

The impact of parental pain- and non-pain-attending responses upon child pain behavior in the context of cancer-related painful procedures: the moderating role of parental self-oriented distress.

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Running title: Parental distress and child pain behavior.

ABSTRACT

Objectives: Literature has demonstrated inconsistent findings regarding the impact of parental responses upon child pain-related outcomes. Yet, research into factors that may underlie inconsistent findings regarding the variable impact of parental responses is lacking. The current study investigated the moderating role of parental distress in understanding the impact of parental pain-attending (e.g., reassuring the child) and non-pain-attending (e.g., distracting the child with humor) responses upon child pain behavior (e.g., crying). **Methods:** Children (≤ 18 years) suffering from leukemia, undergoing a lumbar puncture (LP) and/or bone marrow aspiration (BMA) procedure, and one of their parents, were recruited from the Pediatric Ghent University Hospital. Parent-child interactions were videotaped after the procedure allowing coding of parental responses and child pain behavior. Parents self-reported on experienced personal distress. **Results:** Participants consisted of 42 children (24 boys, 18 girls) with leukemia and one of their parents. Children were 0.6-15 (7.08 ± 4.39) years old. Findings indicated a positive association between parental pain-attending and child pain behavior, but only when parents reported high levels of distress ($\beta = .56$, $p = .001$). No association was observed for parents reporting low levels of distress ($\beta = -.09$, ns). Parental non-pain-attending responses contributed to lower child pain behavior ($\beta = -.24$, $p = .045$), independently from parental distress ($\beta = -.07$, ns). **Discussion:** The current findings point to the moderating role of parental distress in understanding the impact of parental responses upon child pain behavior and highlight the importance of interventions targeting parental emotion regulation to promote more optimal child pain outcomes.

Key Words: invasive medical procedures, childhood leukemia, parental distress, parental responses, child pain behavior

INTRODUCTION

Pain is very prominent during cancer treatment as children with cancer undergo numerous invasive medical procedures, such as venipunctures, lumbar punctures (LP) and bone marrow aspirations (BMA). Despite innovative technologies resulting in less pain during such invasive procedures (1, 2), these procedures often remain major stressors for the child both in the short and long term (1-3). Specifically, in the short term they often provoke significant pain, anxiety and distress in the child (4, 5). In the long term, children may show significantly prolonged changes in behavior, alterations in self-concept, fear, anxiety, and depression, and a greater predisposition to chronic pain in adulthood (6, 7). In addition, these procedures may also be a major stressor for the parent, whose beliefs and responses may, in turn, influence the child's coping with the cancer treatment (4, 8-10).

Empirical evidence has demonstrated that parental responses during painful medical procedures are critically important in understanding child's pain-related outcomes. Certain types of parental responses have been identified as negatively impacting child pain outcomes whereas other responses may promote child positive coping behavior. For instance, literature has indicated that parental protective or pain-attending responses (verbal and non-verbal behavior towards the child that is focused upon the child's pain, such as reassuring and comforting the child), contribute to increased child pain behavior (verbal and non-verbal behavior focusing on the pain experience, such as crying or saying "It hurts a lot") and distress (11-18). Conversely, parental non-pain-attending behavior (verbal and non-verbal behavior towards the child that is not focused upon the child's pain, such as trying to distract the child

with humor) may promote child adaptive coping (19, 20). However, evidence is not unequivocal. Some studies have failed to find expected associations, whereas others observed evidence counter to expectations. For example, Poppert Cordts et al. (2019) (21) recently demonstrated, amongst a sample of children suffering from chronic pain, that parental protectiveness was unrelated to child pain and pain-related interference. Likewise, Kaczynski et al. (2013) (22) observed amongst a sample of children with chronic headaches, that parent protectiveness was not associated with child pain frequency, duration or intensity, which contradicts prior work in youth with acute musculoskeletal pain (23) and pediatric patients undergoing leukemia-related painful medical procedures (11). Other evidence points at complex relationships, moderated by child characteristics. For instance, Connelly et al. (2010) (24) found, in a sample of children with juvenile idiopathic arthritis, that the use of distracting responses by parents significantly predicted less child activity restrictions, but only in children with higher disease severity. They further observed an unexpected trend in which parents' higher use of distracting responses tended to be related to lower child positive mood. To date, systematic research into factors that may underlie inconsistent findings regarding the impact of certain types of parental responses (e.g., pain-attending and non-pain-attending) is lacking. It has previously been argued that chronic pain status (i.e., acute versus chronic) may account for the maladaptive impact of certain types of responses (e.g., protective or pain-attending responses) (17, 25, 26), yet above cited evidence suggests such account is insufficient to explain inconsistent findings.

While a number of variables may influence the variable impact of parental responses on child outcomes, literature suggests that parental *self-oriented* distress elicited by facing child's pain

may be particularly vital in this regard (11, 27). Self-oriented distress can be defined as “feelings of personal discomfort and distress when witnessing another’s negative experience” (28). Specifically, studies have shown that another’s pain activates neural representations of personal pain (29-32), as well as self-oriented aversive emotional responses (33), suggesting that observing pain automatically references the self. Self-oriented parental distress, in turn, has consistently been found to contribute to negative child pain related outcomes such as more child distress, pain, and pain behavior (11, 34, 35), as well as functional disability (36, 37). Whilst evidence has demonstrated that parental distress mainly predisposes parents to engage in protective or pain-attending responses rather than non-pain-attending responses (25, 34), a recently proposed affective motivational theoretical account on interpersonal pain dynamics (27) posits that parental self-oriented distress may underlie *either* category of caregiving behaviors. Critically, the **model** posits that varying levels of self-oriented distress account for observed differential effects of similar types of caregiving. In particular, it is posited that in the absence of adequate regulation of distress, parental protective or pain-attending responses may negatively impact child outcomes, whereas similar behavior may exert more beneficial effects when accompanied by low levels of parental distress. In a similar vein, the effect of parental non-pain-attending responses may largely depend upon whether or not such behavior is accompanied by high levels of parental distress. However, whether parental self-oriented distress modulates the impact of parental responses remains as yet to be examined.

The aim of the current study was to investigate the moderating role of parental self-oriented distress in understanding the impact of parental responses (i.e., protective/pain-attending and

non-pain-attending responses) upon child pain behavior. Study aims were examined amongst children diagnosed with leukemia, and one of their parents. Using observational assessment of parent and child behaviors after LP/BMA procedures, we hypothesized that 1) parental protective/pain-attending behavior would be positively associated with child pain behavior, but with effects being particularly pronounced for parents experiencing high levels of distress and less so for parents experiencing low levels of distress. Conversely, we expected that 2) parental non-pain-attending behaviors would be negatively associated with child pain behavior, with effects being most pronounced for parents experiencing low levels of distress and less so for parents experiencing high levels of distress.

METHODS

Participants

Children (≤ 18 years old) suffering from leukemia, undergoing a lumbar puncture (LP) and/or bone marrow aspiration (BMA) procedure, and one of their parents, were recruited from the Pediatric Oncology/Hematology and Stem Cell Transplantation Department of the Ghent University Hospital. Children were recruited between December 2009 and June 2011. To control for the role of the children's stage of treatment, parents of children in different stages of the treatment process were recruited: recently diagnosed (i.e., induction phase), diagnosed several months ago but still receiving intensive treatment (i.e., consolidation phase), or less intense maintenance treatment (i.e., maintenance phase) were eligible to participate. No quota was set in order to include equal amounts of children in different stages of treatment. Exclusion criteria to participate in this study comprised: 1) any developmental delay in the child or 2) the inability of the parent to speak and write Dutch.

The analyses presented in the current article are additional analyses performed on the clinical sample reported in 3 previous studies by Caes and colleagues (i.e., Investigation of the mediating role of parental distress during the LP/BMA procedures in the relation between state catastrophizing of parents and parental postprocedural pain-attending behavior (11); Prospective longitudinal study to investigate how parents' distress in the context of the LP/BMA procedures evolves over time as a function of parental catastrophizing about the child's procedural pain and child distress (35); Investigation of the relationship between caregivers' distress and sympathy when faced with the child's pain upon caregivers' estimation of the

child's pain (38)). Research questions assessed in the current study (i.e., investigation of the moderating role of parental self-oriented distress in understanding the impact of parental responses upon child pain behavior) are different from previously published work.

Study overview

The present study is part of the “Ghent-Pain in Child Leukemia-study” (G-PICL study), investigating parent-child interactions in the context of childhood leukemia. Parents accompanied their child to the treatment room where the LP/BMA procedure was going to take place. During the pre-procedural phase parents were allowed to be present, as well as during the postprocedural phase (aftercare). According to the standard management of the Ghent University Hospital, parents were not allowed to be present during the LP/BMA procedure itself. The parents had to leave the room as soon as the doctor was ready to start the LP/BMA procedure and were allowed back in as soon as the procedure was completed (i.e., a few minutes after the needle was out and the doctor reported to be ready for the parent to come back in). Each child was entrusted with one of the three child-life specialists of the Department of Pediatric Oncology/Hematology and Stem Cell Transplantation at the Ghent University Hospital at the moment of the diagnosis. The child-life specialists accompanied the children during each painful medical procedure, administered nitrogen peroxide oxygen and promoted child coping behavior during each procedure (e.g. providing procedure-relation information, distracting the child, etc.), as this is the standard care in the Ghent University Hospital. The child-life specialists explained the procedural aspects to the child and parent to prepare them

for the LP/BMA procedures. According to standard practice of the hospital, the parents did not receive specific instructions on how to support their child in coping with the procedures.

For the purpose of the study, parent-child interactions occurring after the LP/BMA procedure were videotaped, as the parent returned to the child's room. During the postprocedural phase parents were asked to rate their experienced level of distress while the child underwent the LP/BMA procedure.

Measures

Parental distress during LP/BMA procedure

Parents reported on self-oriented distress in response to their child's LP/BMA procedure through a series of 4 emotion adjectives (worried, upset, anxious and sad), based on the work of Batson et al. (1987) (39). The use of emotional adjectives is a short and easy-to-use method to assess distress in response to a specific situation (34, 40), in this case parental distress as a reaction to their children's LP/BMA procedure. All emotion adjectives were rated on an 11-point scale ranging from 0 (not at all) to 10 (extremely). The mean score of parental distress, ranging from 0 to 10, was calculated, whereby higher scores represented higher levels of parental distress. This method has proven to be valid and reliable (34, 39, 40). Cronbach's alpha within the present study was high ($\alpha = 0.90$).

Parent and child behavior

Parent-child interaction after the LP/BMA procedure was videotaped, allowing coding of parent and child behavior. Recording started when the parent reentered the treatment room after completion of the LP/BMA procedure until the parent and child left the treatment room. The

coding system used to code the parent and child behaviors was based on a coding scheme developed by Walker et al. (2006) (41) which draws on the CAMPIS-R (Blount, 1997) (19). However, in addition to coding parent/child verbal utterances, also parent/child non-verbal behaviors were coded. Non-verbal behavior codes were derived from those defined in the CAMPIS-SF (42), which includes non-verbal behaviors coded as either neutral (e.g., non-verbal praising), coping-promoting (e.g., using a blower) or distress-promoting (e.g., hugging and pats). Non-verbal behavior categories in the coding scheme of the current study (i.e., pain-attending versus non-pain-attending) are in accordance with the categories used by Walker et al. (2006) (41) (attending versus distracting talk) and the CAMPIS-R (19) (distress- versus coping-promoting behavior). Both the CAMPIS-R and CAMPIS-SF have been used in studies in child and adolescent populations from 6 months to 13 years of age, with identical basic interaction patterns presenting across this wide age range, supporting generalizability and appropriateness of the used coding scheme to the sample of this study with a wide age range (6 months – 15 years old) (11, 12, 43-45).

Our coding procedure comprised the following codes for parents' behavior: 1) Verbal/non-verbal pain-attending behavior, defined as any parental behavior that focused upon the child's pain experience (e.g., 'Did it hurt a lot?', 'Are you still in pain now?', holding the child's hand, stroking or patting the child), 2) Verbal/non-verbal non-pain-attending behavior, defined as parent behavior that did not focus upon the child's pain experience (e.g., smiling, making a joke, coping statement, praising the child by saying for example "You are doing great" or by showing the child a thumbs up) and 3) Other, which included parents' inaudible utterances, statements about technical aspects of the LP/BMA procedure and non-verbal behavior or utterances

directed to the medical staff. Codes for children's behavior included: 1) Child verbal/non-verbal pain behavior, defined as behavior negatively relating to the pain experience (e.g., "I don't want to do this anymore", "I was so scared", "It hurt a lot", crying); 2) Child verbal/non-verbal non-pain behavior, defined as child behavior not related to the pain experience (e.g., talking about something else, playing with a toy, ...); and 3) Other, defined as all other child utterances and behavior. For each 5s interval all parent and child behavior codes were rated as occurring (coded 1) or not occurring (coded 0). One primary coder coded all tapes and a second independent coder performed the same coding procedure for 25% of the tapes. Good interrater reliability for all coding categories was shown by Kappa reliability coefficients ranging from .60 to .93 (46). To control for the duration of the LP/BMA procedure, the total scores for parental pain-attending behaviors and non-pain-attending behaviors, as well as the total scores for child pain behaviors, were divided by the total amount of time intervals and then multiplied by 100.

Procedure

All children diagnosed with leukemia and hospitalized for a LP/BMA procedure between December 2009 and June 2011 were invited to participate together with their parents. Children and parents were informed about the main study objective, i.e., investigating the impact of child pain during LP/BMA procedures on the experiences of the parent with regard to these procedures. They were also ensured that whether they would decide to participate or not, this would have no influence on the child's treatment. A written informed consent was obtained from each parent (and child older than 12 years of age) in case of agreement to participate. After providing consent for participation, parents completed a sociodemographic questionnaire.

As the standard pain management of the clinic prescribes, an eutectic mixture of local anesthetics lidocaine and prilocaine (EMLA® cream) was applied to the child's skin approximately one hour before the start of the LP/BMA procedure (47). Subsequently during the LP/BMA procedure, a mixture of nitrogen peroxide-oxygen (i.e. 50% nitrous oxide and 50% oxygen) was administered by the child-life specialist to the children. This colorless gas brings the child in a conscious sedation and has an analgesic effect on the skin (48). In accordance with the Ghent University Hospital protocol, the LP/BMA procedure started after inhalation of the nitrogen peroxide-oxygen mixture through a face mask for at least 3 minutes. Parent-child interactions were videotaped after the procedure by the principal investigator (L.C.) or by one of the 6 research assistants, allowing coding of parental responses and child pain behavior. Both the investigator and research assistant kept interaction with the staff, parents, and child to the minimum during all phases of the procedure. Once the child and parent(s) had returned to the child's room after the LP/BMA procedure, the parents were asked to report on their level of distress they experienced during the procedure. Ethical approval for this study was obtained from the Ethics Committee of the Ghent University Hospital.

Statistical analyses

Correlation and linear regression analyses were conducted with the statistical software IBM SPSS Statistics 26 (SPSS IBM, New York City, NY). A p-value of less than 0.05 was considered statistically significant. Pearson correlations were performed to examine associations between parental pain-attending behavior, parental distress and child pain behavior. Given we had a priori hypotheses about the direction of effects, we used one-tailed tests of significance ($p < .05$).

Two hierarchical linear regressions were performed to examine the impact of parental pain-attending and non-pain-attending behavior on child pain behavior as well as the moderating role of parental self-oriented distress for these relationships. Given descriptive analyses (see below) indicated the child's age was significantly correlated with the outcome variable (i.e., child pain behavior), the child's age and sex were entered in a first step and time since diagnosis in a second step within each regression analysis to partial out this effect. Parental pain-attending or non-pain-attending and parental self-oriented distress were entered in a third step in the regression analysis, while the cross-product terms of these variables were entered in a fourth block. Moderation analyses followed the procedure as described by Holmbeck et al. (49). The continuous predictor variables parental pain-attending, non-pain-attending behavior and self-oriented distress were centered and significant interactions were examined by testing and plotting significance of the regression lines for high (mean + 1SD) and low (mean – 1SD) values of the continuous moderator variable (i.e., parental self-oriented distress). Variance inflation factors of both regression analyses were acceptable (*range 1.00–1.56*) suggesting there was no substantial problem of multicollinearity. Post hoc power analysis indicated that there was sufficient power (0.81) to detect medium effects ($f^2=0.25$) for parental self-oriented distress and pain-attending behavior as predictor variables for child pain behavior with our sample size of 42 parents.

RESULTS

Descriptive statistics and correlation analyses

Of 52 eligible families invited to participate, only 4 families declined participation (response rate: 92.31%). The main reason to decline participation was being overwhelmed with the child's diagnosis. Additionally, 2 parents did not complete socio-demographic questionnaires. For most participating children data of only one parent was obtained. If data of both parents were available, data of one parent was randomly excluded from the study. Of 4 families, no video data of the postprocedural period could be obtained because of technical issues. The final sample comprised 42 children (18 girls, 24 boys) and one of their parents (32 mothers, 10 fathers). The time since diagnosis ranged from 0 to 26 months (mean = 5.38, SD = 8.67) and is similar to the number of months the child has been in treatment. As a result, the longer the time since diagnosis, the longer the child had been receiving the treatment and the more experienced the family was with the LP/BMA procedures. The children's age ranged from 6 months to 15 years of age (mean = 7.08, SD = 4.39), reflecting the age range in which childhood leukemia is primarily diagnosed and being in accordance with previous research in this population (4, 50). **A summary of the demographic characteristics can be found in Table 1.**

- Insert Table 1 about here -

Means, SD's and Pearson correlation coefficients for all child and parent data are presented in Table 2. **Parents reported a score of 4.38 (\pm 2.84) out of 10 for feelings of distress experienced during the LP/BMA procedure. The average score for parental postprocedural behavior was**

13.29 (± 12.53) for non-pain-attending behavior with scores ranging from 0 to 50, and 31.76 (± 36.78) for pain-attending behavior with scores ranging from 0 to 117. Child pain behavior score ranged from 0 to 100, with a mean score of 17.01 (± 30.23). Parental distress was significantly positively correlated with the parental pain-attending behavior after the LP/BMA procedure ($r = .35$, $p = .024$). Parental postprocedural pain-attending behavior was significantly negatively associated with the age of the child ($r = -.37$, $p = .017$) and positively related to pain behavior in the child after the procedure ($r = .44$, $p = .004$). Child pain behavior after the procedure showed a significant negative relationship with the child's age ($r = -.59$, $p < .001$). Parental non-pain-attending behavior postprocedural was not significantly associated with any of the other dependent or independent variables. Independent t-tests revealed that participating mothers ($M=5.01$, $SD=2.83$) reported significantly more distress during the LP/BMA procedure in comparison with fathers ($M=2.35$, $SD=1.80$, $t_{40} = -2.79$, $p = .008$). There was no significant difference in parental pain-attending behaviors after the procedure between the mothers ($M=33.10$, $SD=37.47$) and fathers ($M=27.45$, $SD=36.05$, $t_{40} = -.42$, ns) or in parental non-pain-attending behaviors (mothers: $M=14.00$, $SD=12.55$; fathers: $M=11.02$, $SD=12.86$, $t_{40} = .65$, ns). Girls ($M=19.11$, $SD=32.80$) and boys ($M=15.44$, $SD=28.78$) did not differ significantly in terms of the amount of pain behavior after the procedure ($t_{40} = -.39$, ns).

- Insert Table 2 about here -

The relationship between parental pain-attending behavior and child pain behavior and the moderating role of parental distress

Regression analysis indicated a significant effect of the child's age ($\beta = -.51$, $p = .002$), indicating that child pain behavior decreases with increasing age of the child. No significant effects of the child's sex ($\beta = -.09$, ns) or time since diagnosis ($\beta = -.04$, ns) were observed. However, a significant parental pain-attending behavior x self-oriented distress interaction ($\beta = .26$, $p = .034$) was shown, indicating that the impact of parental pain-attending behavior upon child pain behavior is dependent upon level of parental self-oriented distress. To illustrate the pattern reflected in this statistically significant interaction term, we plotted regression lines for high (+1 SD above the mean) and low (-1 SD below the mean) values of the moderator variable (i.e., parental self-oriented distress) (see Fig. 1). Significance tests for both slopes showed that the slope for the high parental distress regression line was significant ($\beta = .56$, $p = .001$), indicating that higher levels of parental pain-attending behavior were associated with higher levels of child pain behavior. The slope for the low parental distress regression line did not reach significance ($\beta = -.09$, ns), indicating that higher levels of parental pain-attending behavior were no longer associated with child pain behavior in case parents report low levels of distress (see Fig. 1).

- Insert Figure 1 about here -

The relationship between parental non-pain-attending behavior and child pain behavior and the moderating role of parental distress

Regression analysis indicated a significant effect of the child's age ($\beta = -.65$, $p < .001$), indicating that child pain behavior decreases with increasing age of the child. No significant effects of the child's sex ($\beta = -.19$, ns), time since diagnosis ($\beta = -.08$, ns) or parental self-oriented distress ($\beta = .20$, ns) were observed. Parental non-pain-attending behavior was significantly negatively associated with child pain behavior ($\beta = -.24$, $p = .045$), indicating that higher levels of parental non-pain-attending behavior were associated with lower child pain behavior. The impact of parental non-pain-attending behaviors was not moderated by parental self-oriented distress ($\beta = -.07$, ns).

DISCUSSION

The aim of the present study was to investigate the moderating role of parental self-oriented distress in understanding the impact of parental responses (i.e., pain-attending and non-pain-attending responses) upon child pain behavior. We hypothesized that 1) parental pain-attending behavior would be positively related to child pain behavior, with effects being particularly pronounced for parents experiencing high levels of distress and less so for parents experiencing low levels of distress, and that 2) parental non-pain-attending behaviors would be negatively associated with child pain behavior, with effects being most pronounced for parents experiencing low levels of distress and less so for parents experiencing high levels of distress. Findings of the present study were partially in line with expectations and can be readily summarized. Specifically, results indicated a positive association between parental pain-attending (protective) responses and child pain behavior, but only for children whose parents reported high levels of personal distress. No association was observed amongst parents reporting low levels of distress. Findings furthermore indicated that parental non-pain-attending responses contributed to lower child pain behavior, yet this relationship was not moderated by parental self-oriented distress.

An affective-motivational account on interpersonal pain dynamics posits a number of plausible explanations that may account for the current findings, indicating differential effects of parental pain-attending responses upon child pain behavior depending upon whether parents experience high or low levels of distress. In particular, it is possible that the differential effects of apparently similar caregiving behaviors (e.g., pain-attending responses) may be accounted for by non-

verbal quality characteristics that may subtly differ depending upon associated level of parental distress. Non-verbal characteristics may include a wide range of behaviors, such as tone of voice, interpersonal distance, physical contact or facial expressions (51-54). It is plausible that subtle variations in such non-verbal features may profoundly affect outcomes. Indeed, besides the verbal content, findings have shown that tone of voice and facial expressions are central in understanding the impact of reassurance on children's behavior during painful medical procedures (55). Specifically, McMurtry et al. 2010 (55) found that children indicated that **parental** reassurance and distraction accompanied by a fearful facial expression conducted greater fear as when accompanied by a happy facial expression. The influence of tone on children's perceptions of emotions was found to vary with both verbal content and facial expression. Other researchers likewise demonstrated that protective responses might be provided in diverse ways including a hostile manner, which may, in turn, differentially impact outcomes compared to when provided in a friendly or empathic manner (56). While the coding system in the current study included non-verbal behavior, this assessment tool was quite coarse and did not look at non-verbal behavior in fine detail. Future research employing more fine-grained coding systems tapping into verbal as well as non-verbal aspects of parent-child interactions, such as tone of voice and facial expressions, is highly encouraged to further explore the impact of non-verbal features within the interpersonal context of pain.

Parental sensitivity to feedback cues provided by the **child** may constitute another pathway explaining observed effects. Specifically, self-oriented distress may induce an enhanced self-focus and impede the parent's sensitivity to the child's needs and adjust their behavior

accordingly (57, 58). Parents with lower feelings of distress, on the other hand, might be able to engage in pain-related behavior that is more attuned to the needs of the child. We only examined parental distress and child and parent behavior at one point in time. Time window sequential analysis of fine-grained coded child pain behaviors and parent behaviors within the setting of painful medical procedures such as LP/BMA procedures, could provide greater detail on the contingencies during parent-child interactions and the way these interactions evolve over time as a function of parental distress (59, 60). Further, including assessment of parental distress during different phases of the procedure (e.g., postprocedural) will allow finer conclusions as to when parental distress is most influential in understanding child outcomes. Moreover, adding measurements of parental distress other than self-report (e.g., heart rate and heart rate variability measures (61, 62)) to the sequential data, may provide valuable insights into the role of parental distress in attuning caregiving to specific need of the child.

The results of the current study demonstrate that higher levels of pain-attending behavior of the parent were no longer associated with child pain behavior in case the parent experienced low levels of self-oriented distress, hence suggesting pain-attending responses are not uniformly maladaptive. An explanation for this differential effect compared to parents who experience high levels of distress, may lie in parental validation of the child's emotions and pain-related thoughts. Linton et al. (2012) (63) investigated the impact of validating versus invalidation of emotions during repeated experimental pain tests upon emotions and adherence in healthy students. The results of the study showed significantly more positive affect and significantly less worry in the validation condition compared to the invalidation condition (63). Caution is needed

however when inferring validation effects within the current study whereby only child pain behavior, and no other indices of child well-being (e.g., positive affect) were assessed. We should also be cautious about the adaptiveness of very low or absent levels of child pain behavior in response to stressful painful procedures; expression of emotions, including pain, may be key to elicit caregiving attuned to child's needs (see also (64, 65)). Whether parental pain-attending behaviors can be conceived of validating responses when accompanied by low levels of distress, and hence, constitutes behavior that is more attuned to child's needs, requires further empirical inquiry.

The current findings indicated that the moderating impact of parental distress did not generalize to parental non-pain-attending behaviors. Specifically, our results did not show expected associations and suggest that parental distress does not modulate the impact of non-pain-attending responses. While it is unclear why this is the case, literature to date is much more extended regarding observed variability in the effects of pain-attending or protective responses (see e.g., (56)), versus non-pain-attending responses; suggesting that the impact of the latter may be more fixed. Also in the current study relatively little non-pain-attending behavior was observed among the participating parents compared to pain-attending behavior, with in addition little variability in the observed non-pain-attending responses. Due to this, we might have been limited in power for non-pain-attending behaviors to detect any impact on child pain behavior and moderation by parental self-oriented distress. In addition, we only included child negative pain behavior in the current study. Non-pain-attending responses of the parent appeared not to have much impact on this, but might rather impact more non-pain behavior in

the child. Lastly, parental non-pain-attending behavior was possibly too broad of a category to detect moderation effects of self-oriented distress. Parental non-pain-attending responses included talking about other things, distraction, humor, etc. More specific categories of non-pain-attending responses may be needed for distress to show an impact. Yet, these notions remain speculative at this stage and requires further inquiry. Notably though, parental non-pain-attending responses did also not directly impact child pain behavior in the current study, hence contradicting prior work (19, 20).

The current findings may have some clinical implications. In particular, findings attest to the need for parental emotion regulation to optimize child outcomes associated with parents' caregiving behaviors. Next to involving the parents in the child-life specialist education therapy, as was the case in the current study, a more intensive involvement of the parents (e.g., discussing with parents how to support their child in coping with the procedure in the education therapy (66) and a number of emotion regulation strategies may be employed to further facilitate parental distress regulation (67-69). Of these strategies, attentional deployment (i.e., attentional engagement/avoidance) is considered a central emotion regulation strategy (69-71). For example, findings (72) have demonstrated that parental attentional avoidance of child pain contributed to lower parental distress (indexed by heart rate and self-report) and less engagement in pain control behavior compared to when instructed to attend to pain. Notably though, this effect was only obtained amongst parents who were initially lowly anxious. Parents who were highly anxious benefitted more from attending to child pain. Another study (73) indicated that parental flexible attention deployment (i.e., being able to flexibly shift attention

away from child pain-related attentional sets towards neutral attentional sets and, vice versa, reduced ability to do the reverse) may likewise be key in understanding affective-motivational and associated behavioral outcomes when facing their child in pain. Facilitated attentional shifting by the parent to the pain of the child contributed to more parental pain control behavior when facing increased child facial pain display, while pain control behaviors were equally pronounced regardless of the child's facial display levels amongst parents demonstrating reduced attentional shifting. Besides the above discussed **more intensive involvement of parents in educational therapy and** emotion regulation strategies, mindfulness-based interventions (74, 75) and/or acceptance and commitment (ACT) therapy (76) might be helpful as well to cope with distress and promote psychological flexibility in the parents. Concluding, further research is needed to explore which parents would benefit most from which emotion regulation strategy.

Some limitations need to be noted and taken into account when interpreting the results of the current study. First, the sample size was rather small, due to the monocentric nature of this study. Future multicenter studies could demonstrate more representative findings for the pediatric cancer population. Additionally, the study sample had a wide age range (6 months – 15 years of age). Further research in different age groups is recommended to gain more insight into which types of parental behavior are most relevant for which age group. Second, observed parent-child interactions in the present study are limited to the postprocedural phase. It would be advisable for future studies to include parent-child interactions during the procedure. However, in the participating hospital, parents were not allowed into the treatment room

during the LP/BMA procedures. Parental behavior during such procedures, might influence the pain behavior of the child to a much greater extent, since it is shown that children show most distress during the painful phases of the procedure (13). Third, more than 3 times as many mothers participated in the study than fathers. Future research should aim for equal participation of mothers and fathers, as it is shown in previous research that their behavioral responses towards their child's pain demonstrate different patterns (77). Fourth, we included children who were recently diagnosed with leukemia as well as children who were being treated for cancer for several months already or who were being treated again after relapse. Because of this, not all children had the same experience with the LP/BMA procedure, which may have influenced the results, although no significant effects for the time since diagnosis were observed within the analyses. Moreover, due to the cross-sectional design of the study, causality could not be investigated, implying that the impact of the children's and parents' potential previous experiences with the LP/BMA procedures on their responses in this particular procedure could not be examined and no conclusions regarding causality can be drawn. Finally, non-verbal features such as facial expressions and tone of voice were not included in the coding of non-verbal behaviors within the current study. Including these features in future studies can possibly provide more insight into the differential effects that were found with regard to parents that experienced low versus high levels of personal distress.

Despite the above limitations, the results of the current study **are important as they** add to our understanding of the impact of parental responses upon child pain behavior in the context of painful medical procedures in childhood cancer patients **and provide us with implications for**

practice as well future research. Taken together, study findings provide evidence for the moderating role of parental self-oriented distress on the relationship between parental pain-attending and non-pain-attending responses upon pain behavior exhibited by the child. These findings suggest that psychosocial interventions that focus on parental emotion regulation may be key to promote more optimal outcomes of parental responses in children with cancer undergoing painful medical procedures. Future studies, based on the suggested avenues for future research, are encouraged to further improve our insights on this matter.

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FIGURE LEGENDS

Figure 1: Mean child pain behavior as a function of lower versus higher levels of parental pain-attending behavior and low (-1SD below the mean) and high (+1SD above the mean) levels of parental self-oriented distress (Low parental distress: $\beta = -.09$, ns; High parental distress: $\beta = .56$, $p = .001$)