Singing, sharing, soothing
Family-centred music therapy during painful procedures in neonatal care
"Sometimes the wrong train will get you to the right station"
Thank you for your safe haven Mats, Maria, Eva and Ulrik.

"Success is not final, failure is not fatal:
it is the courage to continue that counts"
You have always encouraged me.
I love you Felicia and Henrik!
Singing, sharing, soothing
Family-centred music therapy
during painful procedures in neonatal care
Abstract

To sing is to communicate. The soothing, comforting and emotional regulating properties of a lullaby are well-known cross-culturally and historically. This doctoral thesis addresses neonatal pain management from a novel and groundbreaking perspective, studying the efficacy of live music therapy on infants’ pain responses during venepuncture. New research is needed to advance the non-pharmacological interventions in neonatal pain care, and neonatal music therapy (NICU MT) offers active methods to involve the parents in pain management. The doctoral thesis includes two empirical and two theoretical articles. In paper I, preterm and term infants (n=38) were subjected to venepuncture with and without live lullaby singing, in a randomised order with a crossover design. Parent-preferred lullabies were performed live by a music therapy student and standard care was provided for all infants. The results did not show any significant pain-alleviating effects, however, the live singing was not stressful for the infants.

In paper II, the microanalysis disclosed that live lullaby singing is a communicative reciprocal intervention that also applies to premature infants during painful procedures. Live lullaby singing is a tool suitable as a means to optimise the homeostatic mechanisms. The results from the theoretical papers III and IV are further developed and synthesised in the thesis into a theoretical strategy; The Nordic NICU MT pain management strategy, featuring the parents and their singing voices as mediators for pain relief. The role of the music therapist in neonatal pain management is as a facilitator and an educator for the parents. Coaching parents to better meet their infant’s attachment needs during a painful procedure may lead to more efficacious interventions. The biopsychosocial parental infant-directed singing is presumably an applicable parent-driven non-pharmacological intervention, which promotes pain relief and attachment formation during painful procedures. Neonatal music therapy is still in its infancy in the Nordic countries, but the societal and healthcare contexts afford important prerequisites to further develop NICU MT as a truly family-centred approach. This doctoral thesis will hopefully contribute to the important interdisciplinary endeavour worldwide of involving and integrating parents in neonatal pain management.

Keywords: music therapy, pain management, premature infants, family-centred, infant-directed singing, venepuncture, parents, dynamic forms of vitality.

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# Table of Contents

LIST OF PAPERS ........................................................................................................... 11

LIST OF ABBREVIATIONS ....................................................................................... 12

PROLOGUE ............................................................................................................ 13

INTRODUCTION ....................................................................................................... 15
  The scope of the doctoral thesis ........................................................................ 15
  Aims and research questions .............................................................................. 17

BACKGROUND ....................................................................................................... 18
  Section 1: Music therapy in healthcare ............................................................ 18
    Development of music therapy in healthcare practice and research ............. 18
    Music therapy versus music medicine ........................................................... 20
    Neonatal music therapy traditions and models of practice ....................... 25
    Protocol-based NICU MT interventions ....................................................... 26
    Interactive NICU MT interventions ............................................................... 27
  Family-centred care informing Nordic neonatal music therapy .............. 28

  Section 2: Pain in early life ............................................................................. 30
    Attachment and pain .................................................................................... 32
    Parents’ role in neonatal pain management ............................................... 34
    Pharmacological and non-pharmacological pain management ............... 36
    Pain physiology in infants ......................................................................... 37
    Ascending nociceptive fibres ....................................................................... 38
    Descending pain modulatory system .......................................................... 39
    Music for distraction and music therapy as integration ......................... 40
    Pain theories and models informing neonatal music therapy ................. 43
    The Gate Control Theory of Pain ................................................................ 44
    Biopsychosocial models ............................................................................. 44
    Procedural support models ......................................................................... 45

THEORETICAL FRAMEWORK AND CONCEPTS .................................................. 47
  Neuroaffective developmental psychology .................................................... 47
    Dynamic forms of vitality ............................................................................ 48
    Proto-musicality ............................................................................................ 50
    Arousal systems ............................................................................................ 51
    Mirror neurons ............................................................................................. 53
    Affect attunement ......................................................................................... 54

ETHICAL CONSIDERATIONS ................................................................................. 56
METHODS ......................................................................................................................... 57
Study design in the RCT ................................................................................................. 57
Live lullaby intervention ............................................................................................... 58
Statistical analyses .......................................................................................................... 60
Pain assessment with BIIP and PIPP-R ......................................................................... 60
Case study with microanalysis ...................................................................................... 62
Theory building papers ................................................................................................. 64
The therapist-researcher’s stance .................................................................................. 64
A SYNTHESIS OF THE MAIN RESULTS ..................................................................... 67
The results of the RCT ..................................................................................................... 67
  Non-significant trends .................................................................................................. 69
Results of the microanalysis in the case study .............................................................. 72
  Irregular live lullaby performance ................................................................................ 72
  Infant-directed speech and affect contagion ................................................................ 77
  Deficiencies with pain assessment ............................................................................... 78
  Affective support versus over-stimulation ................................................................... 79
Live parental infant-directed singing ............................................................................ 81
  The Nordic NICU MT pain management strategy ..................................................... 82
DISCUSSION ..................................................................................................................... 89
Methodological considerations and limitations ............................................................ 89
  The RCT design ........................................................................................................ 89
  The live lullaby intervention ....................................................................................... 92
  The pain assessment ................................................................................................... 93
Inaudible parents in neonatal pain research ................................................................. 95
CONCLUSIONS ............................................................................................................... 100
  Dynamic forms of vitality as the principal link ......................................................... 101
FURTHER PERSPECTIVES ............................................................................................... 104
EPILOGUE AND ACKNOWLEDGEMENTS .................................................................. 106
SAMMANFATTNING (SUMMARY IN SWEDISH) ....................................................... 110
REFERENCES ............................................................................................................... 113
List of papers

This doctoral thesis is based on the following four papers, which are referred to in the text by their roman numerals (I – IV).


# List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ATVV</td>
<td>Audio Tactile Visual Vestibular</td>
</tr>
<tr>
<td>BIIP</td>
<td>Behavioral Indicator of Infant Pain</td>
</tr>
<tr>
<td>dB</td>
<td>Sound level measured in decibel</td>
</tr>
<tr>
<td>DIAPR-R</td>
<td>Development of Infant Acute Pain Responding-Revised</td>
</tr>
<tr>
<td>EBM</td>
<td>Evidence-Based Medicine</td>
</tr>
<tr>
<td>EBP</td>
<td>Evidence-Based Practice</td>
</tr>
<tr>
<td>FCC</td>
<td>Family-Centred Care</td>
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<tr>
<td>GA</td>
<td>Gestational Age</td>
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<tr>
<td>GW</td>
<td>Gestational Weeks</td>
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<tr>
<td>HR</td>
<td>Heart Rate</td>
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<tr>
<td>ITT</td>
<td>Intention-to-Treat</td>
</tr>
<tr>
<td>KMC</td>
<td>Kangaroo Mother Care</td>
</tr>
<tr>
<td>MMS</td>
<td>Music and Multimodal Stimulation</td>
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<tr>
<td>NADP</td>
<td>Neuroaffective Developmental Psychology Theory</td>
</tr>
<tr>
<td>NICU</td>
<td>Neonatal Intensive Care Unit</td>
</tr>
<tr>
<td>NICU MT</td>
<td>Neonatal Music Therapy</td>
</tr>
<tr>
<td>NIDCAP</td>
<td>Newborn Individualized Developmental Care and Assessment Program</td>
</tr>
<tr>
<td>PIPP-R</td>
<td>Premature Infant Pain Profile-Revised</td>
</tr>
<tr>
<td>PP</td>
<td>Per-Protocol</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised Controlled Trial</td>
</tr>
<tr>
<td>RBL</td>
<td>First Sounds: Rhythm, Breath, Lullaby</td>
</tr>
<tr>
<td>RR</td>
<td>Respiration Rate</td>
</tr>
<tr>
<td>SaO₂</td>
<td>Oxygen Saturation</td>
</tr>
<tr>
<td>SSC</td>
<td>Skin-to-Skin Contact</td>
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Prologue

In December 2009, a nurse from the neonatal intensive care unit addressed me about one of their patients who had been in the ward for some months already, an extremely prematurely born boy, who seemed both overwhelmed and under-stimulated by his environment. Perhaps music therapy, she said, could help the boy and his parents to connect?

Children with severe developmental disabilities and their often frustrated and exhausted parents are one of many patient populations I meet in my work as a music and art therapist at the Music and Art Therapy Department, Region Värmland, Central Hospital in Karlstad, Sweden. These families are usually in great need of tools for communicating on a non-verbal level, which music therapy can offer. After a couple of years of working with this patient group, I asked myself if it was possible to prescribe music therapy earlier in the child’s life, at an earlier stage in the healthcare chain, to improve quality of life and communication conditions for these children and their parents.

In March 2010, I received the first referrals from the NICU of two prematurely born infants, one of them was the boy previously mentioned. I was curious to see if this might be the arena I was searching for in order to improve quality of life for impaired children and their parents. Baby V, born in GW 24 and suffering from serious illnesses, had been cared for in the NICU for seven months when I first met him. His stressed cries had become a problem for the staff and other vulnerable infants in the multi-bed open-bay unit. I will never forget baby V’s spontaneous reaction when I, the music therapist, first came to visit him and his mother. When I started to sing his name, he immediately stopped crying. His tensed little body relaxed instantly, and his face lit up as if he was saying to me: “Finally, someone is talking with me”. I was deeply moved by baby V’s response, showing with all his being that he loved to communicate through singing. Both baby V and his parents benefitted from the music therapy interventions I provided, and I strongly felt that the focus for my research should be to hopefully improve the quality of life for the vulnerable hospitalised infants and their families in the NICU and beyond.

In August 2010, I was invited by Joanne Loewy to an international summit for music therapists working in neonatal care. Dr. Loewy is the director of the Louis Armstrong Center for Music and Medicine at Beth Israel Hospital in New York and one of the pioneers in neonatal music therapy research. In this meeting, I met and talked to many of the distinguished music
therapists who have built the neonatal music therapy field with their long experience and significant research. The summit was the starting point for pursuing my PhD and the beginning of my pioneering work to implement music therapy in the neonatal ward in Region Värmland and within Swedish neonatal healthcare. With substantial support from the medical staff and the leadership of the Karlstad NICU, the Central Hospital became the first hospital in the Nordic countries to offer a family-centred music therapy service for hospitalised infants and their parents. Today, nine years later, neonatal music therapy is fully implemented, established, respected and part of the regular neonatal healthcare services in Karlstad.

Cultural sensitivity and cultural context are of crucial importance for knowledge translation and implementation work. The lack of Swedish context-sensitive neonatal music therapy interventions and research became an issue for my implementation work in Karlstad, when existing research literature and models of practice for example lacked a focus on parental involvement (paper IV). I soon understood that as part of the implementation process, I needed research that was based on the Swedish healthcare context with music therapy methods that were sensitive to both context and culture.

In 2011, when I started planning my PhD-project, I was influenced by the context I work in; the hierarchical hospital setting where EBP and randomised controlled trials (RCT) are essential in building new healthcare practices. During my literature studies of neonatal music therapy research and related fields, I identified a knowledge gap. Neonatal music therapy as pain management was an area where research literature was scarce. I challenged myself to initiate a project with live music therapy as pain management and an RCT seemed to best fit the context. Science is still looking for a gold standard to manage infant procedural pain. Therefore, continued research is needed to advance the interventions in neonatal pain care. Perhaps live music therapy could be an adjuvant to the control of infant pain and should therefore be included in a future standard?

During these years as a PhD student (2012-2019) my research work has inspired and informed my clinical music therapy work in the Karlstad NICU and vice versa. The pioneering efforts both in my clinical work and in my research have been exciting and extremely challenging. Thankfully, I have not been alone on this research journey and in the end of this doctoral thesis I express my sincerest gratitude to my fantastic interdisciplinary companions and collaborators along the way.
Introduction

The scope of the doctoral thesis

Music therapy with hospitalised infants and their families is a relatively new but expanding practice in the field of music therapy. More and more music therapy programs are implemented in neonatal intensive care units across the world (Shoemark & Ettenberger, in press). Research in neonatal music therapy is also growing in various parts of the world, but is still in its infancy in the Nordic countries. An important research area to advance is music therapy in neonatal pain management. Pain research in the field of music therapy has mostly focused on older children or adults. There is a dearth of research about live family-centred music therapy as procedural support in neonatal care. Most of the pain research with hospitalised infants has been infant focused, investigating the infant’s physiological and behavioural responses to recorded music undertaken by non-music therapists in the medical and nursing professions (Shoemark & Dearn, 2016). New research is needed to advance the family-centred interventions in non-pharmacological neonatal pain care, interventions like music therapy that offer active methods to involve the parents in infant pain management.

This doctoral thesis addresses critical knowledge gaps in the field of neonatal music therapy as well as in the field of family-centred neonatal pain management. There is a lack of studies investigating the efficacy of live singing during painful procedures in preterm and term infants. There is also an urgent need for more knowledge and research which answers the questions if, how and why live music therapy may alleviate procedural pain in hospitalised infants, how live music therapy interventions should be designed to support the infant and the parents during painful procedures and what the role of the music therapist in neonatal pain management should be. This thesis therefore addresses “a much needed but under-researched population /.../ [and] opens new doorways for NICU music therapy and pain treatment possibilities” (Spintge & Loewy, 2017, p.71).

Pain is a multidimensional phenomenon that is generally researched in interdisciplinary collaborations. Writing a doctoral thesis about music therapy and neonatal pain requires a multifaceted and integrative approach, combining research from areas such as neuroscience, developmental psychology, attachment theory, nursing science and music therapy. These various fields are intertwined in the chapters Background and Theoretical
framework and concepts, contextualising the topic and elaborating on important concepts and prerequisites to guide readers of diverse disciplines to better appreciate the four articles as well as the results, discussion and conclusion of this thesis. The Background is organised in two sections. Section one presents an overview of current knowledge and previous research in music-based interventions in neonatal pain management, distinguishing between music therapy research and music medicine research. Included in section 1 is a historical backdrop to music therapy in health care and in neonatal care, together with neonatal music therapy in the Nordic countries as well as traditions and models of practice in the field of neonatal music therapy. Section 2 gives the reader an overview of neonatal pain physiology, pain management beyond medication and biopsychosocial aspects of neonatal pain management including the role of the parents. This section also presents divergent applications of music-based interventions in pain management such as music for distraction versus music therapy as integration with relational aspects. Those pain theories and pain models that are scaffolding the conclusions and the strategies in this thesis are also presented in section two.

The qualitative and quantitative methods that have been applied in this research are presented in Methods. The main results from the empirical papers I and II are presented in A synthesis of the main results. In the same chapter, the results from the theoretical papers III and IV are further developed and synthesised into a theoretical strategy; The Nordic NICU MT pain management strategy. This strategy, also condensed and presented in a figure, builds on the pain models and theories previously presented in the chapters Background and Theoretical framework and concepts. In the discussion part, the limitations of this doctoral thesis are discussed, as well as the rationale for including music therapy and qualified music therapists as advisors or service delivery experts in neonatal pain research. In the Conclusions, the concept of dynamic forms of vitality is linked to neonatal music therapy and neonatal pain management. The thesis ends with the chapter Further perspectives with implications for future neonatal music therapy research and practice.

At Örebro University where this music therapy research project is situated, the research field of musicology is interdisciplinary with a specific interest in human’s interactions with music. Music therapy researchers and professionals as well as readers from allied healthcare disciplines will conceivably benefit from the interdisciplinary and synthesising content in this doctoral thesis. This is also a thesis that studies infants’ interactions with music during painful procedures analysing the lullaby singing per se, which might be of interest for readers within musicology research.
Aims and research questions

The overarching aim of this doctoral thesis, addressed with empirical and theoretical approaches, is to evaluate live lullaby singing as an adjuvant to the control of infant pain. This aim is divided into the following more specific aims:

1. To test the efficacy of live lullaby singing on behavioural and physiological pain responses during venepuncture in preterm and term neonates.
2. To analyse live lullaby singing for premature infants during venepuncture in comparison to standard care, including infants’ physiological and behavioural responses emerging before, during and after venepuncture.
3. To explore the underlying analgesic aspects and biopsychosocial rationale for involving parents in neonatal pain management in combination with live infant-directed singing through theory construction.
4. To propose a strategy for family-centred neonatal music therapy practice and research in neonatal pain management.

The research questions pursued in this doctoral thesis are therefore:

1. What effect does live lullaby singing have on behavioural and physiological pain responses during venepuncture in preterm and term neonates?
2. How does live lullaby singing for preterm infants influence their physiological and behavioural responses before, during and after venepuncture compared to standard care?
3. What are the respective roles of music therapy, the music therapist and the parents in family-centred non-pharmacological neonatal pain management?

The first aim is pursued in paper I, which answers the first research question with quantitative methods. The second aim and the second research question are explored in paper II within a mixed methods paradigm. In the theoretical papers III and IV, as well as in the chapter A synthesis of the main results, concepts as well as theories and previous interdisciplinary research are synthesised to answer the third research question, fulfilling aims three and four.
Background

Section 1: Music therapy in healthcare

Music, of every kind, is part of almost every human being’s everyday life, creating and shaping our identity, social relations as well as promoting health (Ruud, 2011). Music as a health resource or “health musicking” (Stige, 2016, p. 545) can be curative, palliative, and promote personal strengths, resilience and wellness (Ruud, 2011; Rolvsjord, 2016). The music therapist Even Ruud (2011) describes music as human interaction in context and a tool to increase possibilities for action. Ruud links the concept of health and therapy to a salutogenic orientation, since health includes more than lack of illness.

In the Oxford Handbook of Music Therapy, the editor Jane Edwards defines music therapy by emphasising the interactive, interpersonal and contextual aspects of music therapy practice:

Music therapy is a relational therapy involving the use of music in therapeutic processes with individuals and groups by a qualified practitioner who has undertaken appropriate training and undertakes ongoing professional development. It is a unique way of working in which the dynamic capacities of music and musical relating are harnessed to serve the needs of the client, family, or group who is seeking help (Edwards, 2016a, p. 2).

Bruscia (1998) emphasises the musical relational aspects of music therapy as a source for change, which emerges from a well-structured process with a qualified therapist:

Music therapy is a systematic process of intervention wherein the therapist helps the client to promote health, using music experiences and the relationships that develop through them as dynamic forces of change (Bruscia 1998, p. 20).

Development of music therapy in healthcare practice and research

Music therapy is a rather new discipline in healthcare settings, especially in neonatal care in the Nordic countries (paper IV). As such, music therapists might probably encounter some resistance when entering established healthcare teams and allied research fields (Ledger, 2016; paper IV). A lot of effort is spent negotiating a space for music therapy, securing boundaries and identities to gain credibility (Ruud, 2000). Prior to the establishment of music therapy in healthcare, history tells us how musicians in the late 19th century up until the 1940s in the UK and USA, negotiated a space in the
hospitals to offer live music “treatments” for the patients (Edwards, 2007). The “hospital musicians” longed for appreciation among the hospital staff for their role as health promoters, but their efforts to make music part of hospital care was met with resistance and scornful comments from the medical establishment. At that time, the therapeutic and curative results of the environmental music interventions in the hospitals were mainly anecdotal and testimonial, and were not scientifically established. Furthermore, the musicians were criticised for not being proper educated neither in music nor in medicine (Edwards, 2007).

The discipline of contemporary music therapy formally began after World War I and II, when music both live and recorded was used in the care of traumatised war veterans (American Music Therapy Association, 2019; Hodges & Wilson, 2010). The first music therapy college training programs in the USA were established in the mid-1940s and in the late 1950s in the UK (Edwards, 2007). In Sweden, the first university course in music therapy started 1981.

In the early 1950s when the music therapy profession just started to be recognised, clinicians felt a need to validate the professional status of the field by using a positivist approach to research within a quantitative paradigm (Amir, 1993). Music therapy research became closely aligned with the behavioural and social sciences. The effects of music therapy on behaviours of patients were examined in RCTs, since behaviour modification was feasible to observe and measure (Edwards, 2016b). The music therapy research tradition in the USA has therefore come to favour quantitative methods within a positivist epistemology (Bradt, Burns & Creswell, 2013; Edwards, 2016b; Wheeler, 2016). In Europe and Scandinavia, music therapy practice has mostly involved techniques of interactive, improvisational music-making, which are interventions supposedly difficult to control and replicate in an RCT (Wigram, Nygaard Pedersen & Bonde, 2002). Since the early 1990s, the predominant research methodology in Europe and Scandinavia has been qualitative (Erkkilä, 2016).

When striving for recognition and status of the music therapy profession in healthcare, music therapy research has been influenced by societal requirements. These requirements have followed research trends in other fields, especially the medical field, and this is still the case today (Erkkilä, 2016). Evidence-Based Medicine (EBM), later followed by the overarching term EBP, was introduced in the early 1990s (Edwards, 2004). EBP focuses on positivist research methods accentuating RCT as the gold standard in medical research, to assure that patient treatment is safe, effective and cost-
effective (Edwards, 2016b). Results from clinical studies inform clinical decisions and recommended practices (Goodman, 1999). In order to persist and be accepted within the healthcare system, clinical music therapy research, also in Europe and Scandinavia, has adapted to and complied with the EBP paradigm (Erkkilä, 2016). The qualitative versus quantitative research paradigms have been debated in many allied healthcare fields, so also within music therapy (Amir, 1993; Edwards, 1999, 2002, 2004, 2005, 2012; Bradt et al., 2013; Erkkilä, 2016). Health administrations round the world and also those working in other medical contexts expect the clinical care to be evidence-based, which put demands on music therapists to show documentation of clinical effectiveness for their interventions (Edwards, 2012; Erkkilä, 2016). Yet, music therapy interventions encompass various abstract factors such as aspects of human affects and emotions, interaction, the music itself and its meaning, and is therefore challenging to research (Erkkilä, 2016). Lately, mixed methods, which is viewed as a third research paradigm, has become an approach that intrigue the music therapy theorists (Bradt et al., 2013). Mixed methods, using both qualitative and quantitative research methods, might be an approach that unveils complex music therapy phenomena and answers complex questions that are relevant to music therapy practice though within an EBP framework (Bradt et al, 2013; Erkkilä, 2016).

**Music therapy versus music medicine**

Other healthcare professionals than music therapists are today offering music-based interventions in the context of healthcare. The tradition of “hospital musicians” is also still active round the world. This has urged the music therapy field and professional associations for music therapy to articulate the boundaries and identity of clinical music therapy versus music medicine.

In clinical music therapy practice, the above-mentioned definitions by Edwards (2016a) and Bruscia (1998), are operational. Music medicine is in turn described as the use of recorded music selected by medical personnel for distraction, without involvement of a qualified music therapist as an advisor or a service delivery expert (Stegemann, Geretsegger, Phan Quoc, Riedl & Smetana, 2019).

When it comes to researching the effectiveness of music-based interventions, music therapy and music medicine are two distinct areas of research, as illustrated in Table 1 and Table 2.
Music therapy requires a systematic therapeutic process developed between the patient and a trained music therapist through personally tailored music experiences including listening to live, improvised, or pre-recorded music, playing music instruments, improvising music and composing music. Music therapists use music for symptom management within a biopsychosocial framework (Bradt et al., 2015). In music therapy, the music is used interactively. It is entrained to the patient’s affective, emotional and/or physical state, thus offering integration instead of distraction.

With few exceptions, music medicine research usually uses pre-recorded, randomly selected music of various genres (Table 2). The music is predominately researcher-selected and delivered without any involvement of a systematic therapeutic process (Bradt et al., 2015). In music medicine publications, the musical characteristics are often poorly described, which make them hard to replicate (Robb et al., 2018).

Table 1. Overview of music therapy research related to neonatal pain.

<table>
<thead>
<tr>
<th>First author, year</th>
<th>(N); Age</th>
<th>Intervention</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malone (1996)</td>
<td>(20); 0 - 7 years</td>
<td>Randomisation into groups: 1. Age-appropriate songs accompanied by a steel string guitar, before, during, after a painful procedure. 2. Control group. No meds for pain relief.</td>
<td>Pain measured by behavioural distress. Questionnaire (parents and staff)</td>
<td>Children receiving MT exhibited shorter periods of distress than children without MT. Children 0 to 1 years exhibited significantly less distress during MT than older children. 79% of the parents felt MT was beneficial for their child. Staff positive to MT.</td>
</tr>
<tr>
<td>Whipple (2008)</td>
<td>(60); ≥ 32–37 GA</td>
<td>Randomisation into groups: 1.PAL, 2.Pacifier, 3.Control. Recorded traditional lullabies sung by a female child accompanied by piano delivered before, during, after heel-stick. Sucrose was administered to 16 infants.</td>
<td>Behavioural state (measured by the Continuous response Digital Interface system); Change in HR, RR, SaO2.</td>
<td>Significant difference for PAL and Pacifier-only groups compared to control regarding behaviour state and stress level during and post heel-stick.</td>
</tr>
<tr>
<td>Shah et al. (2017)</td>
<td>(35); &gt;32 GA</td>
<td>RCT. Crossover design. Randomisation into groups: 1.MS, 2.Sucrose 24%, 3. MS + sucrose. MS = Recorded instrumental lullaby music chosen after discussion with a music therapist for stability, repeatability, and presence of minor tones. MS played as a loop 20 minutes before the heel-stick, during, until 7 minutes after. All infants received similar standard non-pharmacologic pain relief such as swaddling and comforting.</td>
<td>Pain measured by PIPP-R. Change in HR and SaO2.</td>
<td>Pain scores were significantly lower in the MS + sucrose group compared to MS or sucrose alone. PIPP scores were similar between the MS and sucrose groups. A combination of MS + sucrose improves pain relief compared to sucrose or music alone. MS alone had a similar effect to the current gold standard of oral sucrose.</td>
</tr>
<tr>
<td>Ullsten et al. (2017)</td>
<td>(38); ≥ 32 - 42 GA</td>
<td>RCT. Crossover design. Random order of: 1. Live lullaby singing + sucrose + facilitated tucking. 2. Sucrose + facilitated tucking. MT performed by a MT student 2.5 min before, during, 2 min after venepuncture.</td>
<td>Pain measured by PIPP-R and BiIP. Change in HR, RR and SaO2.</td>
<td>No significant differences in PIPP-R or BiIP scores between MT and control. Significantly calmer RR in MT condition versus control.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Music medicine research</th>
<th>(N); Age</th>
<th>Intervention</th>
<th>Outcome measures</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td><strong>Bo &amp; Callaghan (2000)</strong></td>
<td>(27); ≥ 30 – 41 GA</td>
<td>Random order of: 1. NNS; 2. MS; 3. NNS + MS; 4. No intervention; 5 min after a heel-stick procedure. MS = recorded intrauterine maternal pulse sound and soothing music. No meds for pain relief.</td>
<td>Pain behavior measured by NIPS. Change in HR and TiPAC02.</td>
<td>MS significantly reduced the infants’ pain in the follow-up period after the heel-stick. MS had a better effect than NNS and NNS+MS on HR and effect was sustained when the intervention was withdrawn. NNS effectively reduced pain but less so than the combined NNS and MT. The TiPACQ2 levels of the neonates were highest in combined MT and NNS condition.</td>
</tr>
<tr>
<td><strong>Butt &amp; Kislavsky (2000)</strong></td>
<td>(14); ≥ 29 – 36 GA</td>
<td>Random order of: 1. Recorded Brahms Lullaby vocal a capella version, 2. Recorded Brahms Lullaby piano solo version, 3. Control. MS played for 10 min after heel-stick. No meds for pain relief.</td>
<td>Pain measured by NFCS.</td>
<td>MS significantly reduced the older infants’ pain (&gt; 31 GA) in the follow-up period after the heel-stick. The older infants (&gt; 31 weeks) HR decreased significantly with MS. No effect of MS on infants &lt; 31 GA. No statistically significant differences in SaO2. With MS the infants &gt; 31 GA returned more rapidly to baseline levels of HR, state-of-awarness and facial expressions and were soothed to even lower levels of arousal. Infants &gt; 31 GA were soothed more by instrumental MS than the vocal MS.</td>
</tr>
<tr>
<td><strong>Chou et al. (2003)</strong></td>
<td>(30); ≥ 28–36 GA</td>
<td>No randomisation of order: 1. Control, 2. MS. Recorded music with a combination of uterine sounds of a pregnant woman blended with synthesised female vocals played during endotracheal suctioning. No meds for pain relief.</td>
<td>Change in SaO2.</td>
<td>Infants receiving MS with endotracheal suctioning had a significant higher SaO2 than without MS. The level of SaO2 returned to baseline level faster with MS than without.</td>
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<tr>
<td><strong>Tramo et al. (2011)</strong></td>
<td>(13); ≥ 30 – 36 GA</td>
<td>Pseudo randomisation into groups: 1. Recorded Western lullabies sung by female in English with simple accompaniment played for 10 min after heel-stick, 2. Control. Some infants were swaddled. No meds for pain relief but 4 infants in control and 4 in MS group were given a pacifier sweetened with sucrose during pre-puncture handling.</td>
<td>Change in HR, RR and SaO2. Behavioural responses.</td>
<td>HR and crying significantly decreased with MS compared to control during the 10-min recovery following the heel stick.</td>
</tr>
<tr>
<td><strong>Bergomi et al. (2014)</strong></td>
<td>(35); ≥ 30 GA</td>
<td>RCT. Randomisation into groups: 1. Mozart music “Sonata in D Major for Two Flautos (K. 448)” played 5 min before heel-stick and 5 min after heel-stick for a maximum of 20 min. 2. Glucose 10%. 3. Control with no pain relief. All infants were given pacifier.</td>
<td>Pain measured by PIPP.</td>
<td>MS significantly decreased pain compared to control without pain relief. No significant difference in pain reduction between music and glucose.</td>
</tr>
<tr>
<td><strong>Cardoso et al. (2014)</strong></td>
<td>(80); ≥ 32 – 37 GA</td>
<td>RCT. Randomisation into groups: 1. Recorded lullaby (not described), 2. Recorded lullaby with 25% glucose. 3. Control with 25% glucose. MS was played 10 minutes before arterial puncture.</td>
<td>Pain measured by PIPP.</td>
<td>MS did not have significant effect on pain scores.</td>
</tr>
<tr>
<td><strong>Zhu et al. (2014)</strong></td>
<td>(250); ≥ 37 GA</td>
<td>RCT. Randomisation into groups: 1. No intervention group, 2. MS, 3. BF, 4. BF + MS. MS = three recorded classical piano pieces (Sonatina D’Amato, A Camino Amor, and Balilla Pour Adeline played by Richard Chamberlain) played on a loop at least 5 min before heel-stick and during heel-stick. Mothers allowed to speak to infants in BF group. Infants swaddled with no skin-to-skin contact with mother.</td>
<td>Pain measured by NIPS.</td>
<td>BF group had a 50% decrease in pain and a 70% decrease in duration of crying time. No statistically significant difference between BF or BF + MS. MS did not have any significant effect on pain scores.</td>
</tr>
<tr>
<td><strong>Azamnejad et al. (2015)</strong></td>
<td>(20); ≥ 37 GA</td>
<td>Randomisation into groups: 1. MS, 2. Control with no pain relief. MS = recorded mothers’ voice, played 10 min before, during, and until 10 min after arterial blood sampling.</td>
<td>Pain measured by NIPS.</td>
<td>MS significantly decreased pain compared to control without pain relief.</td>
</tr>
<tr>
<td><strong>Shabani et al. (2016)</strong></td>
<td>(20); ≥ 29-36 GA</td>
<td>RCT. Crossover design. Randomisation into groups: 1. MS, 2. Control with no pain relief. MS played from 5 min before venepuncture, during, until 10 min after. MS = recorded music with a combination of uterine sounds of a pregnant woman blended with synthesised female vocals played during endotracheal suctioning.</td>
<td>Pain measured by NFCS.</td>
<td>MS significantly decreased HR during and after venepuncture compared to control. 80% decrease in the infants’ mean facial pain expressions with MS.</td>
</tr>
</tbody>
</table>
Neonatal pain research is an interdisciplinary field where music therapy has not yet been established. Paper I in this thesis is the first RCT of its kind (Table 1). Music therapy studies on procedural pain are scarce in all study populations (Loewy, 2019). The limited music therapy literature about pain and pain management mostly refers to music therapy with children in pain and not to infants (e.g. Loewy, 1997; Bradt, 2013; Ghetti, 2012 & 2013). The evidence-based music therapy methods for pain management in children are few; the methods are mostly clinically based and not based on research (Ghetti, 2012; Bradt, 2013).

Music medicine is the predominant approach in neonatal pain research (Table 2). Over the past decade, recorded music with no involvement of a music therapist is increasingly used as so-called music-induced analgesia (Juhl Lunde, Vuust, Garza-Villarreal & Vase, 2019) and as distracting stimulus during skin puncture in hospitalised infants (Loewy, 2019). Recorded music of various kinds has shown statistically significant positive results as an adjuvant pain treatment, but the benefits are inconsistent (Table 2). No study has so far noted negative side effects of music. On the contrary, most studies have observed a stabilising effect of music on both preterm and term infants in MS group had significantly lower PIPP scores and lower decreases in SaO2.

### Table 2. Overview of music stimulation research related to neonatal pain (continued).

<table>
<thead>
<tr>
<th>Study Authors and Year</th>
<th>Sample Size/ GA</th>
<th>Randomisation</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Pain Group Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chirico et al. (2017)</td>
<td>(40) ≥ 29.36 GA</td>
<td>RCT; Randomisation into groups: 1.MS recorded mother’s voice, either singing lullabies or reading nursery rhymes, 2.Control with music. MS played from 10 min before heel-click, during, until 20 minutes after.</td>
<td>Pain measured by PIPP: Change in HR, SaO2; blood pressure.</td>
<td>Infants in MS group had significantly lower PIPP scores and lower decreases in SaO2.</td>
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<tr>
<td>Qiu et al. (2017)</td>
<td>(82) &lt; 27 GA</td>
<td>RCT; Randomisation into groups: 1.MS and touch, 2.Control with no pain relief. MS = lullabies and nursery rhymes (not described). Blood samples were collected from all infants at the beginning of hospitalisation and 2 weeks later. MS + touch was repeated for every painful procedure during the 2-week data collection period. MS was played from 5 min before the experimental procedure until 20 min after the procedure.</td>
<td>Pain measured by PIPP and biological measures of stress - cortisol and β-endorphin serum concentrations.</td>
<td>Infants in MS group had significantly lower pain scores than the comparison group at the end of the study. A combination of MS + touch might decrease the pain response by significantly improving the β-endorphin concentration, but not the blood cortisol concentration.</td>
<td></td>
</tr>
<tr>
<td>Kurdi et al. (2017)</td>
<td>(42) ≥ 29.36 GA</td>
<td>RCT; Crossover design. Random order of: 1.MS with music mothers listened to during pregnancy, 2.Recorded lullabies (not described), 3.Control with no music. MS = Quran chanted by a male singer and traditional Arab music. MS and lullaby intervention was played during, during and after a heel-click. No meds for pain relief in any condition.</td>
<td>Pain measured by N-PASS; Change in SaO2; HR and RR.</td>
<td>Significantly lower pain scores with MS compared to control but equivalent pain scores between MS and recorded lullaby condition. During mother’s music infants spent more time in a quiet alert state, with a significant decrease in RR.</td>
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</tr>
<tr>
<td>Shukla et al. (2018)</td>
<td>(200) ≥ 26.36 GA</td>
<td>RCT; Randomisation into groups: 1.KMC + MS, 2.MS, 3.KMC, 4.Control. All groups received expressed breast milk with cup and spoon as pain relief. MS = instrumental-Indian classical flute music played 10 min prior to heel-lick, during, until 5 min after.</td>
<td>Pain measured by PIPP. KMC with and without MS (+ expressed breast milk) significantly reduced pain scores compared to expressed breast milk alone. PIPP score was not significantly different between control and KMC.</td>
<td></td>
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</tr>
</tbody>
</table>

infants’ physiology (Filippa et al., 2019a). In neonatal music medicine research, music recordings are considered to be a simple, convenient, inexpensive and complication-free intervention (Azarmnejad, Sarhangi, Javadi & Rejeh, 2015; Kurdahi Badr et al., 2017). There is, however, a considerable variability in results and many methodological issues, which display a broad diversity in designs and music types used in the research (Table 2). It is also a question of who is choosing the piece of music. Music medicine research acknowledges that music chosen by the patient/parent has been shown to have a greater analgesic effect than music chosen by the researcher. Personal preference and familiarity have been emphasised as important factors in music-induced analgesia (Kurdahi Badr et al., 2017; Juhl Lunde et al., 2019). There is also a worldwide dilemma in music medicine pain research; a majority of the pain researchers include no treatment or placebo treatment to the control groups when conducting clinical pain trials in newborns, consequently withholding established and effective pain treatments to present significant results (Campbell-Yeo, 2016, Table 2).

Music medicine researchers do not yet know what drives the analgesic effect of music (Juhl Lunde et al., 2019). Cutting-edge research with brain imaging techniques shows that music-based interventions have a beneficial effect on the brain development in hospitalised preterm infants, especially when it comes to emotion regulation capacities (Filippa et al., 2019a; Lordier et al., 2019). The music stimuli are processed on multiple cortical levels in the infant brain beyond auditory cortex and involve a complex process in the brain that includes multisensory responses, triggering both cognitive and emotional mechanisms (Filippa et al., 2019a). In music medicine research, music is used both as a pain reliever on its own and as an adjuvant in connection with other types of interventions. Some researchers state that the analgesic effect of music might be found in the treatment context rather than in the music itself (Juhl Lunde et al., 2019). There are several psychosocial and contextual factors related to the patient’s perception of a treatment that may contribute to a treatment effect, such as pain expectations, information given about the treatment, and the environment surrounding the treatment (Juhl Lunde et al., 2019). To which extent music-induced analgesia is related to the music per se or if the analgesic effect can be explained by general factors embedded in the treatment context, are important questions for future research (Juhl Lunde et al., 2019) and for music therapy. The analgesic effect is probably a result of a mix of these factors,
a theory that is discussed in paper III in relation to neonatal pain management and parental infant-directed singing, and further elaborated on in the chapters A synthesis of the main results and Discussion.

**Neonatal music therapy traditions and models of practice**

The first research findings that showed that premature infants in the NICU benefit from auditory stimulation were published within the music medicine field, in nursing science, in the 1970s (Katz, 1971). Neonatal music therapy research began in the 1980s and 1990s with the pioneering work of Jayne Standley at Florida State University, USA. The study undertaken by Standley’s student Janel Caine (Caine, 1991), who used a study design with recorded auditory stimulation, opened up a new context of practice for music therapy (Shoemark & Dearn, 2016). In the initial stages of developing neonatal music therapy, the music therapy pioneers used a music medicine approach with auditory stimulation through recorded music (Caine, 1991; Standley & Moore, 1995; Shoemark, 1999, Nöcker-Ribaupierre, 1999). Professionals in the NICU were protective of their fragile patients and initially there was resistance to music being present in the NICU since all sounds were perceived as noise (Standley, 2014). Research from the music therapy field, traditionally not included in medical treatment in the NICU, was met with scepticism (Standley, 2014). The existing care focus in neonatal care in the 1980s and 1990s undoubtedly influenced the models of practice and research in music therapy (paper IV). The brief history of NICU MT shows that from early on, neonatal music therapy was infant-focused and emphasised the infant's physical and medical needs. The parents were usually not able, encouraged or allowed to be present in the NICUs on a regular round the clock-basis. The benefits of neonatal music therapy were described using outcome measures which met medical standards and NICU MT research was supposed to comply with medical standards for appropriate research design, methodology, and publication (Standley, 2014). Since NICU MT was first developed within an American healthcare context, the quantitative EBP paradigm with a positivist epistemology shaped neonatal music therapy in the early years (Standley, 2014). This is still the predominant perspective. NICU MT developed in different parts of the world, within different research and clinical contexts, from the late 1990s and onwards in the USA (Loewy, 2000), Germany (Nöcker-Ribaupierre, 1999), and Australia (Shoemark, 1999).

During 30 years of NICU MT, the initial model of practice and research with recorded music stimulation and quantitative research designs has been
modified and developed. Today, the infant-focused music therapy interventions have evolved to include both parents and staff, and they also increasingly include qualitative research perspectives. Current NICU MT can be arranged into two main traditions, protocol-based NICU MT interventions and interactive NICU MT interventions. These traditions will be explicated in this section as a backdrop to the evolving family-centred Nordic approach to NICU MT (paper IV).

Protocol-based NICU MT interventions
Within the quantitative music medicine paradigm and protocol-based care framework, which aim to standardise healthcare delivery and outcomes (Ilott, Rick, Patterson, Turgoose & Lacey, 2006), a behavioural NICU MT program called the Pacifier Activated Lullaby (PAL) has been developed in the USA. PAL is a device that uses recorded music reinforcement for non-nutritive sucking training to improve feeding among premature infants cared for in the NICU (Standley et al., 2010). Music is here used as a reward; when the infants suck strongly and long enough, they will receive music stimulation. Developmental and behavioural training is also the core focus for Music and Multimodal Stimulation (MMS) (Standley, 1998), also termed Developmental Multimodal Stimulation (Walworth, et. al, 2012). This is likewise a protocol-based music therapy treatment for premature infants to enhance faster habituation to stimulation and augment matura-
tion through auditory, tactile, visual and vestibular stimulation. MMS is based on the multimodal stimulation protocol known as the Audio Tactile Visual Vestibular (ATVV) (Burns, Cunningham, White-Traut, Silvestri, & Nelson, 1994), but instead of using speech as the auditory stimulus, live singing of lullabies is used as the initial and ongoing auditory stimulus (Standley, 1998).

Another version of the behavioural and developmental approach is the initial German NICU MT method called Auditory Stimulation with the Mother’s Voice (Nöcker-Ribaupierre, 2004). This was a kind of music medicine intervention with recordings of the mother’s voice when she is humming, singing, talking and reading, with the intention to bridge the gap between mother and infant. This method, which is today used more as a method to encourage and facilitate parental live singing, was first initiated in the 1980s when the NICUs had restrictions on visiting hours for German parents (Haslbeck, Nöcker-Ribaupierre, Zimmer, Schrage-Leitner & Lodde, 2018).
Interactive NICU MT interventions
The NICU MT methods used in the German speaking regions are nowadays moving away from the standardised, infant-focused approaches towards individualised, live, observation- and relationship-based methods with parental involvement based on the theories of the Newborn Individualized Developmental Care (NIDCAP), (Als et al., 1994). Typical German music therapy approaches today are live instrumental NICU MT (vibro-acoustic infant-directed stimulation) within the anthroposophical-oriented music therapy, and live vocal NICU MT (responsive, finely tailored and adjusted infant-directed humming and singing with pauses) within the Nordoff-Robbins approach to music therapy, also known as Creative Music Therapy (Haslbeck et al., 2018). The NICU Creative Music Therapy for premature infants and their families (e.g. Haslbeck, 2012 & 2014) is an observation-based live-singing treatment where improvised humming is based upon the breathing pattern in premature infants together with their facial expression and gestures. The improvised humming is attuned to the rhythms and subtle expressions of the premature infants, ensuring that they are not overwhelmed (Haslbeck, 2012).

Live infant-directed singing is also used in the Australian NICU MT method Contingent singing (Malloch et al., 2012; Shoemark, 2007, Shoemark, 2016), which comprises interactive music therapy or interplay with hospitalised newborn full-term infants (Shoemark, 2007). The Contingent singing method was developed within a post-positivist and constructivist paradigm informed by developmental psychology and neuroscience, using both quantitative and qualitative research methods (Shoemark, 2007). This NICU MT method includes improvised infant-directed singing framed by MMS (Standley, 1998). Shoemark adapted the auditory stimulus with live lullaby singing into improvised singing to acknowledge the social maturity of the older infant (Shoemark, 2007). Contingent singing also includes the principals of Communicative Musicality (Trevarthen & Malloch, 2000; paper III), and employs this theory in the intervention. Contingent singing is an act of shared singing, which has purposely been constructed for therapeutic interplay. It is formed by the spontaneous act of infant-directed singing and speech used by caregivers, but it has been consciously created for a specific therapeutic purpose (Shoemark, 2011). Contingent singing is guided by the infant’s availability for social engagement. The music therapist primarily allows a time of silence to observe the infant before using the voice, combined with facial expressions, posture and gesture to stimulate
reciprocal interaction (Shoemark & Dearn, 2016). The music therapist adjusts the improvised infant-directed singing in response to observed facial, gestural and vocal cues and the moment-by-moment status of the infant to support infant development without causing harm (Shoemark, 2007). Within a family-centred care context, contingent singing offers live contingent interactions with a sensitive counterpart to maintain a healthy pattern of infant neurodevelopment (Malloch et al., 2012).

The New York-based RBL-model, First Sounds: Rhythm, Breath, Lullaby (Loewy, Stewart, Dassler, Telsey & Homel, 2013; Loewy, 2016), is a live, interactive music therapy model within the psychodynamic/psychotherapeutic treatment domain, which provides interventions for both the infant and the parents, together or separately. The RBL-model uses special instruments (ocean disc and the gato box) to simulate womb, heart, and breathing sounds, as well as live lullabies or adapted lullaby versions of parent-preferred songs identified by parents as important to their cultural heritage, so called “Songs of kin”, to enhance bonding and attachment (Loewy et al., 2013). The live music and singing are provided by a certified music therapist with RBL-training and are entrained to the infant’s observed vital signs to improve the infant’s self-regulative abilities. Supportive psychotherapeutic music therapy sessions just for the parents in the NICU are likewise part of the RBL-model. This NICU MT model also acknowledges the physical environment in the NICU where random noxious noise may have negative impact on the infants, staff and parents. Environmental factors have a powerful mediating effect on physiological and psychological factors. In Environmental Music Therapy (EMT) the music therapist uses vocal and instrumental improvisation with the intention of lowering the amount of noise and stress that is perceived in the NICU environment (Nöcker-Ribaupierre, 2013). The sound environment is assessed prior to initiating EMT and is evaluated throughout the intervention, taking into consideration the pitches of machine beeps, the tempo in the ward, the mood and any favourite music of the staff. EMT is an intervention for the traditional multi-bed, open-bay NICUs.

Family-centred care informing Nordic neonatal music therapy
Family involvement in the infant’s care and the parent-infant relationship are of central importance in the family-centred care (FCC) philosophy, which is a cornerstone in current neonatal and paediatric health care (Davidson et al., 2017; paper IV). The family and healthcare staff share responsibility for the infant's hospital care. Two of the core principles in FCC are participation and collaboration. A partnership between staff and parents
can lead to optimal clinical outcomes for the infant and the family, as well as enhanced satisfaction for the staff (Griffin & Celenza, 2014). Since the 1990s, the concept of FCC has been part of an ongoing paradigm shift in neonatal care globally. In the United States and the UK, FCC in neonatal care was evolving as grassroots, consumer-driven movements as patients and families began to seek more control over their care (paper IV). Prior to the middle of the 20th century, most of the children in Sweden were born at home. However, during the 1940s and 1950s, home births decreased, and the infants were born in hospitals where infection control and medical interventions increasingly led to improved health outcomes in perinatal care (Jackson & Wigert, 2013). Parents were only allowed to visit their infants during certain visiting hours and see the child through a windowpane. Members of families were seen as dangerous sources of contamination (Greisen et al., 2009). There were no high-tech intensive care units for premature births and sick newborns in Sweden until the 1970s (Jackson & Wigert, 2013). Even though FCC was introduced in the Swedish NICUs in the 1990s, it was not until the 21st century that the neonatal intensive care units started to implement family-centred care and more actively included both parents, and possible siblings in the infant’s care round the clock.

Neonatal music therapy in the Nordic countries is still in its infancy. In this part of the world the cultural and healthcare contexts constitute a privileged approach to NICU MT (paper IV). The family-friendly parental leave policies within the Nordic healthcare systems, which are quite similar across the Nordic countries, are an important reason why the Nordic countries today are on the front line of welcoming and including parents and partners in the care of their infant round the clock. The FCC approach, which today is considered best practice in the Nordic countries, is an example of a societal requirement that defines and shapes the Nordic neonatal music therapy models of practice as well as research with inclusion of and collaboration with the parents in music therapy treatment (paper IV). In the Nordic countries, neonatal music therapy was first introduced in Finland as a research project in 2006 (Teckenberg-Jansson, Huotilainen, Pölkki, Lipsanen, & Järvenpää, 2011). The first Nordic systematic implementation process started in Sweden at Karlstad Central Hospital in 2010, followed by Norway in 2017. In Denmark, there is no NICU MT practice yet, but a growing interest. Even if most infants in the Nordic countries are still cared for in traditional multi-bed, open-bay NICUs, more and more hospitals are today built, or are under construction, to welcome parents round the clock, with separate family rooms, couplet care with zero-separation, bedside rounds and
opportunities for siblings to stay in family rooms with no restrictions on visiting hours.

Section 2: Pain in early life

Describing pain only in terms of its intensity is like describing music only in terms of its loudness (von Baeyer, 2006).

Pain is a complex phenomenon. The purpose of pain is to alert our body to danger and protect it from psychical or psychological harm. The affective aspects of pain are activated both when a person feels pain herself, including social rejection pain, and when she feels someone else’s pain, regardless of whether this pain is physical or psychological (Hart, 2008).

Preventing and alleviating pain in hospitalised infants is as complex as pain itself. When an infant is born prematurely or with a critical illness, pain is inflicted on the infant for life-saving reasons and numerous painful procedures are often unavoidable. Research shows that infants cared for in the NICU, experience on average between 7 and 17 painful procedures per day and very few receive appropriate pharmacological and non-pharmacological analgesic therapy (Carbajal et al., 2015; Roofthooft, Simons, Anand, Tibboel, & van Dijk, 2014; Cruz, Fernandes & Oliveira, 2016).

Pain is hazardous for vulnerable infants. Exposure to painful stimuli in infancy can alter the physiological and behavioural profile of the adult and predispose individuals to chronic pain disorders (Walker, 2019). Physiological and psychological developmental capabilities may change after substantial exposure to severe or repetitive painful procedures (Walker, 2019). It is therefore essential to assess and manage pain in order to prevent, reduce, or stop pain sensations.

There is still today no biologic gold standard for assessing pain in infants, who cannot verbalise their pain. Pain assessment is based on behavioural and physiological indicators of pain; facial expressions, cry, motor activity, heart rate, oxygen saturation etc. Understanding pain in preverbal infants is a challenge. The infant’s responses to pain are affected by many factors like the presence or absence of the parents, age, frequency of prior painful procedures, time since last procedure, duration of hospitalisation, the use of analgesics, the context in which pain occurs, the psychosocial setting, lights, noise, hunger and stress. All these components influence the infant’s perception and experience of the painful procedure as well as the effectiveness of the pain treatment. Healthy infants might elicit a robust cry in response to pain, but immature or acutely ill preterm and term infants may not cry.
Infants who are ventilated cannot cry in response to pain. Absence of cry cannot discount pain, neither can absence of motor activity. Sometimes it is difficult to distinguish between the absence of pain and the presence of so much pain that the infant cannot muster a response. A pain-exposed infant in constant hyperactive state becomes exhausted, passive and oversensitive to all handling and tries to preserve energy with less crying, weaker grimacing and limp posturing (Franck, Greenberg & Stevens, 2000). Infants who experience multiple painful procedures may also become limp and flaccid in response to repeated pain (Pillai Riddell & Chambers 2007). When pain assessment tools are not designed to capture these manifestations of pain, the risk of undertreatment of the infant’s pain is high. This is something that is discussed in paper II. Moreover, few infant pain measures have been developed or validated with infants with neurological impairments, which might also result in the undermanagement of pain.

Infants process pain within the context of the situation but are unable to understand the meaning or long-term consequences of the noxious stress. Infants have limited capacity to modulate the experience and suffering of the pain and have no concept of coping strategies, attributing meaning to the pain or realising there will be an end to the pain (Pillai Riddell & Chambers, 2007). The infants’ limited ability to moderate their pain places great importance on the parents and other caregivers to accurately assess pain and determining when the infant is suffering.

As recently as the mid-1980s, it was believed that infants did not feel or experience pain. For decades, the prevailing belief was that infants have no memories of painful experiences, nor a present perception or localisation of pain, or capability of interpreting pain in a manner similar to that of adults (Anand & Hickey, 1987). As a consequence of these traditional views, infants underwent numerous painful and invasive procedures, including surgery, without any pain treatment – and many of them died (Anand & Hickey, 1987; Anand, Stevens & McGrath, 2007). In most cases, parents are their infant’s advocate and it was a parent, a devastated mother, who in 1985 started to challenge the neonatal practice and its denial of infant pain (Anand, Stevens & McGrath, 2007, p. 220; Tutelman & Chambers, 2016). This mother had a son who died after surgery and at no point during the surgical procedure had he been given any pain treatment. Other parents supported her efforts and so did the groundbreaking research by Anand & Aynsley-Green (1985), which contributed to the paradigm shift in standards of care in neonatal pain. Today, we know that infants, including premature born infants, feel, experience and have a sensory memory of pain and that they are
more vulnerable to the negative effects of pain than older children and adults (Goksan et al 2015; Noel, Palermo, Chambers, Taddio & Hermann, 2015).

**Attachment and pain**

Infant pain should not be understood outside the interactive process involving both the infant and the parents, who in their turn are influenced by the context of the extended family, community and culture (Anand, Stevens & McGrath, 2007; Craig, 2015). The newborn infant enters a multisensory field of affective resonance with the parents via prosody, facial expressions, eye contact, body movements and timing, and through this resonance, infant and parents share and engage in each other’s nervous systems (Hart, 2008, Ham & Tronick, 2009; Tronick, 1989). Two nervous systems, the infant’s and the parents’, that are activated synchronously, create a resonance phenomenon, which amplifies and co-regulates each other’s activity (Hart, 2008; Filippa et al., 2019a). Thus, when an infant is in pain, a present, stable and responsive parent is also agonising. When the parent regulates the interactions with the infant, the parent is not just regulating her/his own affects but acts as the external regulator of affects and neurochemistry in the infant’s brain as well, including the infant’s endocrine and nervous system, in a dyadic feedback loop. (Hart, 2008). Accordingly, it is of great importance to include parents in pain management techniques for hospitalised infants (Bucsea & Pillai Riddell, 2019).

Understanding infant pain in a dyadic context means considering two specific behavioural reciprocal control systems; the attachment system and the caregiving system. Attachment theory, formulated by Bowlby (1988) and operationalised by Ainsworth (1979), is a framework within which the infant learns how to regulate negative affects during stressful situations where a secure attachment becomes a protective factor for the infant and her/his parents through life. Within the attachment system, the infant strives to attain and maintain proximity to the parent when security is an issue. The infant’s attachment behaviour is especially activated by pain, fatigue and frightening events including separation from the parent (Bowlby, 1988). The innate caregiving system is triggered for example by the parents’ perceptions of danger to the infant. The goal of the caregiving system is to increase the proximity between parent and infant to protect the infant. The infant is wholly dependent on the parents and has an innate need for an unbroken secure early attachment to the parents.
Infants are equipped with innate predispositions to elicit protection. Through smiling, vocalising or crying the infant engages the parents in caretaking behaviours. Similarly, reciprocal predispositions in the parents protect the infant and secure survival of the infant. Separation and ruptures in the processes and functions linked to attachment, for example related to painful procedures, are risk factors, while attachment security and caregiver sensitivity are protective factors against psychopathology in both parent and infant (Fonagy, 1999). Repeated, cumulative and inadequately treated procedural pain in addition to separation from the parents will harm the infant physically and psychologically in the short term, including increasing the risk for abnormally heightened sensitivity to pain (Taddio, Shah, Atenafu, & Katz, 2009; Filippa et al., 2019b). The infant’s nervous system and brain development respond to early extreme or mismatched environmental conditions, like repeated painful procedures, with maladaptation that can hold a negative impact on development, correlating with later neuropsychological deficits (Brummelte, 2017; Filippa et al., 2019a). It might also jeopardise the new family’s attachment process and mental health in the long term and for generations to come (Fonagy, 1999; Cirulli et al., 2010).

The parents’ personal experiences of pain are influential, hence parental behaviour can either promote coping or exacerbate distress in an infant (Pillai Riddell & Chambers, 2007). What seems to be most crucial for an infant before, during and after a painful situation as well as for future painful experiences is the extent to which the parent is emotionally available and stable, capable of noticing and contingently interpreting cues and communications implicit in the infant’s behaviour, responding adequately to the infant’s distress signals and being able to soothe, regulate and share the infant’s states (Pillai Riddell et al., 2011; paper III). Parents’ facial expression and tone of voice during painful procedures influence the infant’s pain experience. A parent who uses a reassuring tone of voice while the infant is in pain does not communicate a shared affect of the painful experience and subsequently the infant shows an increase in pain and distress (Pillai Riddell & Chambers, 2007). A well-informed and emotionally stable parent is however a powerful agent of pain relief for the infant and should therefore be invited and supported as prescribed pain management (Pillai Riddell & Chambers, 2007). Singing, sharing, soothing, holding skin-to-skin, rocking and breastfeeding are simple and cost-effective evidence-based interventions that modify the infant’s pain if the strategies are well-timed (Pillai Riddell & Chambers, 2007; Shahid, Florez & Mbuagbaw, 2019). Parent-driven pain alleviating approaches are efficacious when the infant distress is not too high. High levels of
distress disrupt the infant’s ability to be regulated by otherwise helpful soothing behaviours (Pillai Riddell & Chambers, 2007). These conditions have great implications for music therapy in neonatal pain management (paper III).

**Parents’ role in neonatal pain management**

In the mid-1980s, a surge of research on infant pain was initiated as a result of parental advocacy to acknowledge infant pain. The parents’ role in the pain experience of older children has received considerable attention in research, but parents’ participation in infant pain management has quite recently become a focus for research in nursing pain science (e.g. Axelin, Lehtonen, Pelander & Salanterä, 2010; Franck, Oulton & Bruce, 2012; Axelin et al., 2015; Olsson, Ahlsén & Eriksson, 2015; Palomaa, Korhonen & Pölkki, 2016). Research shows for example that when parents are present, the documentation of nursing pain assessment increases as well as the use of non-pharmacological pain-relieving methods, and parental presence can reduce the child’s pain intensity and behavioural distress (Johnston, Barrington, Taddio, Carbajal, & Filion, 2011; Courtois et al., 2016).

From the parent’s perspective, there is a confusion and frustration about their role in their infant’s pain management (Palomaa et al., 2016). The ongoing global paradigm shift with FCC has come a long way in welcoming and including parents in the everyday care of their infant, but in infant pain management there are still mindsets and staff behaviours that restrict parental participation in neonatal pain relief round the clock (Greisen et al., 2009; Franck et al., 2012; Palomaa et al., 2016). In a study by Axelin et al. (2015), the authors found three types of nursing strategies in pain management. When the nurses were *controlling* the pain management, the parents were absent or passive. The nurse thought this control was better for the infant and that it was protecting the parents from emotional distress. When the nurses *shared* some control with the parents, they provided information and opportunities for parental participation. But with a nurse and parent *collaboration*, the pain management was individually tailored and optimal for the infant. The collaborative approach was most evident for the nurses in the Swedish NICUs but not so common in the NICUs in Finland and the USA (Axelin et al., 2015).

Parents are worried about the effects of pain and pain treatments on their infant and they have a need to fulfil their parental protective role during painful procedures. The desire of parents to be present and to participate in comforting their infant during painful procedures has been investigated
90% of the parents who received evidence-based information about pain plus a hands-on demonstration how to apply the comforting techniques described, expressed a stronger preference to be present and actively involved during painful procedures, which poses a demand on the neonatal units to better respond to parents’ expressed desire for increased knowledge and involvement in infant comfort. (Franck et al., 2011). Thus, interventions to improve parent knowledge and involvement may improve infants’ pain management. The parents in the study by Palomaa et al., (2016) elaborated on this topic; parental counselling was the factor that generated most of the parents' participation, and lack of knowledge inhibited them. Parents want a greater amount of and repeated instructions in various modalities such as verbal counselling, visualisation, hands-on demonstrations, which also take the parents’ diverse individual needs in consideration (Palomaa et al., 2016). According to the parents, there are also environmental factors that need to improve in the NICUs, such as the restrictive caregiving culture and the NICU design, where parent-infant closeness and couplet care with separate family-rooms promote parents' participation and create family-centred pain management (Lester et al., 2016; Palomaa et al., 2016).

Parents are an underused resource in pain management. They have unique knowledge and perspective of their infant’s needs and personality and can be effective partners in the care of the infant, also in neonatal pain management, if they are acknowledged by the NICU-staff (Palomaa et al., 2016; Pölkki, Korhonen & Laukkala, 2018). According to the American Academy of Pediatrics (2016), the prevention and management of infants’ pain should be the goal of all healthcare professionals, and parents should receive education and guidance, not just verbal information, on how to mitigate their infant’s pain (Pölkki et al., 2018). Non-pharmacologic methods have proved useful to reduce pain scores among infants during short-term mildly to moderately painful procedures (American Academy of Pediatrics, 2016). Non-pharmacologic methods are recommended particularly for procedural pain management in infants because there are no adverse effects and parents can use these approaches safely (Pölkki et al., 2018). There are still many non-pharmacologic methods of pain management that are not commonly used during painful procedures, such as singing and breastfeeding. Parents’ use of non-pharmacologic methods is related to the amount of the guidance provided by the nursing staff (Pölkki et al., 2018).
Pharmacological and non-pharmacological pain management

Pharmacological pain management in infants is a complex field and beyond the expertise of this thesis, but in short, most drugs that are used in neonatal pain treatment are not approved for use in infants. For the most common procedure in the NICU, skin puncture by heel-stick, pharmacological agents are not as effective as non-pharmacological approaches (Larsson, Jylli, Lagercrantz & Olson, 1995), e.g. opioid analgesia has a slow onset of effect and is ineffective for procedural pain (Hartley et al, 2018). In addition, the use of analgesic drugs has negative developmental side effects (de Graaf et al., 2011; Shahid et al., 2019). Heel-stick is unfortunately still a common way of taking blood from infants, but it is also a very painful procedure. The recommended blood-sampling method today is instead venepuncture, which causes less pain than heel lance (Shah & Ohlsson, 2011). Oral sweet solutions as sucrose and glucose are today part of standard care in the NICUs and are considered to have a calming and analgesic effect on infants during painful procedures (Fernandes, Campbell-Yeo & Johnston, 2011). Sweet solutions are considered to be pharmacological agents (Norman & Eriksson, 2016) and have been extensively investigated and found to reduce procedural pain from blood-sampling procedures in both preterm and term infants without serious side effects (Stevens, Yamada, Ohlsson, Haliburton & Shorkey, 2016).

It is recommended that pharmacological pain therapies are only used in conjunction with non-pharmacological interventions (Anand & Hall, 2006) and that non-pharmacological interventions should in general be the first choice in procedural pain (Fernandes et al., 2011). Sucrose might for example be more effective in combination with non-pharmacological interventions than sucrose alone (Stevens et al., 2016). Non-pharmacological pain management involves interventions driven by nurses and parents and they are cost-effective and easy to administer (Campbell-Yeo, Fernandes & Johnston, 2011). Swaddling and containment or facilitated tucking are parts of the developmental care, a family-centred nursing care concept, which strives to minimise infant stress and pain. Other nurse-initiated pain alleviating interventions are positioning and non-nutritive sucking (Fernandes et al., 2011). Parents can be included in most of these interventions, but parental presence is not required. Among the non-pharmacological approaches, the biopsychosocial perspective strongly supports parent-driven interventions (paper III). In the parent-driven non-pharmacological interventions, the parent herself/himself is a mediator for pain relief (Campbell-Yeo et al., 2011).
Parent-driven interventions are skin-to-skin care, breastfeeding and multisensory stimulation like vocalisation. They are all a combination of multiple sensory inputs comprising auditory, tactile and olfactory recognition. Research has started to investigate breastfeeding in combination with kangaroo mother care for example, which has shown to be an effective mix (Leite et al., 2015). A multimodal approach that includes a combination of non-pharmacological approaches is considered more effective than single strategies and provides greater pain relief (Norman & Eriksson, 2016). Some approaches are effective during the actual procedure, whereas others promote the infant’s recovery after the procedure.

A painful procedure consists of different stages; the skin breaking procedure followed by a recovery phase. However, there is one more phase that receives less attention in the literature than it deserves, and that is the preparation stage. The pain alleviating interventions should not just be present during the skin puncture. There is always a before and after. Swedish Medical Products Agency has published recommendations concerning procedural pain management in infants and children where age-appropriate pre-procedural preparation is the base in the treatment pyramid and pharmacological agents are placed in the smallest top of the pyramid (Swedish Medical Products Agency, 2014). Parent-driven non-pharmacological biopsychosocial interventions cover the whole procedure; preparation stage, blood-sampling stage and recovery stage. When the infant and the parent experience a high degree of control in a challenging or stressful situation, the event is not always experienced as distressing. It is the perception of the stressful experience that for example determines the amount of stress hormone cortisol that is released. Coping strategies or a sense of control before, during and after the blood sampling reduce the negative experience of stress (paper III). Therefore, combining interventions before, during, and after seems to offer additional benefits (Fernandes et al., 2011).

Pain physiology in infants

Pain sensation is processed in the brain, not in the tissues of the body. A distinction must be made between nociception and pain. Nociception involves the stimulation of nerves that convey information about potential tissue damage to the brain. Pain is the subjective perception that results from the transmission and modulation of sensory information (Gatchel, Peng, Peters, Fuchs & Turk, 2007). There is no specific pain centre in the brain. Pain arises from a distributed network of brain activity, none of which is unique.
to pain. During the experience of pain there are multiple central brain regions involved and these regions process the affective, sensory, cognitive, motor, inhibitory, and autonomic responses stimulated by a noxious event. The “pain network” is viewed as a dynamic and interactive system (Verriotis, Chang, Fitzgerald & Fabrizi, 2016). Pain physiology in infants is complex and more research is needed to understand how infants receive, experience, inhibit and express pain. The following overview will serve as scaffolding for comprehending the pain theories and models described in this thesis and for appreciating the results and conclusions of the same.

Ascending nociceptive fibres
When the infant is exposed to a skin breaking procedure, electrical impulses travel along the nerve cells carrying information to the infant’s spinal cord and further on to the infant’s brain. The spinal cord is a relay station or a gate, referring to the Melzack-Wall Gate Control Theory of Pain (Melzack & Wall, 1965). The electrical impulses are altered and modified in the spinal dorsal horn before they reach the brain. The spinal gating mechanism in the dorsal horn is also modulated by descending nerve impulses from the brain. Because the infant is so small, the sensory nerve cells endings, called nociceptors, in the receptor fields in the infant’s skin are overlapped. A painful procedure therefore activates multiple nociceptors in the infant’s skin simultaneously and more pain signals are consequently sent to the brain, which is one reason why infants are more sensitive to pain than adults. Too much pain is toxic for the nerve cells especially in a nervous system that is growing, and nerve cells may die. This is also a reason for why it is important to prevent and manage pain in infants.

There are two types of ascending nociceptive fibres that carry pain signals to the brain: A-delta fibres (Aδ) and C fibres. In addition to the Aδ and C fibres that carry noxious sensory information, there are primary afferent A-beta (Aβ) fibres that carry non-noxious stimuli. Afferent neurons are neurons that receive information from the sensory organs. Each of these fibre types possesses different characteristics that allow the transmission of different types of sensory information. These fibres differ both in diameter and in the thickness of the myelin sheath that surrounds them. Aβ fibres are large in diameter and highly myelinated and therefore allow rapid signal conduction. They have a low activation threshold and usually respond to light touch and transmit non-noxious stimuli. The Aδ fibres are smaller in diameter and myelinated and therefore fast-pain pathways, which also carry the signals that trigger the withdrawal reflex within a few milliseconds after
a painful stimulus. The even smaller-diameter C fibres are non-myelinated and the transmission of nerve impulses is slower. The pain signals therefore reach the brain at different times. The transmission over Aδ fibres causes the “fast pain”, which goes away fairly quickly. The transmission over non-myelinated C fibres causes the “slow pain”, which persists longer. The pain signals in these two ascending nociceptive fibres guide the brain to locate the sensation of pain and assign it an emotionally unpleasant connotation. There is no longer a dispute about the infant’s ability to perceive pain. However, the infant’s affective pain processing of the noxious stimuli has not been known until a study by Goksan et al., (2015) managed to show that infants are capable of interpreting pain in a manner similar to that of adults, and that almost all regions of the brain that are activated during acute pain in adults are also activated in healthy full-term newborn infants. This suggests that infants have the capacity to experience an affective relevant context related to incoming sensory input.

As previously mentioned, pharmacological interventions are not investigated enough in infants, but recent research implicates that pharmacological interventions are unsuccessful in alleviating procedural pain and can be hazardous for infants in the long term (Carbajal et al., 2005; Anand & Hall, 2006; Shahid et al., 2019). The infant’s kidney and liver mature slowly, and the blood-brain-barrier prevents efficacious concentration in the central nervous system. Therefore, there is a need to research and put into use efficient non-pharmacological pain-alleviating interventions that work through the infant’s own descending pain modulatory system within the interactive and biopsychosocial attachment/caregiving systems. If we look at the infant’s pain physiology again; are infants able to reduce pain signals travelling up the ascending pathways, from the body to the brain? Do infants have the ability to diminish their pain experience? The answer is yes and no.

Descending pain modulatory system
The descending pain modulatory system constitutes a network of widely distributed brain regions whose integrated function is essential for effective modulation of sensory input to the central nervous system and behavioural responses to pain (Goksan et al., 2018). In adults, pain perception is modulated by the descending pain modulatory system, which allows for environmental, contextual and cognitive factors to influence the pain experiences (Goksan et al., 2018). The medical community has so far acknowledged that infants are equipped with descending pain-control pathways, but have on the other hand assumed that these pathways are immature at birth.
and that they develop slowly during the first years of life before they may inhibit pain sensations (Larsson, 2016). For a neonatal music therapist and other professionals who study non-pharmacological pain management interventions, it is essential to know if the descending pain-control pathways are functioning in the infant from birth in order to be able to explain if, when, how and why non-pharmacological interventions alleviate pain in newborn infants. If the descending pain modulatory system functions optimally from birth, it might explain the efficacy of multisensory and multimodal biopsychosocial parent-driven pain alleviating interventions, which are focusing on modifying and modulating the affective aspects of the painful experience. As previously mentioned, cutting-edge research in brain imaging has shown that infants experience the affective dynamics of pain like adults (Goksan et al., 2015), and the results have been confirmed in a study by Goksan et al. (2018). The same research team (Goksan et al., 2018) has now in a new study also proved that the descending pain modulatory system is fully functional at birth in term born healthy infants, similar to that observed in adults. This may suggest that in the newborn term infant, the brain regions involved in descending pain modulation may be influential in dampening down, altering and alleviating the painful experience as well as modifying pain behaviour. It is therefore reasonable to believe that infants are responsive to affective pain-alleviating interventions from birth, for example music and singing.

Findings from the study by Goksan et al., (2018) also show that when brain regions within the descending pain modulatory system are more functionally connected, infants have a greater ability to regulate their brain activity in response to incoming noxious stimulation. Functional connectivity analysis is used to better understand how networks of brain regions are involved in complex functions (Goksan et al., 2018). The study by Goksan et al., (2018) did not investigate preterm infants, so we do not yet know if the descending pain modulatory system operates at birth in a less functionally connected brain, like the preterm infant’s immature brain. This might be one explanation as to why preterm infants are having problems with self-regulation. The self-regulating arousal systems are among the systems most damaged by premature birth (Feldman, Weller, Sirota & Eidelman, 2002).

**Music for distraction and music therapy as integration**

Music for distraction and music therapy as integration are two dichotomous approaches in procedural support for infants and children. Distraction means focusing the attention away from the procedure, versus integration,
which is more established in psychotherapeutic music therapy, where the patient is focusing on the procedure or her/his internal responses in reaction to the procedure. In music therapeutic integration, the effectiveness of music is more than an audio-analgesic (paper III). Music therapy as procedural support also includes interactive and relational aspects. According to Ghetti (2012), procedural support in music therapy is the “use of music and aspects of the therapeutic relationship to promote healthy coping and decrease distress in individuals undergoing medical procedures” (Ghetti, 2012, p.6). Another definition proposed is:

Procedural support in music therapy is the interactive use of music by a board certified music therapist during an invasive or painful medical procedure; the music is designed to specifically address a patient’s needs including reducing anxiety and pain perception, and to encourage healthy coping behaviors. (Beer & Lee, 2017, p. 266)

In the Integrative Model of Procedural Music Therapy (Loewy, 2019), the central concept of integration signifies an emphasis on focusing on the pain while musical expression provides an externalising release, a release or description of pain or anxiety in sounds or words, for the experience of acute pain (Ghetti, 2012). When a patient in pain is crying or making loud unpleasant moans, the healthcare staff usually consider these expressions as negative, while Loewy (2019) argues that these expressions could be defined as a release-oriented coping strategy of self-expression and protection and should be addressed by a music therapist with suitable age-appropriate pain alleviating techniques (paper III).

Entrainment is a fundamental principle in integration. Music and singing entrainment are used by music therapists to change the patient’s physiological responses in order to reduce stress and anxiety. In entrainment, the music therapist first matches the music pulse to the patient’s heart rate or respiratory rate to establish resonance between the music and the physiological responses, then gradually changing the tempo of the music or singing in the therapeutically desired direction. For example, it might involve gradually slowing down the tempo of the music or the singing while the respiratory rate or the heart rate follow the music to encourage deeper breathing or a more calm and regulated heart rate. Music entrainment is based on a process in physics whereby two previously out-of-step oscillators lock into phase with one another, replacing the vibrational rate of one system with the vibrational frequency of another system (the music or the singing) (Bradt, 2013). Entrainment should not be confused with the term synchronisation, which means that the music or singing is matched to the patient’s
external behavioural or physiological responses without the gradual pull from the music (Bradt, 2013). With the psychosocial support from the music therapist the musical release helps the patient to integrate the painful experience, and this integration might induce feelings of empowerment, increase the sense of control, coping and trust, and build a readiness for future procedures. The integrative model of procedural music therapy is an option that in the long run may provide more potency and longevity (Loewy, 2019).

Music as distraction is often used in the music medicine field. Distraction is the most common used tool in interdisciplinary paediatric pain management globally. Current nursing and psychology research, supported by guidelines from for example the Canadian Paediatric Society (2014), suggests that four bundled modalities should be offered for elective needle procedures in order to reduce or eliminate pain experienced by children. A topical anaesthetic is used in both infants and children to numb the skin. Sucrose or breastfeeding is used for infants 0-12 months. Breastfeeding might however be difficult to establish for very preterm neonates. Comfort positioning for infants includes skin-to-skin contact or facilitated tucking and for children six months and older it includes sitting upright, with parents holding them on their laps. The fourth modality is age-appropriate distraction such as singing, talking, or sucking (breastfeeding or soother) before, during, and after the needle, adding rocking of the infant/child after the needle and perhaps toys, books, blowing bubbles, electronic devices etc. (Canadian Paediatric Society, 2014). It is notable that within the interdisciplinary research field of neonatal pain there is a vanishingly small amount of research articles that address the vocal aspects of pain management and the voice of the parent (Jahromi, Putnam & Stifter, 2004). In the guide for parents on how to reduce pain in infants, the Canadian Paediatric Society states: “The way you distract your baby once may not work the next time. Be prepared to change what you are doing to keep your baby distracted” (Canadian Paediatric Society, 2014). Distraction is a momentary intervention in pain management and its efficacy is therefore questionable (Loewy, 2019). Distraction as a pain management technique should not be ruled out as an option for patients who choose such a tool, but it should be formally assessed as one option, and not taken as an assumption (Loewy, 2019). Distraction should imply a child-volitional and engaging shift of attention, distinguished from a “trick” that essentially undermines trust. Trust is a pivotal point in pain management, a cornerstone of effective treatment and the basis for provisions necessary for the context of care throughout the treatment and in future treatment trajectories (Loewy, 2019).
Pain theories and models informing neonatal music therapy

Pain theories and models for pain management and procedural support are presented in Table 3 as a basis for the proposed Nordic NICU MT pain management strategy introduced in the result chapter of this thesis.

Table 3. Transdisciplinary pain theories and models for pain management and procedural support.

<table>
<thead>
<tr>
<th>Pain model/ theory</th>
<th>Author</th>
<th>Description</th>
<th>Age range</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Gate Control Theory of Pain</td>
<td>Melzack &amp; Wall (1965)</td>
<td>The first biopsychosocial model of pain. A gate control system in the spinal dorsal horn modulates sensory input from the skin. By increasing non-painful sensory input, for example in the auditory, visual and tactile domains, the pain perception might be modified via descending inhibitory pathways.</td>
<td>All ages</td>
</tr>
<tr>
<td>Biopsychosocial model</td>
<td>Engel (1977)</td>
<td>Pain is the result of the dynamic interaction among physiologic, psychological, and social factors, which might augment each other over time.</td>
<td>All ages</td>
</tr>
<tr>
<td>DIAPR-R</td>
<td>Bucsea &amp; Pillai Riddell (2019)</td>
<td>A biopsychosocial model grounded in attachment theory underlining the importance of parental inclusion in the implementation of pain management interventions in hospital settings.</td>
<td>Infants, procedural pain</td>
</tr>
<tr>
<td>Social communication model of pain</td>
<td>Craig (2015)</td>
<td>A biopsychosocial model. Infants learn about pain through their families. Culture shapes the pain experience and pain expressions of the family.</td>
<td>Infants, children, procedural pain</td>
</tr>
<tr>
<td>Procedural comfort care</td>
<td>Leroy et al. (2016)</td>
<td>Age-appropriate pre-procedural preparation is crucial for mitigating pain. During the preparation phase and the procedure, the staff should continually monitor and coordinate between the comfort process and procedural process, and only proceed when comfort is optimal. The environment should be child-friendly, non-threatening and family-centred.</td>
<td>Children, procedural pain</td>
</tr>
<tr>
<td>Working model of music therapy as procedural support</td>
<td>Ghetti (2012)</td>
<td>Pre-assessment and ongoing assessment are vital components in this model. The procedural support consists of the music therapist and the role of the music interacting with the responses from the patient. These factors serve as a treatment lens that filters the patient’s experience of the procedure. The music used is live, familiar to or preferred by the patient or improvised, in order to enable procedural support to be individually tailored.</td>
<td>Children, procedural pain</td>
</tr>
</tbody>
</table>
The Gate Control Theory of Pain

Pain theories have moved away from the uni-dimensional biomedical conceptualisation of pain where the pain pathway was viewed as a fixed, direct-line communication system from skin receptor to a pain centre in the brain without any psychosocial interplay, towards multidimensional models that recognise the complex interplay between the physiological, psychological and sociocultural mechanisms that form the pain experience. When Melzack & Wall (1965) introduced their pain theory, this was the beginning of a paradigm shift; viewing pain as a dynamic and interactive system that incorporates sensory, affective and cognitive components. The gate was a metaphor for the gating mechanism in the spinal dorsal horn, a gate control system that modulates sensory input from the skin during a skin puncture before it evokes pain perception and response (Melzack & Wall, 1965). Strategies focusing on coping and stress reduction help to “close” the gate while negative states of mind, such as helplessness, hopelessness and anger, tend to amplify the intensity of the sensory input (Gatchel & Howard, 2008). Pain transmission can be modulated at various levels, including the dorsal horn of the spinal cord and via descending inhibitory pathways from different parts of the brain. The Gate Control Theory was later refined into the neuromatrix theory of pain, suggesting that pain is the consequence of the output of the widely distributed brain neural network rather than a direct response to sensory input (Gatchel et al., 2007). The Gate Control Theory of Pain paved the way for modern transdisciplinary models of pain and is considered the first biopsychosocial model of pain (Pillai Riddell, Racine, Craig & Campbell, 2013). The Gate Control Theory and the subsequent neuromatrix theory have led to the development of various non-pharmacological approaches, including neonatal music therapy, to alleviating pain in infants (Bradt, 2013).

Biopsychosocial models

In the biopsychosocial model, humans are considered to be multidimensional, biological and social beings in a context of family and community (Engel, 1977). The biopsychosocial perspective provides an integrative and relational framework for understanding for example pain and pain management. The model also allows for an interdisciplinary pain management approach, which makes it a relevant model for understanding and including music therapy in neonatal pain management.

A biopsychosocial model of more recent date is the Development of Infant Acute Pain Responding (DIAPR) model, developed specifically for infant procedural pain and grounded in attachment theory (Pillai Riddell et
The model has later been revised into the DIAPR-R-model (Bucsea & Pillai Riddell, 2019). Infants are biologically predisposed to seek the help of their parent in times of distress. The infant signals to the parent to engage in distress-reducing or mitigating interventions. Parents have an innate system that is activated by infants’ distress signals, which prompts the parent to respond in a soothing manner that will help regulate the infant’s negative affect. Positive parent-infant interactions have been demonstrated to employ a buffering effect on the connection between early neonatal pain exposure in preterm infants and subsequent cognitive functioning and mental health outcomes (Bucsea & Pillai Riddell, 2019). The model recognises the parent’s own pain experiences and cognitive pain schemas which will influence her/his autonomic nervous system physiology, her/his pain assessment and her/his management of the infant’s pain, which in turn influences the infant’s pain regulation and reactivity (Pillai Riddell et al., 2013; Bucsea & Pillai Riddell, 2019).

The Social communication model of pain acknowledges pain as a biopsychosocial phenomenon, conceptualising the individual, familial, community, and cultural influences on infant pain. This model describes pain as a process of dynamic interactions between infants/children and parent. The model distinguishes between experience of pain and expression of pain. The pain experience of the infant is influenced by sensory and affective qualities. However, the expression of pain does not only reflect internal experience and processes, but is also influenced by social reinforcement by the parent and by macro-social factors, such as the culture of the family and the healthcare system (Craig & Pillai Riddell, 2003, Craig, 2014).

Procedural support models
Procedural comfort care is mainly focused on the preparation phase where age-appropriate pre-procedural preparation is crucial for mitigating pain (Leroy, Costa, Emmanouil, van Beukering & Franck, 2016). Involving a combination of sensory and procedural information is associated with the largest and most consistent benefits (Suls & Wan, 1989). The physical and emotional environments are equally important to evaluate in the preparation phase. The environment should be child-friendly, non-threatening and family-centred (Leroy et al., 2016). A key factor in the model is that procedural comfort starts with non-pharmacological strategies. These are not considered just as an adjunct to pharmacological interventions. Non-pharmacological strategies result in better procedural care according to the model (Leroy et al., 2016).
The Working model of music therapy as procedural support (Ghetti, 2012) is a model that aims to describe the mechanisms underlying procedural support, which may include support to reduce anxiety and/or pain, as well as promote resiliency and healthy coping. The working model explains how the music therapist, the patient, the music, those around the patient, and the context act as partners in an ongoing reflexive process of supporting a patient through painful or anxiety-producing procedures (Ghetti, 2012). Ghetti’s intention is that this model is work in progress, which could evolve through dialogue and further theoretical development, and could serve as an initial systematic step toward theory construction in this area (Ghetti, 2012). Some vital parts of her results and model will be mentioned here, which will be further developed and elaborated on in a synthesis of the main results.

The assessment prior to the procedure focuses on individual and procedural factors that will moderate the experience of the procedure, such as music preferences, developmental level, coping strategies and demands of the procedure itself. Preparation makes an important contribution to the alleviation of pain and anxiety during the subsequent procedure. During the preparation phase, the music therapist should establish a rapport of trust and cooperation to relieve possible pre-procedural anxiety in the child and parent in order to promote comfort and coping. The ongoing assessment is considered a reflexive process. The music therapist adjusts her/his interventions and role over time according to the responses and changing needs of the individual patient during the course of the procedure, altering the context and the environment within which the patient experiences the procedure. The music must be modified based on patient needs and preferences (Ghetti, 2012).

In the model, the patient’s experience of the painful or anxiety-producing procedure is dependent on a merge of various interacting factors and each situation is unique. The model recognises the influences of context, environment, type of procedure as well as personal variables, such as previous painful experiences, pain sensitivity, family support etc. The procedural support in the model consists of the music therapist and the music, which interact with the responses from the patient. These factors serve as a treatment lens that filters the patient’s experience of the procedure. This ongoing filtering process results in a change of the patient’s perceptions of pain, anxiety and of the procedure itself as well as the patient’s behavioural expressions of this experience (e.g. coping responses and verbalisations). The music therapist uses these outcomes to further adjust the treatment lens to positively influence outcomes (Ghetti, 2012).
Theoretical framework and concepts

As delineated in the Background chapter, music and pain are complex phenomena, described as subjective, multidimensional, perceptual, contextual, biopsychosocial experiences. The complexity in the studied objectives of this doctoral thesis allows for an integrative approach, incorporating research from areas within the biological and the psychosocial realms. The thesis would therefore benefit from a theoretical framework that allows for a mutually enriching dialogue between neuroscience and developmental psychology. The framework chosen for this doctoral thesis is Neuroaffective developmental psychology theory (NADP), which operates as a “holding environment” (Winnicott, 1960) for those theories, concepts and processes presented in the Background as well as for the results, strategies and conclusions further on.

Neuroaffective developmental psychology

The theoretical synthesis of modern neuroscience and theory of developmental psychology began in the 1990s (Hart, 2008; Hart & Lindahl Jacobsen, 2018). In Scandinavia, there has been a strong focus on synthesising developmental psychology based on research from Louis Sander, Daniel Stern and Colwyn Trevarthen, with neuroscience research from for example Paul MacLean, Peter Fonagy and others (Hart & Lindahl Jacobsen, 2018). The NADP is a theory based on relation and attachment theory derived from a psychodynamic tradition, and a psychological understanding of emotional development where neuroscience is used as an overall structural understanding of the complexity between psychological issues and how the nervous system matures (Hart & Lindahl Jacobsen, 2018).

Humans are social beings, born to communicate and share emotions. Culture, in the broader sense, shapes the human brain and mind (Hart, 2011). Our innate potential can only be realised through culture since nature and nurture interact in an interdependent process and are inseparable (Hart, 2011). Human contact creates neural connections and environmental stimuli regulate the anatomical and cellular organisation in the developing nervous system (Hart, 2011; Filippa et al., 2019a). Hormones, stress, social interaction and pain will affect the neural structures in the infant. Early trauma, such as repeated painful procedures early in infancy and separation from the parent, can activate certain genes that lead to a reduced capability for interpersonal adjustment, which makes infants more sensitive to later
trauma (Hart, 2011). On the other hand, a stimulating and enriched environment also has long-term effect on infants’ neurological structure and neurochemistry, enlarging or altering the infant’s brain (Hart, 2008, 2011; Filippa et al., 2019a). The parents shape their infant’s brain and nervous system in unique ways through constant interactions with the infant, since the human brain is designed to mature on the basis of experiences (Stern, 2010; Hart, 2011). It is an ongoing dialogue, as each influences the other and shapes one another. The following paragraphs present the nature and nurture theories and concepts that have been both important in the analysis and reasoning process of paper I-IV as well as operational in the writing of this doctoral thesis. However, one must bear in mind that the following concepts and abilities might be damaged or underdeveloped in infants due to premature birth.

**Dynamic forms of vitality**

In paper III, the concept of vitality affects was one of the basic prerequisites for including parental live singing in neonatal pain management. Stern’s final and more comprehensive concept, dynamic forms of vitality (Stern, 2010), is a cornerstone for the results and conclusions of this doctoral thesis and will be explained in further detail below.

Over many decades, Daniel Stern (2010) was elaborating on the dynamic aspects of experience. His interest began with observations of non-verbal mother-infant interactions and microanalysis of film and videotape of mother–infant face-to-face interaction, where the dynamic features of early human exchanges were more obvious. Stern discovered that the mothers used dynamic forms of vitality when they wanted to show the infant that they understood and shared what the infant was experiencing. Without vitality forms there could not be the exquisite fine-tuning of these interpersonal interactions (Stern, 2010). Vitality forms are difficult to grasp because humans experience them in almost all waking activities, and they are highly subjective phenomena. The domain of dynamic forms of vitality is separate and distinct from the domains of emotion, sensation and cognition; it stands on its own. Vitality is more of a form than content and concerns the how, the manner of the experience (Stern, 2010). Vitality forms colour the experience of the content and are coloured by it as well. Dynamic forms of vitality are ubiquitous and part of all experiences, according to Stern (2010). They may arise in very early development as the central place of arousal in the beginning of life (Stern, 2010).
Stern has throughout the years used different terms to capture this dynamic aspect of experience; vitality affects, temporal feeling shapes, temporal feeling contours, proto-narrative envelopes, vitality contours. He finally merged them all choosing the englobing term *dynamic forms of vitality* (Stern, 2010). In this concept, Stern also includes force, movement, space, directionality and aliveness, as well as time and intensity (Stern, 2010, p. 17). Movement plays the primary role in creating forms of vitality. Each individual has a movement signature and humans experience each other on the basis of the vitality expressed in the other person’s movements; a specific walk or smile that carries the signature of their own unique vitality (Stern, 2010). Humans move constantly, both physically and mentally. For example, the respiration moves in cycles, gestures unfold in time, and the arousal levels shift. There is a time profile of the movement, a force to the movement, a space where the movement happens, and it has intentionality and directionality. Together, these events form the dynamic experience of vitality. The primary essentials of infant-directed singing, whether it is in play-song style or lullaby-style, are the dynamic forms of vitality. Stern suggests that the intimate, well-timed and fine-tuned interactions of parent and infant have musical qualities, where the dialogue between the parent and the infant is saturated with dynamic forms of vitality. Music is sound in motion (Stern, 2000).

It has been established that infants have cross-modal capacities and that there is a multisensory integration early in cortical processing (Stern, 2010). Neuroscience suggests that there are neurons throughout the brain responding to stimuli from more than one single sense, meaning some neurons are multisensory (Stein & Stanford, 2008). The multisensory neurons exist even in brain areas thought to be devoted to only one sensory modality (Stern, 2010; Stein & Stanford, 2008). In particular cortical motor areas, which traditionally were believed to possess functions purely related to movement, are now known to be actively involved in processing sensory information as well (Ammaniti & Ferrari, 2013). These findings may clarify some of the multimodality of dynamic forms of vitality (Stern, 2010). Vitality forms are modality non-specific. They belong to all sensory modalities (vision, audition, touch, smell etc). Vitality is a whole, which emerges from experiences of movement, force, time, space and intention (Stern, 2010). The infant is first and predominantly sensitive to vitality forms and can distinguish vitality forms in their experiences, which makes the infant a multimodal being, though not yet mature enough to discriminate qualitative aspects of the modalities, the content, in their experiences. Dynamic forms of vitality can
therefore exist even for infants, but in a multimodal form with multimodal content, which is compatible with the findings on multisensory neurons (Stern, 2010). The richness of perceptual experience, as well as its usefulness for guiding behaviour, depends on the synthesis of information across multiple senses (Stein & Stanford, 2008). Whether a sound is heard or a movement is visually perceived, the brain will deal with it as a multisensory event (Stern, 2010). However, there might be beneficial as well as harmful experiences in infancy, such as repeated and untreated pain, which also affect the infant’s sensitive brain development in a multisensory way.

**Proto-musicality**

In the womb, the foetus grows familiar with the interior sounds of the mother, continuously enriched by the multimodal sensory environment; the steady rhythm of the mother’s heart and breathing, the flow of her bloodstream and the music of her prosody where the musical qualities of the voice (pitch, volume, timbre and rhythm) are salient in the perinatal experience of speech (Moon, 2011 & 2017). From about three months before birth, the foetus can hear a variety of sounds from the extrauterine world. This enables the developing foetus to share and acquire preferences for the family’s music, culture, voices and language (Moon, 2011; Moon, Lagercrantz, Kuhl, 2013).

Volgsten (2019) suggests that music is fundamentally a social and affective phenomenon. Our developing sense of music emerges from the infant-directed, preverbal and social dialogues between the parent and the infant. The musical elements that are imbedded in the dyad’s early interactions form the basis of musical encounters later in life; they emerge prior to musicking. In other words these musical elements are “proto-musical” (Volgsten, 2019). The proto-musical elements are intensity, contour, tempo, rhythm, timbre, dynamic and shape (Stern, 2000; Volgsten, 2019). Infant-directed singing contains these musical elements and is thus an apt medium for parents and infants to communicate in an affective mutual relationship. The proto-musical relationship between the parent and the infant is a dynamic intentional movement in time and space, where the parent constantly alters the timing, intensity and shape of the singing including her/his actions, based on the dynamic forms of vitality that the infant expresses. The proto-musical elements of infant-directed singing are ideal for arousal regulation and affect coordination as well as for affect sharing between parent and infant, because the proto-musical elements bear resemblance to the dynamic forms of human affects (paper III).
Communicative musicality is a term coined by Colwyn Trevarthen and Stephen Malloch (Malloch & Trevarthen, 2009). Communicative musicality is the duet of movements and sounds between the infant and the parent expressing directionality and intentional states with a synchronisation of the dyad’s behaviours, or with Stern’s words: a coupling of vitality dynamics (Stern, 2010). When the parent and infant interact, communication takes place through the intentions and affects carried by the music-like elements of their joint vocalisations in combination with the joint “dance-like” gestures of their bodies and facial movements (Malloch et al., 2012). Communicative musicality takes place within a shared sense of time through mutually contingent gestures, expression, and timing, which in turn enhance the infant’s ability to modulate feeling states (Malloch et al., 2012). Both Stern and Trevarthen have been key figures in the tradition of microanalysis of film and videotape of mother–infant face-to-face interaction (Beebe, Sorter, Rustin & Knoblauch, 2003). Both have focused on the dynamic features as central for intersubjectivity, but while Stern focuses on affect attunement with time-intensity matching of the inner state or of the dynamic forms of vitality (see below), Trevarthen analyses the interrelationship in the parent-infant dyad through synchronicity and timing remaining at the level of behavioural correspondences (Beebe et al., 2003).

**Arousal systems**

Humans have an innate capacity for self-regulation which the infant develops through daily positive experiences and interactions with an engaged and emotionally available parent. The parent uses her/his own nervous and arousal systems to regulate the infant’s arousal levels (Hart, 2011). The parents are, as Stern so accurately puts it, a “sound-light show” for the infant (Stern, 2010). The stimuli come from the parent’s voice, eyes, face and gestures. The multimodal and multisensory interactions play upon the infant’s states of arousal, creating dynamic forms of vitality. The arousal systems are believed to be active already prenatally. For example, newborns can recognise a musical melody and the voices of significant others at birth, which requires some level of awareness and representation of vitality forms while still in the womb (Stern, 2010). After birth, infants manifest an intense interest in the parents’ affective content in the prosody, and the infants try to synchronise their expressions with those of the parent (Marwick & Murray, 2009). Prosody is the flow of vitality forms (Stern, 2010). Playful infant-directed singing may increase infants’ arousal, which stimulates sustained infant attention or interest, while soothing forms of infant-directed singing
Arousal is problematic to characterise because it does not have clearly defined physical boundaries and has a long history of poor definition (Picard, Fedor & Ayzenberg, 2016a). Arousal is the force for behaviour, the most fundamental force in the nervous system, a force that throws motivations (hunger, attachment etc.) into action, sharpens the attention and initiates movement (Stern, 2010). Arousal determines when to do what we do, and the dynamic manner of doing. Arousal also includes turning off or turning down the arousal, calming the excitement or deactivating the motion. Multiple brain regions contribute to autonomic arousal; multiple sources of arousal interact in the brain and have different kinds of effects on the mind and body (Picard, Fedor & Ayzenberg, 2016b). Stern (2010) states that arousal has a central role in the emergence of the dynamic features of experience and the arousal systems may provide the neuroscientific underpinning for the emergence of vitality forms. The complexity and differentiation of the arousal systems provide support for the idea that the arousal systems could produce a multitude of highly specific and complex arousal profiles, each eliciting a specific vitality form.

Live singing provides a continuum in the regulation of the infant’s arousal systems. Live lullaby-singing is a repetitive emotion communication tool for parents in regulating the infant’s state and arousal levels (Rock, Trainor & Addison, 1999; Trainor, Austin & Desjardins, 2000; Trehub, 2017; Cirelli, Jurewicz & Trehub, 2019). The soothing, comforting and emotion regulating properties of a lullaby are well-known cross-culturally and historically (Fernald, 1989; Rock et al., 1999; Trehub, 2019). The ubiquity of singing to infants, the existence of specific songs for different caregiving occasions across cultures, suggest that music serves a vital function in development with an important communicative function and is therefore a central part of the crucial interaction between parents and infants (Rock et al., 1999; Trehub, 2019). Music is universal because what music does for humans is universally valued in terms of emotional and aesthetic experience and identity formation (Patel, 2008). The human voice is produced within the body, vibrating inward while on the same time connecting us to others (Austin, 2011). Vocalisations to infants are more expressive than vocalisations to adults, and they are often accompanied by gestures in other modalities (Trehub, 2017). Parents also smile more when singing to their infant than when talking. When their infant is absent or out of view, the parents
are unable to produce these smiles and attuned vocalisations (Trehub, Plantinga, Russo, 2016; Cirelli et al, 2019). The parent’s expressiveness is influenced not only by the presence of the infant but also by subtle feedback from the infant (Trehub, 2019). In addition, live parental infant-directed singing is considerably more effective than infant-directed speech in lowering infants’ elevated arousal levels and ameliorating distress (Trehub, 2019). These reciprocal characteristics are intrinsic and individually tailored in the moment, and it is therefore not possible to reproduce them in a recording. Recorded infant-directed singing becomes non-salient for the infant.

**Mirror neurons**

Infants have an innate biological capacity for perceiving temporal forms in other people’s actions, which allows the infant to develop a sense of the other person’s intentions. The discovery of mirror neurons (e.g. Rizzolatti, Fadiga, Gallese & Fogassi, 1996) has been a breakthrough not only in neuroscience but also in child psychology (Ammaniti & Ferrari, 2013). The discovery of mirror neurons in the brain elucidates how the infant can be connected to their parents and other people in their environment from birth (Gerhardt, 2015). Early research found mirror neurons in the prefrontal motor cortex. However, later findings based on a meta-analysis of 125 human fMRI studies (Molenberghs, Cunnington & Mattingley, 2012) suggest that except the core network of brain areas, which are activated by visual observation (executed or imagined visual actions), there are more brain regions with mirror properties. The additional brain areas with mirror properties are involved in somatosensory, auditory and emotional processing. The precise regions that are activated depend on the modality of the task, e.g. visual, auditory, somatosensory (Molenberghs et al., 2012). Research thus shows that the brain regions with mirror properties extend beyond actions to include sharing of emotions as well as understanding the intent of others (Molenberghs et al., 2012). The anterior cingulate cortex (ACC), a brain area just above the corpus callosum at the centre of the brain, is one of the key brain regions within the infant’s descending pain modulatory system, which is influential in dampening down, altering and alleviating the affective components of pain. ACC is a region of interest in the search for a neural mechanism of affect sharing and affect contagion (Carrillo et al., 2019). In animal models, research has shown that ACC contains emotional mirror neurons that respond selectively to pain. These mirror neurons respond when someone is experiencing pain in the self, but they also respond to shared pain, when observing pain in others (Carrillo et al., 2019).
With the mirror neurons, nature and nurture are intertwined. The mirroring process, of which mirror neurons are a part, is the requisite for all relations (Hart, 2007). By the agency of the mirror neurons and the nervous system, the dynamic forms of vitality that are aroused in the infant are for instance visible as an expression in the infant’s face, voice and body. They influence the mirror neurons in the parents to fire in the same pattern, giving the parent a virtual experience of the infant’s experience through the dynamic forms of vitality, initiating actions by the parent. This in turn causes responses from the infant, bringing new dynamic forms of vitality into the dyad in a reciprocal social biofeedback loop (Hart, 2007, 2008; Stern, 2010).

The capacity for imitation, mimicry and gestures is innate (Hart, 2011). The mirror neurons enable humans to empathise with others and engage in interactions. However, infants not only imitate their parents’ expressions and vice versa, but also perceive that the expression corresponds to a particular sensory impression or a set of dynamic forms of vitality (Hart, 2011). When the infant and the parent engage in moments of meeting, they move with synchronised temporal coordination, sharing aspects of each other’s dynamic forms of vitality (Hart, 2011). Lack of synchronisation with the parent will distress the infant, but emotional communication with mutual affect regulation gives the infant a sense of pleasure and vitality and promotes development (Hart, 2011). Being with the other is accomplished by sharing the vitality dynamic flow (Stern, 2010). Affect-regulating mirroring via mirror neurons in the infant’s brain enables infants to self-regulate through the parent’s predictable actions. Since the process is reflexive, the parent’s mental state is communicated to the infant’s state, and the infant thus takes part in the parent’s state and arousal levels (Hart, 2008). The mirror neurons make situations and the environment predictable, both beneficial as well as adverse situations, like a painful procedure (Hart, 2007). However, pain, anxiety, tension and stress reduce the sophistication of the mirror neurons, confining the parent’s ability to attune to their infant’s dynamic forms of vitality in order to regulate their infant well, but may also weaken the infant’s capacity to express her/his dynamic forms of vitality (Hart, 2007, 2008; Gerhardt, 2015).

**Affect attunement**

The mirror neurons make it possible for a parent to resonate on a neurobiological, intrapsychological and interpersonal level with the infant, an action that Stern termed *affect attunement* (e.g. Stern, 2000, 2010). Affect
attunement is the matching of the dynamic forms of vitality. Both the parent’s and the infant’s attunement is amodal, i.e. cross-modal (Hart, 2011). The parent shares the infant’s subjective experience through matching the dynamics of the infant’s vitality form but not the modality because the parent is not just imitating, the match becomes a match of internal feeling states not overt behaviours (Stern, 2010). The infant’s response is through amodal perception. The mirror neurons provide the infant with the innate general capacity to receive information derived from one sensory modality (e.g., hearing) and translate it into another sensory modality (e.g., motion). Such amodal perception plays a key role in affect attunement whereby the intention, through the characteristics of intensity, timing and shape in the interaction, can be perceived by the infant and parent on an implicit level and evoke an intersubjective reciprocally-related response from both parties, each changing with the other. This creates an experience of emotional connectedness and a subjective experience of “I feel that you feel that I feel” (Stern, 2005, p. 91). For example, the parent’s prosodic contour, with crescendos and diminuendos, and duration, are matching the infant’s facial-kinetic contour in a playful interplay (from seen action to heard sound). The affect attunement carries the parent’s unique time-intensity signature, showing the infant that the parent also felt what it felt like to do what the infant just did in this playful situation. Through affect attunement a sense of mutual understanding and sharing has been established, creating intersubjectivity; the sharing of another’s experience (Stern, 2010).
**Ethical considerations**

Ethics of this neonatal music therapy study was approved by the Regional Ethical Review Board in Sweden (2012/1097-31/2; 2012/1754-32). Since critically ill infants are included in this research, written informed consent was acquired from each and one of the participating infants’ parents. In medical research, most interventions involve risks and burdens. Infants are a vulnerable group that should receive specifically considered protection in research. According to the ethical principles of the World Medical Association Declaration of Helsinki for medical research involving human subjects (2013), research in infants is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. Pain management for infants is a top priority in neonatal care. There is a great need for advancing the non-pharmacological interventions in neonatal pain care, which rationalises this study with infant-directed singing with live lullaby singing. The participating infants in the “lullaby-study” all received standard pain management. Standard care entailed facilitated tucking done by a nurse or the parent, oral glucose (300 mg/ml) and the opportunity to suck on a pacifier or on a parent’s or a nurse’s plastic gloved finger. The parents were invited to attend both the venepuncture procedure with and the one without live lullaby singing. Only infants who were referred by a physician to have two routine venepunctures during the study period were eligible to participate in the study, which meant that no extra pain burden was inflicted on the infants for research reasons. Infant-directed singing with live lullaby singing as a non-pharmacological intervention in neonatal pain care has no known side effects.
Methods

This doctoral thesis consists of four papers (Table 4). Two of the papers are based on the clinical trial performed in the NICU at Danderyd-Karolinska University Hospital in Stockholm, Sweden in September 2012 to April 2013. The other two are theoretical theory building papers.

Table 4. Overview of included papers.

<table>
<thead>
<tr>
<th>Paper</th>
<th>Design</th>
<th>Sample &amp; setting</th>
<th>Data collection</th>
<th>Data analysis</th>
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<tbody>
<tr>
<td>I</td>
<td>RCT with crossover design. Infants served as their own control</td>
<td>Level 2 NICU Danderyd-Karolinska University Hospital in Stockholm, Sweden</td>
<td>Oxygen saturation (SaO2) Heart rate (HR) Respiratory rate (RR)</td>
<td>Pain assessment: Premature infant Pain Profile-Revised (PIPP-R) Behavioral Indicators of Infant Pain (BIIP) Statistical analyses</td>
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<td></td>
<td>Random order of: 1. Live lullaby singing + sucrose + facilitated tucking 2. Sucrose + facilitated tucking</td>
<td>Infants (N=38) ≥ 32 - 42 GA 15 female and 23 male infants were recruited for venepuncture on two occasions</td>
<td>The procedures including the lullaby singing were videotaped The sound levels were measured 10 cm from the infant’s ear on dBA slow, A scale</td>
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<td></td>
<td>Interactive infant-directed singing performed before, during, after venepuncture by a student in training to become a professional music therapist Parent-preferred lullabies or a traditional Swedish lullaby</td>
<td>Different specialist nurses and midwives performed the venepunctures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Case study</td>
<td>Level 2 NICU Danderyd-Karolinska University Hospital in Stockholm, Sweden</td>
<td>SaO2, HR, RR Video recording of all procedures The lullaby and environmental sounds were recorded with the built-in camera microphone Detailed transcriptions of the two lullaby episodes into conventional music notation</td>
<td>Hand-coded second-by-second video microanalysis of 2 episodes/infant and of the transcriptions into conventional music notation Pain assessment: BIIP</td>
</tr>
<tr>
<td></td>
<td>Interactive infant-directed singing performed before, during, after venipuncture by a student in training to become a professional music therapist Parent-preferred lullabies or a traditional Swedish lullaby</td>
<td>Infants (N=2) Premature girl, 35 + 4 GA, 1870 grams BW Premature boy, 34 + 5 GA, 2535 grams BW</td>
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<tr>
<td></td>
<td></td>
<td>2 episodes/infant, lullaby episode &amp; standard care only episode</td>
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<td></td>
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<tr>
<td>III</td>
<td>Theoretical study Argumentative research article</td>
<td>Database search PsycINFO, CINAHL, PubMed, Google Scholar Snowballing search method for reviewing literature</td>
<td>A synthesis of concepts, theories and interdisciplinary research</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Theoretical paper Essay</td>
<td>Database search in CINAHL, PubMed, Google Scholar Snowballing search method for reviewing literature</td>
<td>A review of concepts, theories and interdisciplinary research</td>
<td></td>
</tr>
</tbody>
</table>

Study design in the RCT

An RCT with a crossover design, where the infants served as their own control, was chosen for this study. All infants cared for in the NICU ≥ 32 GA who were referred by a physician to have two routine venepunctures during the study period were eligible to participate in the study if a written informed consent was acquired from each and one of the infant’s parents. Infants with known congenital malformations, severe illness, respiratory
support or on-going treatment with sedatives or analgesics were excluded. The infants received infant-directed live lullaby singing pre-, during and post venepuncture. The order of the lullaby intervention and the control situation was randomised. 48 infants were eligible for entering the study, seven declined participation and 41 were enrolled. Three of those were excluded because of incomplete data, such as equipment malfunction or blood sample collection failure. The study encompassed 38 infants (15 female and 23 male infants) for venepuncture on two separate occasions; lullaby intervention with standard care and the silent control with standard care only (Fig. 1). Standard care entailed facilitated tucking done by a nurse or the parent, oral glucose (300 mg/ml) and the opportunity to suck on a pacifier or on a parent’s or a nurse’s plastic gloved finger. The venepuncture procedures were performed in the infant’s crib or on an examination bed.

Figure 1. Overview of lullaby intervention with standard care and control with standard care (period 1 to period 5) and of pain assessment periods with Behavioral Indicators of Infant Pain (BIIP) and Premature Infant Pain Profile-Revised (PIPP-R). PIPP-R 2 and PIPP-R 3 are titled in parallel to the equivalent BIIP periods. According to the instructions no PIPP-R 1 was assessed.

Live lullaby intervention
The live lullaby intervention was based on previous neonatal music therapy research; the “Song of kin” intervention (Loewy, 2015), the musical sedation procedure and singing as entrainment (Loewy, 2004, 2009, 2013), and contingent singing (Shoemark, 2011).
Infant-directed singing was chosen as the foundation for the live intervention. Infant-directed singing provides a consistent and appealing communicative message to the infant, which may provide familiarity, safety and regulation. Songs provide predictable patterns of expectation and improvised song is a profound source of contingency (Shoemark, 2007).

The lullaby mode was chosen because of its intrinsic qualities to calm and sedate an infant. The songs used in the clinical study were parent-preferred traditional lullabies. In the cases where the parents did not identify a favourite lullaby, the music therapy student, in training to become a professional music therapist, chose a traditional Swedish lullaby. Even though the lullaby of choice was a pre-composed song, the lullaby was supposed to be performed in responsiveness with the infant, being sensitive to any possible signs of stress related to the singing and modifying the singing according to the infant’s state. In an attempt to standardise the lullaby intervention, a music therapy student was singing, not a parent. Since previous studies had shown it to be likewise effective in a non-painful setting, we chose a female singer, unknown to the infants, to perform the lullaby interventions (de L’Etoile, 2006; Teckenberg-Jansson et al., 2011).

The start of the lullaby intervention was informed by Shoemark (2007), where the singing is supposed to start with quiet, short “sing-song” vocal phrases of reassurance, which is downwardly inflected until the infant is oriented to the therapist and the physiological signs are stable. The lullaby melody should be sung a capella without lyrics, initially matching the state of the infant and gradually allowing the infant to entrain to and transition into a sedative state. The lullaby should be performed in a simple, repetitive, recognisable and sedative mode in 3/4 or 6/8, in a low pitch with slow steady and predictable pulse and rhythm, entrained to the breathing of the infant, with small variations in fundamental frequency, in consonant harmony, with a soft timbre in the voice without sudden shifts or modulations, with stable dynamics and with pauses between phrases. The infant-directed lullaby singing should start before the venepuncture, in order to lull the infants. The singing should continue during the blood sampling to support and provide a holding environment (Wigram et al., 2002; Winnicott, 1960) and continue after the venepuncture procedure to soothe and facilitate self-regulation. The protocol states that the singing should maintain a constant sound level, between recommended ≤55–65 dB on the A-scale (Neal & Lindeke, 2008; Philbin, 2000).
Statistical analyses
Together with the interdisciplinary research team and a statistical consultant, the author of this doctoral thesis discussed and formulated a statistical analysis plan where efficacy variables were defined as well as statistical methods. Because of the complex study design and the many variables in the data, the actual statistical analysis was performed by the statistical consulting group. The statistical analyses of the data in the clinical study was performed on two groups, the Intention-to-Treat (ITT) population, where all randomised infants were included (N=38), and the Per-Protocol population (PP), where all randomised subjects with no significant protocol violations were included (N=25). Procedures with only lullaby procedure or only control procedure was regarded as a protocol violation.

The primary efficacy variable for the clinical study was pain measured with PIPP-R from first skin puncture and 30 seconds onward (Fig. 1). The secondary efficacy variables for the study were changes in HR, RR and SaO2 during blood sampling as well as in the other periods, change in BIIP 3-score at skin puncture and in BIIP 4-score. The analysis included the total duration of the intervention versus control from the start of period 1 until the end of period 5, the number of skin punctures per intervention versus control, the duration of all skin punctures per intervention versus control (the total time for period 3), and the duration of time for handling before first venepuncture, that is the time from the beginning of period 3 until skin puncture.

For comparison between two groups, Mann-Whitney U-test was used for continuous variables, Fisher’s exact test was used for dichotomous variables and Mantel-Haenszel chi-square test was used for ordered categorical variables. Continuous variables and changes in continuous variables were described by mean, standard deviation (SD), median, minimum and maximum. Categorical variables were described by numbers and percentages. All tests were two-tailed and conducted at 0.05 significance level. All analyses were performed by using SAS® v9.3 (Cary, NC).

Pain assessment with BIIP and PIPP-R
Two pain scales were chosen to assess pain in the infants who participated in the clinical study; BIIP (Holsti & Grunau, 2007), which was also used in the case study, and PIPP-R (Stevens et al, 2014). The infants’ pain expressions were assessed from video films by a neonatal nurse expert on pain assessment who was blinded to the situation and whether the video showed intervention or control. Primary efficacy variable was pain measured with
PIPP-R from first skin puncture and 30 seconds onward (Fig. 1). Secondary efficacy variables were among others, the BIIP-score at skin puncture in period 3 compared to the primary efficacy variable of PIPP-R 3, and the BIIP-score from the last 60 seconds of period 4 to measure the infants’ ability to recover from the painful procedure with and without lullaby singing (paper I).

Both BIIP and PIPP-R are validated tools for assessing procedural pain intensity in preterm and term infants. BIIP evaluates behavioural parameters in the infant’s state, level of arousal, face actions and hand actions (Fig. 2 & paper II). PIPP-R combines behavioural (face actions), physiological (HR and SaO2) and contextual parameters (GA and behavioural state).

The PIPP-R uses weightings to adjust for varying gestational ages and sleep/wake states. For example, there are additional pain score points if an infant is in quiet sleep. In the PIPP-R, GA and behavioural state are scored after the painful event only if there are changes in any of the physiological and/or behavioural variables in response to the painful stimulus (Stevens et al, 2014). The BIIP tool on the contrary, does not apply weightings to the scoring of GA and the sleep/wake states. The authors of the BIIP (Holsti & Grunau, 2007) argue that it is not possible to determine whether or not infants in deep sleep feel greater pain, and that weighting may hide important information with regard to arousal in these infants. In the BIIP tool, deep sleep, active sleep, drowsy and quiet awake states, are understood generally to be indicative of low distress and are assigned a score of 0 (Holsti & Grunau, 2007).

Figure 2. Illustration of five facial actions and two hand actions indicating pain in the Behavioral Indicators of Infant Pain (BIIP), a tool for assessing pain in preterm and term infants. Illustration by Isabell Pettersson. (Reprinted with permission)
For paper I, pain assessment with BIIP was assessed in five periods, chosen by the research team (Fig. 1). PIPP-R score was assessed according to the instructions of the PIPP-R tool, in two periods during the procedures, corresponding to the second and third BIIP scoring. In the case study (paper II), behavioural responses on pain were assessed with BIIP by the author of this thesis, according to the BIIP manual, for the first blood test in each intervention, from the skin puncture and 60 seconds onward (Holsti & Grunau, 2007).

**Case study with microanalysis**

Paper II is an explorative case study with microanalysis. The micro-details in the lullaby improvisations in interaction with the infants’ behaviours were studied. The sampling strategy was purposive with two premature infants chosen from the larger RCT data set (Table 9). When looking through all video recordings of the 38 infants in the RCT data set, there was one infant, a prematurely born boy, who performed a strikingly synchronised moving pattern during the lullaby intervention. This pattern would be important to analyse to better understand the interactions in infant-directed singing in conjunction with painful procedures. The strategy was then to find another infant, approximately the same GA but of opposite gender, because there are implications in previous research that there are gender differences in responses to pain and to singing (Grunau & Craig, 1987; Standley & Walworth, 2010). Preferably, the infants in the case study would receive the same lullaby and have their parents present during venepuncture, at least in the lullaby condition. There was one prematurely born girl in the data set that matched these criteria.

The two procedures with interactive live lullaby singing were transcribed into conventional music notation. These transcriptions were also peer-reviewed by two university teachers in music and composition. In total four episodes, two episodes per infant with and without lullaby singing, were hand-coded second-by-second. All episodes, including the music notation, were analysed with the microanalysis method described in paper II. Two prematurely born infants and four episodes may not be representative or typical of the larger population in the clinical study, but the hand-coded data collection and the microanalysis were fruitful and generated rich data on many levels (Table 5), especially relevant for the neonatal music therapy field.
Table 5. Example of a hand-coded second-by-second microanalysis of the videotape of the lullaby intervention with the prematurely born girl in the case study. Each video description included different layers over the same timescale, presented in tables using Excel software as a basic structure.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Video Events</th>
<th>Microanalysis of the Lullaby Intervention</th>
<th>Microanalysis of the Skin Puncture</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.30.01</td>
<td>Lullaby</td>
<td>00:06:16</td>
<td>00:06:16</td>
</tr>
<tr>
<td>12.30.02</td>
<td>Skin puncture</td>
<td>00:06:16</td>
<td>00:06:16</td>
</tr>
</tbody>
</table>

There is a long tradition within developmental psychology research to analyse video and audio recordings and to use microanalysis to study parent-infant moment-to-moment communication. Microanalysis was an ideal method for the case study in uncovering subtle occurrences and changes in a) the infant’s intrapersonal responses to the infant-directed singing, the skin puncture and environmental noise, b) interpersonal communication and interactions among the individuals present, c) the live lullaby singing itself and the verbal communication nearby the infant. These micro processes were studied with qualitative methods (hand-coded data collection, lullaby transcripts and microanalysis) and quantitative methods (pain assessment, change in HR, RR, SaO2 and dB). Validity was secured through a thorough and systematic process, analysing each of the four videos until no new details was discerned, about 30 times per episode. A validated pain assessment tool (BIIP) was used in this process. Validity was also secured through peer reviewing of the lullaby transcripts by comparing the transcripts to the original singing on the videos. Two independent researchers and university teachers in music conducted the reviews, which resulted in some minor changes. The results were discussed within the theoretical framework of developmental psychology. The pre-understanding of the author of this doctoral thesis is disclosed at the end of Methods.
Theory building papers

Paper III and IV are theoretical papers. Paper III is an argumentative research article investigating the pros and cons of inviting parents as prescribed pain management for their infant, determining the validity of the hypothesis that biopsychosocial parental infant-directed singing has the potential to alleviate infants’ pain. The theoretical framework for paper III is the NADP theory. The theoretical paper III was motivated by the results in paper I. Paper I stated that a research area of great future interest is to investigate how live lullaby singing can be further individualised to empower the infant during painful procedures and encourage parents to participate more actively in the pain management of their infant. Since the analgesic aspects of parental infant-directed singing have not yet been empirically explored, a theoretical paper would fill some of the knowledge gap and lay a foundation for such a study. Paper III synthesises concepts, theories and previous interdisciplinary research to map the underlying analgesic aspects of the unexplored parental infant-directed singing intervention and to position neonatal music therapy and the music therapist within neonatal pain management. The published literature was systematically reviewed in the databases PsycINFO, CINAHL, PubMed and Google Scholar using the keywords “parents”, “infant”, “pain management”, “oxytocin”, “biopsychosocial”, “music therapy”, “infant-directed singing”. A snowballing search method was also used for reviewing peer-reviewed literature within the scope of the paper. The literature was critically appraised.

Paper IV has the form of an essay, reflecting upon and discussing the efforts and benefits of complying with the principles of family-centred care when establishing a Nordic NICU MT approach with parental participation. The essay also covers a historical review of the development of NICU MT and the Nordic cultural adaption process of NICU MT in Sweden and Norway. The published literature on family-centred care was systematically reviewed in the databases CINAHL, PubMed and Google Scholar using the keywords “family-centered care”, “NICU”, “parents” and “history”. A snowballing search method was used for reviewing peer-reviewed literature in the neonatal music therapy sections of the article.

The therapist-researcher’s stance

NICU MT implementation round the world has often been initiated by single music therapists attempting to start a new program where the acceptance within the medical community is still being generated one NICU at a time.
(Standley, 2014). Each neonatal music therapist usually has her/his own ontological and epistemological foundation informing the clinical practice and research. These eclectic and local versions of NICU MT practices are influenced by for example the music therapist’s training background, the healthcare setting, the general social security system and the cultural context. Diversity of practice is a strength of the music therapy discipline in that the therapist is not restricted to one philosophical orientation but may base treatment approaches on the particular needs of the infant and the family as well as the demands of the specific work setting (Scovel & Gardstrom, 2012). Consequently, “References to workplace practices in music therapy must be contextualized otherwise they run the risk of producing research and techniques that when implemented elsewhere are either ineffective or run the risk of causing harm” (Edwards, 2016a, p. 6). So, what is the context of the workplace practice of the writer of this doctoral thesis?

When I, the music therapist, come to visit an infant who is cared for in the Swedish NICU, usually both the mother and the father/partner are present. Music therapy is rarely offered without one or both parents participating. The NICU at the Central Hospital in Karlstad is one of the most modern level 2 units in Sweden. As a music therapy clinician, I am trained in a psychodynamic music therapy tradition and my clinical work in the NICU is humanistic resource-oriented (Rolvsjord, 2016), informed by developmental psychology, attachment theories, cognitive theory formation and the biopsychosocial neuroaffective developmental psychology model (Hart, 2008; Hart, 2011). As one of the “grandparents” of RBL, I have based the NICU MT practice in Karlstad on this model (Loewy, 2016). In my work, I emphasise the voice as the main instrument in the sessions since singing is a resource that parents always have available but perhaps not use purposely. When appropriate, a nylon string guitar is used as accompaniment. The RBL-instruments, gato box and ocean disc, are seldom applied. As a music therapist, I am role modelling and mentoring the parents to use their own voice with their infant to enhance mutual co-regulation, interaction and attachment and promote salutogenesis. Improvised contingent singing (Shoemark, 2011) is used to endorse the social, emotional and neurological development of the hospitalised medically stable infant (Malloch et al., 2012). Another important objective is to identify Songs of kin, culturally specific and preferred songs in the families, which often inspire parents to continue ‘musicking’ with their infant between the music therapy sessions as well as at home after discharge. Research shows that infants exhibit greater social engagement in songs that are familiar to them, especially
songs learned from their parents (Cirelli, Trehub, & Trainor, 2018). Other music therapy techniques used with the families are for example singing as entrainment (e.g. Loewy, 2015), lullabies, play songs, musical sedation (Loewy, 2009; Loewy 2016), and music psychotherapy for caregiver support (Loewy, 2015). Receptive music therapy is also offered. Sometimes the parents want to rest, sitting skin-to-skin with their infant while I sing lullabies or adapted lullaby versions of parent-preferred songs. The lullaby singing affords easily repeatable and recognisable affective patterns, to which the parent–infant dyad may attune. The songs foster intimacy and affectionate touch, relaxing the parents and often inspiring them to hum along, which helps to regulate the infant to sleep. These moments create a space for the parents to share their thoughts and emotions in a therapeutic dialogue. On other occasions, the slightly faster rhythms of the children’s songs and nursery rhymes engage both parents and infant in shared social affective interactions with mutual positive facial and vocal responses, where eye contact is made and perhaps the infant’s first social smiles will appear. These shared present moments (Stern, 2005) offer the family a sense of coherence (Hart, 2008), empowerment and togetherness (Shoemark, 2016). In my position as a Swedish NICU MT clinician and neonatal music therapy researcher, I build on the predecessors’ music therapy work, trying to establish a family-centred Nordic approach to NICU MT, which is culturally sensitive to the Nordic public healthcare system and collaborative with the parents and the NICU staff.
A synthesis of the main results

The results are presented separately for paper I and paper II. The results from the theoretical papers III and IV are here further developed and synthesised into a theoretical strategy, condensed and presented in a figure.

The results of the RCT

The participants in the RCT (paper I) are presented in Table 6.

<table>
<thead>
<tr>
<th></th>
<th>Total n (%)</th>
<th>Median (Min-Max)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, weeks+days</td>
<td>34 + 4 (25 + 0 - 42 + 0)</td>
<td>34 + 6 (4 + 3)</td>
<td></td>
</tr>
<tr>
<td>Birth weight, grams</td>
<td>2 460 (736 - 4 245)</td>
<td>2 519 (1 019)</td>
<td></td>
</tr>
<tr>
<td>Post-natal age at first blood test, days</td>
<td>3 (1 - 100)</td>
<td>13 (24)</td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>15 (40)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All comparisons in the statistical analysis were between groups; live lullaby intervention with standard care versus control with standard care only, conducted at the 5% significance level. There were an intention-to-treat (ITT) population and a per protocol population (PP) in the study. ITT included all 38 infants and in the PP 25 infants fulfilled both the lullaby and the control test situation. Primary efficacy variable for the study was pain measured for the ITT population as well as for the PP population with the assessment tool PIPP-R in episode 3, from skin puncture and 30 seconds onward (Fig. 1). There was no statistically significant difference in PIPP-R score between lullaby intervention and control in either population, thus the primary hypothesis could not be supported. The absence of significant differences in PIPP-R and BIIP scores indicates an already effective standard pain management. The live lullaby singing compared to standard treatment did not negatively affect the primary outcome, and the effects must be discussed from other perspectives, for instance live singing as a means for involving parents promoting attachment formation. Among the secondary efficacy variables there was a significantly calmer breathing pattern in the lullaby intervention versus control in both ITT and PP populations before skin-puncture, in the pre-needle stage, p=0.028 for ITT (Fig. 3) and p=0.0074 for the PP population (Fig. 4). This is an effect that probably carries clinical significance as an indicator of a relaxation response, thus suggesting that the live lullaby singing lowers stress and contributes to clinical stability (paper I).
Figure 3 and 4. Box-plots showing distribution of respiratory rate (RR) during five periods (1-5) in intention-to-treat population (ITT) (Fig. 3), and in per protocol population (PP) (Fig. 4). O mean control, + mean lullaby intervention. Puncture stage (3) starts at the time of the first puncture. The top of the rectangle shows the third quartile (Q3), the horizontal line near the middle shows the median, the bottom shows the first quartile (Q1). The vertical line extending from the top of the rectangle shows the maximum value within 1.5 * interquartile range (IQR) and the vertical line from the bottom indicates the minimum value within 1.5 * IQR. O and + = scores more than 1.5 times the IQR below Q1 or above Q3.
Non-significant trends
The statistical analysis also revealed some trends, which although not being significant, indicate positive effects of the live lullaby singing.

The mean difference in the duration of the total procedure of the live lullaby intervention versus control, from the start of period 1 until the end of period 5, is shown in paper I (table 2 and 4 in paper I). In the ITT population, the duration of the total procedure was 15.7 (4.1) minutes in the lullaby condition and 17.3 (6.5) minutes in the control condition (p=0.46). In the PP group, 15.6 (4.2) minutes in the lullaby condition and 17.7 (6.8) minutes in the control condition (p=0.13).

In the ITT population, enough blood was collected during the first skin puncture in 73 % of the cases in the lullaby condition, versus in 57 % in the control (p=0.18). In the PP population, the corresponding numbers were 72% versus 52% (p=0.45).

The duration of all skin punctures per procedure, which means the total time for period 3 (Fig. 1), showed non-significant trends in favour of the lullaby condition in both the ITT (p=0.58) and PP (p=0.16) populations (tables 2 and 4 in paper I).

The change in mean RR from baseline to the last 60 seconds of the post-needle stage was in the ITT population 0.833 (11.064) in the lullaby condition and -1.72 (11.46) in the control condition (p=0.20). In the PP population the corresponding numbers were 1.28 (11.42) for the lullaby intervention and -3.04 (11.42) in the control condition (p=0.20).

The change in mean SaO2 from baseline to last 60 seconds of post-needle stage was in the ITT population -0.604 (1.236) in the lullaby condition and -0.005 (2.695) in the control condition (p=0.26). In the PP population the corresponding numbers were -0.600 (1.225) in the lullaby intervention and 0.103 (2.392) in the control condition (p=0.26).

The change in HR shows on the contrary slightly raised HR levels in the lullaby condition compared to the control condition during and after skin puncture in both populations. The change in mean HR from baseline to last 60 seconds of post-needle stage was in the ITT population 2.76 (13.65) in the lullaby condition and -0.603 (12.443) in the control condition (p=0.54). In the PP population the corresponding numbers were 2.69 (15.43) in the lullaby condition and -1.71 (10.47) in the control condition (p=0.23). The physiological results by situation are shown in Table 7 for the ITT population and in Table 8 for the PP population.
Table 7. Summary of secondary efficacy variables by situation in ITT population.

<table>
<thead>
<tr>
<th>Situation</th>
<th>Variables</th>
<th>Song (n=33)</th>
<th>Quiet (n=30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (1)</td>
<td>HR</td>
<td>138.0 (18.9)</td>
<td>139.6 (20.9)</td>
<td>0.93</td>
</tr>
<tr>
<td></td>
<td></td>
<td>138.2 (98.1; 175.5)</td>
<td>136.9 (99.9; 198.5)</td>
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</tr>
<tr>
<td></td>
<td>RR</td>
<td>49.2 (11.8)</td>
<td>53.8 (11.6)</td>
<td>0.10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>47.3 (29.8; 68.9)</td>
<td>54.9 (28.8; 73.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SaO2</td>
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<td>97.2 (2.6)</td>
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<td></td>
<td></td>
<td>98.4 (95.3; 100.0)</td>
<td>97.5 (87.3; 100.0)</td>
<td></td>
</tr>
<tr>
<td>Pre-needle stage (2)</td>
<td>HR</td>
<td>138.7 (17.0)</td>
<td>140.6 (16.9)</td>
<td>0.69</td>
</tr>
<tr>
<td></td>
<td></td>
<td>136.9 (105.9; 174.9)</td>
<td>138.6 (103.8; 193.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RR</td>
<td>47.2 (11.9)</td>
<td>52.7 (0.1)</td>
<td>0.028</td>
</tr>
<tr>
<td></td>
<td></td>
<td>45.1 (27.6; 80.8)</td>
<td>52.0 (35.5; 69.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SaO2</td>
<td>97.8 (1.7)</td>
<td>96.6 (3.3)</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>97.8 (93.6; 100.0)</td>
<td>97.1 (84.9; 100.0)</td>
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<tr>
<td>Puncture stage (3)</td>
<td>HR</td>
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<td>148.4 (18.9)</td>
<td>0.91</td>
</tr>
<tr>
<td></td>
<td></td>
<td>151.4 (108.5; 187.1)</td>
<td>150.3 (113.8; 192.0)</td>
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</tr>
<tr>
<td></td>
<td>RR</td>
<td>49.3 (13.5)</td>
<td>50.9 (10.9)</td>
<td>0.54</td>
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<tr>
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<td>46.8 (24.8; 90.6)</td>
<td>49.6 (30.7; 80.9)</td>
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<td>Post-needle stage (4)</td>
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<td>146.2 (107.4; 177.9)</td>
<td>143.9 (98.7; 178.5)</td>
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<td>48.2 (25.1; 87.8)</td>
<td>50.1 (28.4; 78.9)</td>
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<td></td>
<td>SaO2</td>
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<td>96.7 (3.9)</td>
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<td>97.8 (80.8; 100.0)</td>
<td></td>
</tr>
<tr>
<td>Silence stage (5)</td>
<td>HR</td>
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<td>136.4 (14.6)</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>137.3 (108.2; 174.6)</td>
<td>137.7 (102.8; 166.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RR</td>
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<td>51.3 (10.5)</td>
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<td>96.4 (2.9)</td>
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<td></td>
<td>97.7 (93.2; 100.0)</td>
<td>97.3 (86.9; 100.0)</td>
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</table>

For continuous variables Mean (SD) / Median (Min; Max) / n= is presented.
For comparison between groups the Mann-Whitney U-test was used for continuous variables.
Table 8. Summary of secondary efficacy variables by situation in PP population.

<table>
<thead>
<tr>
<th>Situation</th>
<th>Variables</th>
<th>Song (n=25)</th>
<th>Quiet (n=25)</th>
<th>p-value</th>
</tr>
</thead>
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<tr>
<td>Baseline (1)</td>
<td>HR</td>
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<td>138.3 (17.3)</td>
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<tr>
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<td>n=25</td>
<td>138.2 (98.1; 172.7)</td>
<td>136.4 (99.9; 189.3)</td>
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<tr>
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<td>RR</td>
<td>49.3 (11.7)</td>
<td>53.5 (12.4)</td>
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<td>n=25</td>
<td>47.5 (29.8; 68.9)</td>
<td>52.1 (28.8; 73.8)</td>
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<td>SaO2</td>
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<td>97.7 (1.9)</td>
<td>0.081</td>
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<td>98.5 (92.6; 100.0)</td>
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<td>Pre-needle stage (2)</td>
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<td>138.2 (14.3)</td>
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<td>138.5 (103.8; 175.3)</td>
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<td>Puncture stage (3)</td>
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<td>147.5 (17.6)</td>
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<td>151.4 (108.5; 177.6)</td>
<td>149.8 (113.8; 184.0)</td>
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<tr>
<td></td>
<td>RR</td>
<td>48.1 (11.7)</td>
<td>50.7 (10.8)</td>
<td>0.50</td>
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<td></td>
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<td>46.8 (24.8; 66.4)</td>
<td>50.3 (30.7; 80.9)</td>
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<tr>
<td></td>
<td>SaO2</td>
<td>96.0 (3.3)</td>
<td>96.3 (5.9)</td>
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<td>139.1 (15.5)</td>
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<td>SaO2</td>
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<td>97.9 (93.9; 100.0)</td>
<td>98.0 (80.8; 100.0)</td>
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<tr>
<td>Silence stage (5)</td>
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<td>134.6 (13.1)</td>
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<td>137.9 (102.8; 166.8)</td>
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<td>97.2 (2.1)</td>
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<td>n=25</td>
<td>97.8 (94.4; 100.0)</td>
<td>97.5 (91.9; 100.0)</td>
<td></td>
</tr>
</tbody>
</table>

For continuous variables Mean (SD) / Median (Min; Max) / n = is presented.
For comparison between groups the Mann-Whitney U-test was used for continuous variables.
Results of the microanalysis in the case study

For the case study (paper II), two infants were chosen from the larger RCT study, a premature girl and a premature boy (Table 9). The lullaby performance was analysed directly from the videotape and through the music transcriptions. The two infants’ procedures with only standard care were also analysed with microanalyses. In the procedures with lullaby singing, 12 different layers were discerned and in the standard care procedures 10 layers, for example the infants’ physiological and affective responses emerging before, during and after the painful procedure (Table 5).

Table 9. Background data of the premature infants in the case study.

<table>
<thead>
<tr>
<th></th>
<th>Premature Swedish-born girl</th>
<th></th>
<th>Premature Swedish-born boy</th>
<th></th>
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</thead>
<tbody>
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<td></td>
<td>35 + 4 weeks of gestation</td>
<td>birth-weight 1870 grams</td>
<td>34 + 5 weeks of gestation</td>
<td>birth-weight 2535 grams</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>First intervention</td>
<td>Second intervention</td>
<td>First intervention</td>
<td>Second intervention</td>
</tr>
<tr>
<td>Standard care</td>
<td>Live lullaby singing</td>
<td>Live lullaby singing</td>
<td>Standard care</td>
<td></td>
</tr>
<tr>
<td><strong>Song</strong></td>
<td>Vyska lulla litaet barn</td>
<td>F sharp major/minor</td>
<td>Vyska lulla litaet barn</td>
<td>F major/minor</td>
</tr>
<tr>
<td>(trad. Sweden)</td>
<td>58 bpm, 3/4 time</td>
<td>55 bpm, 3/4 time</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age at intervention</strong></td>
<td>2 days</td>
<td>4 days</td>
<td>4 days</td>
<td>5 days</td>
</tr>
<tr>
<td><strong>Parental presence</strong></td>
<td>Mother</td>
<td>Both parents</td>
<td>Both parents</td>
<td>No parent</td>
</tr>
<tr>
<td><strong>Duration of intervention</strong></td>
<td>21 min and 42 sec</td>
<td>10 min and 52 sec</td>
<td>11 min and 40 sec</td>
<td>18 min and 16 sec</td>
</tr>
<tr>
<td><strong>Number of skin punctures</strong></td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Irregular live lullaby performance

The results of the microanalysis of the lullaby performances disclosed problems with the intervention fidelity with violations to the singing protocol, which affected the infants’ physiological and affective responses. There was a surprising irregular pattern in the singing style before, during and after the skin puncture. The intervention protocol stated that the lullaby intervention was supposed to start with simple, short, calm, descending “sing-
song” vocal phrases of reassurance, informed by Shoemark’s contingent singing model (Shoemark, 2007), which should be sung until the infant was oriented to the therapist and the physiological signs were stable. The transcriptions of the live lullaby singing identified these vocal phrases of reassurance shown in the transcription as an improvised irregular introduction hummed by the music therapy student before she began singing the repetitive lullaby melody. This intro, which in paper II is called the prelude, turned out to be performed in another key than the actual lullaby, that is, there was a key change from major to minor key in the start of the infant-directed singing in both lullaby interventions (Fig. 5 and Fig. 6).

![Figure 5. Improvised irregular introduction hummed for the girl by the music therapy student prior to the repetitive lullaby melody.](image)

![Figure 6. Improvised irregular introduction hummed for the boy by the music therapy student prior to the repetitive lullaby melody.](image)

The case study showed that the infant-directed interaction with the infants before venepuncture bears a resemblance to infant-directed speech. The interaction in the preludes was irregular in rhythm and pitch contour and had
a bell-shaped melody contour, similar to the shape, intensity and temporal structures in infant-directed speech, which is more engaging than soothing.

The actual lullaby melody, which the intervention protocol specified to be performed in a repetitive regular soothing style, was ornamented with extra notes in the melody during the intervention and was also interrupted by reassuring infant-directed speech in response to the infants’ reactions during venepuncture (Fig. 7 and Fig. 8). Previous research shows that a reassuring tone of voice while the infant is stressed or in pain, does not communicate a shared affect of the painful experience and subsequently the infant becomes more distressed.

Figure 7. Interruption in the lullaby singing for the girl with reassuring infant-directed speech during skin puncture.

Figure 8. Interruption in the lullaby singing for the boy with reassuring infant-directed speech during handling and skin puncture.
The transcription of the lullaby performances also revealed that the lullaby interventions ended with a sort of improvised coda, which was performed in an irregular style of singing (Fig. 9 and Fig. 10).

Figure 9. Improvised coda in six bars with descending minor thirds and long extended final notes at the end of the lullaby performance for the girl.

Figure 10. Improvised coda at the end of the lullaby performance for the boy with an improvisational cadence, where the last phrase in the lullaby was repeated three times, bar 121–141. The cadence dissolved in a descending perfect fifth and a minor sixth, performed with glissandi and finally a descending minor third.

As shown in the figures, the vocal performance in the lullaby interventions was not predictable and regular all the way through in the temporal, shape and intensity structures, as intended. The singing did not start with a repetitive and regular lullaby melody but with an irregular prelude that was perhaps arousing the infants more than soothing them because of the similarities to the shape, intensity and temporal structures of infant-directed speech, which is engaging infants. The prelude for the girl was shorter and more repetitive than the prelude for the boy, which might be one answer as to why the girl responded with less pronounced behavioural reactions and needed less time to self-regulate during her prelude. The boy’s rotating hand movements, finger splays and hand covering face responses during his prelude, could be interpreted as signs of an infant trying to self-regulate from an over-stimulating interaction with infant-directed speech (Fig. 11). On the other hand, if one observes the boy’s smooth hand gestures while listening to the prelude, one can almost believe that it is the boy who is directing the
singer not vice versa. With his sense of time in movement, his hand gestures were synchronised with the impulses in the actions of the singer’s prosody in the prelude, and with her alterations of the regularity in the prelude. Through amodal perception and auditive mirror neurons, the boy perceived common temporal, shape and intensity levels in the prelude performance and, across modalities, transferred these into an attuned kinetic hand-dance. This response could be interpreted as a matching of the dynamic forms of vitality, where the boy is resonating on a neurobiological, intrapsychological and interpersonal level with the singer and her expressed affects in the vocal performance. The boy’s response is either a result of affect attunement or affect contagion. Since anxiety, tension and stress reduce the sophistication of the mirror neurons, limiting the ability to attune to and express dynamic forms of vitality, the boy’s expressions and gestures during the prelude are probably more related to a manifestation of dynamic forms of vitality and affect attunement. It was not the intention or the purpose of the lullaby singing to engage the infants in arousing communication before, during and after the painful venepuncture. The vocal performance was supposed to be performed in a predictable style of singing to foster safety and ensure regular comfort from the start of the live singing intervention, to offer the infants a repetitive and soothing melody pattern to which they could attune and gradually feel supported by, thus promoting self-regulation in the infants.
Infant-directed speech and affect contagion
Infant-directed speech is more arousal-eliciting than infant-directed singing, but both infant-directed singing and infant-directed speech must be prac-
ticed cautiously within a pain context, so as not to cause adverse and undesirable effects. In the control condition for the girl, infant-directed speech also caused problematic responses. There was a situation where the infant girl was responding negatively to the discouraging prosody in the nurse’s voice as well as to the nurse’s affective expression of no hope, when the nurse realised that she had to take a second blood sample from the girl (paper II). The girl showed signs of a 30-second-long freeze response in her face and body. The body turned dull and limp, followed by a radical drop in HR as well as in RR. Compared to the boy’s hand-dance, this was a more obvious case of affect contagion; the induction of an affect in one person from seeing or hearing someone else’s affect display. In traumatic situations, which are perceived as hopeless and fear-provoking, a freeze response might automatically get activated, which involves behavioural immobility and marked drop in HR and RR.

**Deficiencies with pain assessment**

In the case study (paper II), the infants’ pain expressions were assessed with BIIP by the author of this doctoral thesis (Table 10). The highest possible score in BIIP is 9, and the scoring range is: 0–2 minimal or no pain, 3–6 moderate pain and 7–9 significant pain (Holsti & Grunau, 2010).

*Table 10. Pain assessment with Behavioral Indicators of Infant Pain (BIIP) for the girl and the boy during venepuncture (from skin puncture and 60 seconds onward) in standard care only and in lullaby intervention with standard care.*

<table>
<thead>
<tr>
<th>Score</th>
<th>State</th>
<th>The girl Standard care only</th>
<th>Lullaby intervention</th>
<th>The boy Standard care only</th>
<th>Lullaby intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Deep sleep</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>Active sleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>Drowsy</td>
<td></td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>Quiet awake</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Active awake</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Agitated/Crying</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Brow bulge</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Eye squeeze</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Naso-labial furrow</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Horizontal mouth stretch</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Taut tongue</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hand</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Finger splay</td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Fistng</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td></td>
<td>8</td>
<td>2</td>
<td>2</td>
<td>8</td>
</tr>
</tbody>
</table>

The problem with assessment of behavioural observations like the BIIP is the difficulty in discriminating between stress from causes other than pain,
for example environmental noise. The background was noisy in all test situations in this case study. The microanalysis of the infants’ overall pain expression revealed that the BIIP did not capture long time-out periods or signs of exhaustion. Lack of visible pain-related responses does not necessarily imply absence of experienced pain. This was the case in the boy’s intervention with standard care only, with no parents present, where his BIIP score indicated minimal pain. At the same time, the physiological measurements displayed stressed vital signs, as well as behavioural signs of exhaustion, with a 2-minute long time-out period at the end of the second attempt to sample blood. His physiological variables also indicated stress caused by handling during the control situation. A pain-exposed infant in a constant hyperactive state becomes exhausted, passive and oversensitive to all handling, trying to preserve energy with less crying, weaker grimace and limp posturing. These manifestations are unfortunately not included in BIIP and are therefore not considered as related to pain.

**Affective support versus over-stimulation**

The case study showed the reciprocity of physiological and behavioural activity linked to live infant-directed singing and infant-directed speech before, during and after painful procedures.

Despite the irregular singing style, the microanalysis of the overall physiological and behavioural responses, as well as the pain assessment with BIIP, showed that live singing appeared to offer a general affective support to both infants, with decreased stress before the skin puncture and after, facilitating recovery and homeostasis (Fig. 12). The premature girl in the case study also seemed to benefit from the live lullaby singing during blood sampling. The case study highlighted the importance of preparation. The infant’s regulatory style and responses must be observed prior to the painful procedure. During venepuncture, the infant’s vital signs and behavioural responses must be constantly assessed during live singing in order to refocus the affective support within the present moment, to maintain emotional regulation. Live singing is a communicative reciprocal intervention which is also applicable for premature infants during painful procedures, used as a means to optimise the homeostatic mechanisms of the infant, provided that the vocal performance is repetitive, predictable and unceasing, and not interrupted by infant-directed speech. In order to be audible and soothing, the vocal performance should use elongated breathy vowels instead of a closed humming and it is vital that the singing is predictable in the temporal, shape and intensity structures from the start until the end of the live singing.
Figure 12. Physiological responses for (A) the girl during standard care only, (B) the girl during lullaby intervention, (C) the boy during standard care only and (D) the boy during lullaby intervention. From the top and down on the y-axis: (green) heart rate (min$^{-1}$), (red) saturation (%), (blue) respiration rate (min$^{-1}$), (purple) blood sampling episodes. The duration of the procedures (h: m: s) is shown on the x-axis. The procedures with standard care only are longer than the procedures with lullaby intervention. In graph A, there are a few measurement errors with a sequence of zero values, probably caused by unattached electrodes. (Reprinted with permission)
The case study also generated an important overall question for live vocal interventions during venepuncture. Is the combination of vocal interaction and painful stimuli increasing the risk for over-stimulation during the skin puncture and therefore is live lullaby singing more beneficial in the pre- and post-needle stages? For the boy in the case study, infant-directed singing seemed to be arousing during some parts of the intervention, while the girl on the contrary seemed to be helped by the singing during the whole procedure. Gender differences, which have been noted for example in speed of response following a heel-lance (Grunau & Craig, 1987), might be one reason for these discrepancies in responses, the girl being neurologically more mature and the boy showing shorter time to cry and to display facial action following venepuncture. There might be individual differences in the infants’ functional brain connectivity and abilities to regulate. Another answer to this important question might be found in the style of singing, which was more regular in the performance for the girl and more irregular and arousing for the boy. An additional explanation could be the noise in the infants’ soundscape during the two lullaby interventions. A very important consideration when using singing in an already busy environment like the NICU is to assess the environmental noise. Background noise with loud conversations in the background, as well as high-pitched sounds from monitors and phones, was an issue in all situations in the RCT and likewise in the case study, which could certainly have influenced the effect of the affective support. Non-pharmacological comfort and coping strategies like live lullaby singing applied in painful and stressful conditions, while other distracting events are occurring in the environment, become less effective. It was obvious in the microanalysis that background noise stressed both infants and that noise in the NICU should be eliminated. In what phase the live lullaby singing is more beneficial during a blood sampling procedure is probably of less importance if a parent would sing the lullaby with an attuned soothing and loving prosody, preferable having the infant in their arms with skin-to-skin contact, close to the heart.

**Live parental infant-directed singing**

In paper III and IV, the parent as prescribed pain management for the pain exposed infant is discussed from the perspective of a biopsychosocial neuroaffective developmental psychology approach and within a family-centred care context. The results in paper III and IV are in this thesis condensed into a plan of action; a strategy for the family-centred neonatal music therapy
The Nordic NICU MT pain management strategy
A venepuncture procedure consists of three stages, the procedural preparation phase, the skin-breaking blood-sampling procedure followed by a recovery phase. During the first weeks of life, the hospitalised infant undergoes repeated invasive procedures. Therefore, a referral to music therapy as early as possible in the family’s NICU care process is desirable. From a music therapeutic point of view, preparing the parents to use their voices during a painful procedure starts already in the first music therapy session in the pre-procedure phase (Fig. 13). In the Nordic NICU MT pain management strategy, the music therapist uses music therapy methods and techniques to gradually prepare the parents and the infant for a painful procedure, enhancing self-efficacy and coping. Knowledge translation and psychoeducation is a vital part of the Nordic NICU MT pain management strategy, since education is considered an efficacious component of pain treatment (Zernikow et al., 2017). The role of the music therapist in family-centred neonatal pain management is as guide, role model and facilitator for the parents, coaching the parents to identify emotionally important songs or lullabies that are easy and comfortable to sing in conjunction with painful procedures (paper III & IV). Together with the parents, the music therapist also assesses the intra- and interpersonal factors that are influencing the dyad’s pain experience and pain expressions in order to acknowledge these factors
and process them together with the parents. Influencing factors are a) individual factors (both in the infant and the parent) such as age, sex, development, temperament, affective state, prior pain experiences and possible experiences of separation, b) social factors such as environment, type of procedure, culture, pain beliefs, musical preferences and c) ethnic and psychobiological factors such as nociceptor density, endogenous opioids, stress and pain sensitivity (c.f. Social communication model of pain, Craig, 2015, and DIAPR-R model, Bucsea & Pillai Riddell, 2019).

![Intra/interpersonal factors influencing dyad's pain experience and pain expression](image)

**Figure 13.** In the music therapy sessions before the procedure (in the Pre-procedure phase), the music therapist prepares the parents to use their voices during a painful procedure and assesses the intra- and interpersonal factors that are influencing the dyad’s pain experience and pain expressions.

When the painful procedure is about to take place, the parents already know how to use infant-directed lullaby singing to regulate themselves and the infant during the preparation phase (Fig. 14). As previously mentioned, the core principle in procedural comfort care is for the infant and parent to be well regulated before the painful procedure begins (c.f. Procedural comfort care, Leroy et al., 2016). To become an emotionally available, stable and loving parent who is capable of noticing the infant’s signals and able to share and regulate the infant’s states during blood sampling, the parent needs time to prepare and become well-informed about non-pharmacologic methods. Parental infant-directed singing is a parent-driven non-pharmacological intervention that matches the prerequisites of the age-appropriate
pre-procedural comfort care. The live parental infant-directed singing is non-verbal, multisensory, multimodal and affective, tailored to the individual infant’s affect state and includes the parent in the infant’s pain management (c.f. Bucsea & Pillai Riddell, 2019). During the procedural preparation phase, the parent should use the singing to match the level of the infant’s affective intensity, gaining an emotional connection, before the parent gradually modifies and fine-tunes the singing to regulate the infant. The age-appropriate pre-procedural preparation is crucial for mitigating pain. In the Nordic approach of NICU MT (paper IV), the parents are present and available for their infant round the clock. The music therapist is not. Venepunctures are performed day and night and it is not feasible to expect a music therapist to be stand-by and present for all painful procedures for all the families admitted to the NICU. In the Nordic approach of NICU MT (paper IV), the parents are the most important pain alleviating mediators, not the music therapist. Though, the music therapist is very important as a consultant, educator and therapist.

Figure 14. Since each painful situation is unique the procedural preparation needs to be individually tailored to the infant and parent. Live parental infant-directed singing is an intervention that aims for the infant and parent to be well regulated before the painful procedure is performed. The parent is emotionally available and stable, loving and caring, and capable of attuning and being responsive to the infant’s signals in order to help the infant reach homeostasis and a state of regulation before the painful procedure.
During the painful procedure (Fig. 15), the procedural support in the Nordic NICU MT pain management strategy consists of multisensory and multimodal biopsychosocial parent-driven interactions with live parental infant-directed lullaby singing in combination with standard care such as skin-to-skin contact, breastfeeding and sweet solutions.

The concept of the treatment lens appears in the working model of music therapy as procedural support (Ghetti, 2012). The concept, which according to Ghetti (2012) focuses on the role of the music therapist, music and client, is adapted to instead encompass the biopsychosocial factors arising from parental lullaby singing (Fig. 16). These multisensory and multimodal biopsychosocial factors serve as a treatment lens that filters the infant’s and the parent’s experiences of the procedure. Coping strategies or a sense of control may reduce the negative experience of stress and pain (paper III). During the painful procedure the emotionally available, stable and well-informed parent uses her/his dynamic forms of vitality to perceive the infant’s pain experience and to vocally and bodily adjust the biopsychosocial response and regulation, i.e. the biopsychosocial filter in the treatment lens, in the moment to positively alter infant’s outcomes.
The parent continuously assesses the infant’s affective state (Fig. 17), using dynamic forms of vitality to show the infant that she/he understands and shares what the infant is experiencing in the moment. The concept of reflexivity as a process in ongoing assessment (Ghetti, 2012) is herein adapted to reflect how the parent (instead of the music therapist) alters and adjusts her/his biopsychosocial intervention over time in reaction to the infant’s responses and changing needs. The constant assessment may determine for example what type of vocal adjustments are needed in the lullaby singing. The parent’s reflexive assessment and filtering process may modulate and modify the infant’s and parent’s perceptions of the painful procedure in an ongoing infant-parent regulatory feedback loop (c.f. Bucea & Pillai Riddell, 2019). It may maintain homeostasis and alleviate pain through release of endogenous pain-alleviating hormones and opioids in the dyad, decreasing stress and promoting attachment formation. The parent constantly refocuses the biopsychosocial intervention lens to positively influence outcomes (c.f. Ghetti, 2012).
Figure 17. The blood-sampling phase of the Nordic NICU MT pain management strategy. In an ongoing assessment the parent alters and adjusts her/his biopsychological intervention in a reflexive process over time in reaction to the infant’s responses and changing needs to positively influence outcomes. (Modified from Ghetti, 2012).

During the recovery phase (Fig. 18), the live parental infant-directed singing may function as a real-time emotion regulator for the infant as well as for the parent, increasing self-regulation and stabilising affect. The parent uses the infant-directed singing to entrain to the infant’s affective state and gradually modify and fine-tune the style of singing to match, share and modulate the painful experience’s intense dynamic forms of vitality (c.f. Loewy, 2019). Instinctively, parents might want to calm a distressed infant without first matching the infant’s distress, indirectly leaving the infant to calm down on her/his own. If the parent first shares the infant’s dynamic forms of vitality by entraining to the infant’s rhythm, before trying to calm the infant, the infant will feel supported by the parent in a shared attuned down-regulating process.
During the recovery phase, the parent uses the infant-directed singing to entrain to the infant’s affective state and gradually modify and fine-tune the style of singing to match, share and modulate the painful experience’s intense dynamic forms of vitality in a shared attuned downregulating process.

This Nordic family-centred parent-driven non-pharmacological biopsychosocial NICU MT pain management strategy covers the whole process; the pre-procedural music therapy treatments, the procedural preparation phase, the blood-sampling phase and recovery phase. The live parental infant-directed lullaby singing may offer the parent–infant dyad experiences of pleasure, happiness, love and joy instead of pain, worry and fear. Shared pleasure has the capacity to dissolve a negative painful affective spiral (paper III). In family-centred pain management, the music therapist is a facilitator and an educator, collaborating with the parents to empower them to communicate with their infant in an infant-directed mode. The music therapist can provide emotional verbal and non-verbal support for the whole family, the parents together with the hospitalised infant and possible siblings during the pre-procedural music therapy sessions. Live parental infant-directed singing also provides the parents with a pain management tool they can use at home after discharge. The theoretical biopsychosocial rationales give opportunities for live parental infant-directed singing and neonatal music therapy to be included in the gold standard for non-pharmacological neonatal pain management (paper III).
Discussion

Methodological considerations and limitations

The following paragraphs in this chapter will not just discuss the chosen methods and the limitations of these choices, but they also include an explanatory methodological background of the considerations and decisions concerning the design and methods used in this doctoral thesis.

The RCT design

The very first study protocol in Spring 2012 was called “The efficacy of non-pharmacological parental infant-directed singing and multimodal stimulation in management of procedural pain in preterm neonates”. The initial suggestion in the research team was to randomise infants between the age of ≥ 34 GA to < 37 GA and their parents into an intervention group, with parental infant-directed singing in combination with multimodal stimulation treatment (Whipple, 2000) and compare with a control group. This soon changed to a crossover design where the infants served as their own control. Recruiting infants to a separate control group would have been too time consuming. The parents in the intervention group were originally supposed to be trained in how to use their voice in combination with the multimodal stimulation before, during and after a venepuncture. A separate training/information session was planned for the participating nurses. The blood sampling was supposed to be performed while the infant was resting in the arms of the parent. A mixed methods study design was discussed where the physiological and behavioural measurements were combined with a qualitative semi-structured interview study with the participating parents.

However, to train that many parents in infant-directed singing and multimodal stimulation was unfortunately not feasible within the time frame we had. Instead, a music therapy student in training to become a professional music therapist sang to all infants, and the intervention with multimodal stimulation treatment was dismissed. The two research nurses who were supposed to perform all venepunctures left for other assignments and consequently different specialist nurses and midwives performed the venepunctures with some differences among the nurses concerning blood-sampling preparation routines. During the initial phase of data collection, we became aware of the limitations of the inclusion criterion for GA and applied for a supplement approval by the Regional Ethical Review Board to
include all infants cared for in the NICU, both preterm and term born infants, ≥ 32 GA.

A dilemma for the study was the lack of sufficient previous research to inform the design of the music therapy intervention concerning time frames and power calculations. The sample size for the RCT was motivated by previous exploratory pain studies with neonates using recorded music. Sample sizes in these studies have been small, ranging from 13 up to 35 participants, yet demonstrating significant modulations of both behavioural and physiological pain responses (Table 2). A major question in the beginning of the study was how many minutes the lullaby singing should continue before the skin puncture was initiated. There were also questions about how long the baseline was supposed to be and the silent period in the end of each procedure (Figure 1). At that time, in the year of 2012, there were to our knowledge no other pain studies that had studied the effectiveness of live infant-directed singing before, during and after the skin puncture on infants’ pain expression. The available music medicine studies all used recorded music interventions. We hypothesised that non-pharmacological interventions, like the live singing, needed some time to have an impact on the infant’s state before the blood sampling was introduced. Half through the study, a book chapter by Axelin, Eriksson & Grdin, (2013) was somewhat reinforcing this reasoning; “it takes between one and two minutes for the infant to adapt to and relax after a new sensory stimulus” (Axelin et al., 2013, p. 117). We decided to start the lullaby singing 2 minutes and 30 seconds before the painful procedure so that the infant would adapt and relax to the singing. For the same reason, the time for the baseline and the silent period at the end of the intervention was set to two minutes each (Figure 1). Critically ill infants are vulnerable, and the time frame was also carefully set so as not to risk exhaustion of the infants. At the time of writing, the dosage and timing of live singing as well as recorded music stimulation are still not clearly defined and established. In recent published research, various dosages are described (Table 2). It varies from for example 5 minutes or 10 minutes before the blood sampling, continuing during the skin puncture until 5, 10 or 20 minutes after the skin puncture and some music medicine studies decided not to play the recorded music during the painful procedure, but only after, to support recovery (Table 2).

The NICU context where the RCT-study was conducted also influenced the design of the study and there were some conflicts between research design and clinical practice. The NICU in Stockholm had a NIDCAP care profile where standard care was blood sampling through venepuncture, not
heel-lance. Venepuncture is considered less painful for the infant than heel-lance (Shah & Ohlsson, 2011), but on the other hand, venepuncture can be a difficult and somewhat complicated and drawn-out procedure, searching for these small and fragile veins in which to put the needle. Some blood-sampling procedures in the RCT were more complicated and lengthier than others, since the nurse had up to three attempts per procedure to achieve the required amount of blood (Figure 1). After three attempts, the policy in the NICU was to change nurse or if possible, postpone the procedure if the infant needed rest. The skin punctures were performed in the infant’s crib or on the examination table, not in the arms of a parent, so we had to adapt to that routine in the design. Standard pain care comprised facilitated tucking by an assistant nurse or a parent and oral glucose two minutes before the venepuncture as well as on demand during the venepuncture. The infant was given the opportunity to suck on a pacifier or on a parent’s or a nurse’s finger. Before the blood sampling the infant was supposed to be newly fed.

During the planning of the RCT, as an inexperienced researcher, I was not fully aware of how standard pain care would influence the measurements of the effectiveness of the live lullaby intervention. The absence of significant results in PIPP-R and BIIP scores indicates an already effective standard pain management. The infants were in minimal or no pain in the control condition as well as in the lullaby intervention with mean pain scores less than 6 in both conditions measured with PIPP-R (paper I). The majority (70 %) of the neonatal clinical pain trials round the world that study interventions to reduce pain, include a no treatment or placebo control group in their studies, which means these studies purposely expose infants to unnecessary harm to get a positive trial with a large effect (Campbell-Yeo, 2016). In our RCT, we took all the necessary precautions to ensure the ethical conduct of neonatal pain trials by providing standard pain management for all involved infants. In this real-world research, we also had to ethically accept that not all infants underwent two routine blood-sampling procedures, which affected the balance in the crossover design. We did of course not impose an extra skin puncture on the infants just to get a full data set.

Although the parents were always invited to attend the venepuncture procedures, a limitation in the design was that they were instructed not to sing, hum or talk to their infant, which some parents felt to be a restraint. Another dilemma was the policy in the NICU to cover the infant’s eyes during blood-sampling procedures, since the bright light might arouse the infant. The pain assessment was done from video recordings of the infants’ face.
and hands. To cover half of the face would be detrimental for the core of the study. The assistant nurse or the parent was consequently instructed to shadow the infant’s eyes from the light with their hands like a cap so the video could still record the facial expressions. Some nurses felt very uncomfortable about this adjustment.

Another limitation in the study design was for example the handling before blood sampling. The handling of the infant before the skin puncture, with divergent routines across the nurses, could also cause much distress influencing the pain experience, but it was not possible to account for in any assessment tool. The individual differences among the infants in the study were many and mixing results from both premature and term born infants was problematic. The sample size was too small to form subgroups in the statistical analysis. The background noise in the NICU was surprisingly high, which could have influenced the effectiveness of the lullaby singing. A further problem was that the project had almost no funding and could not continue until the study was fully powered.

**The live lullaby intervention**

At the time of the planning of the RCT, there were no previous studies evaluating live music therapy in conjunction with painful procedures in a neonatal context and there was therefore no music therapy research to inform the design of the live music therapy intervention. The music therapy tradition in Scandinavian practice involves techniques of active and improvised music-making. In combination with the family-centred care perspective in Swedish NICUs, it was obvious that the music therapy intervention should be live. Live singing can be responsive to the infant in pain since live singing can be used to entrain to the infant’s state and induce calm, thus assisting the infant to self-regulate. Live singing is flexible in the moment and multisensory, which recorded music is not. A useful source in deciding the music therapy content of the study was previous NICU MT research with infants in a non-painful situation that showed how live music therapy influences infant behaviour. Hearing is closely linked to the arousal systems (Shoemark, 2007), and in the clinical study we hypothesised that in a painful situation the music therapy intervention should be designed to diminish stress, stimulation and arousal while maximising calm, trust, stability and the infant’s self-organising capacities, in order to alleviate the infant’s pain. There could be an advantage as well as a problem with choosing one singer for all infants; the female student in training to become a professional music therapist. This was an attempt to standardise the interventions complying
with medical standards for appropriate research design. On the other hand, we might have increased the risk of a “music therapist effect”, as described in Kain et al. (2004).

**The pain assessment**

A limitation with the pain assessments in the study was that either the BIIP nor the PIPP-R discriminate between pain stress and stress from causes other than pain, for example environmental noise. The loud background noise might have added extra stress to the painful situation. Another limitation with the assessment tools was that they did not capture the infants’ signs of exhaustion during and after skin puncture. Pain consists of more dimensions than just pain intensity. Absence of expressions in the infants’ state, face or hands during time-out periods did not generate any scores and were therefore not measurable items in the scales. On the other hand, in the PIPP-R there are additional pain score points if a prematurely born infant is in quiet sleep, since prematurity and quiet sleep dampen pain response (Johnston et al., 2008). Using weightings to adjust for varying gestational ages and sleep/wake states may hide important information with regard to arousal in these infants (Holsti & Grunau, 2007). This may decrease any differences between conditions if lullaby singing puts infants into a quiet state/sleep (c.f. Johnston et al., 2008). The issue of when to take baseline measures for the PIPP-R when the intervention begins many minutes before the venepuncture procedure also needs addressing. According to the PIPP-R guidelines, baseline measures of state, heart rate and oxygen saturation levels are recorded just prior to the venepuncture. In studies such as this when the intervention starts prior to when the baseline measures would normally be recorded, the values of state, heart rate and oxygen saturation levels are not at baseline levels, because the lullaby singing has a modifying effect on each of these parameters. Future research with lullaby singing should take the baseline measures into consideration.

In measuring and capturing biopsychosocial phenomena like pain and the influence of lullaby singing on infants’ pain experiences, BIIP and PIPP-R are relatively blunt and reductionistic tools. Pain intensity is obviously only one dimension of the pain experience (Andersen, 2018). Researchers and clinicians use a structured pain measurement scale to quantify the infants’ biobehavioural pain responses to obtain a numerical pain score for statistical analysis or for effective treatment of pain. To self-report pain is standard in healthcare today. However, non-verbal individuals, for example
infants, cannot self-report their pain and they are in the hands of an observer who interprets and assesses if and how much pain the infant expresses (Andersen, 2018). There is always a risk for both under- and overestimation of the non-verbal infant’s pain, even though a scale is used (Andersen, Langius-Eklöf, Nakstad, Bernklev & Jylli, 2017). A crucial factor in pain assessment is that the chosen pain scale is valid. Validity, reliability and responsiveness are important measurement properties. If a pain scale has inadequate measurement properties, it might not measure pain magnitude adequately or identify changes in pain intensity (Andersen, 2018). The validity of a scale must be tested in repeated studies with different approaches, which is time consuming and expensive. Therefore, many published scales today have limited validity testing, and the pain assessment field has been more focused on developing new scales than on validating the existing scales (Andersen, 2018; Eriksson & Campbell-Yeo, 2019). A systematic review of reviews (Andersen et al, 2017), showed that there are today at least 65 pain scales for assessing pain in infants and children and the systematic review showed that there is little consensus on which of the published scales to recommend. The systematic review also found that the methodological quality was low in the studies that had evaluated the various pain scales and the included reviews of the various pain scales were flawed with high risk of bias. In sum, the recommended pain scales that are used in clinical practice and in research have low evidence value and should be interpreted with caution (Andersen et al., 2017).

In medical and nursing research, pain scales are considered to be a quantitative measurement of infants’ pain expressions, but one has to remember that the numerical pain score rests heavily on qualitative and subjective interpretation of the infant’s behaviour. The assessed pain score is then followed by a new qualitative interpretation when the score is evaluated as minimal/no pain, moderate pain or significant pain as in the BIIP scale (Holsti & Grunau, 2007). The result of the pain assessment is also dependent on who is assessing the pain and their previous training. The pain score may also vary depending on which variables of pain expressions are selected and included in the specific pain scale. There is a risk that the scales simplify the pain experience too much. Perhaps the best way for the future is to take a step back and reflect on how infants’ pain could be evaluated in a more consistent and comprehensive way, where the pain scales are one parameter of many in the assessment of pain, with a more individualised approach that also include the parents’ perspective and assessment (Randi Dovland Andersen, personal communication, 11 March 2019).
Inaudible parents in neonatal pain research

The quintessence of this doctoral thesis is articulated straightforward in the following quote:

Often, all that a child needs to get through a pain experience is to have someone nearby who understands and will share that experience (Muller, 1997, p. 80).

The infant has an innate need for her or his parents, a physiological, psychological and social need to be close to the parent and share the painful experience, and receive love and support from the parent before, during and after a painful procedure. The goals of pain management in infants are to minimise the pain experience along with other factors that can contribute to pain and stress (such as noise, handling and parental separation) and maximise the infant’s coping capacities to recover from the painful experience (Walter-Nicolet, Calvel, Gazzo, Poisbeau & Kuhn, 2017). There is a consensus that non-pharmacological strategies should be the first choice in procedural pain management (Swedish Medical Products Agency, 2014). These strategies reduce pain by for example blocking nociceptive transmission or by activating descending inhibitory pathways, which are supposed to be functioning at term birth.

Neonatal pain research has studied a range of non-pharmacological pain alleviating strategies and has so far found that a combination of parent-driven interventions has the best effect on pain expression, especially combinations of multimodal and multisensory strategies such as SSC, KMC plus breastfeeding (Leite et al., 2015). These results fully harmonise with the fact that infants are multisensory, biopsychosocial beings with an innate ability for amodal perception (Stern, 2010). The researchers in the study by Leite et al., (2015) discuss what aspects are in fact involved in pain relief when combined with SSC and breastfeeding:

The analgesic mechanisms of maternal skin-to-skin contact are not known with certainty. This nonpharmacological measure brings together various stimuli such as the smell, voice, warmth, skin texture, sound of the heartbeat, movement of the chest during maternal breathing, restraint and prone positioning (Leite et al., 2015, p. 6).

The aspects that the authors in the study by Leite et al. (2015) mention engages all senses at the same time in the dyad, and the mother’s multisensory and multimodal voice is of course included in the list. Daniel Stern and his colleagues in developmental psychology research studied naturalistic mother-infant moment-to-moment communication, using microanalysis to
discern for example the dyad’s coordinated vocal turn taking. They recognised that multimodal actions, including music-like vocalisations, were overall present in a healthy naturalistic regulatory parent-infant interaction (Beebe, 2014). Nevertheless, in pain studies that are investigating non-pharmacological approaches, the involved parents are surprisingly quiet. Supposedly, these reciprocal multimodal music-like vocalisations must also be present in painful procedural situations, if the parents are permitted to participate. In the study by Leite et al., (2015), the researchers sensibly state: “Another aspect that deserves to be better evaluated in future studies is the maternal behavior during breastfeeding and maternal skin-to-skin contact, as these strategies enable the active participation of mothers and may modify the response of newborns to the painful event” (p. 7).

The efficacy of multimodal, soothing vocalisation behaviour has been established in the study by Jahromi et al. (2004). The study was a naturalistic observation of mother-infant mutual regulatory interactions and the specific soothing behaviours used by the mothers, as well as the effectiveness with which these maternal behaviours relieved infant distress during immunisation. At 2 and 6 months, holding/rocking and vocalising combined were significantly related to reductions in infant crying at all levels of distress, even when the infant was highly distressed (Jahromi et al., 2004). Vocalisations in this study involved any vocalisations the mother made directed at the child, including talking, singing, “shushing,” and unrecognisable vocal sounds. The combination of holding/rocking and vocalising behaviours were found to be among those most frequently used by mothers at both 2 and 6 months, implying that mothers are aware of the efficacy of these behaviours and consequently use them more frequently. Holding/rocking and vocalising behaviours were only effective if they occurred together (Jahromi et al., 2004). The second most effective behaviours, the feeding/pacifying behaviours when the mother gave the infant a bottle or pacifier or began breastfeeding, was found most effective when the infant was either at a low or moderate level of crying (Jahromi et al., 2004).

These results lend support to later research results regarding the efficacy of SSC, KMC, breastfeeding and also the pharmacological agent sweet solutions. Combined parental soothing behaviours that provide rhythmic (holding/rocking/vocalising) or orogustatory/orotactile (feeding/pacifying) stimulation that keep the mother/parent close are more effective in a painful context than those that take the mother away from addressing the pain, such as distracting behaviours, which require the mother/parent to focus their attention on something other than the infant. The study by Jahromi et
al. (2004) suggests that varying levels of infant distress may warrant different types of parental regulatory behaviours and that parents change their use of behaviours to reflect infants’ developmental maturation.

The results of the study (Jahromi et al., 2004) also clearly show that distraction interventions are ineffective strategies at all levels of distress at both 2 and 6 months, and that distraction behaviours are significantly less likely to reduce crying since distraction behaviours do not address the primary concern of the infant (Jahromi et al., 2004). Early maternal soothing behaviours also predict later infant distress (Jahromi & Stifter, 2007). Efficient and sensitive parent-driven pain management early on in infancy in terms of affection, touching, and vocalising have both immediate and long-term effects on infants’ self-regulation (Jahromi & Stifter, 2007; Atkinson, Gennis, Racine & Pillai Riddell, 2015; Filippa et al., 2019a).

The study by Jahromi et al. (2004) is, to my knowledge, the only naturalistic music medicine study so far that has observed the efficacy of the parents’ singing behaviours in conjunction to painful procedures, though during an outpatient routine immunisation visit. It is worth mentioning that when neonatal pain researchers study parent-driven pain-alleviating interventions they do not generally report, and perhaps do not even register or measure, the dyadic music-like vocalisations occurring in the interventions, not even as “confounding factors”. Verbal communication is certainly easier to detect and assess than interactive subtle vocalisations in the dyad, which requires microanalytic work. Perhaps the researchers in pain studies even prevent parents from using their full range of multimodal and multisensory communicative comfort strategies, including their voices, in order to distinguish certain single effects?

The most significant, most multimodal and multisensory aspect of the dyadic relationship is the mother’s, and later on, the fathers voices (Filippa et al., 2019a). The first voice the foetus hears and ascribes significance to is the mother’s voice and the music of her prosody (Moon, 2017). The mother’s behaviour, the way she moves and acts, i.e. her dynamic forms of vitality, also become familiar to the foetus and is reflected in the mother’s voice. The musical qualities of the mother’s voice are salient in the perinatal experience of speech, enculturation and attachment. The mother’s voice is a multisensory and multimodal event both prenatally and after birth. The mother’s voice is accompanied by motion conjoint with sound intensity and rhythm, as well as motions in the mother’s diaphragm and through her gestures. After birth the infant perceives the motion in the mother’s and father’s
facial expressions, eye contact, body movements, affectionate touch and timing (Moon, 2017).

For decades, research has shown that infants, already at birth and perhaps even earlier, are sophisticated musical communicators. Considering this, it is bewildering that hardly any research so far has investigated the impact of and the adjuvant role of the multimodal and multisensory parental voice on infants’ pain expressions. Not even the RCT in this thesis managed to investigate the live parental infant-directed singing on infants’ pain responses. The RCT in this thesis studied the additional effect of live lullaby singing performed by a female stranger. Her voice and style of singing was probably not multimodally, multisensory or affectionately significant enough for the infants to alleviate their behavioural pain responses during venepuncture. As previously mentioned, a limitation of this study was the study design, where the parents were confined to use their voices in connection to the venepuncture in favour of a stranger’s voice.

However, the results from the live lullaby RCT did not indicate that live singing was harmful. On the contrary, the power of a repetitive lullaby is still something to consider in painful situations in future research. Live parental infant-directed singing may augment the parent’s focus on the infant in the moment, enhancing the parent’s emotional availability and responsiveness in the painful context and decrease stress, which have been confirmed in previous research in non-painful contexts (Loewy et al., 2013; Fancourt & Perkins, 2018). From research, we know that parents who are more emotional available use less verbal reassurance behaviours (Atkinson et al., 2015). The risks with using reassuring infant-directed speech during painful procedures have previously been investigated (McMurtry, Chambers, McGrath & Asp, 2010), and have also been confirmed in this thesis. Verbal reassurance during painful procedures is known to increase the infant’s pain stress, while infant-directed singing decreases infant stress (Bieleninik, Ghetti & Gold, 2016).

One of the objectives for this doctoral thesis was to theoretically investigate and present rationales for including vocalisation, or more specifically, infant-directed live singing performed by a parent among multimodal parent-driven pain alleviating interventions before, during and after painful procedures. Parental live singing is a highly unexplored biopsychosocial, multimodal and multisensory contributor especially in combination with SSC, KMC, breastfeeding and sucrose. One reason for the effectiveness of parent-driven pain management is something as fundamental as love, a parent’s love and empathy (Anand & Hall, 2008). Parental presence enables a
range of comforting parental interventions such as skin-to-skin contact, breastfeeding, rocking and soothing vocalisations, all of these are expressions of a parent’s love for the infant (Anand & Hall, 2008). The attachment theory (Bowlby, 1988) is essentially about love, parents’ love for their infant expressed within a multimodal and multisensory modality, which cannot be replaced by random persons in the environment, for example a music therapist. Singing with your infant might be a highly common activity among parents, but it is certainly not in the hospital context, and parents need instructions and support to implement this simple yet potent strategy (Shoemark & Dearn, 2008). The loss of “normal”parenthood in a hospital may result in the loss of opportunity for valuable contingent interaction, which is the basis of attachment (Shoemark & Dearn, 2008). NICU MT is a triadic relationship with the parent/s and the infant, in which they together share an expanded competence. The music therapist may serve as a source of respite or direct support for the parents (Shoemark & Dearn, 2008).
Conclusions

This doctoral thesis has generated conclusions within macro (paper I), micro (paper II), biopsychosocial and relational (paper III), organisational and societal (paper IV) dimensions within the framework of Neuroaffective Developmental Psychology Theory.

The first research question addressed in paper I was: What effect does live lullaby singing have on behavioural and physiological pain responses during venepuncture in preterm and term neonates? There was no statistically significant difference in PIPP-R score between lullaby intervention and control in either ITT or PP population, thus the primary hypothesis could not be supported. The live lullaby singing compared to standard treatment did not negatively affect the primary outcome, and the effects must be discussed from other perspectives. There was a significantly calmer breathing pattern in the lullaby intervention versus control in both ITT and PP populations in the pre-needle stage, suggesting that live lullaby singing lowers stress and contributes to clinical stability.

The second research question addressed in paper II was: How does live lullaby singing for preterm infants influence their physiological and behavioural responses before, during and after venepuncture compared to standard care? The microanalysis disclosed that live infant-directed lullaby singing is a communicative reciprocal intervention, which also applies to premature infants during painful procedures. Lullaby singing is a communicative interaction tool suitable as a means to optimise the homeostatic mechanisms of the premature infant. Live singing affords the infants a soothing melody pattern to which they can attune and gradually feel supported by, provided that the vocal performance is repetitive and predictable in the temporal, shape and intensity structure, continuous from the start until the end of the procedure and not interrupted by infant-directed speech. The infant must be constantly observed during singing in order to refocus the affective support within the present moment, to maintain emotion regulation.

Research question three, covering aims three and four, is addressed in papers III and IV as well as in the chapter A synthesis of the main results. The third research question was: What are the respective roles of music therapy, the music therapist and the parents in family-centred non-pharmacological neonatal pain management? Coaching parents to better meet their infant's attachment needs during a painful procedure may lead to more efficacious interventions. The biopsychosocial rationales for including the parents’ live singing in neonatal pain management are demonstrated in the
literature. The biopsychosocial parental infant-directed singing is presumably an applicable parent-driven non-pharmacological intervention, which promotes pain relief and attachment formation during painful procedures. The music therapist, specialised in neonatal music therapy methods, is an important role model, coach and educator in family-centred neonatal care. The music therapist can support the parents to be sensitive, responsive, emotionally available, stable and well-informed in using attuned live infant-directed lullaby singing in combination with other parent-driven interventions in connection with painful procedures. The strategy proposed in this doctoral thesis, the Nordic NICU MT pain management strategy (Fig. 18), elucidates how and why it is vital and relevant to include parents’ live singing as well as the music therapy expertise in a gold standard, in order to advance the interventions in non-pharmacological parent-driven neonatal pain management and contribute to the overall health outcomes of hospitalised infants and their parents. Cultural sensitivity and cultural context are of crucial importance for knowledge translation and implementation work when establishing and building neonatal music therapy services. The family-centred care approach in the Nordic NICUs, combined with the progressive family politics in the Nordic countries with generous parental leave schemes and gender equality in childcare, afford advantageous prerequisites to further develop NICU MT into a family-integrated approach also in neonatal pain management.

**Dynamic forms of vitality as the principal link**

The overarching aim of this doctoral thesis is to evaluate live lullaby singing as an adjuvant to the control of infant pain. To evaluate this objective, the theoretical framework NADP and the concept of dynamic forms of vitality (Stern, 2010) have been operational.

Pain is a biopsychosocial experience. Parental infant-directed singing is a biopsychosocial interactive intervention. The reciprocal interactions between the attachment system and the caregiving system are found to be biopsychosocial and proto-musical (Volgsten, 2019). The common denominator in this complex mix of physiological, psychological and social processes, the link between a) the dyad’s biopsychosocial pain experiences, b) the biopsychosocial parental infant-directed singing and c) the biopsychosocial attachment/caregiving systems, is the concept of affect or more specifically, the dynamic forms of vitality.
Dynamic forms of vitality may elucidate how and why live parental infant-directed singing in combination with other non-pharmacological parent-driven strategies facilitates pain alleviation (Fig. 19). When an infant is in pain, dynamic forms of vitality related to pain are aroused in the infant influencing mirror neurons in the parent to fire in the same pattern. The dynamic forms of vitality, which are aroused in the parent, give the parent a virtual experience of the infant’s pain experience.

Through affect attunement using multimodal and multisensory protomusical elements, the parent matches the infant’s dynamic forms of vitality, showing the infant that she/he understands the infant’s affects and shares the experience with the infant, sending a message to the infant that she/he is not alone in this situation.

Simply sharing vitality affects might not be enough for mitigating the painful experience. The parent needs a down-regulating, real-time arousal regulator for the infant to attune to. Live parental infant-directed singing provides a continuum in the regulation of the infant’s arousal systems. The music therapist plays an important role coaching the parents to identify emotionally important songs or lullabies that are comfortable to sing in conjunction with painful procedures.

The proto-musical elements used in infant-directed singing are intensity, contour, shape, tempo, rhythm, dynamic, the same elements as the pain experiences comprise and the same type of elements of which dynamic forms of vitality consist. Since the live parental singing process is reflexive, the mental state of the responsive and stable parent is communicated to the infant through proto-musical elements, and the infant thus takes part in the parent’s state and arousal levels and is helped to self-regulate back to homeostasis. In live parental infant-directed singing, both the infant and the parent become active agents in pain management and can modify their own affective state.

When a parent sings, the music moves the infant in a multimodal and multisensory manner via the parent’s expressions of dynamic forms of vitality. In this reflexive process, contingent upon the infant’s dynamic forms of vitality-response, the emotionally available and stable parent uses the repetitive lullaby singing to constantly alter the timing, intensity and shape of the singing and her/his other actions to regulate, comfort and soothe the infant before, during and after a painful procedure.

When the parent interplays with both her/his own and the infant’s dynamic forms of vitality through live singing, the parent is resonating on the neurobiological, intrapsychological and interpersonal level to alleviate the
infant’s pain experience. Love and joy are important elements to provide a secure, safe and shared affective base. Shared positive dynamic forms of vitality enhance the release of endogenous pain-alleviating hormones and opioids in both infants and parents, which promotes pain relief and attachment formation.

Figure 19. When the infant and the parent experience a painful procedure, dynamic forms of vitality related to pain are aroused in the dyad. Dynamic forms of pain affects are interwoven on physiological, psychological and social levels in the dyad. Biopsychosocial interventions, including parental lullaby singing, love, joy and comfort as well as reciprocal attachment interactions, gradually match, share, modify, and modulate the intense dynamic forms of vitality of the painful experience. The principal link between a) the dyad’s biopsychosocial pain experiences, b) the biopsychosocial parental infant-directed singing and c) the biopsychosocial attachment/caregiving systems, is the concept of dynamic forms of vitality. Family-centred multimodal standard pain management, such as SSC, KMC, breastfeeding and sucrose, is the scaffolding condition for the parental infant-directed singing intervention.
Further perspectives

During the past 30 years, music therapy research has built evidence-based knowledge and practice in the neonatal context. However, research about music therapy as pain management for infants and their parents is a new research field that needs to be explored further. Neonatal music therapy is a salutogenic, resource-oriented and cost-effective approach, which involves parents in caregiving activities, including pain relief, and goes very well with the family-centred care philosophy. NICU MT could play an important role in family-centred preventive perinatal medicine and deserves to be considered and researched.

One important question that is raised in this doctoral thesis is who should deliver the lullaby singing intervention during painful procedures. Is it allied healthcare professionals with recorded music? The music therapist with live lullaby singing? Or the parents, singing live in combination with other parent-driven non-pharmacological strategies? Another consideration is when and where in the pain management process the music therapy service would be most wisely and successfully administered. Providing emotional support to the parents is today a recognised challenge for the NICU staff and the least developed aspect of FCC globally (Raiskila et al., 2016). Based on existing evidence, new guidelines (Davidson et al., 2017) have identified best practices for family-centred care in the NICU and have for example recommended that family support and education programs should be included as part of clinical care. These programs have demonstrated beneficial effects in reducing anxiety, depression and stress and improved parental confidence and competence in the caregiving role, as well as improved parental psychological health during and after the NICU stay. By improving the parents’ knowledge and involvement, the infants’ pain management is also improved, and parental counselling is one of the most important factors in this improvement. It is not just the infants’ pain management that needs to be individually tailored and adjusted in the moment. The instructions and training in parent-driven non-pharmacological strategies also need to be individually tailored and adjusted to the parents’ diverse individual needs. The music therapist, specialised in neonatal music therapy methods, can partner up with staff and parents in addressing these specific care needs. She or he can mentor parents in a non-confrontational manner to use non-pharmacological combinations in connection to painful procedures. The supportive and coaching functions could be most relevant for the music therapist to pursue and to research, preferably in participatory collaboration with the
parents. An important future research study would be to frame the results of this thesis into a strengths-based psychoeducation service for parents, building on for example Helen Shoemark’s program Time Together (Shoemark, 2017), but for painful contexts, and to investigate the usefulness of the proposed Nordic NICU MT pain management strategy.

Parents need to and want to participate actively in their infant’s pain management. In future research, parents coached by a music therapist in advance can use their infant-directed singing to prepare the infant before the skin puncture, aiming for the infant and the parent to reach homeostasis and become well-regulated prior to the painful procedure. During the procedure, the infant and parent could share the painful experience while the parent comforts the infant through attuned moment-to-moment responsive lullaby singing, and after the skin puncture, parental infant-directed singing offers a means for the dyad to recover in an attuned, soothing down-regulating process, where the parent leads the infant into a new but safer affective state.

Being one of a handful of NICU MT music therapists in the Nordic countries, pioneering NICU MT research and practice in Sweden, I do not have the luxury of being too much of a professional protectionist. However, it is not merely pragmatic causes which lead me to suggest the Nordic NICU MT pain management strategy with parental infant-directed singing, but the infant’s and the parents’ needs. Searching for what is best for the patient and the family in a painful situation is what really unites all professions in the interdisciplinary research field of family-centred infant pain management. A current trend in music therapy in general, as well as in interdisciplinary neonatal pain management research, is user involvement (for example participatory action research). To perform research together with the parents is a democratic power sharing process, in line with the music therapeutic ideas and the FCC philosophy, which could also be the link to narrowing the 17-year research to practice gap (Morris, Wooding & Grant, 2011), like a reversed translation.

To sing is to communicate and singing belongs to all. A parent’s singing is love embodied in sound. This doctoral thesis will hopefully contribute to the important interdisciplinary endeavour worldwide of involving and integrating parents in neonatal pain management, because “if a community values its children, it must cherish their parents” (Bowlby, 1951, p. 84).
Epilogue and acknowledgements

Baby V is 10 years old today and he goes to a special needs school assisted by his personal assistant. Together with the school, I recently initiated a music therapy group for pupils with intellectual disabilities, including V. I meet V and the other children, together with their personal assistants, every second week at their school, singing and musicking together for developmental purposes. After so many years, it is fascinating to resume the music therapy contact with V. Since V is blind, his hearing is his strongest but also most sensitive sense. His love for music is unquestionable and he is very expressive through sounds and in musical interplay. Musicking with V is like playing on him as an instrument; he entrains with dynamic shifts in the interplay and follows intuitively the temporal, shape and intensity contour in the musical communication. Just like when he was an infant, V still gets easily overwhelmed and overstimulated by his environment. The musical interplay with V in the music therapy group at his school must therefore be carefully fine-tuned to his individual needs, as well as taking the other children’s needs into consideration, which is a balancing act many times. However, if or when the musical communication becomes too intense, a repetitive and soothing lullaby will always rapidly regulate V and the other group members into a calmer state. The principles in this doctoral thesis are now in the process to be implemented in the NICU context within the health care in Region Värmland as well as in a wider community context. Thank you, baby V, and all my other patients and families for the inspiration to pursue this research project and for all the learning experiences you have offered me during these years!

Pursuing a PhD is a lifestyle. For me personally, these years as a PhD student could be compared to a roller coaster ride with ups and downs, a 7 year-long emotional, nerve-racking but highly enriching and insightful journey involving a lot of people to whom I owe sincere appreciation.

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Sammanfattning (Summary in Swedish)


Musikterapeutisk forskning om för tidigt födda och sjuka fullgångna spädbarn, har bedrivits internationellt under nära 30 år, företrädesvis i USA, Tyskland och Australien. Det område som är minst utforskat inom neonatal musikterapiforskning är musikterapiins möjligheter att erbjuda de sjuka nyfödda smärtlindring vid smärtsamma procedurer som exempelvis blodprov. I Sverige har tidigare ingen forskning bedrivits inom neonatal musikterapi. Avhandlingsprojektet, som stöttats av Region Värmland, Örebro universitet, Kungl. Musikhögskolan, Karolinska Institutet och Karolinska Universitetssjukhuset, är därmed det första i sitt slag nationellt och internationellt.


Från den randomiserade kontrollerade studien valdes två prematurt födda spädbarn ut, en flicka och en pojke, till en fallstudie (artikel två). Sammanlagt fyra provtagningar med och utan vaggsångsintervention analyserades; två per spädbarn. Provtagningarna, som videofilmer, handkodades och analyserades på sekundnivå med mikroanalys. Spädbarnens beteenden, fysiologiska reaktioner och smärtuttryck före, under och efter blodproven samt omgivningsfaktorer analyserades i detalj. Vaggsången som framfördes live i interaktion med de för tidigt födda spädbarnen, transkriberades till notskrift och analyserades med mikroanalys. Mikroanalysen visade att


Smärta framkallar vitalitetsaffekter som varierar i rytm, tempo, intensitet, dynamik, skepnad och kontur från individ till individ och därmed formas en individuell smärtupplevelse. Späd barnets vitalitetsaffekter ”smittar” föräldern. Varje gång ett späd barn genomgår en smärtsam provtagning upplever även föräldern smärta. En förälder som är stabil, lugn, receptiv och tillgänglig använder multisensoriska och multimodala uttryck, bland annat sin sångröst, för att tona in och dela späd barnets vitalitetsaffekter av smärta utan att själv överväldigas av dem. Förälderns vitalitetsaffekter av trygghet, kärlek och delad upplevelse hjälper barnet att omforma och reglera de intensiva vitalitetsaffekterna i den smärtsamma upplevelsen och därmed dämpas smärta. Den repetitiva vaggsången blir ett redskap för den emotionellt tillgängliga föräldern att smärtlindra späd barnet genom biopsykosocial intoning och regleringen av späd barnets vitalitetsaffekter av smärta. Detta minskar smärtstressen i dyaden och kan bidra till frisättning av de kroppsegna smärtlindrande hormonerna hos både barnet och föräldern.

Utifrån resultaten i de tre tidigare nämnda delstudierna har en strategi utformats. I artikeln fyra samt i avhandlingskappan utvecklas och förklaras strategin, som har sin bas i den familjecentrerade omvårdnadsfilosofin. Enligt strategin sker regleringen av späd barnets vitalitetsaffekter före, under och efter ett blodprov, mest optimalt genom späd barnsriktad vaggsång, som framförs av föräldern i kombination med andra multimodala och multisensoriska icke-farmakologiska interventioner som exempelvis amning och hud-mot-hud. Musikterapeutens roll i denna biopsykosociala smärtlindrande strategi är att på förhand inspirera, utbilda och vägleda föräldrarna i processen att vilja och kunna delta aktivt som smärtlindrar för sitt späd barn. En ökad förmåga hos föräldrarna att läsa av och reglera sitt späd barns affekter kan komma till stånd genom exempelvis musikterapeutisk behandling. Slutsatsen är: ingen effekt utan reglerad affekt!
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