergent validity. Each subscale will be used as an individual predictor.

Mother's Relationship Style: (Relationship Scales Questionnaire [RSQ]; Griffin & Bartholomew, 1994). This 30-item measure provides a continuous measure of one's characteristic style in close relationships. Each item maps onto one of four relationship subscales (i.e., Secure, Fearful, Dismissing and Preoccupied) and upon completion, a participant receives a score on each of the four relationship styles. Individuals who strongly endorse secure relationship styles have positive views of themselves and of other people – building close relationships are a priority and a skill for individuals who strongly endorse this style. People who have negative perceptions of themselves and others and have difficulty making and maintaining close relationships often endorse a fearful relationship style. The preoccupied relationship style is defined by a negative view of self and a positive view of others. This combination results in individuals who constantly seek out close relationships but are often let down by these relationships. Finally, the dismissing strategy is related to the inverse pattern of preoccupied individuals

– people who have high levels of self-confidence but more negative views of others.

These individuals tend to avoid intimacy and prefer to rely on themselves. This measure has been demonstrated to have strong convergent and divergent validity (Griffin & Bartholomew, 1994). Each relationship subscale will be analyzed as a potential independent variable.

Maternal Feelings toward her Infant (Maternal Postnatal Attachment Scale; Condon & Corkindale, 1998). This is a 19-item self-report questionnaire designed to tap into a mother's emotional tie to her infant¹. A factor analysis supports the three main subscales (i.e., Quality of attachment, Absence of hostility [towards infant] and Pleasure in interaction). Moderate internal consistency, test-re-test reliability and convergent validity have been reported.

2.3.5 Measure of Maternal Individual Context

Maternal Mental Health (Brief Symptom Inventory [BSI]; Derogatis, 1993). The BSI is a 53-item self-report screener that provides scores on 9 primary symptom dimensions of psychological functioning (i.e., Depression, Anxiety, Somatization, Obsessive-Compulsive, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism). Over the past decade, a substantial body of literature has confirmed a consistent factor structure, moderate inter-item and test-retest reliability and high convergent validity. Two scales of overall functioning were calculated and used as predictors. The first, the Global Severity Index, provides the average endorsement level across all 53 symptoms on the measure (higher scores indicative of higher average endorsement of distress across all symptoms). The second scale, the Positive Symptom Distress Index, provides the

¹ Despite the title it is important to note that this measure does not measure “attachment” as classically defined in the developmental psychology/psychiatry traditions and is best interpreted as an indicator of mother's feelings toward her child.

average endorsement level for only symptoms that were acknowledged as present by the mother (higher scores indicate that, on endorsed symptoms, the mother had a higher average levels of reported distress). Due to the sensitive nature of this measure, an emergency procedure was put in place in case a mother divulged harm to herself or her child. No mothers required emergency care.

2.4 Statistics

As no comparable work in this area exists to base variance estimates for a power analysis, sample size was based on guidelines for multiple regression analysis; eight times the number of predictors plus 50 (Green, 1991). We conservatively assumed final predictor models with 4 predictors (one from each block of predictor variables; see following paragraph describing hierarchical strategy of entering predictor variables into the regression equation) and aimed to recruit 82 dyads in the clinic (all the final models ended up having three or less significant predictors).

Because the power analysis strategy was focused on power for detecting significance based on blocks of predictors rather than individual predictors (see below), dropping non-significant individual predictors to form a final model may represent Type II errors, and may bias the beta coefficients of the significant predictors retained for the final model. Thus, following Cohen, Cohen, West, and Aiken (2003, p. 144), sensitivity analyses were conducted to determine whether the magnitude and significance of the predictors in a final model were substantially different from the corresponding results in the complete model containing all predictors. For each dependent variable, this sensitivity analysis suggested that dropping the non-significant predictors did not change the interpretation of the relationships between the predictors and dependent variables in the

final models. Therefore, we followed the recommendation from Cohen et al. (2003, p. 186) of reporting a more parsimonious final model with fewer predictors that does not include predictors with small effects.

Four hierarchical multiple regressions were planned with each of the maternal and behavioral measures of infant pain as a dependent variable [maternal ratings of pain in clinic (NRS DAY 0); maternal report of infant pain for the day after immunization (NRS DAY 1); neonatal facial pain reactivity directly after the immunization (NFCS) and a composite pain behavior score for directly after the immunization (MBPS)]. These models focused on elucidating the relative predictive value of maternal variables after infant factors were controlled. Accordingly, using the Sociocommunication Model (Craig & Pillai Riddell, 2003) as a framework, it was pre-determined that independent variables would be entered in 4 blocks: Block 1 - infant pain behavior variables (e.g. MBPS, NFCS); Block 2 - infant variables (such as infant age or infant pre-needle irritability); Block 3 - maternal behavior in clinic; Block 4 - maternal psychosocial variables (e.g. global level of psychological distress, acculturation). If independent variables were inter-correlated greater than .7, only the predictor with the largest correlation with the dependent variable was retained to avoid multicollinearity (Tabachnick & Fidell, 2001). Finally, to contextualize the regression models, Bonferroni-corrected post-hoc analyses using t-tests were conducted to look at the differences on pain scores (i.e. the four dependent variables used in the regressions) across specific immunizations.

To maximize sample size, imputed means were used to replace missing data. Missing values that were replaced: NFCS 38/525 = 6%; Pre-needle irritability 3/75 = 4%

and MAISD $4/75 = 5\%$. To ensure that this procedure did not artificially inflate alpha levels nor change the estimated relations of individual predictors with the dependent variables, the 4 final models were also run using a listwise deletion strategy to handle missing values ($n=63$). No important differences were detected in terms of size or significance of Beta weights or in the R-square of each model. All variables were screened for outliers both at the univariate and multivariate stage and no significant outliers were detected. **Skewness and kurtosis for all variables were examined, and there were no strong indications of violation of normality assumptions for regression. However, the variable representing mother's pain judgment for the day after immunization (NRS Day 1) had a non-extreme violation of normality. The below analyses with this variable were replicated with a normalized transformation suggesting that non-normality did not bias that particular analysis.** Furthermore, four variables were excluded from further analysis due to extremely low variability (i.e., restriction of range)².

3. Results

3.1 Regression Analyses

3.1.1 Zero-order Correlations

Zero-order correlations were examined to determine potential predictors for each model (see Tables 1, 2, 3 and 4 for significant correlations). Surveying the correlation tables, different patterns were noted among the different dependent variables. When examining mother's pain judgment directly after immunization, the largest relationships were with infant variables (pain variables had the strongest relationships) while maternal

² Offer Toy, Offer Pacifier, Offer Food and Offer to Nurse were excluded. An examination of these variables indicated that >85% of mothers did not enact that behavior once during the entire study period.

behavior was less strongly related. However, when predicting maternal pain judgments for the day after the immunization, only maternal psychosocial variables were significant. Examining the correlations with both pain behavior measures, both infant and maternal factors were significant.

3.1.2 Regression Models (See Table 5 for Summaries of Final Models)

3.1.2.1 Model 1: Maternal Pain Rating Directly After Immunization: Using the hierarchical regression strategy described above, after all blocks were entered into the model, only the MBPS was a significant predictor of mother's pain judgment. The final model was estimated with only MBPS as a predictor. The adjusted R^2 for this model was .375.

3.1.2.2 Model 2: Maternal Pain Rating for Day After Immunization: The issue of multicollinearity arose in this model due to a large correlation between two of the predictor variables (Global Severity Index [GSI] and Positive Symptom Distress Index [PSDI]). Thus, the PSDI was excluded from the analysis. After all blocks were entered into the model, only two variables had significant Beta weights. The final model was estimated with only the GSI and the scale measuring one's identification with North American culture as predictors. The adjusted R^2 for this model was .191.

3.1.2.3 Model 3: Pain Facial Activity Directly After Immunization: After all blocks were entered into the model, two of the seven variables had significantly predicted NFCS scores. The final model was estimated with only the MBPS and the Dismissing subscale as predictors and the adjusted R^2 was .356.

*3.1.2.3 Model 4: **Composite** Measure of Pain Reactivity Directly After Immunization:* After all blocks were entered into the model, three variables had significant Beta-weights.

The final model was estimated with only NFCS, pre-needle irritability and maternal pain judgment as predictors. This model had an adjusted R^2 of .522.

3.2 Post-hoc Analyses

The previous analyses were interested in predicting subjective and objective measures of infant pain, regardless of the actual pain intensity. However, due to the cross-sectional nature of these analyses, infants were administered different types of immunizations. Moreover, 60% percent of the infants received more than one type of immunization injection during the visit. Small sample sizes and/or significant violations of homogeneity of variance precluded any comparative analysis of infants who received only one immunization versus those who received two or more. Thus, in order to contextualize our previous models, post-hoc analyses were conducted to explore if different combinations of immunizations resulted in differences among the maternal and behavioral measures of infant pain (see Table 6).

3.2.1 Age: The mean infant ages for each immunization combination (that utilized one of 6 specific immunizations) demonstrated that Menigitec and Hepatitis B were administered to the youngest children, while Varicella was administered to the oldest cohort of children.

3.2.2 Mean Number of Needles: MMR and Prevnar were most likely to be administered with another immunization (93.3% and 84.8% of the time, respectively) with the Varicella and Hepatitis B least likely to be administered with another immunization (40% and 60% of the time, respectively).

3.2.3 Mean Pain Ratings of Immunization Combinations with a Specific Vaccine: Mean pain ratings for infants who received each of the 6 specific immunizations (collapsed

over infants who received only that specific immunization and infants who received that specific immunization in combination with another immunization) was calculated for each of the four pain measures (See “Yes” columns in Table 6) .

3.2.4 Comparing Pain Scores: Immunization Combinations with a Specific Vaccine

versus without the Specific Vaccine: For each immunization type, mean scores on each of the four pain measures were compared using 24 independent samples t-tests (i.e. comparison of “Yes” versus “No” cells within each column; see Table 6). A Bonferroni-correction was applied to a family-wise error rate of 10% (.0042 per test). For the following vaccines, no differences were found between combinations that involved the vaccine versus combinations that did not: Prevnar, Menigitec, MMR, and Penta.

Only on the Modified Behavior Pain scale were significant differences found. Infants who received a combination involving the Varicella vaccine ($M = 7.70$, $SD = 1.05$; $n = 10$) had higher pain scores than infants that did not ($M = 5.70$, $SD = 1.82$; $n = 65$); while infants who received the Hepatitis B vaccine ($M = 5.00$, $SD = 2.25$; $n = 20$) had lower pain scores than infants that did not ($M = 6.33$, $SD = 1.59$; $n = 55$). Although not significant using the Bonferroni alpha level of .0042, it was noted that maternal pain judgements right after the immunization also suggested ($p = .011$) that infants who received the Varicella vaccination had higher pain scores than infants who did not.

4. Discussion

4.1 Discussion of Findings

To our knowledge, this study provides the first empirical confirmation that maternal variables from domains hypothesized by the Sociocommunication Model of Infant Pain (individual, familial, community, cultural) significantly predict infant pain.

Mother's immediate pain judgment was most strongly related to the composite measure of infant pain (MBPS). No other predictor produced a significant relationship with maternal pain judgment, including the specific facial pain measure, once the MBPS was controlled. The importance of facial expression to making pain judgments in infancy has been substantiated by a number of empirical studies, reviewed by Craig, Prkachin & Grunau (2001) and through studies that asked the parents themselves (Pillai Riddell, Badali et al., 2004). Although supporting the importance of facial expression, the current findings further suggest that maternal pain judgments of their non-verbal infants is more heavily determined by the combination of the infant's general display of negative face, body and cry, rather than the infant's specific pain face. Further supporting this relationship was the model that demonstrated maternal judgments predicted the composite pain measure even after the infant variables (infant pain face and irritability) were entered. From an evolutionary perspective, it appears adaptive that mothers would base assessments on, and infants would be capable of mounting, a concurrent display of different pain-related behaviors. However, it is important to qualify that these findings may not be generalizable to ambiguous situations (e.g., when mother is not sure why infant is distressed and is required to assess infant pain).

The choice of using a measure that tapped into the specific pain facial display (NFCS) and a pain measure that more generally evaluates face, body movement and cry (MBPS) was a deliberate one. An examination of the model that predicted specific facial pain reactivity directly after an immunization results in different findings than the model described above predicting the MBPS. After controlling for the composite of distress behavior, a significant amount of variance was predicted by mothers' self-report of

dismissive relationship tendencies. The negative relationship suggests that the more dismissive a mother reports she is in relationships (e.g., avoiding dependence on others or having other depend on her), the less pain reactivity was seen in the infant's face. It is noteworthy that the negative relationship between maternal avoidance strategies in caregiving and infant distress behavior has also been found in research using non-pain distress paradigms (Goldberg, 2000; Bradley, 2001).

Comparing these two models predicting the objective measures of pain, an interesting question arises regarding why mothers' dismissing relationship style was only related to the specific pain facial measure but not the composite pain measure. The composite pain measure is based on the intensity of cry, face and body movement. Although created for a pain context, an examination of the subscales suggests that an infant could also score highly if distressed by a non-pain stimulus (e.g. facial activity is scored used anchors of 0 = definite positive expression and 3 = definite negative expression). Pragmatically, there is nothing about the behavioral descriptions provided in the measure is specific to a pain-distress response. However, the specific infant pain facial measure was initially based on an adult coding system that demonstrated discriminant validity with adults expressing different emotions such as sadness or anger (Craig, Prkachin et al. 2001). Thus, perhaps the relationship between the dismissing relationship style and NFCS could be related to the fact that NFCS is measuring a pain factor that is above and beyond a general distress display. Thus, although speculative, a mother who strongly endorses a dismissive relationship style could be conditioning an infant to try and reduce his/her specific display of pain-related distress (in order to avoid mother's avoidance). However, the immediate general distress after an immunization

may be less under the control of the infant and not related to maternal contingencies. Further research using more in-depth measures of adult attachment style (such as the Adult Attachment Interview; George, Kaplan et al, 1996) or adult close relationship style (such as the History of Attachments Interview (Bartholomew, Henderson et al. 2000) in the infant pain context would be needed to follow up on these hypotheses.

The issue of what different pain measures are actually measuring was also seen in the post-hoc analyses exploring the different pain levels across immunization combinations. Absolute comparisons of the pain level associated with a particular type of immunization cannot be answered because of the commonplace practice of administering more than one immunization. However, when comparing the pain levels of immunization combinations, across the four different dependent variables, only two significant differences were found - both on the MBPS. When comparing infants who received a combination involving Varicella to infants who did not receive the Varicella vaccine, it was found that the Varicella group had significantly higher composite pain ratings (MBPS). Conversely, the infants who received a combination involving Hepatitis B vaccine had lower pain scores than infants who did not receive the vaccine. Although a stringent alpha level was necessitated by the number of statistical tests run, even using a more liberal alpha (such as $p < .01$, with a resultant family-wise error rate $\leq .24$) would not result in more significant findings across pain measures. These findings suggest that as a measure of infant reactivity after a noxious stimulus is applied, the Modified Behavior Pain Scale is a more sensitive measure than both maternal ratings via NRS and infant facial activity using NFCS.

To further understand why these injections were significantly different, the nature of the immunizations were examined. The Hepatitis B vaccine is the vaccine with the smallest volume injected (.5 millilitres [ml]; all others were .25 ml); however, it is not entirely clear why only the Varicella vaccine resulted in significantly more distress, as it is similar in route, volume and pH level to the MMR vaccination (all the other vaccines are given intramuscularly in the thigh). These speculations should be taken with caution as there could be order effects (Varicella is never administered first in the series of infant immunizations), age biases (Hepatitis B had some of the youngest infants, while Varicella had the oldest infants) or another product in the vaccine (adjuvants), which could be impacting these findings.

The final point for discussion appears to be the most surprising. Two maternal psychosocial variables (general level of maternal psychopathology and mother's identification with North American culture) were the only significant determinants of Day 1 maternal pain recall. Both higher psychopathology and lower levels of identification with mainstream culture could be considered significant stressors. In this vein, this model suggests that significant stressors in the mother's life are linked to greater recall of infant pain for the day after an immunization.

The emergence of maternal psychosocial factors as strong predictors of a pain recollection but not for an immediate pain judgment of pain is a novel finding. As high levels of stress and psychopathology have been linked to negative attribution biases and negative recall biases (Lovejoy, Graczyk et al 2000; Seifer & Dickenstein, 2000), perhaps mothers who reported greater psychopathology and acculturative stress had higher recall of infant pain due to negative cognitive biases. However, as this was not an experimental

study, causation cannot be inferred. Therefore another feasible hypothesis is that stressed mothers have infants who are more stressed and stressed infants take longer to regulate after a painful stimulus; thus, mothers are accurately remembering the infant's pain level.

In conclusion, we have provided preliminary empirical validation for the theoretical premise that maternal factors are related to measures of infant pain, even after infant variables are controlled. In order to better understand the nature of these relationships, an important direction for future research is to examine the interaction of infant and maternal factors over time.

4.2 Discussion of Limitations

Due to the vigorous behavioral movement in the period immediately following the immunization, roughly 20% of raw facial data was lost due to infant movement. Whereas the application of the constancy rule helped to alleviate a systematic bias against infants who were more vigorously responding post-immunization, this may have impacted our results. Also, other infant and maternal factors that could account for study findings such as infant age, maternal age, number of prior born children and maternal education level need to be included in future research. Moreover, although all our questionnaires asked mothers to respond based on the "last two weeks" (thus covering the period of the immunization), the maternal questionnaire variables were obtained after the in-clinic video footage. Finally, because of the sample size and sample composition (all mothers were English speaking), more research is needed to examine the effects of the variables that were dropped to form the final models before discounting their role in predicting infant pain.

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References

Agency for Health Care Policy and Research. Acute Pain Management: Operative or Medical Procedures and Trauma. Clinical Practice Guidelines (Rep. No. AHCPR Pub. No. 92-0032). Rockville: U.S. Department of Health and Human Services, 1994.

American Psychological Association. Guidelines on multicultural education, training, research, practice and organisational change for psychologists. *Am Psychol* 2003; 58:377-402.

Bartholomew K, Henderson AJZ, Marcia JE. Coded semi-structured interviews in social psychological research. In: Reis HT, Judd CM, editors. *Handbook of Research Methods in Social Psychology*. Cambridge: Cambridge University Press, 2000. pp. 286-312.

Blount RL, Cohen LL, Frank NC, Bachanas PJ, Smith AJ, Manimala RM, Pate JT. The Child-Adult Medical Procedure Interaction Scale-Revised: An assessment of validity. *J Pediatr Psychol* 1997; 22: 689-705.

Bowlby J. *Attachment*, 2nd ed. USA: Tavistock Institute of Human Relations, 1969/1982.

Bradley SJ. *Affect Regulation and the Development of Psychopathology*. New York: The Guildford Press, 2001.

Cohen LL, Bernard RS, McClellan CB, MacLaren JE. Assessing medical room behavior during infants' painful medical procedures: The measure of adult and infant soothing and distress (MAISD). *Children's Health Care* 2005; 34: 81-94.

Cohen, J., Cohen, P., West, S.G., & Aiken, L.S. (2003). *Applied multiple regression/correlation analysis for the behavioral sciences* (3rd ed.). Mahwah, NJ: Lawrence Erlbaum.

Condon JT, Corkindale CJ. The assessment of parent-to-infant attachment: Development of a self-report questionnaire instrument. *J Reprod Infant Psychol* 1998;16:57-76.

Craig KD, Lilley CM, Gilbert CA. Social barriers to optimal pain management in infants and children. *Clin J Pain* 1996;12: 232-242.

Craig KD, Prkachin KM, Grunau RE. The facial expression of pain. In: Turk DC, Melzack R, editors. *Handbook of Pain Assessment*, 2nd Edition. The Guildford Press: New York, 2001. pp. 153-169.

Craig KD, Pillai Riddell R. Social influences, culture and ethnicity. In: Finley GA, McGrath PJ, editors. *Pediatric pain: biological and social context*. Seattle: IASP Press, 2003.

Craig KD, Whitfield MF, Grunau R, Linton J, Hadjistavropoulos HD. Pain in the preterm neonate: behavioral and physiological indices. *Pain* 1993;52:287-299.

Crockenberg S, Leerkes E. Infant Social and Emotional Development in Family Context. In: Zeanah CH Jr, editor. *Handbook of Infant Mental Health*. New York: The Guilford Press, 2001. pp. 60-90.

Derogatis L. *The Brief Symptom Inventory: Administration, scoring, and procedures manual* (3rd ed.). Minneapolis: National Computer Systems, Inc, 1993.

Ekman P, Friesen WV. *Facial Action Coding System Investigator's Guide*. 1978.

George C, Kaplan N, Main M. Adult Attachment Interview Protocol 3rd Edition. University of California at Berkeley: Unpublished Protocol, 1996.

Goldberg S. *Attachment & Development*. London: Oxford University Press, 2000.

Goubert L, Craig KD, Vervoort, T, Morley S, Sullivan MJL, C. de C. Williams A, Cano A, Crombez G. Facing others in pain: the effects of empathy. *Pain* 2005; 118:285-288.

Green SB. How many subjects does it take to do a multiple regression analysis? *Multivariate Behavioral Research* 1991;26: 499-510.

Griffin D, Bartholomew K. Models of the Self and Other: Fundamental Dimensions Underlying Measures of Adult Attachment. *J Pers Soc Psychol* 1994;67:430-445.

Grunau RV, Craig KD. Pain expression in neonates: facial action and cry. *Pain* 1987; 28: 395-410.

Jensen MP, Karoly P, O’Riordan EF, Bland F Jr, Burns RS. The subjective experience of acute pain. An assessment of the utility of 10 indices. *Clin J Pain* 1989;5:153-159.

Jensen MP, Karoly P. Self-Report Scales and Procedures for Assessing Pain in Adults. In: Turk DC, Melzack R, editors. *Handbook of Pain Assessment*. New York: The Guilford Press, 2001. pp. 15-34.

Lovejoy MC, Graczyk PA, O’Hare E, Neuman G. Maternal depression and parenting behavior: A meta-analytic review. *Clin Psychol Rev* 2000;20: 561-592.

Oberlander TF, Grunau R, Whitfield MF, Fitzgerald C, Pitfield S, Saul JP. Biobehavioral Pain Responses in Former Extremely Low Birth Weight Infants at Four Months' Corrected Age. *Pediatrics* 2000;105:e6.

Pillai Riddell R. The Attribution of Pain to The Infant: A Comparative Analysis of Parent, Nurses and Pediatricians. Dissertation (University of British Columbia) 2004.

Pillai Riddell R, Badali MA, Craig KD. Parental judgments of infant pain: importance of perceived cognitive abilities, behavioral cues and contextual cues. *Pain* 2004;9:73-80.

Pillai Riddell RR., Chambers CT. Parenting and pain during infancy. *Pain in Neonates and Infants*, 3rd Edition. Edinburgh: Elsevier Limited, in press.

Pillai Riddell RR, Stevens BJ. Invited Response to Boyle, Freer, Wong, McIntosh & Anand's commentary on Looking Beyond Acute Pain in Infancy (in press). *Pain*.

Ryder AG, Alden LA, Paulhus DL. Is acculturation unidimensional or bidimensional?: A head-to-head comparison in the prediction of personality, self-identity, and adjustment. *J Pers Soc Psychol* 2000; 79: 49-65.

Seifer R, Dickenstein S. Parental mental illness and infant development. In: Zeanah CH Jr, editor. *Handbook of Infant Mental Health*, 2nd Edition. New York: The Guilford Press, 2000. 145-160.

Solodiuk J, Curley MA. Pain assessment in nonverbal children with severe cognitive impairments: the Individualized Numeric Rating Scale. *J Ped Nurs* 2003; 18:295-299.

Stevens B, Pillai Riddell RR, Oberlander T, Gibbins S. Assessment of pain in neonates and infants. *Pain in Neonates and Infants*, 3rd Edition. Edinburgh: Elsevier Limited, in press.

Tabachnick BG, Fidell LS. *Using Multivariate Statistics*, Fourth Edition. Boston: Allyn and Bacon, 2001.

Taddio A, Nulman Irena, Koren BS, Stevens B, KorenG. A revised measure of acute pain in infants. *J Pain Symptom Manage* 1995;10:456-463.

Winnicott, DW. The theory of the parent-child relationship. *Intl J Psychoanal* 1960;41: 585-595.

Zimet GD, Dahlem NW, Zimet SG, Farley GK. The Multidimensional Scale of Perceived Social Support. *J Pers Assess* 1988; 55: 610-617.

Figure 1: Participant Flowchart

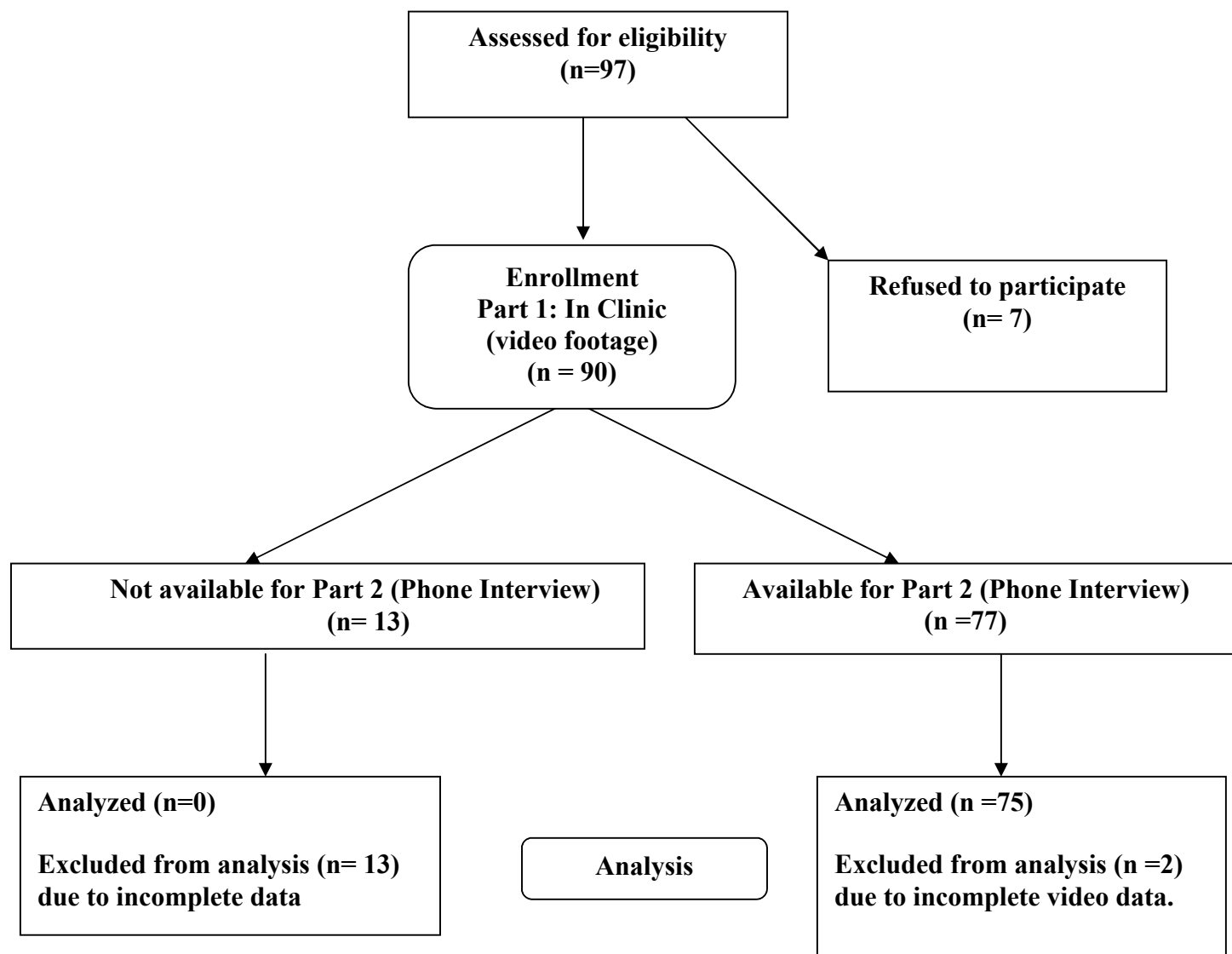


Table 1: Variables with a Significant Zero-Order Correlation with Maternal Judgments of Infant Pain in clinic (NRS-DAY 0)

	NRS-DAY 0 (Maternal judgment of infant pain in clinic)	NFCS (Facial Pain Measure)	MBPS (Global Pain Measure)	Infant Age	Pre-needle Irritability (MBPS-baseline)	Mother Behavior: MAISD - Physical Comfort	Mother Behavior: MAISD-Rocking
NFCS	.448***	1.0	.573***	.074	.186	.307**	.266*
MBPS	.619***	.573***	1.0	.237*	.431***	.263*	.312**
Infant Age	.247*	.074	.237*	1.0	.355**	-.117	.177
Pre-Needle Irritability (MBPS-baseline)	.338**	.186	.431***	.355**	1.0	-.020	.310**
MAISD-Physical Comfort	.271*	.307**	.263*	-.117	-.020	1.0	.236*
MAISD-Rocking	.290*	.266*	.312**	.177	.310**	.236*	1.0

Note: Column one (NRS-DAY 0) delineates all variables with significant correlations with NRS-DAY 0. Columns 2 to 7 indicate intercorrelations among all the variables that have significant correlations with NRS-DAY 0.

*significant at $p < .05$

**significant at $p < .01$

***significant at $p < .001$

Table 2: Variables with a Significant Zero-Order Correlation with Maternal Judgments of Infant Pain for Day After Immunization (NRS-DAY 1)

	NRS DAY 1 (Maternal recall of infant pain for day after immunization)	Global Severity Index of the Brief Symptom Inventory (GSI)	Positive Symptom Distress Index of the Brief Symptom Inventory (PSDI)	Absence of Hostility subscale of the Maternal Postnatal Attachment Scale (HOST)	Acculturation to North America subscale of the Vancouver Index of Acculturation (America)	Dismissive Relationship Style subscale of the Relationship Scales Questionnaire (Dismiss)
GSI	.367**	1.0	.860***	.431***	.029	.154
PSDI	.337**	.860***	1.0	.353**	-.024	.210
HOST	.231*	.431***	.353**	1.0	-.059	-.079
America	-.270*	.029	-.024	-.059	1.0	-.148
Dismiss	.257*	.154	.210	-.079	-.148	1.0

Note: Column one (NRS-DAY 1) delineates all variables with significant correlations with NRS-DAY 1. Columns 2 to 6 indicate intercorrelations among all the variables that have significant correlations with NRS-DAY 1.

*significant at $p < .05$

**significant at $p < .01$

***significant at $p < .001$

Table 3: Variables with a Significant Zero-Order Correlation with Neonatal Facial Coding Scale Summary Score (NFCS)

	NFCS (Facial Pain Measure)	Dismissive Relationship Style subscale of the Relationship Scales Questionnaire (Dismiss)	Pre-needle Irritability (MBPS-baseline)	Mother Behavior: MAISD - Physical Comfort	Mother Behavior: MAISD-Rocking	MBPS (Global Pain Measure)	NRS-DAY 0 (Mother Pain Judgment in Clinic)
Dismiss	-.241*	1.0	.176	-.148	.013	-.050	-.199
MAISD-Physical Comfort	.307**	-.148	-.068	1.0	.236*	.263*	.271*
MAISD-Rocking	.266*	.013	.188	.236*	1.0	.312**	.290*
MBPS-baseline	.573***	-.050	.422***	.263*	.312**	1.0	.619***
NRS-DAY 0	.448***	-.199	.339**	.271*	.290*	.619***	1.0

Note: Column one (NFCS) delineates all variables with significant correlations with NFCS. Columns 2 to 7 indicate intercorrelations among all the variables that have significant correlations with NFCS.

*significant at $p < .05$

**significant at $p < .01$

***significant at $p < .001$

Table 4: Variables with a Significant Zero-Order Correlation with Modified Behaviour Pain Scale Score (MBPS)

	MBPS (Global Pain Measure)	NRS-Day 0 (Mother Pain Judgment in Clinic)	NFCS (Facial Pain Measure)	Infant Age (age)	Pre-Needle Irritability (MBPS-baseline)	Mother Behavior: MAISD-Rocking	Mother Behavior: MAISD - Physical Comfort
NRS Day-0	.619***	1.0	.448***	.247*	.338**	.290*	.271*
NFCS	.573***	.448***	1.0	.074	.186	.266*	.307**
Infant Age	.237*	.247*	.074	1.0	.355**	.177	-.117
Pre-needle irritability (MBPS-baseline)	.431***	.338**	.186	.355**	1.0	.310**	-.020
MAISD-Rocking	.312**	.290*	.266*	.177	.310**	1.0	.236*
MAISD-Physical Comfort	.263*	.271*	.307**	-.117	-.020	.236*	1.0

Note: Column one (MBPS) delineates all variables with significant correlations with MBPS. Columns 2 to 7 indicate intercorrelations among all the variables that have significant correlations with MBPS.

*significant at $p < .05$

**significant at $p < .01$

***significant at $p < .001$

Table 5: Final Regression Model Summary Table for the Maternal and Behavioural Pain Scales

Outcome	Predictor	Beta	<i>Actual p-value</i>	Final Model R ²	Adjusted R ²
NRS-0	MBPS	.619	.001	.383	.375
	GSI	.375	.001	-	-
NRS-1	America	-.281	.009	.213	.191
	MBPS	.562	.000	-	-
NFCS	Dismiss	-.213	.025	.374	.356
	MBPS	.350	.000		
MBPS	Irritability	.236	.007		
	NRS-Day 0	.378	.000	.542	.522

NRS-Day 0= Maternal Pain Judgment after immunization

NRS-Day 1= Maternal Pain **Recall** for the day after the immunization

NFCS = Neonatal Facial Coding Scale **post-needle**

MBPS = Modified Behaviour Pain Scale- post needle

GSI = Global Symptom Index **of the Brief Symptom Inventory** (GSI)

America = Identification with North American Culture **subscale of the Vancouver Index of Acculturation**

Dismiss = Dismissing subscale of the Relationship Scales Questionnaire

Irritability = Modified Behaviour Pain Scale – baseline pre-needle

Table 6: Table with Age, Mean Number of Immunizations and Mean Pain Values (using NRS-DAY 0, NRS DAY 1, MBPS, NFCS) for Infants Receiving a Specific Vaccination (Pevnar, Varicella, Menigitec, MMR, Penta, Hepatitis B) versus Infants that did not.

Specific Immunization administered (number of infants who received vaccination)	Mean Age of Infants Receiving Specific Immunization- in Months (SD in brackets) and Age Range	Mean Number of Needles given to Infants Receiving Specific Immunization (% of babies receiving more than 1 needle in brackets)	Mean Maternal NRS-DAY 0 (Range 0-10) in Clinic for all babies who received specific immunization versus not (SD in brackets)	Mean Maternal NRS-DAY 1 (Range 0-10) for day after immunization for babies who received specific immunization versus not (SD in brackets)	Modified Behaviour Pain Scale – MPBS (Range 0-10) for babies who received specific immunization versus not (SD in brackets)	Neonatal Facial Action Coding Scale - NFCS (Range 0-35) for babies who received specific immunization versus not (SD in brackets)
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			Yes	No	Yes	No	Yes	No	Yes	No
Pevnar (33)	11.07 (4.57) Age Range: 5 to 20	1.85 (84.8 % received Pevnar and another immunization)	5.00 (2.38)	5.14 (2.79)	1.36 (1.83)	2.09 (2.55)	6.03 [^] (1.28)	5.92 [^] (2.23)	23.24 (7.96)	21.94 (8.81)
Varicella (10)	15.50 (1.77) Age Range: 13 to 20	1.4 (40%)	7.00 ^{**} (1.82)	4.78 ^{**} (2.59)	2.80 (2.48)	1.61 (2.22)	7.70^{***} (1.05)	5.70^{***} (1.82)	25.76 (5.74)	22.01 (8.68)
Menigitec (15)	7.80 (4.22) Age Range: 5 to 16	1.86 (73.3%)	4.93 (2.57)	5.11 (2.63)	1.46 (1.80)	1.85 (2.39)	5.66 (1.44)	6.05 (1.96)	21.93 (5.99)	22.66 (8.95)
MMR (15)	13.07 (2.25) Age Range: 12 to 19	1.93 (93.3%)	6.20 (2.67)	4.80 (2.53)	1.26 (2.08)	1.90 (2.32)	6.40 (1.76)	5.86 (1.89)	23.78 (7.48)	22.20 (8.66)
Penta (25)	11.10 (5.93) Age Range: 5 to 20	1.76 (68%)	4.52 (2.55)	5.36 (2.61)	1.80 (2.17)	1.76 (2.35)	5.84 (1.46)	6.04 (2.04)	22.67 (7.95)	22.43 (8.71)
Hepatitis B (20)	7.95 (3.25) Age Range: 5 to 17	1.65 (60.0)	4.40 (2.82)	5.12 (2.51)	1.95 (2.74)	1.71 (2.11)	5.00^{***} (2.25)	6.33^{***} (1.59)	20.10 (8.98)	23.39 (8.11)

NOTE: The last 4 columns indicate pain ratings (on each of the 4 infant pain measurements indicated) for infants who received an immunization combination involving the immunization indicated by the row ("Yes" sub-column) versus those that received an immunization combination that did not involve the immunization indicated by the row ("No" subcolumn).

[^]Violated homogeneity of variance assumption, Welch's statistic used

^{**}T-test significant at p < .05;

^{***} T-test significant at p < .0042