TREATING INVISIBLE SCARS

Psychological outcomes & effectiveness of EMDR after pediatric hospitalization

Maya Meentken

About the Author

Maya Meentken was born during the sunny season on July 26th, 1989 in Osnabrück, Germany, as third and last child of *Dr.* Josef Meentken and Elisabeth Gerkens-Meentken. She grew up in Osnabrück together with her two older brothers: *Dr.* Moritz Meentken and *Dr.* Felix Meentken. During high school she spent a full academic year (2006-2007) in Venezuela living with host families as part of the Rotary youth exchange program. After graduating from high school in 2009 (Gymnasium 'In der Wüste' Osnabrück) she spent another year in Latin America working at a rehabilitation center for street children in Nicaragua.

In 2011 she started studying Psychology at the University of Utrecht in the Netherlands. She finished her Bachelor (including Von Humboldt honors program) in 2014. During her Master she specialized in clinical child and adolescent psychology. For her clinical internship she worked at the department of Medical Psychology and Social Work of the Wilhelmina Children's Hospital, University Medical Center (UMC) Utrecht. After obtaining her Master's degree in 2015, she worked at the Dutch National Psychotrauma Center for Children and Youth & Dutch Sexual Assault Center in Utrecht. In 2016 she started her doctoral research, as described in this thesis, which was conducted at the Child and Adolescent Psychiatry/Psychology department in cooperation with the departments of Pediatrics and Pediatric Cardiology of the Erasmus Medical Center in Rotterdam. In November 2019, she started working as a therapist and researcher for Hulphond Nederland.

Maya recently moved to Noordwijk together with her boyfriend Roy and their dog Bright where they enjoy the beach life.

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COLOFON

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Scars on your soul
scars on your skin
Some on the outside
some are within
Some have a story
some are unwritten
Some you can see
but most are quite hidden

-E.P.

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CHAPTER 1

General introduction

There are wounds that never show on the body that are deeper and more hurtful than anything that bleeds

Laurell K Hamilton

PART I: PSYCHOLOGICAL OUTCOMES AFTER PEDIATRIC HOSPITALIZATION

Trauma is the Greek word for *wound*. Within physical medicine, trauma refers to severe physical injury. However, nowadays it also refers to a severely disturbing experience that can lead to lasting psychological or emotional impairment [1].

Pediatric injury and illness

Physical injury and illness are very common experiences during childhood and adolescence. Each year, about 1,4 million children in the Netherlands (almost 40%) are treated in hospitals and around 400.000 pediatric hospitalizations take place [2, 3]. Hospitalizations encompass a variety of possible stressors such as physical discomfort, painful medical procedures, and separation from caregivers, siblings and/or friends. In the first part of this thesis, we will investigate the psychosocial impact of pediatric hospitalizations for *acute* physical injury and illness and *chronic* illness.

Hospitalizations for *acute* physical injury and illness usually take place after a visit to the emergency department (ED). Yearly, approximately 174.000 emergency department (ED) visits of children (aged 5-14) take place in the Netherlands and about 37% of Dutch ED visits lead to hospitalizations [4, 5]. **Physical injury** is one of the major acute causes of hospitalization. In 2015, about 13.700 hospitalizations of children between 4 and 18 years took place after consultation at a Dutch ED because of injury [6]. Another emergent cause for hospitalization is **acute illness**, which is characterized by a sudden onset and/or short duration [7]. There are various minor and major acute illnesses that can occur in all bodily systems, such as musculoskeletal (e.g. aches, pain), respiratory (e.g. pneumonia, dyspnoe), gastrointestinal (e.g. appendicitis, intussusception), neurological (e.g. migraine), and dermatological (e.g. rashes, abces) [8].

In contrast, **chronic illnesses** are defined as long-lasting (minimal 6 weeks) and permanent [9]. About 18% of all adolescents have a chronic condition and they account for more than half of all pediatric hospitalizations [10, 11]. A very common condition that can be considered as chronic nowadays is pediatric heart disease. Due to its commonness and associated regularity of medical follow-up, we will focus on this type of chronic illness in this thesis. Pediatric heart diseases can be

categorized as congenital (present at birth) or acquired. **Congenital heart disease** (ConHD) is the most common congenital defect and occurs in 8 per 1000 births in Europe [12, 13]. ConHD involves structural abnormalities of the heart that are present at birth and can vary from small and mild to very serious and fatal. Due to enormous improvements in medical, surgical, and intensive care treatment most children (more than 80%) survive into adulthood [14]. Life-long medical checkups are recommended, with hospital visits being a routine part for the rest of the patient's life [15]. About 900-1100 children are hospitalized in the Netherlands every year because of a ConHD [16].

The psychological sequelae of injury and illness

The main goal of hospitals is to restore physical health which is critical for overall well-being. However, according to the World Health Organization (WHO) health is defined as "a state of complete physical, mental and social well-being" [17]. Despite the inclusion of mental and social well-being in this definition, the psychological impact of hospitalization has not been recognized until some decades ago. Before, children were separated from their parents while being hospitalized [18]. With the emergence of family-centered care (FCC) and new scientific insights, more attention was drawn to the importance of meeting the emotional needs of hospitalized children and their caregivers [18, 19].

As a consequence of improved health care during the last decades, the percentage of children living with chronic illnesses and/or physical impairments is still growing [20]. This brings along new psychosocial issues and challenges. Children who have experienced illness or injury are more likely to develop psychosocial problems than healthy peers and may be traumatized by the medical treatment and/or the hospital environment. Medical procedures (e.g. injections, surgeries) and hospitalizations (including scary surroundings and sounds) can be highly stressful [21]. Posttraumatic stress, emotional and behavioral difficulties, and lower quality of life have been reported as psychological sequelae of illness and injury in children [22, 23].

Pediatric Medical Traumatic Stress

Pediatric Medical Traumatic Stress (PMTS) has been defined as "a set of psychological and physiological responses of children and their families to pain,

injury, serious illness, medical procedures, and invasive or frightening treatment experiences" [24]. These responses are related, but not limited, to posttraumatic stress symptoms (PTSS). Key symptom categories of posttraumatic stress according to the Diagnostic and Statistical Manual of Mental Disorders 4 (DSM-IV) are:

- re-experiences of the traumatic event (e.g. flashbacks, nightmares),
- avoidance of stimuli associated with the event (e.g. thoughts, places, persons) and/or numbing of general responsiveness (e.g. withdrawal from activities, feeling of detachment from others), and
- increased arousal (e.g. hypervigilance, concentration problems) [25].

These categories have recently been adapted in the DSM-V to intrusion, avoidance, negative alterations in cognitions and mood, and alterations in arousal or reactivity [26]. Children who have experienced a traumatic event have an increased risk of developing posttraumatic stress reactions compared to children who have experienced a nontraumatic stressful life event [27]. The burden of PTSS is high as it places children's emotional, social, physical, and academic development and well-being at risk [28-32].

When an individual experiences the required number of posttraumatic stress symptoms, as described in the DSM, for more than a month and suffers from significant distress or functional impairment, this person meets the criteria for a posttraumatic stress disorder (PTSD) [25]. The estimated lifetime prevalence of PTSD in children is about 0.4-9% [33, 34]. The chance of developing PTSD is highest after interpersonal trauma (e.g. violence, physical/sexual abuse), but non-interpersonal trauma (e.g. accidents, serious illness) is more common [35, 36].

Research suggests that PTSS can best be seen as a continuum of symptoms with PTSD at the higher end and a few mild symptoms as normal reactions at the lower end of the spectrum [37]. A growing body of literature states that there is a group of individuals situated in the middle of that spectrum showing meaningful PTSS with similar impairment as PTSD, but without meeting all criteria for a full diagnostic PTSD [38, 39]. This has been named **subthreshold PTSD** (also called partial, subclinical, or subsyndromal PTSD). The first definition of subthreshold PTSD has been suggested in the early 90's [40]. While there is still no widely accepted consensus on a definition of subthreshold PTSD, the World Health Organization recommends to define it as meeting two or three of the four DSM-V

symptom criteria [41]. The estimated lifetime prevalence of subthreshold PTSD in children varies depending on the definition used between 2-14% [33, 34]. Again, the prevalence rates are higher in trauma-exposed children. About 25-38% of all ill and injured children develop subthreshold PTSD [22]. Impairment has been found to be similar in children with subthreshold PTSD and in those with a full diagnostic PTSD after interpersonal trauma [38]. However, research into the prevalence and consequences of subthreshold PTSD in children after potentially traumatic medical events (PTME) is underrepresented.

Therefore, the present thesis aimed to focus on subthreshold PTSD as a consequence of PTME's.

Medically related trauma types

Single potentially traumatic events (PTE's) encompass one-time events, also called type I trauma [42]. In a medical setting, this kind of trauma is often seen at EDs where children with acute one-time illnesses or injuries are presented. On the other hand, children with chronic medical conditions or severe injuries often experience prolonged or recurrent medical treatments and hospitalizations. The multiple potentially traumatic experiences of those children can be categorized as trauma type II. Scientific literature suggests that the experience of trauma type II might increase the risk of developing posttraumatic stress reactions compared to trauma type I [43, 44]. To date, it is unsure whether this also accounts for medically related trauma. Therefore, we were interested in investigating posttraumatic stress reactions after pediatric hospitalization, specifically studying the role of medically related trauma type (I versus II).

Psychiatric comorbidity

Since posttraumatic stress symptoms have been reported to be accompanied by other mental health problems (e.g. anxiety, depression), we also wanted to study psychiatric comorbidity after medically related PTE's [45]. The worldwide prevalence of any anxiety disorder in children and adolescents is 6.5% with a lifetime prevalence of 15-20% [46, 47]. In pediatric medical care samples, the prevalence rates for anxiety disorders increase to up to 30% [48, 49]. The worldwide prevalence rate for any depressive disorder in children and adolescents is 2.6% with a lifetime prevalence in the Netherlands of 15% [46, 50]. The experience of a traumatic

event increases the odds of a diagnosis of depression in children by 2.6 times [51]. Children who have experienced illness show prevalence rates of depressive disorders in up to 18% [49].

In addition, sleep problems are often seen in children after acute and chronic diseases possibly due to disease-related mechanisms (e.g. feeling unwell, breathing problems), medical treatments (e.g. pain, medication), or hospitalization (e.g. separation from caregivers, anxiety) [52].

Finally, health-related quality of life (HRQoL) is a broad concept which is considered crucial in medical care settings [53, 54]. Research suggests that HRQoL of children decreases in the first period after the medical event but can improve later on [55, 56].

Considering the problems associated with medically related PTE's described above, we aimed to examine the level of elevated symptoms of anxiety, depression, sleep problems, and HRQoL in addition to PTSS after pediatric hospitalization in the first part of this thesis.

Parental mental health

Hospitalizations and medical procedures not only affect the mental health of the child itself, but can also be highly stressful for parents. The PTSD prevalence in parents of children with chronic illnesses is 23% [57]. However, this prevalence rate is mainly based on studies regarding parents of children with cancer. In addition to mental health problems of children after pediatric hospitalization, we also aimed to review mental health problems in their parents. We focused on parents of children with a congenital heart disease as this is a very common pediatric condition (described above). Parents having a child with ConHD can be confronted with overwhelming stress and challenging emotional, social, and financial burdens [58]. Therefore, the first part of this thesis also includes a review of mental health problems in parents of children with ConHD.

PART II: EFFECTIVENESS OF EMDR AFTER PEDIATRIC HOSPITALIZATION

While the majority of ill or injured children and their families are resilient (defined as being able to adapt or manage significant sources of stress or trauma), a substantial proportion develops psychiatric morbidity with potential long-lasting effects [23, 59, 60]. Untreated clinically significant PTSS can decrease naturally but often last for years [61]. However, psychosocial resources are scarce within medical settings and mental health problems often remain unrecognized and untreated. Parents and children express a need for psychosocial care and individual psychotherapy within medical settings [62].

Very few evidence-based psychosocial interventions are available for ill and injured children [63, 64]. With regard to PTSD, the general international guidelines recommend trauma-focused cognitive behavioral therapy (TF-CBT) or eye movement desensitization and reprocessing (EMDR) [65, 66]. It has been argued that EMDR might work faster than CBT [67]. Three to six sessions of EMDR are often sufficient to significantly reduce PTSS [68]. EMDR has not only been shown to reduce PTSS, but also to improve other comorbid conditions such as depression and anxiety [69]. EMDR was originally developed for adults and later adapted for the use with children. Whereas its effectiveness for adults has already been proven in various meta-analyses, studies into its effectiveness in children are underrepresented [70-75]. Furthermore, only three studies were found focusing on EMDR after medically related trauma in children of which only one was a randomized controlled trial [76-78]. All three studies focused on PTSD symptoms after traffic accidents and had small sample sizes. Promising improvements were found in all three studies. Furthermore, another RCT investigating the effectiveness of EMDR for children who had experienced different kinds of traumas, including a small subsample of children with medically related trauma (23% accidents, 7% serious illness), also found promising results [79].

Summing up, EMDR might provide a fast treatment option that shows promising results for the treatment of PTSD in children. However, the few earlier studies into the effectiveness of EMDR for children with medically related trauma did not focus on subthreshold PTSD and only included children who had experienced a traffic accident [76-78]. Therefore the second part of this thesis aimed to investigate the effectiveness of EMDR in children with medically related subthreshold PTSD after hospitalization for illness and injury.

Eye Movement Desensitization and Reprocessing

EMDR, initially called EMD, was developed by Francine Shapiro in 1987 to treat posttraumatic stress reactions [80]. The eight phases of the standard EMDR protocol for children and adolescents can be found in **table 1**. During EMDR, patients are instructed to concentrate on a currently distressing memory while simultaneously engaging in bilateral stimulation (typically horizontal eye movements). The adaptive information processing (AIP) model offers a theoretical framework for the therapeutic effects of EMDR [80]. According to AIP, all experiences are processed within an innate information processing system that integrates new experiences within existing memory networks. However, some experiences might be stored dysfunctionally because of their distressing and traumatic nature. EMDR is thought to facilitate adaptive processing and integration of such distressing memories. The underlying working mechanism of EMDR has been studied repeatedly but is not yet fully understood. The theory that currently receives the most empirical support is the working memory theory [81]. This theory states that dual tasks (i.e. thinking about a distressing memory and simultaneously engaging in bilateral stimulation) challenge the limited capacity of the working memory. When this process occurs repeatedly, the vividness and emotional intensity of the distressing memory is thought to decrease and neutralize.

Table 1. Overview of the eight EMDR treatment phases

Phase	Purpose
Client history & treatment planning	Assess child's suitability for EMDR treatment Identify distressing memories for therapy (target sequence plan)
Preparation	Establish therapeutic relationship, explain EMDR procedures and train self-control techniques
Assessment	Elicit distressing image, current negative belief, desired positive belief, current emotion, and physical sensation
Desensitization	Standardized protocol including bilateral stimulation
Installation	Installing positive cognitions
Body scan	Check whether child feels any lingering physical sensations
Closure	Reflect on positive insights gained during the session Explain possible sensations between sessions and use of journal
Re-evaluation	Monitor progress and treatment effect

A randomized controlled trial

The main aim of the RCT described in this thesis was to investigate the short and longer term effectiveness of EMDR for children and adolescents with medically related subthreshold PTSD. Children aged 4-15 years who had been hospitalized because of injury or illness were included. Since earlier studies did not focus on subthreshold PTSD, we only included children with subthreshold PTSD. We were interested whether 1) EMDR is also effective in reducing subthreshold symptoms, and 2) EMDR can prevent a worsening of symptoms that otherwise might lead to full diagnostic PTSD (secondary prevention).

The main aim of the RCT was to study the following two research questions:

- What is the prevalence of mental health problems (symptoms of PTSD, depression, anxiety) in children after hospitalization for illness (acute illness and chronic pediatric heart disease) and injury, and what is the role of medically related trauma type as to these symptoms?
- What is the short-, and long-term effectiveness of EMDR on subthreshold PTSD (primary outcome), anxiety, depression, sleep problems, and HRQoL (secondary outcomes) in hospitalized children?

Participants

Included were children and adolescents (referred to as children throughout the thesis) aged 4-15 years, who had underwent a hospitalization for minimally one night 1) after consultation at an ED due to acute injury or illness, or 2) at a pediatric cardiology department due to a congenital or acquired heart defect. The last hospitalization or additional invasive medical procedure needed to have taken place at least 4 weeks up to 5 years before recruitment.

Exclusion criteria were: (1) intellectual disability (IQ<70); (2) parental inability to read or write Dutch; (3) diagnosis of a chronic illness for the emergency department subgroup; (4) previous successful treatment for medically related PTSD; and (5) current psychological treatment.

Procedure

Participants were recruited continuously from July 2016 until May 2018. Most participating children were recruited from the Erasmus MC Sophia children's hospital (divisions of pediatrics and pediatric cardiology) and the Maasstad hospital (division of pediatrics) in Rotterdam. At the Erasmus MC, approximately 7000 children (0-16 years) are seen at the ED every year and about 19% are admitted to the hospital afterwards [82, 83]. The ED of the Maasstad hospital, also treats about 7000 children (0-16 years) yearly [83]. Furthermore, children were recruited at the pediatric cardiology division of the Radboud UMC Nijmegen, by the Dutch Association for patients with a congenital heart defect, and by the Dutch non-profit organization Heartchild Foundation (Stichting Hartekind).

After written informed consent, children ≥6 years and all parents participated in a baseline screening. The purpose of this assessment was to screen children and divide them into three groups: 1) no/low PTSD symptoms, 2) subthreshold PTSD, and 3) full diagnostic PTSD. Only children with subthreshold PTSD participated in the randomized controlled trial. Children with subthreshold PTSD were randomized to EMDR or care-as-usual (CAU; i.e. no EMDR, regular medical care 'only') using a 1:1 allocation ratio stratified by trauma type (i.e. I vs. II) and age (i.e. 4-11 vs. 12-15 years). Randomization was done by an independent research psychologist using opaque envelopes. Children with full diagnostic PTSD were referred directly for psychosocial care and were not randomized.

Variables

We used standardized instruments with adequate psychometric properties and Dutch normative data where possible. The following variables were measured during the study:

- *Primary outcome*: PTSD symptoms
- *Secondary outcomes*: anxiety, depression, HrQoL, sleep problems, self-perception, attention problems, school functioning, social validity, and impact of PTSD questionnaire
- *Other variables*: demographic variables, cognitive coping styles, stressful life events, parental stress, family functioning, somatic complaints, and medical information.

For an extensive overview and description of the used instruments, see Methods sections of Chapter 4-7.

OUTLINE

In *chapter 2*, we reviewed the literature on prevalence rates of posttraumatic stress in children with a congenital heart disease. In *chapter 3*, we examined the existing literature on mental health problems in parents of children with a congenital heart disease. Then, in *chapter 4*, we describe the baseline data of our RCT, including prevalence rates of elevated symptoms of PTSD, depression, general anxiety and Blood-injection-injury (BII) phobia. Furthermore we investigated risk factors for the development of PTSD symptoms in children. *Chapter 5* represents the study design of the RCT. In *chapter 6*, we present the short-term results of the RCT. More specifically, we describe the effectiveness of EMDR on symptoms of PTSD, depression, general anxiety, BII-phobia and sleep problems of the child. The subjective evaluation of the EMDR treatment by the participants is also reported. Subsequently, *chapter 7* presents the longer-term effectiveness of EMDR on symptoms of PTSD, depression, BII-phobia, sleep problems and HRQoL. Finally, in *chapter 8* we provide a general discussion of all findings, clinical implications and future directions for scientific research.

PART 1

Psychological outcomes after pediatric hospitalization

CHAPTER 2

Medically related post-traumatic stress in children and adolescents with congenital heart defects

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Abstract

Children and adolescents with a congenital heart defect (ConHD) frequently undergo painful or frightening medical procedures and hospitalizations. They often need multiple invasive procedures at a very young age and require regular checkups during their entire life. From other pediatric populations, it is known that these kinds of experiences can result in acute stress reactions and even in post-traumatic stress disorder (PTSD) in the long-term. PTSD and also subthreshold PTSD can lead to serious (psychosocial) impairment. However, limited information is available about PTSD in children with ConHD. Therefore, the aim of this review is to provide a summary of the current literature on post-traumatic stress (PTS) in children and adolescents with ConHD describing the prevalence of PTSD and its predictors/correlates. This review indicates that a range of 12–31% of children undergoing cardiac surgery develop PTSD. A range of 12–14% shows elevated post-traumatic stress symptoms (PTSS). These findings are comparable to those of hospitalized children without ConHD. Noteworthy, most studies used varying self-report questionnaires to measure PTSD and only one study used a semistructured interview. Although all studies point in the same direction of elevated PTSD and PTSS, systematic research is necessary to be able to draw firm conclusions. At present, as far as we know, in most clinics treating patients with ConHD, there is no regular screening for PTS in children with ConHD. In the reviewed literature, there is strong consensus that screening for PTSS and (preventive) psychological care for children and adolescents with ConHD is urgently needed.

Introduction

Medical events are often experienced as stressful and frightening. Especially in young patients, this can be overwhelming. Medical procedures and treatments often cause pain, fear, a feeling of helplessness, and may give a sense of life threat [21, 22]. Furthermore, such procedures can challenge the beliefs of youngsters about the world as a safe place and can give rise to uncertainty about the future. Therefore, it is normal and understandable that some kind of postoperative stress occurs after the experience of such an event. The majority of young patients and their parents can handle this stress quite well [22, 84]. However, some develop persistent traumatic stress reactions such as post-traumatic stress disorder (PTSD). This, in turn, can have a negative influence on medical adherence and consequently morbidity or even mortality and can lead to an increase in health care service use [28, 85]. Furthermore, PTSD is associated with rehospitalizations, worse sleep quality, and impaired quality of life [30, 86, 87]. Children and adolescents with congenital heart defects (ConHDs) often undergo various invasive medical procedures at a very young age and some need lifelong checkups at the hospital and re-interventions [88]. Therefore, children with ConHD seem to have a heightened risk for developing PTSD. Considering this and the impact that PTSD can have on medical and psychosocial functioning, research into this topic should be a priority. However, research regarding PTSD in youngsters mostly has focused on abuse, violence, accidents, and natural disasters [89]. Disproportionately, few studies have looked into traumatized children and adolescents with ConHD. This review aims to give an overview of what is known in the field of medically related post-traumatic stress (PTS) in children and adolescents with congenital heart disease and suggests future directions. To find all relevant articles, a multi- database search was done with support from the Biomedical Information Specialist of the Medical Library of the Erasmus MC. The databases used were Embase, Medline, PsychInfo, Web of Science, Scopus, and Google Scholar. The search was limited to English language articles published from the year 2000 onward. Keywords included in the search were posttraumatic stress disorder and congenital heart disease (with a variation of corresponding terms).

Overview of definitions of PTSD in literature

In researching literature, different terms and abbreviations are used for posttraumatic stress (disorder). This variability makes it difficult to compare results across studies.

In the following, all relevant terms and abbreviations are shortly discussed to highlight the differences. We suggest that future studies should use similar terms to make results more comparable across studies.

Post-traumatic Stress (PTS)

The word "trauma" is often linked to physical injury. However, it can also refer to psychological injury or pain [90]. Immediately after the experience of an unpleasant or stressful event, people may express unusual physical and emotional reactions. This acute distress in response to a traumatic event is called PTS. It is considered a normal and often adaptive response [23, 91]. Stress reactions enable people to react directly to threatening situations and most people can return to a normal emotional state without help from professionals after such an event [92].

Post-traumatic Stress Symptoms (PTSS)

The wide range of distressing physical and emotional reactions is sometimes also referred to as "symptoms" [93]. PTSS is the term given to symptoms that can be experienced after a traumatic event. These symptoms include flashbacks, bodily sensations (e.g., sweating), avoidance of trauma-related aspects, emotional numbing, negative feelings, trouble with sleeping, anger, attention problems, hypervigilance, and others [26]. As mentioned earlier, people are often confronted with some of these complaints after the experience of a traumatic event. However, the presence of some PTSS symptoms does not automatically lead to significant long-term impairment and must not be confused with a PTSD.

Post-traumatic Stress Disorder (PTSD)

Fortunately, most people do not experience long-term negative reactions after a stressful event but cope with the distress in an adaptive way. However, some develop persistent traumatic stress reactions, such as PTSD. When we speak of PTSD, a specific constellation of PTSS is present in a persistent and significantly distressing way. In the recent fifth edition of the diagnostic and statistical manual of mental health (DSM-V), the definition of PTSD has been considerably changed as compared to the formerly used DSM-IV. Yet, most psychological diagnostic and screening instruments (used in scientific research) are based on the DSM-IV criteria [94]. Therefore, both will be addressed in the following.

PTSD in the DSM-IV

According to the DSM-IV, there are 17 PTSS which are grouped into three clusters: re-experience (cluster B), avoidance (cluster C) of the traumatic event, and increased arousal (cluster D) [25]. To meet the diagnostic threshold for PTSD of the DSM-IV, individuals must experience at least one symptom of cluster B, three symptoms of cluster C, and two symptoms of cluster D in reaction to a traumatic event for more than a month.

PTSD in the DSM-V

The DSM-V lists 20 symptoms and divides them into 4 clusters instead of 3. They are called intrusion (cluster B), avoidance (cluster C), negative alterations in cognition and mood (cluster D), and alterations in arousal and reactivity (cluster E) [26]. Compared to the DSM-IV, the number of symptoms that must be present for a diagnosis did not change, but the distribution over the different clusters did, as the individual must experience at least one cluster B, one cluster C, two cluster D, and two cluster E symptoms for more than a month. Besides, the DSM-V introduced a PTSD subtype for children 6 years and younger. The major change for preschool children is that in order to obtain a PTSD diagnosis only one symptom in either the "avoidance" or the "negative alterations in cognition and mood cluster" is needed.

Subthreshold PTSD

Individuals can suffer from various PTSS without completely meeting all criteria for a PTSD. When this is the case, the literature speaks of "subthreshold," "partial," "subclinical," or "subsyndromal" PTSD [95]. Some authors also refer to elevated PTSS [23, 96]. We suggest to use the term subthreshold PTSD as it refers best to patients who do not meet full PTSD criteria, and this term is also preferred by the World Health Organization (WHO) [41]. Patients with subthreshold PTSD suffer from several PTSS but show too few symptoms to obtain a clinical diagnosis of PTSD [97]. In literature, there is no strong consensus about a precise definition of subthreshold PTSD [95]. Clinicians do not agree about the number of symptoms that must be experienced and to what extent all clusters must be present in order to determine the diagnosis of subthreshold PTSD. Therefore, there is a lot of variation in definition and nomenclature of this variable throughout the literature. However, all definitions agree that even the presence of subthreshold symptoms can lead to serious impairment of everyday functioning and must not be ignored [39, 97].

Unfortunately, subthreshold PTSD is not part of any official classification and is likely to be under-diagnosed. To improve the comparability of scientific findings regarding subthreshold PTSD, the WHO introduced the following definition: meeting two or three of the DSM-V criteria B–E [41]. However, most screening questionnaires and diagnostic interviews used in the clinical practice and for research purposes still rely on the DSM-IV criteria, which makes it impossible to use the definition of the WHO. Therefore, updated versions of the instruments are highly needed. The three most frequently used DSM-IV definitions for subthreshold PTSD are (1) meeting criterion B plus C or D, (2) meeting two of the three criteria B, C, and D, and (3) having at least one symptom of each criterion [39]. Despite the varying definitions across studies, prevalence rates were found to be most influenced by sample composition rather than definition [39].

Pediatric Medical Traumatic Stress (PMTS)

Another term, which has been developed recently, is PMTS. PMTS refers to "a set of psychological and physiological responses of children and their families to pain, injury, serious illness, medical procedures, and invasive or frightening treatment experiences" [98]. PMTS is related to subthreshold PTSD in the way that it represents a concept of PTSS when not all criteria for a PTSD are met. However, PMTS is limited to the pediatric setting. The underlying theory of PMTS offers a framework for comparable psychological responses in reaction to a variety of different pediatric injuries and illnesses [23].

Diagnostic Instruments

About seven different types of validated instruments have been used to measure PTSS in children and adolescents in the pediatric setting [94]. Three of them were used in scientific research into PTSD in children and adolescents with ConHD.

1. The Diagnostic Interview Schedule for Children (DISC) [99] is a structured diagnostic instrument to screen for more than 30 developmental psychiatric diagnoses. The child version is suited for youngsters aged 9–17 years. There is also a parallel parent version for children aged 6–17 years. Furthermore, there is an interviewer-administered computer-assisted and paper-and-pencil version and a self-administered computerized audio version. The DISC contains 24 modules that can be administered individually. One of those modules is the

anxiety disorder module that, among others, addresses the DSM-IV criteria of PTSD. Yet, no DSM-V version is available. The DISC has been shown to be a reliable and valid instrument [100, 101].

2. The University of California at Los Angeles post-traumatic Stress Disorder Reaction Index (UCLA PTSD-RI) has a child, adolescent, and parent version. It can be administered verbally (questions are read out loud) or as a self-report (completed on paper). Norms for children and adolescents between 7 and 18 years are available. It was not designed to provide a PTSD diagnosis. The psychometric properties are good, and the UCLA PTSD-RI has been used widely [102, 103]. A DSM-V version has been developed recently.
3. The Impact of Event Scale-Revised (IES-R) [104] is a self- report instrument to measure subjective distress after a traumatic event. This questionnaire has not been developed to diagnose PTSD. However, research shows that it seems to be a solid instrument for the screening of PTS [105, 106]. The IES-R has not yet been updated to the DSM-V criteria.

PTS in Children and Adolescents with ConHD

In the early 1970s, Aisenberg et al. [107] for the first time raised attention to the psychological impact of cardiac catheterization and noted that especially young children showed post procedural emotional stress reactions. Despite the medical advances in pediatric cardiology and cardiac surgery over the last 30 years, a negative impact of those medical treatments on psychosocial functioning remains [108, 109]. Since 2000, in total, five studies were published studying PTS in children and adolescents with a heart disease (see **Table 1** for an overview). These few studies had heterogeneous samples, as only three studies included children and adolescents diagnosed with a *congenital* heart disease. Another study included children and adolescents with a genetic heart disease, and the remaining study did not mention the exact diagnoses of the participating patients.

PTS after Cardiac Surgery

Connolly et al. [110] studied 43 children between 5 and 12 years who underwent some type of cardiac surgery. No child had a diagnosis of PTSD pre-operatively. At postoperative assessment (4–8 weeks after discharge from the hospital), 12% of the children met diagnostic criteria for PTSD measured with the anxiety disorder module of the DISC. Both, the child and the parent versions of the DISC, were

administered and scored jointly. It is stated that 12% of the sample showed PTSS. Furthermore, no follow-up assessment was done.

Toren and Horesh [111] studied PTSD in adolescents who had an operation for congenital cyanotic heart disease. Thirty-one adolescents between 10 and 21 years participated, of which 29.03% scored "full PTSD likely" on the adolescent version of the UCLA PTSD-RI. Interesting fact is that PTSS were measured 13.7 years (*SD* = 2.48) after cardiac surgery in this study. Thus, PTSS seemed to be present in adolescents with ConHD long after surgery.

PTS after Transplantation

Mintzer et al. [112] studied 104 adolescent organ transplant recipients, of which 13 adolescents received a heart transplant. The adolescents were 12–20 years old. PTSD symptoms were measured with the adolescent version of the UCLA PTSD-RI. The authors categorized respondents as "full PTSD likely," when PTSD criteria were met, and "partial PTSD likely," when adolescents met criteria for two of the three DSM-IV symptom clusters. They found that 16.3% were "full PTSD likely" and an additional 14.4% were "partial PTSD likely." The assessment took place 7.3 years (*SD* = 7.3) after transplantation surgery. No difference in PTSD symptom severity was found between the organ types (liver, heart, and kidney). Evan et al. [114] did a retrospective chart review to look for PTSS in pediatric heart transplant recipients aged 0–20 years. They reviewed 51 consecutive patients (of which 12 were known with a ConHD) and checked the medical history for any PTSS; 34% were found to have PTSS (at least 1 PTSD symptom according to the DSM-IV) up to 1 year after transplantation. Presence of PTSS was even higher around surgery: 43% were found to have PTSS in the peritransplant period. No patient was reported to have a full PTSD. It must be noted that these findings are speculative as they do not rely on prospective data from validated instruments.

PTS after ICD implantation

Ninety patients (15 years and older, mean = 49 years, SD = 14) with a clinical diagnosis of a genetic heart disease and an ICD implant participated in the study of Ingles et al. [113]. Only those who had experienced at least one ICD shock (*n* = 31) were asked to complete the IES-R. Thirty-one percent reported a score above the cutoff of 22, indicative of PTSD. Notably, 50% of the females who reported a shock showed PTSS.

Table 1. Overview of studies into PTSD and PTSS in children and adolescents with ConHD.

Reference	Sample size (*n*)	Age range (in years)	Sample population	Design	Instrument	PTSD (%)	PTSS (%)
Connolly et al. [110]	43	5-12	**Cardiac surgery**	Longitudinal follow-up study	DISC	12	12
Mintzer et al. [112]	104	12-20	Organ transplant (13 x heart)	Cross-sectional descriptive study	UCLA PTSD-RI	16	14
Toren and Horesh [111]	31	10-21	**CCHD**	Cross-sectional descriptive study	UCLA PTSD-RI	29	
Ingles et al. [113]	31	>15	ICD implant (for genetic heart disease)	Cross-sectional descriptive study	IES-R	31	50[a]
Evan et al. [114]	51	0-20	**Heart transplant**	Retrospective study	Retrospective chart review	0	34

Studies including children with congenital heart disease are given in bold.

PTSD, post-traumatic stress disorder; PTSS, post-traumatic stress symptoms; CCHD, congenital cyanotic heart disease; ICD, implantable cardioverter defibrillator; DISC, Diagnostic Interview Schedule for Children; UCLA PTSD-RI, University of California at Los Angeles Post-traumatic Stress Disorder Reaction Index; IES-R, Impact of Event Scale – Revised; ConHD, congenital heart defect.

[a]*PTSD rate in females.*

Predictors and Correlates

Connolly et al. [110] found that ICU length of stay (48 h and more) was the only predictor of postoperative PTSD symptoms in children aged 5–12 years who underwent cardiac surgery. The amount of hours spent at the ICU ranged between 0 and 1008 hours in this study. Cognitive level, negative reactivity and approach/withdrawal dimensions of temperament, and family support were no predictors of postoperative PTSD symptoms. Mintzer et al. [112] found no association between any demographic (gender, ethnicity, age at interview) or illness-related (organ type, time since transplant, age at transplant) variables and PTSS severity. However,

they found that illness onset (acute versus chronic) and medical complications in the past year (mild versus moderate/severe) did act as a significant predictor of PTSS when combined in the regression analysis. It is striking that adolescents with mild complications, rather than moderate/severe, had a higher chance of reporting PTSS. Furthermore, an acute onset also increased the risk for PTSS.

In the *general pediatric setting*, different factors predict the development of PTSS in children after injury [115]:

- Child characteristics: prior internalizing (e.g., anxiety and depression) and externalizing (e.g., aggressive behavior) problems,
- Environmental characteristics: parental PTSS,
- Trauma-related factors: elevated heart rate immediately after injury and perceived severity of the event, and
- Cognitive processes: dysfunctional cognitive strategies/ beliefs.

Remarkably, the *subjective* experience of life threat (trauma severity), rather than objective factors (mechanism, type, and severity of the injury), seems to contribute to the development of PTSS [115].

PTS in Children and Adolescents without ConHD after Hospitalization

Since few studies focused on PTS in children and adolescents with ConHD, other pediatric populations can serve as an important reference framework. From other pediatric populations without ConHD, it is known that the experience of an injury or illness can lead to traumatic stress reactions in children and adolescents. Hospitalization, admission to the emergency department, entering intensive care, and undergoing medical interventions all heighten the risk for psychological problems alongside the evident physical complaints [115]. Research shows that even mild to moderate physical injury leads to heightened PTSS [116]. The PTSD prevalence in children undergoing admission to the pediatric intensive care unit (PICU) has been shown to be between 5 and 28% [117]. Despite the overlapping medical context, it seems that PTSD prevalence rates differ between young patients with a (chronic) illness and those with an injury [22]. Both illness and injury often result in invasive procedures and hospitalizations. In addition, however, children who suffer an injury were also confronted with some kind of accident that may have been a traumatic experience itself. This might explain why injured children

and adolescents show higher rates of PTSD than ill children and adolescents. Furthermore, young patients rate the perceived trauma severity and/or life threat higher when injured, compared to children with an illness. However, this might also be due to differences in follow-up measurements. Across research, children who experienced an injury were followed up for a shorter time span. Nevertheless, it is recommended to disentangle the traumatic impact of illness and injury samples when studying PTSD.

Conclusions and Clinical Implications

Only five studies have been found that focused on PTSD in children and adolescents with different heart diseases, of which one did not use standardized measurements. The four studies using standardized instruments to measure PTSD in children with a (congenital) heart disease found PTSD prevalence between 12 and 31% even up to many years after the traumatic experience. This is comparable to 11–21% found in adults with ConHD [118]. Compared to a lifetime PTSD prevalence of 5% in the general adolescent population (13–18 years) [119], youngsters with ConHD show a clearly heightened risk for PTSD. Two of the four described articles that used standardized measurements also studied the prevalence of subthreshold PTSD and found a prevalence of 12–14% in children and adolescents with ConHD. This is comparable with the mean subthreshold PTSD prevalence of 14.7% found in a meta-analysis of Brancu et al. [39]. Methodological weaknesses of the studies described are use of small sample sizes, different time intervals in follow-up assessments, the use of different instruments, and single- versus multi-informant approaches. Moreover, it is uncertain to what extent selection bias influenced the results. Only five studies into PTSD were found regarding children with ConHD using very specific samples. This lends to limited generalizability to the overall pediatric ConHD population. However, results are comparable to outcomes in other pediatric medical populations (such as children in the PICU).

In summary, children and adolescents with ConHD have an elevated risk of developing PTSD. Given the fact that both PTSD and subthreshold PTSD lead to serious psychological and behavioral impairments and increased health-care use [39], it is astonishing that only very few studies investigated the prevalence, correlates, and impact of PTSD in children and adolescents with ConHD. Even more concerning is that no study has evaluated an evidence-based treatment in this

pediatric population yet. For adults, it has been proven already that eye movement desensitization and reprocessing (EMDR) is an effective psychotherapeutic treatment to reduce (symptoms of) PTSD [71]. A large randomized controlled trial into the effectiveness of EMDR for children and adolescents with ConHD is now being executed in the Erasmus MC – Sophia Children's Hospital, Rotterdam, the Netherlands. The authors of this review recommend early screening of psychosocial problems in children with ConHD, given the fact that those children have a heightened risk of developing PTSS. If indicated, referral for psychosocial treatment (trauma-focused cognitive behavioral therapy or EMDR) should be arranged.

Author Contributions

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Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

CHAPTER 3

Mental health problems in parents of children with congenital heart disease

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Abstract

This review will provide a concise description of mental health problems in parents of children with a (non-syndromic) congenital heart disease (CHD) during different stressful periods. Predictors of these problems and also implications for clinical practice will be mentioned. Having a child with CHD can be very stressful for parents, who have to face overwhelming emotions and also extra physical, financial, and other practical challenges. Parental distress has been reported in 30–80% of parents and appears not to be related to severity of CHD. Parental mental health, parenting, the parent–child relationship, and parental quality of life can all be affected. Parents, and especially mothers, are at risk of psychological distress, anxiety, depression, somatization, hopelessness, and posttraumatic stress symptoms, which in turn may influence mother's responsiveness. In the long term, the majority of parents adapt successfully to living with a child with CHD, but approximately 40% report a need for psychosocial care. These families may be helped by early psychosocial interventions to alleviate stress and reduce children's emotional and behavioral problems. A holistic approach to early psychosocial interventions should aim at improving coping and enhance parenting. During routine medical checkups, medical professionals should ask about parental stress, family functioning, and psychosocial functioning of the child and, when needed, adequate psychosocial care should be provided.

Introduction

Approximately 36,000 infants (1% of total live births) are born with a congenital heart disease (CHD) in the USA each year [120]. It is well known that due to huge improvements in the medical and surgical treatment of CHD in the last three decades, 85% of infants are expected to survive [121]. In a retrospective cohort study, Oster et al. found that 1-year survival for infants with critical CHD improved from 67.4% for the 1979–1993 birth era to 82.5% for the 1994–2005 birth era ($P < 0.001$) [121]. Because of the improved survival rates, more and more studies have looked into the psychological outcomes of children with CHD and their parents. Having a child with CHD can be very stressful for parents; the overwhelming emotions and experiences at the time of diagnosis, cardiac surgery, and thereafter may impact parental quality of life and their capacity for optimal parenting. Research indicates that parents, and especially mothers of children with CHD, report mental health problems (such as depression, anxiety, and feelings of guilt), adjustment problems, and poor quality of life more often than parents of healthy children or children with other medical problems [122, 123]. These parental mental health problems can be present during different phases of the lives of the children and their medical trajectories. A recent systematic review revealed that up to 30% of parents of children with critical CHD have posttraumatic stress (PTS) symptoms, 25–50% of them reported symptoms of depression and/or anxiety and 30–80% severe psychological distress, particularly shortly after children's cardiac surgery [124]. In addition, parents have to face various extra physical, financial, and other practical challenges.

In this chapter, we give a short overview of parental mental health problems across different stressful or even traumatic periods, e.g., pre- and postnatal diagnosis, the time around cardiac surgery and hospital admissions, and parental wellbeing on the long term. Due to limited space, this mini review does not have the aim to give a complete systematic review, but rather aims to describe the most prominent problems concerning parents of children with CHD (**Table 1**).

Table 1. Details of studies included in the mini review.

Reference	Population studied	Measures
Parental mental health problems at the time of diagnosis		
Lawoko and Soares [122]	*N* = 632 parents of children with congenital heart disease (CHD; 58% women)	Symptom Checklist – 90 – Revised (SCL-90-R). The Hopelessness Scale
Fonseca et al. [123]	*N* = 42 infants with congenital anomalies (40% CHD) and *N* = 42 healthy controls	Symptom Inventory-18, World Health Organization Quality of Life-Brief instrument
Jackson et al. [125]		Systematic review of 25 studies that were selected, using the PRISMA guidelines
Solberg et al. [126]	*N* = 162 mothers of infants with CHD and *N* = 44,400 mothers of healthy controls within the Norwegian Mother and Child Cohort Study	Hopkins Symptom Checklist (SCL-8)
Bevilacqua et al. [127]	*N* = 38 parental couples of infants with CHD	General Health Questionnaire-30 (GHQ-30), Beck Depression Inventory (BDI), Quality of Life: SF-36
Cantwell-Bartl and Tibballs [128]	*N* = 16 mothers and *N* = 13 fathers	Structured Clinical Interview for Diagnosis-Clinical Version (posttraumatic stress disorder (PTSD) module)
Fischer et al. [129]	*N* = 38 neonates	State Trait Anxiety Scale (STAI)
Solberg et al. [130]	*N* = 141 mothers of infants with CHD and *N* = 36,437 mothers from the Norwegian Mother and Child Cohort Study	SCL-8

Risk factors	Main findings/types of problems
Gender: mothers had more severe symptoms of depression, anxiety, somatization, and hopelessness than fathers. Parental caregiving burden, feeling dissatisfaction about care, social isolation, and financial difficulties were associated with an elevated risk of long-standing parental psychopathology	Parental depression (18%), anxiety (16-18%), somatization (31-38%), and hopelessness (16%)
Being a mother and postnatal diagnosis are risk factors for more adjustment difficulties	Parents of infants with a congenital anomaly had higher distress than parents of healthy infants
Families with fewer psychosocial resources and lower support are at risk of higher parental psychological distress	Higher anxiety, depression, somatization, hopelessness in parents of children with CHD compared to parents of healthy children or those with other diseases
CHD was a substantial risk factor for parental mental health problems	Mothers of CHD children had increased depression and anxiety compared to controls; mothers of infants with severe CHD had different postpartum mental health compared to healthy controls at 6, 18, and 36 months postpartum
Prenatal diagnosis was associated with higher depression in mothers and postnatal diagnosis with more maternal stress	Mothers had higher stress and depression levels, compared to fathers (81.8 versus 60.6 and 45.7 versus 20.0%, respectively) The majority of parents (88% of mothers and 66% of fathers) had PTSD (only five parents were free of traumatic stress)
Higher education and less medication associated with higher parental anxiety	Low trait and higher state anxiety scores in parents
Severity of child's CHD is associated with higher levels of depression and anxiety symptoms	Mothers of infants with severe CHD are at risk of anxiety and depression from delivery to 36 months postpartum

table continues

Reference	Population studied	Measures
Landolt et al. [131]	*N* = mothers of 408 children with CHD	Fussy/Difficult Scale from the Infant Characteristics Questionnaire, Child Behavior Checklist, SCL-8
Parental mental health problems at postsurgery period		
Woolf-King et al. [124]		A systematic review of 30 studies that were selected using the PRISMA guidelines
Helfricht et al. [132]	*N* = 135 mothers and *N* = 98 fathers of 139 children with CHD undergoing surgery	Posttraumatic Diagnostic Scale
Vrijmoet-Wiersma et al. [133]	*N* = 114 mothers and *N* = 82 fathers of 131 children	Pediatric Inventory for Parents-short form, GHQ, Parental Stress Index-short form, STAI, Child Vulnerability Scale
Üzger et al. [134]	*N* = parents of 73 patients with CHD undergoing cardiac catheterization	BDI, Beck Anxiety Inventory
Hearps et al. [135]	*N* = 39 caregivers (28 mothers) of 29 children with CHD	Adapted version of Psychosocial Assessment Tool
Farley et al. [136]	*N* = parents of 52 pediatric heart transplant recipients	Questionnaires on illness-related parenting stress and PTS symptoms
Nelson and Gold [117]		A review of descriptive, observational, and controlled studies on pediatric intensive care unit and PTSD
Helfricht et al. [137]	*N* = 61 parents of children following surgery and *N* = 52 patients with an acute cardiac event	German version of Acute Stress Disorder Scale (ASDS)

Risk factors	Main findings/types of problems
More negative child behavior at 18 months was associated with poorer maternal mental health at 36 months in CHD and controls	CHD explained 31% and 39% of the variance in child and maternal mental health problems
	30% of parents have PTS symptoms, 25-50% depression/anxiety symptoms, and 30-80% severe distress
PTS symptom severity at discharge predicted PTSD severity 6 months later	16.4% of mothers and 13.3% of fathers had acute PTSD; 15.7% of mothers and 13.3% of fathers had PTS symptoms
Number of surgical procedures, time past since last one, and ethnicity were risk factors for higher parental anxiety	Parents of children with CHD had higher levels of perceived vulnerability than parents of healthy children; state anxiety was higher in mothers of children with CHD
Cyanosis: mothers of cyanotic children had more anxiety and depression than mothers of acyanotic children	Increased parental depression and anxiety symptoms in parents of children with CHD
Increased risk for psychosocial problems is associated with higher emotional distress (in 38.5% of parents)	61.5% of parents at risk comparable to that of the general population, 35.9% at subclinical level, and 2.6% at clinical risk
	19% of parents had PTSD and almost 40% of them had moderately severe to severe PTS symptoms
More serious disease was associated with PTSD development. Positive association between children's PTS symptoms and their parents' symptoms. Mothers at increased risk to develop PTSD (and more severe PTSD) compared to fathers	PTSD in 5-28% and PTS symptoms in 35-62% of parents of children admitted to intensive care unit
Surgery versus acute cardiac event	25% of parents of children with CHD met diagnostic criteria for ASD

table continues

Reference	Population studied	Measures
Franich-Ray et al. [138]	*N* = 77 mothers and *N* = 55 fathers of infants who underwent cardiac surgery before 3 months of age	ASDS
Van Horn et al. [139]	*N* = 38 mothers of children with CHD aged 3-16 years	Modified Semistructured Interview (developed by Beardslee et al., 1992)
López et al. [140]	*N* = 40 parents of children with CHD and *N* = 115 parents of healthy children	GHQ, Basic Psychological Needs Scales, Self-Determination Scale, Beck Hopelessness Scale, a socioeconomic survey
Longitudinal studies of parental mental health problems		
Lawoko and Soares [122]	*N* = 632 parents of children with CHD (58% women)	Symptom Checklist – 90 – Revised (SCL-90-R), The Hopelessness Scale
Lawoko and Soares [141]	*N* = 1,092 parents of children with CHD, *N* = 112 parents of children with other diseases, and *N* = 293 parents of healthy children	Symptom Checklist – 90 – Revised (SCL-90-R), The Hopelessness Scale
Berant et al. [142]	*N* = 63 mothers of newborns with CHD	Mothers' interview on mental health and attachment style, Children's Apperception Test
Menahem et al. [143]	*N* = parents of 39 children	Parents were assessed (e.g. mental health, locus of control) prior to and 12-50 months following their children's surgery

Risk factors	Main findings/types of problems
Gender: mothers had higher ASD mean scores than fathers for all symptoms (except dissociation)	33.8% of mothers and 18.2% of fathers had ASD
Mothers' perceptions of medical severity were associated with distress about psychosocial issues postdischarge	Maternal distress, anxiety and depressed mood decreased postdischarge
	Children's surgery decreased parental hopelessness. Parents of children with CHD had worse GHQ scorings than parents of healthy children
Parental caregiving burden, feeling dissatisfaction about care, social isolation, and financial difficulties were associated with a higher risk of long-term parental mental health morbidity	Parental depression (18%), anxiety (16-18%), somatization (31-38%), and hopelessness (16%) at both measurement points
Employment status and financial situation were risk factors for parental distress and hopelessness	Parents of children with CHD at higher risk of distress and hopelessness. Mothers within all parent groups had higher distress and hopelessness than fathers. Fathers of children with CHD were doing worse than fathers of the other groups
Maternal avoidant attachment at initial assessment was the best predictor of worsening of her mental health at 7-year follow-up	Mothers of children with severe CHD were more vulnerable in terms of their mental health
	Mothers with increased anxiety and a tendency to attribute events to chance greater than normal; their anxiety decreased at follow-up

Parental Mental Health Problems around the time of child's CHD diagnosis

Several studies showed that during the period of diagnosis, parents of children with CHD experience more psychopathology (e.g., anxiety, depression, and somatization) compared to parents of children with other medical illnesses or healthy controls [122, 125, 126]. Parents can experience difficulties at different time points. One possible stressful period is the time around the child's diagnosis.

As to timing of diagnosis of CHD (e.g., prenatal, postnatal), Fonseca et al. showed that parents of children with a congenital anomaly (40% of which were CHD) were more distressed compared to parents of healthy children, even if they had similar quality of life [123]. Interestingly, learning the diagnosis in the prenatal period was related to a higher maternal quality of life compared to receiving the diagnosis after the baby was born.

Bevilacqua et al. found no differences in stress and depression levels in both fathers and mothers, who received the diagnosis of CHD in their child prenatally or postnatally [127]. However, mothers who had received the diagnosis prenatally were more depressed, while those who had received a postnatal diagnosis were more stressed. In this study, parental self-reported stress and depression levels within 2 weeks after hospitalization of their infants in the first 3 months of life were significantly higher in mothers compared to fathers.

In a study of Cantwell-Bartl and Tibballs, of the total 18 parents whose infants were diagnosed with hypoplastic left heart syndrome (HLHS) *in utero*, eight of nine mothers and six of nine fathers had posttraumatic stress disorder (PTSD) [128]. Of those parents whose infants were diagnosed with HLHS postbirth, six of seven mothers had acute stress disorder (ASD) and one mother had PTSD. Furthermore, two of the four fathers had ASD and one father had PTSD. These parents were clinically assessed with a semistructured interview and the PTSD module of the Structured Clinical Interview for Diagnosis. Only five parents were free of traumatic symptoms. This was the first study with parents of infants with HLHS in the ICU. The high prevalence of traumatic stress of parents in this study is related to the multiple stressors experienced by them, including the CHD diagnosis received after birth of their infant (for 50% of parents) and the life-threatening nature of HLHS, the ICU environment, and surgery.

Fischer et al. studied parental anxiety levels during the first month of their neonates' life with CHD (upon hospital discharge), using the State Trait Anxiety Scale (STAI) [129]. They found low (5% with significant and 2% with borderline) trait anxiety scores, indicating stable personality levels of anxiety in caregivers, whereas higher numbers of caregivers reported clinically significant (5%) and borderline (14%) state anxiety. Higher education was associated with higher level of state and trait anxiety.

In a Norwegian Mother and Child Cohort Study (*n* = 36,437), Solberg et al. studied a subgroup of 141 children with CHD. They found that postpartum mental health of mothers of infants with severe (but not mild/moderate) CHD was different compared to that of cohort controls at 6, 18, and 36 months postpartum. The mothers of CHD children had been experiencing significantly elevated levels of depression and anxiety symptoms [126, 130]. In the same cohort, CHD was a substantial risk factor for parental mental health problems in children and their mothers at all time points [131]. Both familial and individual factors contributed to risk for developing mental health problems, and mutual influences between mother's and child's mental health at 18 and 36 months over time were found.

In sum, despite different methodologies, most studies agree that the period of the child's CHD diagnosis is generally a stressful period for parents, which may jeopardize the parental mental health. Nevertheless, the mentioned studies have limitations such as small sample size [127-129], reliance on retrospective memory, low participation rate and attrition [126, 130], oversimplification in CHD severity grading [126, 130], use of self-reports, lack of clinical assessment of parental mental health problems [127, 130], and lack of data on possible confounding factors [130].

Parental Mental Health Problems after child's cardiac surgery

Parents of children with CHD undergoing cardiac surgery may also be at increased risk for psychological malfunctioning particularly in the weeks and months immediately following cardiac surgery [124, 132]. In the study of Vrijmoet-Wiersma et al., predictive factors for increased parental anxiety appeared to be: the time interval since last procedure, the number of surgeries, and ethnicity [133].

Preprocedural mental health of parents of patients with (a) cyanotic CHD was studied by Üzger et al. [134]. They found that an upcoming angiography was associated with depression and anxiety in parents of children with CHD. Mothers

of children with cyanotic CHD had significantly higher levels of depression and anxiety compared to mothers of children with acyanotic CHD.

In Hearps et al.'s sample, the majority of parents appeared to have adjusted to the acute stress of their infant's CHD 4 weeks following cardiac surgery. However, 38.5% of them were classified at increased psychosocial risk [35.9% at a targeted (/subclinical) and 2.6% at a clinical level]. This risk was measured using the Psychosocial Assessment Tool (PAT), a brief parent report screener that was adapted to include also sleeping, feeding, crying, and bonding difficulties. PAT scores were associated with higher levels of emotional distress compared to universal psychosocial risk (the lowest 61.5% of parents) [135]. As the authors report, the distribution of risk for psychosocial problems in parents of CHD children undergoing surgery is comparable to that of parents of children with other serious pediatric diagnoses such as pediatric cancer. There were no differences between families of infants who received prenatal versus postnatal diagnosis or single ventricle versus biventricular repair. In addition, a higher parent education significantly predicted a lower total psychosocial risk score.

Farley et al. found a PTSD prevalence of 19% in parents of children who underwent pediatric heart transplantation [136]. This is a clearly heightened risk in comparison to a PTSD lifetime prevalence of 5.6% in the general population [144]. This high rate of PTSD is comparable to that of parents, following their child's admission to the pediatric intensive care unit (10.5–21%) [117]. Fifty-six percentage of the CHD parent sample showed moderate levels of PTSD symptoms and 39% indicated moderately severe to severe PTSD symptoms.

Helfricht et al. reported that acute PTS symptoms in parents following discharge from hospital after cardiopulmonary bypass surgery in their child are a major risk factor for the development of chronic PTSD. Their research showed that following discharge, 16.4% of mothers and 13.3% of fathers of CHD children met diagnostic criteria for acute PTSD, using the Posttraumatic Diagnostic Scale. Another 15.7% of mothers and 13.3% of fathers experienced significant PTS symptoms. Six months after surgery, PTSD rates were 14.9 and 9.5%, respectively. In another study, Helfricht et al. found that 25% of parents of children with CHD met diagnostic criteria for ASD assessed with the German Acute Stress Disorder Scale [137].

Almost similar levels of ASD were found by Franich-Ray et al. in 77 mothers and 55 fathers of infants (younger than 3 months old), 1 month after their child was

discharged from hospital following cardiac surgery [138]. More specifically, one-third of mothers and almost one-fifth of fathers experienced ASD symptoms. Most of them experienced at least one symptom at a clinical level, while dissociative symptoms were the most commonly experienced group of symptoms.

Van Horn et al. studied mothers of children with CHD and their concerns during hospitalization and 2–4 weeks after discharge from hospital [139]. Distress due to concerns decreased postdischarge, as did mother's anxiety and depressed mood.

In a Latin American study (Chile), parents of children with CHD had a decreased well-being (measured with the General Health Questionnaire-12) compared to parents of healthy children. On the other hand, they had a similar level of agency (a concept from developmental studies defined as "the ability to act on behalf of what you value and have a reason to value") [140]. Their children's surgery significantly decreased parental feelings of hopelessness, but had no influence on their well-being or agency.

In sum, most of the reviewed studies show that in the period surrounding a child's cardiac surgery, parents are at elevated risk for developing mainly traumatic reactions, i.e., ASD and PTSD, but also anxiety and depression symptoms; psychological distress may gradually decrease following cardiac surgery. Limitations of reviewed studies include, e.g., small sample size or use of non-standardized instruments [140], underestimation of ASD [138], assessment of mental health symptoms "only," and not of specific psychiatric diagnoses [132-134, 136-138, 140].

Long-term parental mental health problems

Several studies investigated parental mental health problems at longer term (after at least 1 year or longer thereafter) following diagnosis or cardiac surgery of their child. In a longitudinal study, Lawoko and Soares studied psychological morbidity and its determinants in parents of children with CHD, with a 1-year follow-up interval. Parents reported a variety of psychological problems: depression (18%), anxiety (16–18%), somatization (31–38%), and hopelessness (16%) during both measurement points. Moreover, 7–22% reported persisting problems during the 1-year follow-up period. Mothers reported more severe mental health problems than fathers. Children's clinical severity did not explain parents' psychological morbidity over time. Nevertheless, parental caregiving burden, feeling dissatisfaction about care, social isolation, and financial difficulties were associated with an elevated

risk of long-standing parental psychopathology. In their previous study, the same researchers found that parents of children with CHD overall were at higher risk of distress and hopelessness than parents of children with other diseases and parents of healthy children [141]. Across all parent groups, mothers had higher levels of distress and hopelessness than fathers, with the highest levels among mothers of children with CHD compared to mothers in the other groups. Fathers of children with CHD were doing worse than fathers belonging to the other groups.

In a 1-year and 7-year follow-up study of children with CHD, maternal avoidant attachment at the time of diagnosis was the best predictor of worsening of mothers' mental health and maternal satisfaction over this period, especially in a subgroup of whose children had severe CHD [142]. In addition, mothers' attachment insecurities to their own and their children's psychological functioning (both anxiety and avoidance) at the time of diagnosis were associated with their children's emotional problems and children's poor self-image 7 years later.

In the study of Menahem et al., a substantial increase in the emotional distress, e.g., anxiety of mothers of children with CHD at the time of surgery significantly resolved by 12–50 months following the surgery while they still seemed not to feel in "control" at follow-up [143]. At baseline, these mothers reported increased anxiety and a tendency to attribute events to luck and/or chance greater than community norms.

In sum, the few longitudinal studies on mental health problems of parents with CHD available show conflicting results, i.e., decline of parental symptoms over time or persistence, especially in more severe CHD cases.

Clinical implications – the need for psychosocial care

Despite high variability in methodologies and measurements used in outcome studies, it can be concluded that parents of children with CHD experience numerous stresses and mental health problems. High percentages of them show traumatic stress, anxiety, depression, and other psychiatric morbidities [124, 128, 139]. Levert et al. have recently reported that more than 40% of parents and more than 50% of their children with CHD reported a need for psychosocial care on each of five domains studied, i.e., physical/medical, emotional, social and educational/occupational functioning, and health behavior [62]. Needs for psychosocial care

for parents themselves were highest for parents of 0–12-year-old children. Parents and/or patients reported that they would like to be referred to mental health professionals in case of problems on the domains studied.

The PICU environment, where also the diagnosis is given for many children with CHD, may impact the parent–infant attachment and parental adaptation. The PICU staff may, therefore, help parents in dealing with their new traumatic situation [128]. This can be done by providing parents information and psychoeducation, involving them in taking care of their infant as much as possible and strengthening their role as parents, to enhance bonding with their child. Also, other studies point to the need for providing support both to children/adolescents with CHD and their parents, especially mothers [131]. There is a need for early identification and screening of parents at risk of stress and mental health problems. Specific interventions to improve parental coping and adjustment are needed. Practitioners working with these children and families should ask about, e.g., parental mental health, stress, and family functioning, in the context of routine medical checkups [145]. In this modern digital era, we recommend to screen for mental health problems and parental stress during outpatient consultations, by having parents complete questionnaire digitally on an iPad, in the waiting room during outpatient consultations.

Considering the findings of studies on psychosocial interventions to promote adjustment in families of child with CHD, a holistic approach is recommended [125]. The pediatric cardiology group from Belfast (United Kingdom) has highlighted the importance of maternal mental health for child behavioral outcomes at 1-year follow-up. Their psychosocial intervention has been shown to have a positive impact on maternal mental health and functioning of families with children with CHD [146].

Finally, parents and families can be helped by educational interventions such as the use of narrative therapy, strengthening protective factors, cognitive behavioral techniques (relaxation, helpful thoughts, and cognitive restructuring), and provision of psychoeducation to deepen parents' understanding of their child with CHD [122].

Conclusion

Despite great methodological variability between reviewed studies, the majority of studies show that parents, and especially mothers, of children with CHD are at higher risk and experience a variety of mental health problems (e.g., PTS, anxiety, depression) at different time periods of their offspring medical condition. Those parents with mental health problems can be helped by mental health professionals. In addition, prospective studies of parental mental health problems, with larger samples of families and use of standardized instruments and interviews.

Author contributions

All the authors (GK, MM, and EU) have substantially contributed to the conception of the work. GK has drafted the manuscript, and MM and EU revised it. All the authors (GK, MM, and EU) have made a final approval of the version to be published and have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

CHAPTER 4

Psychological outcomes after pediatric hospitalization: the role of trauma type

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Abstract

Physical injury and illness are common potentially traumatic events during childhood and adolescence. Many children experience psychosocial difficulties after medical events. The sample consisted of 399 children aged 4 to 15 who had been hospitalized for physical illness or injury. Elevated psychological symptomatology (PTSS, depression, anxiety) was more frequent after multiple (type II) compared to single (type I) medical events, but only a few differences were statistically significant. The strongest risk factor of child PTSS was parental stress. Type II trauma and low parental education were significant risk factors only for parent report of child PTSS (not for child report). The analyzed risk factors did not differ for type I versus II trauma. We recommend standardized screening and monitoring for mental health in the standard pediatric health care. Furthermore, pediatricians should be trained in signaling stress signs of parents.

Introduction

Events related to acute or chronic illness, injury, and medical treatment are among the most common potentially traumatic events during childhood and adolescence [27]. Research has shown that being hospitalized for illness or injury can lead to posttraumatic stress, depression, anxiety, and other psychological difficulties [22, 147]. Posttraumatic stress symptoms (PTSS) are considered one of the most common psychological consequences which can be experienced even years after illness or injury [61, 148, 149]. These symptoms consist of re-experiencing the event, avoidance of trauma-related stimuli, negative thoughts or feelings, and alterations in arousal and reactivity [26]. Approximately 25-38% of all ill or injured children experience some of these symptoms to some extent [22]. Next to PTSS, symptoms of depression and anxiety are also often reported, with prevalence rates of 7-13% and 7-40% respectively [59, 150]. PTSS, depression, and anxiety are associated with reduced health-related quality of life [53], functional impairment [86], and increased health care service use [28]. Furthermore, comorbidity between PTSS, depression, and anxiety is common; also in a medical setting [45].

Illness and injury can encompass single, but also multiple potentially traumatic events (PTEs). Single PTEs in a medical setting are often seen at the emergency department (ED), such as sudden minor accidents or acute illnesses. Often, only one hospitalization is needed. The experience of multiple potentially traumatic medical events (PTMEs) is more common in children with a chronic illness (e.g. congenital or acquired heart disease) or severe injuries, who need repeated hospitalizations and/or medical procedures. Terr [42] was the first to state that distress caused by single PTEs (type I trauma) might differ from distress caused by multiple PTEs (type II trauma). Several studies found that the experience of multiple traumatic events, compared to single events, seems to heighten the chance of developing PTSS [34, 43, 44]. However, an overview of the prevalence of PTSS and its psychological comorbidity in both trauma types in a pediatric medical setting is still missing.

As there is reason to believe that type I and type II trauma differ in symptomatology, one might argue that this difference is based on distinct risk factors. Nevertheless, differential risk factors for developing PTSS after medically related type I versus type II trauma have not yet been investigated. In the general child trauma literature, the strongest support exists for parental risk factors. Parental stress, family functioning and socioeconomic status were all found to be significant risk factors for the

development of PTSS in the child in various studies [22, 151, 152]. Findings regarding the role of child characteristics in predicting PTSS are inconsistent [45, 115]. Aspects of the illness/injury itself as risk factors for PTSS also receive less support. A general belief is that the subjective perception rather than objective characteristics of the illness/injury are of importance in predicting PTSS in children [115]. However, there are studies that found number of operations [153] and length of hospitalization [154] to be significantly associated with mental health problems of adolescents.

Objectives

The main aim of the present study was to identify possible parental, child, and medical risk factors for PTSS after medically related type I versus type II trauma. The research questions were as follows: (1) what is the prevalence of PTSS, depression, and anxiety in hospitalized children after medically related type I versus type II trauma, and 2) what parental, child, and medical variables are risk factors for PTSS in medically related type I versus type II trauma? We hypothesized that type II trauma would show higher prevalence rates on all outcomes than type I trauma. Furthermore, we hypothesized that parental stress, family functioning, parental education and other stressful life events would be significant risk factors for child PTSS. We also hypothesized that the associations of risk factors with PTSS would depend on trauma type.

Method

The data were collected between July 2016 and May 2018 during the baseline screening for a randomized controlled trial studying the effectiveness of eye movement desensitization and reprocessing (EMDR) in children with elevated PTSS after medically related trauma [155]. Participants were mainly recruited from the Erasmus MC-Sophia Children's Hospital (pediatrics and pediatric cardiology divisions) and the Maasstad hospital (pediatric division) in Rotterdam, the Netherlands. In addition, participants were recruited nationally through the Dutch Association for patients with a congenital heart defect, the Dutch non-profit organization Heartchild Foundation (*Stichting Hartekind*), and through the pediatric cardiology division of the Radboud UMC in Nijmegen, the Netherlands. Participation rate was 24%. See figure 1 for more details.

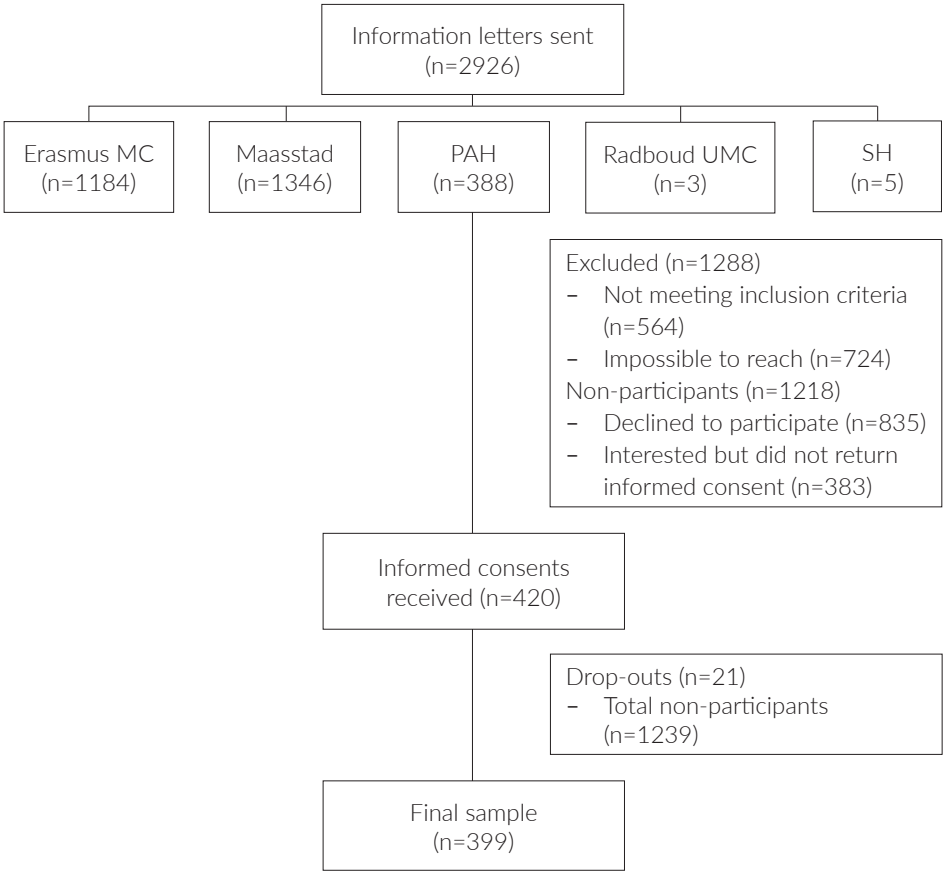

Figure 1. Flowchart of the study

*MC, Medical Center; PAH, Dutch Association for patients with congenital heart defect; UMC, University Medical Center; SH, Stichting Hartekind (Dutch non-profit organization supporting research into congenital heart disease). Participation rate = 100/(total non-participants + final sample)*final sample.*

Participants

Patients aged 4- 15 years who had been hospitalized for minimally one night in a Dutch hospital were included. The last hospitalization or additional invasive medical procedure needed to have taken place at least 4 weeks up to 5 years before recruitment. We included children who had been hospitalized after consultation at either 1) the emergency department (due to all types of injury or acute illness, mainly type I trauma) or 2) at the pediatric cardiology department (due to a congenital or acquired heart defect; mainly type II trauma).

Excluded were patients with (1) intellectual disability (IQ<70); (2) parental inability to read or write Dutch; (3) diagnosis of chronic illness within the ED subgroup (4) previous successful treatment for medically related posttraumatic stress disorder (PTSD); (5) current psychological treatment.

Procedure

All participating departments and organizations identified eligible patients who subsequently received an information letter. It was explained that participation was valuable regardless of whether or not the child experienced distress. By returning a response letter, patients could indicate if they were interested in participating. Then, during a telephone call, questions were answered and inclusion and exclusion criteria were checked. In total, 420 participants returned a signed informed consent.

Outcome variables

Participating children aged 6-15 and their parents were asked to fill out questionnaires. For 4-5 year old children, only parents were asked to fill out questionnaires. Questionnaires were filled out online via a secured website after written informed consent was provided by parents/guardians and children ≥12 years. We categorized scores as elevated according to the cut-offs for above average scores provided in the relevant manuals. All questionnaires investigated current complaints.

Medically related PTSS of the child was measured by the self-reported and parent-reported PTSD total score of the Children's Responses to Trauma Inventory (CRTI; norms 4/8-18 years). Participants were asked to fill out the questionnaire specifically thinking about a medical event of the child. The PTSD total score was computed with the 24 PTSD-items. Furthermore, all children (for self-report only children ≥8 years) with a PTSD total score above the 60th percentile and/or fulfilling two or three of the three symptom criteria were categorized as showing 'elevated PTSS'.

Child symptoms of depression were measured through the self-reported (28 items) and parent-reported (17 items) Children's Depressive Inventory (CDI-2; norms 8-21 years). A total score and a categorical score were computed. Children ≥8 years with a score above the 70th percentile were categorized as having 'elevated symptoms of depression'.

Anxiety symptoms of the child were measured with the Dutch Screen for Child Anxiety Related Emotional Disorder (SCARED-NL; norms 7-19 years). This questionnaire contains 69 items concerning 9 different anxiety disorders (subscales). We computed the total score, based on all items. Additionally, children ≥7 years that scored more than one standard deviation above the normative mean were categorized as having 'elevated anxiety symptoms'. The categorical scores could not be computed for SCARED-NL parent-report due to lack of normative data for parents.

Risk factors

Medically related trauma type was dichotomized: type I trauma was defined as a single hospitalization; type II trauma was defined as ≥2 hospitalizations or at least one additional invasive medical procedure in day-care/outpatient clinic next to a single hospitalization. Hospitalization was defined as a minimum stay of one night.

Other stressful life events were measured to control for the experience of other (not medical) stressful life events, by using the life events scale of the Cognitive Emotion Regulation Questionnaire (CERQ) [156, 157]. We removed two questions about illness and injury of the child. Scores were dichotomized in 'experienced other stressful life events: yes/no'

Parental risk factors included educational level, parental stress, and family functioning. *Parental education* (high, middle and low) was based on the highest educational level of both parents [158]. *Parental stress* was measured by the total score of all problem domains of the Distress Thermometer (LTO, 34 items) [159]. *Family functioning* was measured through the score on the general functioning scale of the Family Assessment Device (FAD, 12 items) [160].

Child risk factors consisted of the child's age and gender. The child's *age* was defined as years between the date of birth and date of informed consent.

Medical risk factors included length of hospitalization, time since last hospitalization/ invasive medical procedure, and type of hospital department. All medical variables were retrieved from the medical records of the child and/or asked to the parents by the research psychologist. *Length of hospitalization* was computed by adding up the

number of days of all hospitalizations. To compute *time since the last hospitalization/ medical procedure* the years that elapsed between the last hospitalization/ invasive medical procedure (end date) and study-participation (date first questionnaire was filled out) were calculated. Invasive medical procedures were defined as any kind of operation (e.g. surgery, catheterization), magnetic resonance imaging (MRI), computed tomography (CT), or lung perfusion scans. Type of h*ospital department* was dichotomized into pediatric cardiology and emergency department.

Statistical analyses

Descriptive statistics were computed for the study variables and differences between both medically related trauma types were tested with χ^2 tests and t-tests. To investigate differences in prevalence rates of elevated psychological symptomatology (categorical scores) between trauma types, we used χ^2 tests.

To examine associations of risk factors with PTSS, we conducted a multiple regression analysis in four steps separately for parent- and child-reported PTSS (total scores). First, we wanted to test whether medically related trauma type is associated with PTSS. Therefore, a linear regression analysis was conducted with PTSS as outcome variable and medically related trauma type as an independent variable. Trauma type was only included in further analyses when significant. Second, we controlled for other stressful life events and parental factors as indicated by previous studies. To do this, stressful life events, parental stress, family functioning and parental education were added to the model. Only factors that reached significance were included in the further analyses. Third, interactions of trauma type with factors that remained from the second step were tested to examine the hypothesis that the associations of risk factors with PTSS depend on trauma type. If significant, interaction terms were included in further analyses. Fourth, child and medical risk factors were selected by backward elimination as there is less consensus on the association between these factors and PTSS in literature. Missing data were imputed for the regression analyses using a fully conditional specification method with 20 imputations and continuous variables were standardized into z-scores. P-values of $<.05$ were considered significant. All analyses were performed using SPSS 24.0.

Results

Baseline characteristics

The final sample consisted of 174 girls (44%) and 225 boys (56%) and the mean age was 9.33 (*SD*=3.18, age range 4-15). Type I trauma was present in 115 children (29%) and type II trauma was present in 284 children (71%). Compared with the type I trauma group, the type II trauma patients were significantly older, more likely to be a male and a cardiology patient, had more hospitalizations, and had a longer total length of hospitalization. See table 1 for more details.

Table 1. Child, parental and medical characteristics of the sample and differences between trauma type.

	N	Total	Type I Trauma n=115	Type II Trauma n=284	*p*
Child					
Age in years, M (SD)	399	9.3 (3.2)	8.8 (3.3)	9.6 (3.1)	.026*
Gender, n (%)	399				.049*
Girls		174 (43.6)	59 (51.3)	115 (40.5)	
Boys		225 (56.4)	56 (48.7)	169 (59.5)	
Ethnicity, n (%)	377				
Dutch		305 (80.9)	82 (75.2)	223 (83.2)	.165
Other Western		21 (5.6)	9 (8.3)	12 (4.5)	
Non-Western		51 (13.5)	18 (16.5)	33 (12.3)	
Other stressful life events, n (%)	314				.998
Yes		229 (72.9)	62 (72.9)	167 (72.9)	
No		85 (27.1)	23 (27.1)	62 (27.1)	
PTSD score self-report, M (SD)	323	32.0 (12.3)	30.9 (11.6)	32.4 (12.6)	.347
PTSD score parent-report, M(SD)	396	31.0 (12.1)	28.7 (11.1)	31.9 (12.4)	.017*
Parental					
Informant gender, n (%)	392				.581
Female (mothers)		325 (82.9)	91 (81.3)	234 (83.6)	
Male (fathers)		67 (17.1)	21 (18.8)	46 (16.4)	
Education, n (%)	391				.334
High		231 (59.1)	71 (63.4)	160 (57.3)	
Medium		140 (35.8)	34 (30.4)	106 (38.0)	
Low		20 (5.1)	7 (6.3)	13 (4.7)	
Parental stress, M (SD)	390	5.2 (5.6)	4.9 (5.5)	5.4 (5.7)	.453
Family functioning, M (SD)	387	1.5 (.4)	1.5 (0.4)	1.5 (0.4)	.811

table continues

	N	Total	Type I Trauma n=115	Type II Trauma n=284	*p*
Medical					
Department, n (%);	399				<.001*
Cardiology		200 (50.1)	20 (17.4)	180 (63.4)	
Emergency unit		199 (49.9)	95 (82.6)	104 (36.6)	
No. of hospitalizations, M(SD)	388	3.1 (3.3)	1.0 (0)[a]	3.9 (3.6)	<.001*
Length of hospitalization(s) in days, M(SD)	340	23.1 (40.1)	4.3 (6.4)	32.6 (46.2)	<.001*
Time since hospitalization in years, M(SD)	390	1.9 (1.4)	2.0 (1.3)	1.9 (1.4)	.749

*M, mean; SD, standard deviation; PTSD, posttraumatic stress disorder; no., number; p, p-value. χ2 tests were used for categorical variables. T-tests were used for continuous variables. *significant.*

Prevalence of psychological outcomes

Prevalence rates are presented separately for child report, parent report and combined. See table 2 for more details.

Child report

22% of the children reported elevated PTSS and 31% reported elevated symptoms of depression. Furthermore, 7% reported an elevated total anxiety score. The highest percentages found on the anxiety subscales where on situational phobia (25%), social phobia (21%), blood-injection-injury (BII) phobia (15%), and posttraumatic stress disorder/acute stress disorder (PTSD/ASD; 15%). Children did not report any significant differences between type I and type II trauma with regard to prevalence rates.

Parent report

21% of the children were categorized as having elevated PTSS by their parents. Parent-reported elevated PTSS of the child was significantly more present in type II trauma (24%) than type I trauma (15%). The prevalence rates of children that were reported to have elevated symptoms of depression was 36%. There was no significant difference between both trauma types on parent-reported elevated depressive symptoms of the child.

Combined

Combined scores of child and parent report were computed for elevated PTSS and symptoms of depression. It has been argued that a combined symptom report is

valuable when identifying posttraumatic reactions [161]. Combined means that a child was categorized as having elevated symptoms when either the child and/or the parent score was categorized as elevated. When child and parent report were combined into one score, 26% of the children had elevated PTSS. The combined elevated PTSS score was significantly higher after type II trauma (29%) than type I trauma (17%). The combined prevalence rate of elevated depressive symptoms of the child was 31%, which also differed significantly between type I trauma (22%) and type II trauma (34%).

Table 2. Prevalence rates of elevated PTSS, anxiety and depression in the total sample and each trauma type.

	N	Total		Type I Trauma		Type II Trauma		*p*
		n	%	n	%	n	%	
Elevated PTSS								
Child Report	249	54	21.7	10	16.7	44	23.3	.279
Parent report	398	85	21.3	17	14.9	68	23.9	.047*
Combined	399	103	25.8	20	17.4	83	29.2	.014*
Elevated depressive symptoms								
Child report	246	77	31.3	16	26.7	61	32.8	.373
Parent report	267	96	36.0	19	28.4	77	38.5	.134
Combined	399	122	30.6	25	21.7	97	34.2	.015*
Elevated anxiety symptoms								
Child report								
Total	280	20	7.1	2	2.8	18	8.7	.095
SAD	280	20	7.1	2	2.8	18	8.7	.095
Panic	280	26	9.3	5	6.9	21	10.1	.427
Animal phobia	280	0	0	0	0	0	0	
BII phobia	280	43	15.4	9	12.5	34	16.3	.435
Situational phobia	280	70	25.0	16	22.2	54	26.0	.528
Social phobia	280	58	20.7	11	15.3	47	22.6	.187
OCD	280	8	2.9	0	0	8	3.8	.091
GAD	280	25	8.9	4	5.6	21	10.1	.244
PTSD/ASD	280	43	15.4	13	18.1	30	14.4	.461

*n, number of children with elevated scores; SAD, separation anxiety disorder; Panic, panic disorder; BII phobia, Blood-injection-injury phobia; OCD, obsessive-compulsive disorder; GAD, generalized anxiety disorder; PTSD, posttraumatic stress disorder; ASD, acute stress disorder; p, p-value. Prevalence rates were analyzed using $\chi 2$ tests. *significant.*

Risk factors for child PTSS

Child report

Trauma type was not associated with PTSS reported by the child (see table 3). Only parental stress was significantly related to child-reported PTSS. The interaction between parental stress and trauma type was not significantly associated with PTSS. There were no significant child and medical risk factors. In the final model, parental stress was the only significant risk factor for child-reported PTSS.

Parent report

Trauma type was significantly associated with child PTSS reported by parents in the first step of the regression analyses. Furthermore, we found parental stress and parental education (low versus high) to be significantly associated with child PTSS. However, the interactions of trauma type with parental stress, respectively, parental education were not significant. Besides, no child or medical risk factors were significant. The final model showed trauma type, parental stress and parental education to be significantly related to child PTSS reported by parents.

Table 3. Results of the linear multiple regression analyses.

	Self-report			Parent-report		
Risk factors	*b*	*CI*	*p*	*b*	*CI*	*p*
Step 1						
(Constant)	.042	-.088, .172	.526	.071	-.045, .188	.231
Trauma Type (I vs II)*	-.126	-.366, .115	.306	-.245	-.463, -.026	.028*
Step 2						
(Constant)	-.058	-.282, .166	.610	.069	-.138, .276	.512
Trauma Type (I vs II)*	---	---	---	-.216	-.412, -.020	.030*
Stressful life events (yes vs no)*	.077	-.168, .322	.538	.080	-.296, .136	.468
Parental stress	.278	.165, .391	.000*	.402	.304, .500	<.001*
Family functioning	.071	-.041, .184	.213	.086	-.013, .184	.088
Parental education (medium vs high)*	-.027	-.249, .195	.810	.087	-.101, .274	.365
Parental education (low vs high)*	.256	-.208, .720	.279	.431	.024, .838	.038*
Step 3						
(Constant)	.005	-.101, .110	.932	-.007	-.145, .132	.925
Trauma Type (I vs II)*	---	---	---	-.183	-.435, .069	.156
Parental stress	.286	.165, .406	.000*	.429	.325, .532	<.001*
Parental education (medium vs high)*	---	---	---	.146	-.074, .365	.194
Parental education (low vs high)*	---	---	---	.292	-.212, .796	.256
Trauma Type*Parental stress	.089	-.139, .317	.443	.002	-.199, .203	.984
Trauma Type*Parental education (medium vs high)*	---	---	---	-.178	-.606, .250	.415
Trauma Type*Parental education (low vs high)*	---	---	---	.471	-.385, 1.328	.281
Step 4 (final model)						
(Constant)	.004	-.102, .109	.944	.003	-.127, .132	.965
Trauma Type (I vs II)*	---	---	---	-.213	-.410, -.017	.033*
Parental stress	.310	.208, .413	.000*	.429	.341, .518	<.001*
Parental education (medium vs high)*	---	---	---	.100	-.088, .287	.296
Parental education (low vs high)*	---	---	---	.460	.054, .866	.027*

*b, unstandardized coefficient; CI, 95% confidence interval; p, p-value; --- , this variables were only included in further steps for parent report as they were not significant for child report. *Reference values were type II trauma, no stressful life events, and high parental education. R2 = .10 for Step 4 self-report. R2 = .21 for Step 4 parent-report.*

Discussion

The main findings of this study were that 1) we only found very few significant differences (i.e. elevated PTSS and depressive symptoms) between type II trauma (mostly ConHD patients) and type I trauma (mostly ED patients) and 2) the strongest risk factor for PTSS in children was parental stress followed by low parental education and trauma type.

Prevalence rates of elevated PTSS and elevated symptoms of depression and anxiety were higher in our sample of hospitalized children compared to the normal population [39, 162, 163], but comparable to earlier research in ill/injured children [22, 59, 150]. Our study supports that psychological difficulties can be present even years after a hospitalization and/or medical procedure. Elevated symptoms of depression were most frequently reported. A general belief is that symptoms of depression might be overestimated in a medical setting because of the overlap between symptoms of the illness/injury itself and symptoms of depression (e.g. fatigue, loss of energy, reduction of physical movement) [164]. However, the high percentage might also be due to the fact that more than two thirds of the participants have experienced repeated hospitalizations, which might worsen symptoms of depression due to school absence and consequent isolation from peers. Furthermore, methodological choices (e.g. questionnaires and cutoffs) could account for differences in prevalence rates between studies.

Children did not report any significant differences in prevalence rates between both trauma types. Parents reported elevated PTSS of the child significantly more often after type II than type I trauma. It might be possible that recurrent hospitalizations are experienced as especially traumatic by parents. It has been found earlier that parents' mental health influences their report of the child's wellbeing [165]. Parents' mental health (such as parental PTSS) was not measured in this study so we couldn't control for possible bias. Future research should investigate this.

Parental stress predicted child and parent reported PTSS of the child. This is in line with earlier studies [151, 166]. Against our expectations, family functioning was not found to be a significant risk factor for child PTSS after hospitalization. However, this is in line with a study of Coakley et al. who found that family functioning was associated with parental PTSS, but not child PTSS after unintentional pediatric injury of the child [167]. Type II trauma and low parental education were also associated with higher child PTSS, but only for parent report. Child and medical predictors

were not significantly associated with PTSS of the child. Earlier research found ambiguous outcomes regarding these factors [115]. The current study presents more evidence for the assumption that gender and age of the child and objective medical factors do not seem to be associated with child PTSS after potentially traumatic medical events, controlled for other stressful life events.

Strengths & Limitations

The strengths of this study include a large sample size of an underrepresented group in trauma research. Furthermore, we compared medically related type I and type II trauma and therefore add important information to the literature. Lastly, we used a multi-informant approach and measured parent and child information on all outcomes.

When interpreting the results of this study some limitations should be kept in mind. First, no judgements can be made about causality as this study used a baseline cohort sample. Second, we focused on elevated symptomatology and not psychiatric disorders. Prevalence rates of subthreshold symptomatology have been shown to be higher than those of psychiatric disorders [163]. Third, parent-reported prevalence rates of child anxiety symptoms could not be analyzed due to the lack of Dutch normative data for the parent version of the SCARED-NL. Future research should provide these norm data. Furthermore, young children might have had assistance of their parents when filling out the questionnaires which could have biased their answers. Moreover, generalizability of the findings may be influenced by the low participation rate and the overrepresentation of highly educated parents. However, this phenomenon is seen frequently in scientific research [168]. Additionally, we defined medically related type I and type II trauma mainly based on the number of hospitalizations. One might argue that hospitalizations differ in terms of length, amount of invasive medical procedures and other factors. However, we did measure those objective factors and they were not associated with PTSS in our sample. Another limitation is that medical risk factors of the participants recruited through the RUMC and both non-profit organizations had to be collected through parent report due to no access to the medical record. Faulty memory might have biased their report. However, we asked parents to check data with the treating physician before reporting. Finally, medically related trauma type and other stressful life experiences of the child were measured dichotomous. For future research, it would be interesting to investigate cumulative effects of medical and other stressful life events using continuous scores.

Implications for Practice

The results of this study show that children who have experienced one or more hospitalizations experience high levels of PTSD, depression, and anxiety symptoms. Implementation of a trauma-informed health care approach and early identification of symptoms could be crucial to reduce the emotional and psychological impact of medical events. We recommend to integrate routinely mental health screening after pediatric hospitalizations.

Furthermore, our analyses of possible risk factors for child PTSS made clear that sources of parental stress within pediatric health care settings should be limited as much as possible. Especially parents with a low educational level and parents of children who experienced multiple medical events should be monitored closely and should receive adequate support if needed.

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Data accessibility

The data that support the findings of this study are available from the corresponding author upon reasonable request.

PART 2

Effectiveness of EMDR after pediatric hospitalization

CHAPTER 5

Eye movement desensitization and reprocessing (EMDR) in children and adolescents with subthreshold PTSD after medically related trauma: design of a randomized controlled trial

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Abstract

Background

Three in every 10 children and adolescents admitted to a hospital or undergoing medical treatment develop subthreshold symptoms of posttraumatic stress disorder (PTSD). When untreated, subthreshold PTSD can have a serious impact on psychosocial functioning, quality of life and long-term psychopathology. However, research investigating subthreshold PTSD and its treatment following paediatric medical interventions and/or hospitalization is scarce. Eye Movement Desensitization and Reprocessing (EMDR) is a fast and non-invasive psychosocial treatment for posttraumatic stress complaints. However, the effectiveness of EMDR in paediatric patients with subthreshold PTSD has not previously been systematically investigated.

Objective

Describing the design of a randomized controlled trial (RCT) set up to evaluate the effectiveness of EMDR in children with subthreshold PTSD after hospitalization.

Method

Children aged 4–15 years who have undergone a one-time (trauma type I) or repeated (trauma type II) hospitalization up to five years ago will be included. Participating children will be first screened with a standardized questionnaire for PTSD-symptoms. Subsequently, children with subthreshold PTSD will be randomly assigned to (1) approximately six sessions of standardized EMDR or (2) care as usual (CAU). Children with full diagnostic PTSD do not participate in the RCT, but are referred for direct treatment. Follow-up measurements will take place after eight weeks and eight months.

Discussion

Considering the scarce evidence for the effectiveness of EMDR in children with medically related trauma, clinicans, researchers and children treated in hospitals can benefit from this study. Potential strengths and limitations of this study are discussed.

Trial Registration

Netherlands Trial Register NTR5801

Highlights

- This RCT specifically focusses on the effectiveness of EMDR in children and adolescents (4–15 years) with subthreshold PTSD after medically related trauma.
- Short- and long-term effectiveness of EMDR on PTSD symptoms will be measured.
- Data about the prevalence of subthreshold PTSD and possible predictors of the treatment effect is also obtained.
- If EMDR proves to be evidence-based, it can be structurally implemented in the (psychosocial) care of children with subthreshold PTSD in Dutch hospitals.

Background

Children and adolescents admitted to hospitals often undergo invasive, painful and potentially traumatic medical procedures. Apart from possible physical health consequences, such as reduced exercise capacity, scars or chronic pain, medical events can impact mental health and lead to posttraumatic stress symptoms (PTSS) including flashbacks, avoidance or numbing of memories of the event and hyperarousal. If symptoms are disturbing and persistent, children may even develop a posttraumatic stress disorder (PTSD). About one in every 10 children develops PTSD due to hospital admission and medical procedures [169]. Some children fail to meet all criteria for a PTSD diagnosis, but still suffer from similar impairments [23, 38, 170]. In general, the presence of impairing posttraumatic stress symptoms that do not meet the full diagnostic criteria for PTSD is referred to as subthreshold PTSD [41]. About 25-38% of children develop subthreshold PTSD after illness or injury [22]. Despite growing evidence for the negative impact of medically related trauma on child development, it has received less scientific attention than other forms of childhood trauma, such as physical or sexual abuse [147, 166]. Furthermore, research has mainly focused on multiple-incident trauma and only a few studies have examined the impact of multiple versus single trauma [171].

Currently, trauma-focused cognitive behavioural therapy (TF-CBT) is the most acknowledged, evidence-based treatment for PTSD in children [172]. A drawback of this treatment is that reliving and replaying feared thoughts and memories are psychologically very intensive. Another treatment for PTSD is eye movement desensitization and reprocessing (EMDR) [173]. EMDR is a standardized treatment method based on bilateral stimulation to help process traumatic memories. Compared to TF-CBT, "EMDR does not involve (a) detailed descriptions of the event, (b) direct challenging of beliefs, (c) extended exposure, or (d) homework" [174]. Furthermore, EMDR seems to work faster (often <8 sessions at 45-60 min; [175]) than traditional TF-CBT (8-12 sessions at 90 min; [176]) and is thus cheaper and more efficient [67, 177].

The effectiveness of EMDR on PTSD in adults has been demonstrated in various reviews and in a meta-analysis [68, 71, 178]. Together with TF-CBT, EMDR is recommended as a first-choice treatment for PTSD in various international practice guidelines [174, 176, 179, 180]. However, research examining the benefit of EMDR in children is scarce. Two recent meta-analysis of small studies (mostly RCTs)

demonstrated that EMDR had positive results in children with PTSS and PTSD [73, 74]. However, the studies in these meta-analyses had mostly small sample sizes (*N* = 14 – 67) and covered diverse traumas varying from natural disasters to interpersonal trauma. Even though some studies examining the effectiveness of EMDR included children with subthreshold PTSD in their sample [67, 78, 79, 181], no research has yet specifically focused on the effect of EMDR to reduce distress in children with medically related subthreshold PTSD, nor on predictors of EMDR treatment effect in this population. It is very important to identify and reduce subthreshold PTSD in children with medically related trauma to prevent these children developing full diagnostic PTSD and growing up with unresolved trauma and anxieties regarding medical treatment, since this may harm their medical adherence and their (mental) health later in life.

With regard to predictors of treatment effect of EMDR in children, the literature is scarce. Hensel [182] found that increasing age, higher pre-treatment severity of PTSS and longer time since the traumatic event positively influenced the treatment effect of EMDR for children and adolescents with diverse single-incident trauma. Moreno-Alcázar, Treen [74] suggested that gender might play a role in predicting treatment effect, stating that the effect size for EMDR was nearly zero in studies that included mostly boys. Predictors of EMDR treatment effect in a medical setting are still unknown

The hypotheses of this study are that (1) EMDR will lead to significant improvements of psychosocial functioning, quality of life, school functioning and sleep in children with subthreshold PTSD and (2) older age, female gender and higher initial PTSS of the child will be associated with better outcomes in the EMDR group. Other potential medical, parental and child predictors of the EMDR treatment effect will be analysed.

Objectives

The main aim of this randomized controlled trial (RCT) is to study the effectiveness of standardized EMDR on reducing PTSS in children with subthreshold PTSD following hospitalization in the Netherlands. Further, we aim to identify factors predicting treatment success of EMDR in children with medically related trauma.

Method

Design

This study represents a prospective single-blind RCT. Prior to randomization, all participants complete a screening measurement (see Assessments). After screening, only participants with subthreshold PTSD are randomized on a 1:1 basis to either EMDR or care-as-usual (CAU; medical care only if necessary). Randomization is stratified by trauma type (I/II) and age (4-11/12-15). This study represents a single-centre study, as all therapy sessions take place in the Erasmus MC Sophia Children's Hospital. However, patients are not only recruited at the paediatrics and paediatric cardiology division of the Erasmus MC, but also by the Dutch Association for patients with a congenital heart defect (PAH), the Dutch non-profit organization *Stichting Hartekind*, the paediatric division of the Maasstad Ziekenhuis Rotterdam and the paediatric cardiology division of the Radboud UMC. The study protocol has been approved by The Medical Ethics Review Committee of the Erasmus MC in the Netherlands. The study is registered in the Dutch Trial Register as NTR5801.

Participants

The target group of this study consists of children and adolescents (4-15 years old) suffering from subthreshold PTSD after one or more hospitalization(s) or additional medical treatment that occurred at least four weeks up to maximally five years before recruitment. Inclusion period is from July 2016 until May 2018, and follow-up assessments will be complete in September 2018 (T2) and March 2019 (T3).

In this study, subthreshold PTSD is defined as either fulfilling two of the three DSM-IV PTSD symptom criteria (re-experience, avoidance or hyperarousal) and/or having a score above the cut-off on the primary outcome measuring PTSS (without a full diagnostic PTSD score on a semi-structured interview afterwards; see Assessments). The group will consist of children with trauma type I and trauma type II. In this study, we defined trauma type I as a *first hospitalization* of previously healthy children after consultation at the emergency department (due to injury or *acute* illness) or the paediatric cardiology department (due to a heart disease). Trauma type II is defined as *recurrent hospitalizations* (after consultation at the emergency department or the paediatric cardiology department) or an additional medical procedure (e.g. surgery) next to a one-time hospitalization.

Exclusion criteria are: (1) intellectual disability; (2) parental inability to read or write Dutch; (3) diagnosis of a chronic illness for the Emergency Department subgroup; (4) previous successful treatment for medically related PTSD; and (5) current psychological treatment. Additionally, exclusion criteria for participation in the randomization are: (6) not meeting the study criteria for subthreshold PTSD; and (7) a full diagnostic PTSD score on the semi-structured interview.

Procedure

All eligible patients receive an information letter and are invited to participate in the study. Additionally, flyers about the study are distributed in the waiting areas of the participating departments. Interested patients are asked to give informed consent. For patients younger than 12 years, informed consent is obtained from their parents/guardians. For patients between 12-15 years, informed consent is obtained from both the patient and his/her parents/guardians.

After informed consent, all participants (6-15 years), their parents/guardians and teachers are asked to complete an age-appropriate screening measurement. The questionnaires are valid for two weeks so that every participant has enough time to fill out the questionnaires. For the 4-5-year-olds only parents (and teachers) are asked to complete questionnaires. If parents and/or the child report subthreshold PTSD (or higher) at the screening assessment, the child (8-15 years) or one parent (4-7 years) is invited for a semi-structured clinical interview. If patients meet all criteria for a full diagnostic PTSD diagnose during the semi-structured interview, they are not randomized but referred directly for psychosocial care. Only children with subthreshold PTSD are asked to participate in the RCT, since this is the focus of the study. Moreover, it would be unethical to randomize children with full diagnostic PTSD to the control group. Children without subthreshold PTSD symptoms only perform the baseline assessment. An independent researcher allocates the participants with subthreshold PTSD in either the EMDR or CAU group. Considering the nature of EMDR, it is not possible to blind the participants nor the therapists providing EMDR. However, the research psychologist and research assistants performing all outcome measurements and completing the interviews with participants are blinded. Participants are instructed not to discuss their allocation with the interviewer. All participants receive a voucher and all travel costs are compensated.

Follow-up assessments will take place eight weeks and eight months after the start of EMDR/CAU. **Figure 1** shows the flowchart of the study.

Assessments

Almost all questionnaires are completed online by parents, children (6-15 years) and teachers. Only one questionnaire is filled out on paper. All questionnaires have adequate psychometric properties. In **table 1**, all instruments and measurement time-points are listed.

PTSD symptoms (primary outcome). The Children's Responses to Trauma Inventory (CRTI; in Dutch: Schokverwerkingslijst, SVLK) is used to measure PTSD-symptoms [183, 184]. The CRTI consists of 24 PTSD-items plus 10 non-specific items. In this study, only the 24 PTSD-items are administered. The PTSD-items can be divided into three subscales related to the DSM-IV-TR symptom clusters of PTSD: intrusion, avoidance and hyperarousal [26]. The PTSD-total score is computed and used as a primary outcome. Both the parent and the child version are administered. Normative data is available from 4-18 years for the parent version and 8-18 years for the child version.

Additionally, a diagnostic psychiatric semi-structured interview is administered to every participant that reports PTSD (full or subthreshold) on the CRTI. This is done only to differentiate between participants with subthreshold PTSD and those with full diagnostic PTSD. The scores are not used for statistical analysis. The semi-structured interviews used in this study are the Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA) [185, 186] and the PTSD module of the Diagnostic Infant and Preschool Assessment (DIPA). The CAPS-CA is administered to children aged 8-15. The CAPS-CA is the international gold standard for determining the presence of PTSD. For children aged 4-7, one parent is interviewed with the PTSD module of the Diagnostic Infant and Preschool Assessment (DIPA) [187]. This module consists of 55 items, assessing the presence of PTSD according to the DSM-V criteria.

Anxiety is assessed with the Dutch version of the Screen for Child Anxiety Related Emotional Disorders (SCARED-NL) [188]. This is a 69-item screening instrument for anxiety symptoms in children aged 7-19 years. The child and parent version are administered.

Table 1. Instruments used in the RCT into effectiveness of EMDR in children/adolescents with subthreshold PTSD after medically related trauma.

Variable	Instrument	Format	Informant	T1	T2	T3
Key outcome						
PTSD symptoms	Dutch Children's Responses to Trauma Inventory (CRTI)	Online questionnaire	Parent, child[a]	x	x	x
Exclusion criteria RCT						
PTSD	Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA)	Child interview	Child[b]	x	x*	x*
PTSD	Diagnostic Infant and Preschool Assessment (DIPA)	Parent interview	Parent[c]	x	x*	x*
Secondary outcomes						
Anxiety	Screen for Child Anxiety Related Emotional Disorders (SCARED-NL)	Online questionnaire	Parent, child[a]	x	x	x
Depression	Child Depression Inventory 2 (CDI-2)	Online questionnaire	Parent, child[a]	x	x	x
Quality of life	Child Health-Related Quality Of Life (TACQOL)	Online questionnaire	Parent, child[a]	x	x	x
Sleep	Sleep Self-Report (SSR) / Child Sleep Habits Questionnaire (CSHQ)	Online questionnaire	Parent, child[a]	x	x	x
Self-perception	Self-Perception Profile for Children (SPP-C) / Self-Perception Profile for Adolescents (SPP-A)	Paper questionnaire	Child[a]	x	x	x
Attention (Problems) and school functioning	Child Behavior Checklist (CBCL) / Teacher Report Form (TRF)	Online questionnaire	Parent, teacher	x	x	x
Social validity	n.a.	Conceptualized questions	Parent, child[a]		x	
Impact CRTI questions	n.a.	Conceptualized question	Child[a]	x		
Predictors						
Demographic factors	Rotterdam Quality of Life Interview	Online questionnaire	Parent	x		
Cognitive coping styles	Cognitive Emotion Regulation Questionnaire for Children (CERQ-C)	Online questionnaire	Child[a]	x		
Stressful life events	Life events scale of CERQ	Online questionnaire	Child[a]	x		
Parental stress	Distress thermometer (LTO)	Online questionnaire	Parent	x		

table continues

Variable	Instrument	Format	Informant	T1	T2	T3
Somatic complaints	Questionnaire Somatic Complaints in children	Online questionnaire	Parent, child[a]	x		
Family functioning	Family Assessment Device (FAD)	Online questionnaire	Parent	x		
Information about hospitalizations and medical interventions	n.a.	Medical records	Clinican/ researcher/ parent	x		

*[a]Only for children aged ≥ 6 years; [b]only for children aged ≥ 8 years; [c]only for children aged ≤ 7 years; *only if necessary.*

Note. T1=before intervention; T2=eight weeks after start of intervention; T3= eight months after start intervention.

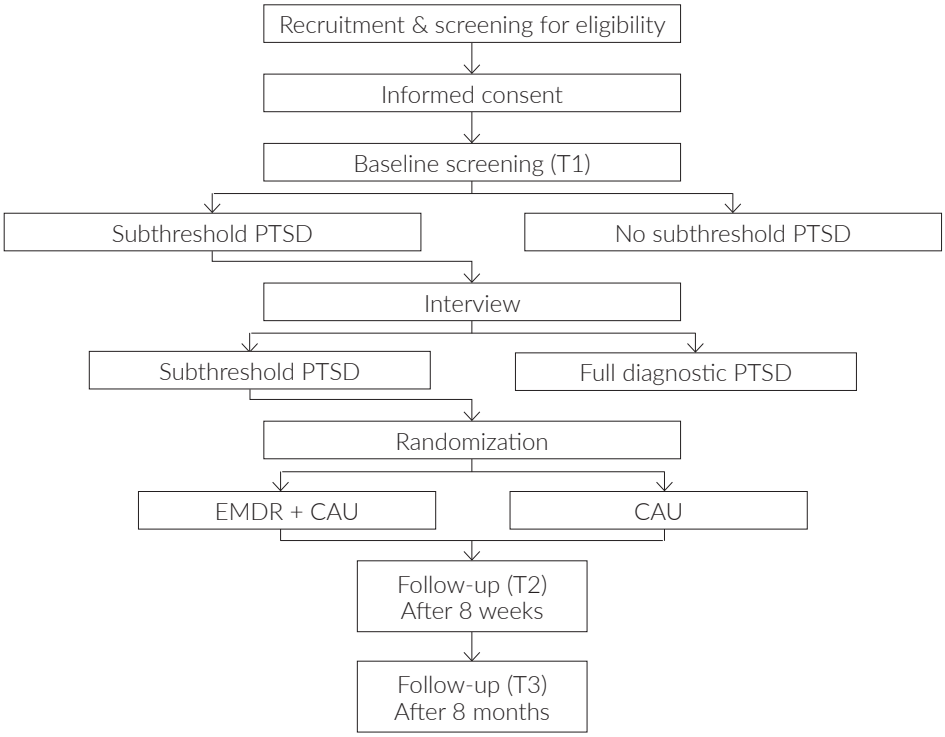

Figure 1. Study Design.

Depression is measured using the Child Depression Inventory 2 (CDI-2) [189, 190]. The CDI-2 is designed for children aged 8-21 years, with a child (containing 28 items) and parent (containing 17 items) form. Both are administered.

The *Quality of Life* of the participants is assessed with the TNO-AZL Questionnaire for Children's Health-Related Quality of Life (TACQOL; 63 items) for children aged 6-15 years [191, 192]. The child, as well as the parent form, are administered.

Sleep quality and disturbances are measured with the Sleep Self-Report (SSR; 26 items, 7-12 years) [193] and the parallel parent version which is called Child Sleep Habits Questionnaire (CSHQ; 35 items, 4-10 years) [194].

Self-perception is evaluated using the Dutch versions of Harter's Self-Perception Profile for Children (SPP-C; in Dutch CBSK, 8-12 years) and Adolescents (SPP-A, in Dutch CBSA, 12-18 years) [195, 196]. The questionnaires consist of 36 (SPP-C) and 35 (SPP-A) items. The same subscales can be computed for both questionnaires. These questionnaires are filled out on paper by children because of licence reasons. There is no parent version of this questionnaire.

Attention problems and school functioning are measured with the Child Behavior Checklist (CBCL 6-18) [197, 198]. Only its subscale attention problems (10 items) and the items about school (4 items) are administered to parents. We also used the complete Teacher Report Form (TRF 6-18), which is a parallel version of the CBCL, to obtain standardized reports from teachers. The original CBCL & TRF recall-period is six months. Because of the treatment period, the instruction will be changed into six weeks for the T2-assessment only.

To evaluate the *subjective satisfaction* (hereby referred to as *social validity)* regarding EMDR, questions specifically designed for this study are asked to patients and parents who were randomized to the EMDR group: (1) "How satisfied are you with the EMDR treatment that you(r child) received as part of this study?", (2) "How meaningful was EMDR?" and (3) "Would you recommend EMDR to others?". Scores are on a 10-point scale, with 0 representing a very negative score and 10 a very positive score.

To measure the subjective *impact of the trauma-related questions* of the CRTI, the specifically for this study designed question "How did you experience it to be reminded of the unpleasant event through the herefore asked questions?" is asked to all participating children (6-15). The child has four different answer options, namely 'I did not feel upset at all because of the questions', 'I did feel a little upset because of the questions', 'I did feel quite upset because of the questions' or 'I did feel very upset because of the questions'.

Demographic factors, such as education and ethnicity, are assessed with the general scale of the Rotterdam's Quality of Life Interview (RKvL) [199].

Cognitive coping (towards negative life events) is assessed with the Cognitive Emotion Regulation Questionnaire (CERQ). It has a child version for 9-11-year-olds (CERQ-K) [157] and a version for 12-18 year old adolescents [156]; both have 36 items. The only difference between both version is the age-appropriate formulation of the questions. The additional life events scale is also administered.

Parental stress. The Distress Thermometer (DT; in Dutch Last Thermometer, LTO; Haverman, 2013) and its problem list is used to assess the parent-reported amount of impairment due to stress and the problems causing this stress (46 items). It was designed for parents with a child aged 0-18 years that needed treatment in a hospital.

Somatic complaints of the child are measured with the Questionnaire Somatic Complaints (in Dutch Vragenlijst Lichamelijke Klachten, VLK) [200]. The child version and parent version (40 items) were designed for children aged 8 to 13 years.

Family functioning is evaluated with the 'General Functioning subscale' of the Dutch version of the Family Assessment Device (FAD-N) [201]. This subscale contains 12 items and will be completed by the parents.

Intervention

Participants allocated to the EMDR group will receive approximately six weekly sessions of 60 minutes, depending on how many sessions are needed. The intervention is terminated when (1) Subjective Units of Distress (SUDs) of all selected memories regarding the medical trauma are zero and/or (2) positive cognitions are established (rated by the child) and/or (3) child, parents and therapist agree that PTSD symptoms sufficiently decreased. EMDR is performed by EMDR-licensed and experienced health psychologists of the Erasmus MC Sophia Children's Hospital. In this study, the standard Dutch EMDR protocol for children and adolescents [202] or the adapted version for young children [203, 204] are used. It consists of a structured eight-phase approach to address the past, present and future aspects of the traumatic memory. During the sessions, a child is asked to select a memory that is currently most distressing with regard to a previous hospitalization. The painful thoughts are then desensitized through controlled rhythmic eye

movements, and pleasant and positive thoughts are programmed [205]. Visual stimulation is done with an official EMDR lightbar to enhance standardization of the treatment. When administration with the lightbar was not feasible, pads or self-tapping were used consistent with the official EMDR standards. There are different theoretical frameworks behind the mechanism of EMDR. The most prominent one is the working memory theory [e.g.206]. The rationale is that humans have limited working memory capacity and engaging in dual-attention tasks therefore reduces the vividness and emotional intensity of memories. All sessions are videotaped and 20% will be randomly evaluated on treatment integrity using an EMDR-specific treatment integrity checklist. To ensure further protocol adherence, the trained EMDR therapists receive regular supervisions by a licensed EMDR supervisor.

The participants in the care-as-usual group receive standard medical care if that is necessary, as do all participants in the study.

Sample Size

The effectiveness of EMDR in this study sample for treating PTSD symptoms is measured by the difference in CRTI-PTSD total score at T2 between the EMDR and the CAU group. A meta-analysis has shown that the effect size (Cohen's d) of EMDR on PTSD symptoms in children is 0.67 versus a waiting list control group, 0.65 versus care-as-usual and 0.25 versus CBT [73]. This meta-analysis studied the efficacy of EMDR in children aged 4-18 years with PTSS after single and multiple heterogeneous trauma's. With an effect size of 0.65, an alpha of 0.05 (two-tailed) and a power of 0.80, a sample size of 78 (39 per group) is needed to detect differences in the primary outcome between the EMDR and CAU group.

Data analysis

To evaluate differences in demographics, trauma-related and other baseline clinical characteristics between the two groups, descriptive statistics will be computed. The primary analysis will be conducted using an intention-to-treat analysis. There are two follow-up measurements (T2 and T3) to assess treatment results over time. Linear mixed models will be used to test the effectiveness of EMDR on the primary outcome (CRTI-PTSD total score) assessed at three time points. The first follow-up measurement (T2) will be considered the primary endpoint. T3 will be considered as a secondary endpoint. Trauma type, gender and age will be included

as covariates. P-values of <0.05 will be considered significant.

For the secondary outcomes (psychosocial functioning, quality of life, etc.) linear mixed models will be used as well.

To identify predictors (demographic factors, coping, parental stress, etc.) for treatment response to EMDR, we will first run univariate regression analyses with all potential predictor variables and the PTSD total score as outcome (separately for child and parent report) on T2 in the EMDR sub-group. Second, we will test for moderation by entering interaction terms between the significant predictor variables from the first step and treatment condition in the linear mixed model.

Multiple imputation methods will be used to deal with missing values. Separate analyses will be done for every informant (child, parent and teacher).

Discussion

This paper describes the study design and protocol of the first randomized controlled trial to test the effectiveness of EMDR on reducing subthreshold PTSD in children and adolescents after medically related trauma. Given the scarcity of research in this area, this study will provide essential information for psychologists considering the use of EMDR in paediatric patients. Another strength of this study is that we include children with single and multiple trauma so we can explore differences in prevalence of subthreshold PTSD and EMDR effectiveness. Posttraumatic stress symptoms are measured not only by self-report but also through parent-report and a validated semi-structured interview. Short- and long-term outcomes and possible predictors of the treatment effect are also measured.

Currently, the majority of children and adolescents do not receive any psychosocial care after medical procedures or hospitalization. If EMDR proves to be an effective and evidence-based intervention in this population, then there is good evidence to structurally implement EMDR into the psychosocial care of Dutch hospitals. Screening for PTSS and other co-morbid mental health complaints is not currently part of standard paediatric medical care in many hospitals. This study introduces mental health screening for young patients after hospitalization at several hospitals throughout the Netherlands. This will provide new information about the prevalence

of subthreshold PTSD and other psychiatric comorbid difficulties in children and adolescents with medically related trauma type I and II in the Netherlands.
Despite its strengths, this study might also face some limitations. This is a single-centre study as all EMDR sessions were provided in the Erasmus MC only. However, patients were recruited from all over the Netherlands, enhancing the generalizability of our findings. As we used a care-as-usual control group, statements about the unique treatment effect of EMDR will not be possible. Any treatment effect observed could also be due to general contact aspects of a psychosocial intervention. However, it has repeatedly been shown that EMDR is as effective as TF-CBT or even more effective [67, 73, 79, 177]. It is also possible that some of the participants in the care-as-usual group will nonetheless search psychological treatment during the assessment period. The screening procedure may raise awareness about their posttraumatic stress symptoms and thus motivate them to seek help. Parents are asked to communicate it with us if they seek help on their own during the study.

Despite these possible limitations, this study represents the largest RCT up-to-date focusing on the effectiveness of EMDR in children with subthreshold PTSD after medically related trauma and will therefore contribute to the knowledge of clinicians and researchers and the well-being of children in hospitals.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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CHAPTER 6

EMDR for children with medically related subthreshold PTSD: short-term effects on PTSD, blood-injection-injury phobia, depression and sleep

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Abstract

Background

Paediatric illness, injury and medical procedures are potentially traumatic experiences with a range of possible negative psychosocial consequences. To prevent psychosocial impairment and improve medical adherence, evidence-based psychotherapy should be offered if indicated. Eye movement desensitization and reprocessing (EMDR) has been found to reduce symptoms of posttraumatic stress disorder (PTSD) in adults. The evidence for the use with children is promising. Furthermore, recent studies indicate its effectiveness for the treatment of other psychological symptomatology. However, the effectiveness of EMDR in children with subthreshold PTSD after medically related trauma has not yet been investigated.

Objective

Investigating the short-term effectiveness of EMDR on posttraumatic stress, anxiety, depression and sleep problems in children with subthreshold PTSD after hospitalization through a randomized controlled trial (RCT).

Method

Following baseline screening of 420 children from various Dutch hospitals, 74 children (4–15 years old) with medically related subthreshold PTSD were randomized to EMDR (n = 37) or care-as-usual (CAU; n = 37). Follow-up assessment took place after *M* = 9.7 weeks. Generalized Estimating Equation (GEE) analyses were performed to examine the effectiveness of EMDR compared to CAU.

Results

Children in both groups improved significantly over time on all outcomes. However, the EMDR group improved significantly more as to child-reported symptoms of blood-injection-injury (BII) phobia and depression, and child-, and parent-reported sleep problems of the child. There was no superior effect of EMDR compared to CAU on subthreshold PTSD symptom reduction.

Conclusions

EMDR did not perform better than CAU in reducing PTSD symptoms in a paediatric sample of children with subthreshold PTSD after hospitalization. However, the study results indicate that EMDR might be superior in reducing symptoms of blood-injection -injury phobia, depression and sleep problems.

Highlights

- First RCT evaluating the effectiveness of EMDR in children with medically related subthreshold PTSD.
- EMDR was equally effective as CAU in reducing PTSD symptoms.
- EMDR was more effective than CAU in reducing symptoms of BII phobia, depression and sleep problems.

Background

A growing number of studies have confirmed posttraumatic stress reactions and other psychopathological symptoms in children and adolescents after hospitalization and medical procedures [22, 23]. Although many children are resilient and show a reduction in symptoms in the weeks after the medical event, some experience long-term impairing symptomatology or even develop a mental disorder. Common symptoms after medical events are posttraumatic stress, anxiety (especially blood-injection-injury phobia), mood and sleep problems [23, 52, 207, 208]. Prevalence rates of posttraumatic stress disorder (PTSD) in children after chronic illness (e.g. heart disease) or acute injury (e.g. after traffic accidents) vary from 12 to 31% [209, 210]. PTSD is a serious mental disorder which is associated with substantial impairment in cognitive, academic, social and emotional functioning [211-214]. Similar impairment is seen in children with subthreshold PTSD (i.e. not meeting all criteria for a full diagnostic PTSD), which is even more common than full diagnostic PTSD, namely 25-38% [22, 23, 38, 170]. These findings underscore the clinical significance of subthreshold PTSD and suggest a need for appropriate treatment options. However, subthreshold PTSD is often overlooked and stays untreated which can lead to worsening of the symptoms and full diagnostic PTSD [97]. While treatment possibilities for full diagnostic PTSD are widely studied, evaluations of treatment options for subthreshold PTSD are very scarce [215, 216].

Eye movement desensitization and reprocessing (EMDR) is one of the most studied evidence-based psychotherapies for PTSD treatment in adults [71, 72, 178]. Like many psychotherapies, EMDR was developed for adults and was later adapted for children. Consequently, scientific studies into the effectiveness of EMDR for children are underrepresented [70, 217]. Two meta-analyses and one review including only a few studies show promising results regarding EMDR for children [73, 74, 218]. Interestingly, a recent meta-analysis comparing the effectiveness of EMDR and cognitive behavioural therapy (CBT) showed that children with subthreshold PTSD exhibited significantly greater reductions in PTSD symptoms following treatment than those who were reported to have full diagnostic PTSD [75]. However, the effectiveness of EMDR for children has not yet been investigated focusing solely on children with subthreshold PTSD.

EMDR has originally been developed as PTSD treatment, but it has also been shown to be useful for the treatment of other mental health issues [69]. Evidence

suggests that EMDR reduces symptoms of anxiety and depression in children [74, 177, 219, 220] and sleep problems in adults [221]. However, these EMDR treatment outcomes have not yet been studied in paediatric medical settings.

The use of EMDR in medical settings was recently recommended by the developer of EMDR herself [68]. However, studies into the effectiveness of EMDR in a paediatric medical setting are scarce. Kemp, Drummond, and McDermott [78] found significant PTSD symptom reduction after four EMDR sessions in children (6-12 years) who were injured in motor vehicle accidents and initially met two or more PTSD criteria. However, this study had a very small sample size (controls *n*=14, EMDR *n*=13). Another small study with children who experienced a road traffic accident (*n*=11) found significant reductions of PTSD, general anxiety, and depression after an average of 2.4 EMDR sessions [76]. However, this study did not use a control group. A very small quasi-experimental study in Iranian children who survived serious traffic accidents also claims to show positive results of EMDR, but no firm conclusions can be drawn from the article due to methodological reasons [77]. Furthermore, a study in children who had experienced different kinds of traumas, including a small subsample of children with medically related trauma (23% accidents, 7% serious illness), also found promising results for EMDR in reducing PTSD symptoms [79]. Again, the sample size was small (CBT *n*=23, EMDR *n*=25).

Overviewing this rather unexplored field, systematic research in larger samples remains urgently needed. Our study represents the first randomized controlled trial that specifically aims to investigate the effectiveness of EMDR in reducing medically related subthreshold PTSD after hospitalization for paediatric illness or injury. Secondary aims were to test the effectiveness of EMDR in reducing children's anxiety (especially blood-injection-injury phobia), depression and sleep problems. The outcome variables investigated in this article (subthreshold PTSD, symptoms of anxiety and depression, and sleep problems) were selected a priori. The choice for anxiety, depression and sleep problems next to subthreshold PTSD was based on their close association with each other [222]. Anxiety and depression appear to be strongly correlated and highly comorbid with PTSD [22, 223]. Furthermore, there is also a significant symptom overlap with sleep [222].

Methods

Design

This randomized controlled trial (RCT) represents a single-centre study. All therapy sessions took place in the Erasmus MC - Sophia children's hospital in Rotterdam, the Netherlands. Participants were recruited via the Sophia children's hospital (divisions of paediatrics and paediatric cardiology), the paediatrics division of the Maasstad hospital in Rotterdam, the paediatric cardiology division of the Radboud UMC Nijmegen, and nationally through the Dutch Association for patients with a congenital heart defect, and the Dutch non-profit organization Heartchild Foundation (*Stichting Hartekind)*. A detailed article about the study protocol has been published previously [155]. The study was approved by the Medical Ethics Committee of the Erasmus Medical Centre in the Netherlands, registered in the Dutch Trial Register (NTR5801), and performed conform the Declaration of Helsinki [224].

Participants

The target group was 4-15-year-old children with medically related subthreshold PTSD after ≥1 hospitalization(s) of at least one night. The presence of subthreshold PTSD was first investigated with the Children's Responses to Trauma Inventory [CRTI; 184]. Subthreshold PTSD was defined as either (1) fulfiling at least two of the three DSM-IV PTSD symptom criteria (re-experience, avoidance or hyperarousal) and/or (2) having an above average score (>60th percentile) on the CRTI; without a full diagnostic PTSD score on a semi-structured interview afterwards. The last hospitalization or additional medical procedure(s) should have occurred at least 4 weeks and at most 5 years ago. The inclusion period was from July 2016 until May 2018.

The screening for subthreshold PTSD took place during a baseline assessment (T1). For this assessment, we included children who had been hospitalized (1) after consultation at an emergency department due to acute injury or illness, or (2) at a paediatric cardiology department due to a congenital or acquired heart defect. Both groups encompassed children who experienced single (type I trauma) or multiple (type II trauma) medical events. In this study, we defined type I trauma as a first hospitalization of previously healthy children. Type II trauma was defined as ≥2 hospitalizations or an additional medical procedure (e.g. surgery) next to an one-time hospitalization.

Exclusion criteria were: (1) intellectual disability (IQ<70); (2) parental inability to read or write Dutch; (3) diagnosis of a chronic illness for the emergency department subgroup; (4) previous successful treatment for medically related PTSD; and (5) current psychological treatment.

Procedure

After informed consent was obtained, 420 participants were asked to fill out questionnaires to screen for PTSD symptoms (primary outcome) and other related psychosocial symptoms (secondary outcomes) during a baseline assessment [225]. Subsequently, children (aged 8-15 years) with baseline scores indicating at least subthreshold levels of PTSD were invited for a semi-structured interview (Clinician-Administered PTSD Scale for Children and Adolescents, CAPS-CA; [186]). For children aged 4-7 years with at least subthreshold levels of PTSD, one parent was interviewed using the PTSD module of the Diagnostic Infant and Preschool Assessment (DIPA; [187]). Since our study focused on children with subthreshold PTSD, children with a full diagnostic PTSD score on the interview were excluded and referred for treatment. Seventy-four children with subthreshold PTSD were randomized on a 1:1 ratio into the EMDR (*n*=37) or care-as-usual group (CAU; *n*=37). Randomization was stratified by trauma type (i.e. type I vs. type II trauma) and age (i.e. 4-11 vs. 12-15) using blocks. Randomization was performed by an independent researcher (using opaque envelopes) and concealed from the researcher enrolling and assessing participants. Questionnaires were filled out at baseline (T1) and during a follow-up assessment *M*= 9.7 (*SD*=2.5) weeks after the first EMDR session (T2). Of the 74 randomized children, three (EMDR *n*=2; CAU *n*=1) were erroneously randomized due to misinterpretation of their score (two children scored only one point below the cut-off). Within the EMDR group, four children did not start with EMDR at all after randomization. See **figure 1** for an overview.

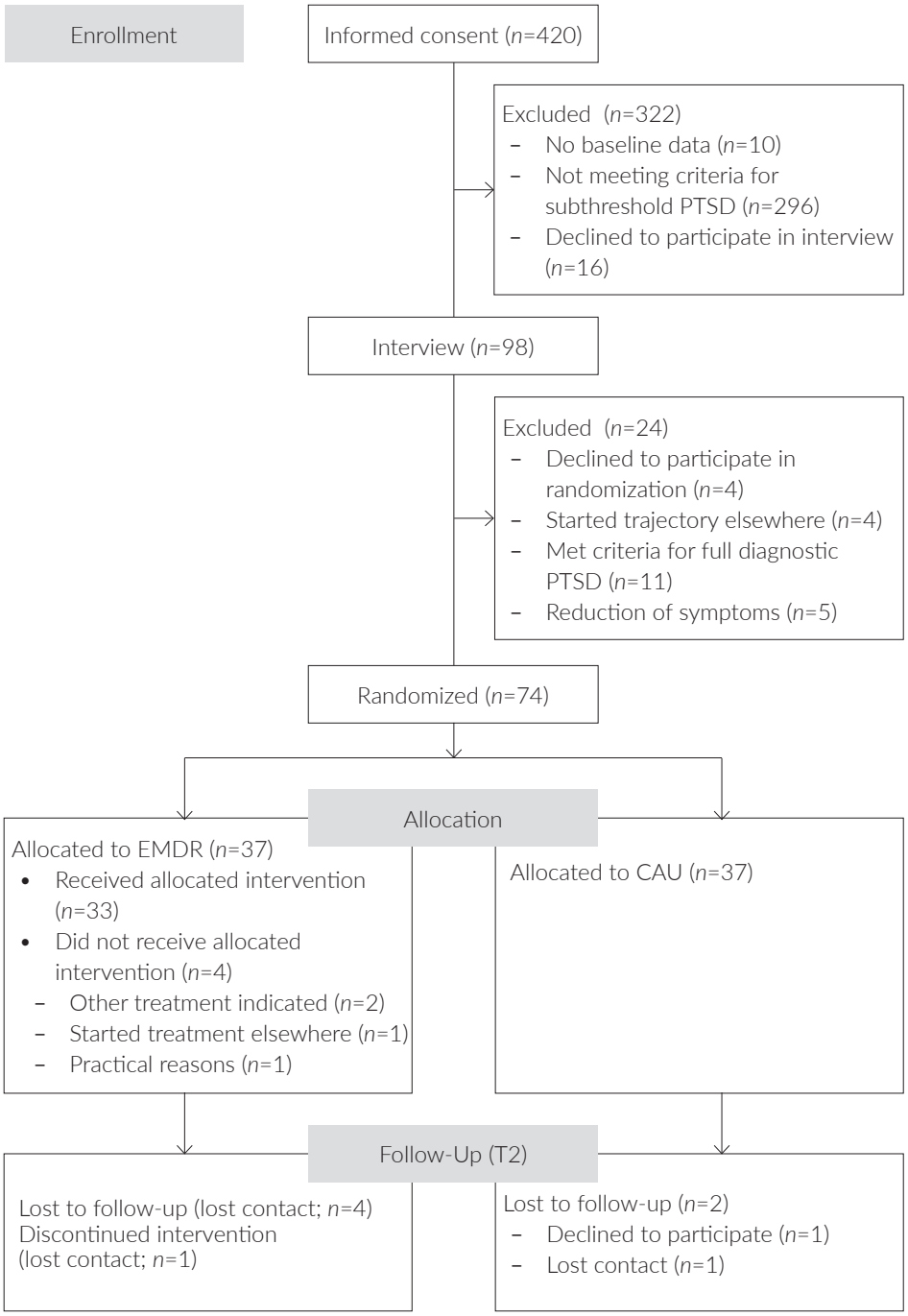

Figure 1. Flow chart.

Measures

Children ≥6 years of age were asked to fill out questionnaires. Parent-report was asked for children of all included ages. Participants were asked to fill out the questionnaires with regard to a medical event. All questionnaires have adequate psychometric properties.

Primary outcome

PTSD symptoms were measured using the Dutch version of the Children's Responses to Trauma Inventory [CRTI; 184]. The CRTI contains 24 PTSD items which can be divided into three subscales related to the DSM-IV-TR symptom clusters of PTSD (intrusion, avoidance, and hyperarousal). The total PTSD score can range from 17 to 85, with a higher score indicating more problems. The scores on the subscales intrusion and hyperarousal can range from 5-25 and on avoidance from 7-35.

Secondary outcomes

Symptoms of depression were measured through the total score of the Dutch Children's Depression Inventory 2 [CDI-2; 190]. The parent version contains 17 items with a 4-point Likert scale and the child version contains 28 items with a 3-point Likert scale. Scores can range from 0 to 51 (parent-version) or 56 (child-version). A higher score indicates more problems.

Symptoms of blood-injection-injury (BII) phobia and anxiety in general were measured through the BII subscale (7 items) and the total score (69 items) of the Dutch Screen for Child Anxiety Related Emotional Disorders [SCARED-NL; 188]. Responses are scored on a 3-point Likert scale (0-2) with a maximum score of 14 (BII subscale) and 138 (total score). A higher score indicates more problems.

Sleep problems were measured using the total score of the Dutch Sleep Self Report [SSR, 23 items; 226] and the Dutch parallel parent version called Child Sleep Habits Questionnaire [CSHQ, 35 items; 194]. Responses are rated on a 3-point Likert scale (1-3) with maximum total scores of 69 (SSR) and 99 (CSHQ). Again, a higher score indicates more sleep problems.

Social validity questions were added to investigate parents' and children's subjective evaluation of the EMDR treatment. Three aspects of social validity (satisfaction with EMDR, usefulness of EMDR and recommendation of EMDR) were assessed in the EMDR group at T2. A 10-point Likert scale (0-10) was used with a higher score

indicating more satisfaction, perceived usefulness and willingness to recommend EMDR.

Intervention

EMDR is based on the assumption that traumatic memories are stored inadequately. During therapy, the child is asked to think about a currently disturbing memory while simultaneously focusing on a bilateral stimulation (i.e. eye movements). This initiates processing of the memory. The working mechanism of EMDR is still unclear. The hypothesis with most support is that engaging in two simultaneous tasks (i.e. eye movements and thinking about a disturbing memory) draws on the limited capacity of the working memory and therefore decreases the vividness of the image [81].

Children in the EMDR group received *M*=3.5 (*SD*=1.9) EMDR sessions (intake included) of approximately 50 minutes. Parents were allowed to be present during the sessions when the child agreed on this with the therapist. EMDR therapy was provided by five licenced and experienced clinical psychologists following the standard Dutch EMDR protocol for children and adolescents [202] or the adapted version for young children [203, 204]. EMDR treatment was completed when (1) Subjective Units of Distress (SUDs) of all selected memories regarding the medical trauma were zero and/or (2) positive cognitions were established (rated by the child) and/or (3) child, parents and therapist agreed that PTSD symptoms had sufficiently decreased.

Children in the CAU group only received standard medical care.

Treatment integrity

All five EMDR-therapists participated in regular supervision sessions provided by a EMDR Europe consultant (licenced supervisor). All EMDR sessions were video-taped. If no consent for videotaping was obtained, the therapists provided detailed written records. All sessions of 10 randomly chosen children (27%) were rated on protocol adherence by a trained research psychologist and two trained Master students in psychology, supervised by the aforementioned research psychologist. Rating was done with an EMDR-specific treatment integrity checklist with a total score ranging from 0-16. There was good agreement between all three independent raters: all total scores given ranged between 13-16. Treatment integrity was high with 95%.

Statistical analyses

We conducted *t*-tests and χ^2-tests to test differences between the EMDR and CAU group baseline characteristics. Correlations between child and parent report were analysed using Pearson's *r* and differences were tested using paired sample *t*-test. To test for differences in outcome scores between both groups in the total sample, Generalized Estimating Equations (GEE) with an unstructured correlation matrix were performed following the intention-to-treat principle. We conducted a GEE analysis for each outcome separately. In each analysis, we first added time (T1 vs. T2) and group (EMDR vs. CAU) as factors. Interactions between time and group were tested for significance with Wald χ^2 tests. Second, if the interaction was significant, we ran the GEE analyses again adding age, gender and whether the child had experienced ≥1 other non-medical stressful life events as covariates. Third, for all significant interactions, we also added trauma type, hospital department, and time since last medical event as covariates and, for explorative analyses, their interaction with time and group.

In addition, we ran the analyses of the first step again 1) following the per-protocol principle and 2) without the three erroneously randomized children. Effect sizes were measured with Cohen's *d* by dividing the difference between the estimated means of both groups at T2 by the pooled standard deviation at T1 [227]. SPSS version 24.0 was used for all statistical analyses.

Results

Baseline characteristics

At baseline, no differences were found between the EMDR and CAU group with regard to baseline demographics. See **table 1** for more information. However, the EMDR group had a significantly higher mean score at baseline on the child-reported total sleep problem score than the CAU group [$t(65) = -2.3$, $p < .05$].

Parent-child agreement

PTSD symptoms

The correlation between child and parent report on the primary outcome (CRTI) was moderate ($r=.31$) at T1 and high ($r=.56$) at T2. Differences between child and parent report at the two time points were not significant.

Symptoms of depression
The correlation between parent and child report on depression was high at T1 (r =.58) and T2 (r =.76). Differences between child and parent report could not be tested due to incomparable questionnaires.

Symptoms of BII phobia and anxiety in general
Parent and child report for BII phobia was high at T1 (r =.71) and T2 (r =.75). There were significant differences in the T1 scores for parent report (M=5.06, SD=3.16) and child report (M=5.76, SD=3.21); t(66)=-2.35, p=.02. The correlation between parent and child report on the SCARED-NL total score was also high at T1 (r =.53) and T2 (r =.75). There were no significant differences between child and parent report.

Sleep problems
The correlation between child and parent report on sleep problems were high at T1 (r =.53) and T2 (r =.79). To test for differences between child and parent reported sleep problems, CSHQ total scores were divided by 35 (number of CSHQ items) and then multiplied by 23 (number of SSR items). At both assessment points, children (M_{T1}= 37.09, SD_{T1}=5.97; M_{T2}=34.18, SD_{T2}=6.36) reported significantly more sleep problems than parents (M_{T1}= 32.70, SD_{T1}=5.47; M_{T2}=30.23, SD_{T2}=5.50); t_{T1}(66)=-6.47, p=.00 and t_{T2}(56)=-7.56, p=.00.

Primary outcome

Outcomes of the EMDR and CAU group are shown in **table 2**. Children in both groups showed a similar reduction in PTSD symptoms from baseline to follow-up. EMDR was not significantly superior compared to CAU in reducing child-reported (b=-0.5, p=.853) and parent-reported (b=-3.5, p=.275) PTSD symptoms of the child. The same was true for all three PTSD subscales.

Table 1. Baseline demographics.

	N	Total	EMDR group n=37	CAU group n=37	*p-value*
Child					
Age in years, M ± SD	74	9.6 ± 2.9	9.8 ± 2.7	9.4 ± 3.1	.604
Gender, n (%)	74				.806
Girls		25 (33.8)	12 (32.4)	13 (35.1)	
Boys		49 (66.2)	25 (67.6)	24 (64.9)	
Ethnicity, n (%)	72				.202
Dutch		59 (81.9)	32 (88.9)	27 (75.0)	
Other Western		4 (5.6)	2 (5.6)	2 (5.6)	
Non-Western		9 (12.5)	2 (5.6)	7 (19.4)	
Other stressful life events, n (%)	67				.864
Yes		55 (82.1)	29 (82.9)	26 (81.3)	
No		12 (17.9)	6 (17.1)	6 (18.8)	
Parental					
Education, n (%)	74				.836
High		41 (55.4)	21 (56.8)	20 (54.1)	
Medium		30 (40.5)	15 (40.5)	15 (40.5)	
Low		3 (4.1)	1 (2.7)	2 (5.4)	
Medical					
Department, n (%);	74				.816
Cardiology		39 (52.7)	19 (51.4)	20 (54.1)	
Emergency unit		35 (47.3)	18 (48.6)	17 (45.9)	
Trauma Type, n (%)	74				.572
I		16 (21.6)	9 (24.3)	7 (18.9)	
II		58 (78.4)	28 (75.7)	30 (81.1)	
No. of hospitalizations, M ± SD	71	4.01 ± 4.00	4.5 ± 4.4	3.6 ± 3.5	.331
Length of hospitalization(s) in days, M ± SD	59	28.14 ± 47.23	31.7 ± 54.9	24.2 ± 37.6	.545
Time since last medical event in years, M ± SD	71	1.76 ± 1.42	1.7 ± 1.5	1.8 ± 1.4	.789

M, mean; SD, standard deviation; no., number. χ^2 tests were used for categorical variables. T-tests were used for continuous variables.

Table 2. Outcome measures for EMDR vs. CAU.

	EMDR group (n=37)	
Outcome measure	**T1**	**T2**
Posttraumatic stress symptoms		
Child-report		
Total PTSD score	45.00 ± 9.17	32.00 ± 11.80
Intrusion	12.20 ± 4.19	8.29 ± 3.60
Avoidance	18.77 ± 3.85	13.10 ± 5.32
Hyperarousal	14.03 ± 4.11	10.61 ± 4.82
Parent-report		
Total PTSD score	44.51 ± 10.80	32.94 ± 10.44
Intrusion	11.86 ± 4.18	8.42 ± 3.64
Avoidance	17.97 ± 5.12	13.58 ± 5.26
Hyperarousal	14.68 ± 4.14	10.94 ± 3.42
Symptoms of depression		
Child-report	11.23 ± 6.04	6.17 ± 5.27
Parent-report	17.59 ± 6.42	12.06 ± 6.03
Symptoms of blood-injection-injury phobia		
Child-report	6.31 ± 3.23	4.30 ± 2.83
Parent-report	5.38 ± 3.06	4.52 ± 3.05
Symptoms of anxiety		
Child-report	46.09 ± 22.87	28.73 ± 17.39
Parent-report	38.97 ± 16.76	27.39 ± 13.87
Sleep problems		
Child-report	38.63 ± 6.48	33.80 ± 6.04
Parent-report	51.14 ± 8.61	46.12 ± 8.20

*Mean ± Standard deviation. *p < .05.*

[a]GEE analyses. Uncorrected interaction of time x group.

[b]GEE analyses. P-values indicate level of significance of the uncorrected time x group interaction.

[c]Cohen's d

CAU group (n=37)				
T1	T2	*B*[a]	*P*-value[b]	Effect size[c]
44.37 ± 8.32	31.54 ± 11.76	-0.509	0.853	-.06
11.53 ± 3.08	7.50 ± 2.93	-0.044	0.966	-.01
18.69 ± 4.27	13.50 ± 5.06	-0.601	0.658	-.15
14.16 ± 4.30	10.54 ± 5.37	0.293	0.790	0.07
43.46 ± 9.78	35.43 ± 12.58	-3.468	0.275	-.34
11.14 ± 3.56	9.14 ± 3.80	-1.420	0.214	-.37
17.76 ± 4.91	14.37 ± 5.55	-1.038	0.482	-.21
14.57 ± 3.84	11.91 ± 4.81	-0.990	0.355	-.25
9.03 ± 6.38	7.07 ± 6.55	-2.473	0.037*	-.40
14.65 ± 6.63	12.14 ± 7.20	-2.551	0.050	-.39
5.16 ± 3.12	4.37 ± 3.20	-1.463	0.034*	-.46
4.49 ± 3.05	4.17 ± 3.48	-0.541	0.364	-.18
39.91 ± 16.86	29.63 ± 21.13	-6.834	0.101	-.34
37.49 ± 20.43	30.43 ± 20.84	-3.833	0.288	-.20
35.41 ± 4.92	34.59 ± 6.80	-3.614	0.003*	-.63
48.76 ± 7.96	47.35 ± 8.15	-2.751	0.032*	-.33

Secondary outcomes

From baseline to follow-up, child-reported symptoms of blood-injection-injury phobia decreased significantly more in the EMDR group than in the CAU group (*b*=-1.5, *p* = .034). This effect remained significant in a secondary GEE analysis controlling for age, gender and other stressful life events (*b*=-1.5, *p*=.034, Cohen's *d*=-.46). In contrast, parent-reported BII phobia symptom reduction in the child did not differ significantly between the EMDR group and the CAU group (*b*=-0.5, *p*=.364).

As to child-reported anxiety symptoms, EMDR was not superior in reducing child-reported total anxiety symptoms compared to CAU (*b*=-6.8, *p*=.101). The same was true for parent-reported total child anxiety symptoms (*b*=-3.8, *p*=.288).

Child-reported symptoms of depression declined significantly more in the EMDR group than in the CAU group (*b*=-2.5, *p*=.037). This effect remained significant after controlling for age, gender and other stressful life events (*b*=-2.5, *p*=.037, Cohen's *d*=-.40). As to parent-reported symptoms of depression of the child, a trend towards significance in favour of the EMDR group was found (*b*=-2.6, *p*=.05).

With regard to child-reported sleep problems we found a significant larger reduction from baseline to follow-up for the EMDR group compared with the CAU group (*b*=-3.6, *p*=.003). This effect remained significant after controlling for age, gender and other stressful life events (*b*=-3.6, *p*=.003, Cohen's *d*=-.63). Children's sleep problems reported by the parents also reduced significantly more in the EMDR group than the CAU group (*b*=-2.8, *p*=.032). However, this effect was not significant anymore after controlling for age, gender and other stressful life events (*b*=-2.6, *p*=.059, Cohen's *d*=-.31).

Explorative analyses

No significant differences in treatment effect were found for trauma type and hospital department. However, the effect of EMDR in reducing child-reported symptoms of depression and sleep problems were larger the longer ago the last medical event happened.

Additional analyses

Per-protocol analyses revealed some minor deviations regarding the secondary

outcomes compared to intention-to-treat analyses. In addition to the findings that EMDR was superior to CAU in treating BII phobia (child-report), depression (child-report) and sleep problems (child-report and parent-report), per-protocol analyses showed that EMDR was also superior in treating parent-reported symptoms of depression of the child and child-reported total anxiety score.

Furthermore, we did another analyses without the children who were erroneously randomized. In contrast to the previous analyses, improvements between baseline and follow-up regarding child-reported depressive symptoms and parent-reported sleep problems of the child were not significantly larger for the EMDR group anymore. However, the superior effects of EMDR on child-reported BII phobia symptoms and child-reported sleep problems remained significant.

Social validity

On a scale of 1 to 10, mean child (*n*=29) and parent (*n*=31) ratings of satisfaction with EMDR treatment were 8.2 (*SD*=1.6) and 8.0 (*SD*=1.1), respectively. The mean level of perceived usefulness of EMDR rated by children was 7.8 (*SD*=1.9) and by parents 6.8 (*SD*=2.3). On average, the willingness to recommend EMDR to others was rated with a 7.9 (*SD*=2.3) by children and with a 7.7 (*SD*=1.7) by parents.

Discussion

This study presents outcomes of the first randomized controlled trial investigating the effectiveness of EMDR compared with CAU for children with medically related subthreshold PTSD after hospitalization for illness or injury. Children of both groups improved over time, but EMDR was superior in reducing symptoms of depression and BII phobia, and sleep problems.

We found significant improvements for both the EMDR and the CAU group over time on all outcomes. This could be due to the fact that children in the CAU group participated in a baseline psychological screening and an interview with a psychologist and, thereby, received additional attention from a professional. Participating in a structured assessment and hearing that PTSD symptoms were of subthreshold nature might be therapeutic in itself by acknowledging and normalizing the child's symptoms. Furthermore, research suggests that participating

in a psychological study can decrease psychosocial symptomatology [228, 229]. With regard to PTSD symptom reduction, EMDR was as effective as CAU. This is in contrast to two meta analyses reporting on smaller studies [73, 74]. However, these studies did not specifically focus on medically related trauma and subthreshold PTSD. It is possible that with medically related subthreshold levels of PTSD, receiving attention from a mental health professional is enough to reduce symptoms and that EMDR, therefore, had no superior effect compared to CAU in our sample. Bearing in mind the limited resources of psychotherapists, a stepped-care model might be most efficient and cost-effective for monitoring and treating symptoms. This model proposes that mental health care is provided in steps and based on the needs of the child, with only those with persistent severe symptoms progressing to psychotherapy [64]. Additionally, natural remission from PTSD symptoms can also occur [97, 230]. Exact remission rates, however, of children with medically related subthreshold PTSD are unknown. Future research should provide more insights into predictors of the EMDR treatment effect. It is important to note that we did not find any harmful effect of EMDR and that parents and children evaluated EMDR as very satisfactory.

Sleep problems are part of the DSM-V criteria for PTSD. However, sleep problems are rarely investigated as treatment outcome of EMDR. The present study presents support for the use of EMDR to reduce sleep problems in children after hospitalization. This is in line with Raboni et al. [221], who showed that EMDR treatment of PTSD improved sleep quality in adults.

Furthermore, PTSD tends to be closely related to specific phobias as these often have a traumatic origin too [231]. Interestingly, we found a superior effect of EMDR in reducing child-reported symptoms of blood-injection-injury phobia. This is in line with previous research indicating a positive effect of EMDR on dental phobia [232, 233]. Our finding that EMDR can reduce BII is clinically very relevant: it may be beneficial for future medical adherence as phobic patients tend to avoid the source of their fear.

Level of medical adherence has also been found to be smaller in patients who suffer from depression [234]. In line with previous findings, our results indicate that child-reported symptoms of depression decreased significantly more in the EMDR group than in the CAU group [67, 219] and thereby possibly improved medical adherence.

As to our multi-informant approach, correlations between child and parent report were moderate to high. Still, children reported significantly higher mean scores on BII phobia at T1 and sleep problems at T1 and T2 compared to parent-report. Earlier research has also found that child report tends to be higher than parent report on both outcomes [235, 236]. It has been argued that some aspects of internalizing problems and sleep may manifest beyond parent's awareness and therefore child-report might be more reliable [237, 238]. However this might not be true for young children.

The additional analyses revealed that per-protocol analyses showed additional superior effects of EMDR on reducing child-reported anxiety and parent-reported symptoms of depression of the child. However, per-protocol analyses represents the best-case scenario and may therefore show an exaggerated effect [239]. Furthermore, we also tested whether the benefits of EMDR remained when the three erroneously randomized children were eliminated from the statistical analyses. The superior effects of EMDR on child-reported BII phobia and sleep problems remained significant. Since results were changing during the additional analyses, results of this study should be interpreted with caution.

Finally, we also explored whether trauma type (I vs. II), type of department (emergency vs. cardiology) or time since last medical event (0-5 years) influence the found treatment effects. In accordance to Diehle, Opmeer [79], treatment effect was not related to trauma type. The same was true for hospital department. However, the time elapsed since the last medical event did influence the treatment effect. The longer ago the last medical event happened, the more effective was EMDR in reducing child-reported symptoms of depression and sleep problems. This finding is explorative and should be tested in future studies.

Strengths and limitations

This study presents several strengths. First, our sample size was relatively large compared to earlier research into the effectiveness of EMDR in children. Second, we used parent and child report for all outcomes and included a broad age range. Third, we recruited participants throughout the Netherlands which increases generalizability. Fourth, all therapists received regular supervision and treatment integrity was assessed by multiple independent raters. Fifth, randomization was stratified and done by an independent researcher. Sixth, the researcher who was

responsible for all assessments was blinded for randomization outcome. Finally, we specified the trauma type that children in our sample had experienced and explored the effects of trauma type during analyses.

Some limitations should also be noted. First, it should be noted that the CAU group did not represent real care-as-usual as this group received a psychological screening and interview in addition to regular medical care. No similar attention placebo control group was provided. Second, follow-up questionnaires were sent to participants 8 weeks after the first EMDR session regardless of whether EMDR was completed or not for methodological reasons. Therefore, the time between completion of EMDR and follow-up was different for every participant and six participants had not completed therapy when filling out the follow-up assessment. Third, EMDR might be more effective in children with more severe PTSD symptoms. However, it would have been unethical to randomize children with full diagnostic PTSD into a CAU group when other treatment options for PTSD are available. Fourth, due to the nature of EMDR it was not possible to blind participants to their group allocation. Finally, we did not assess parental mental health which is associated with parent report of the child's emotional wellbeing [165] and we did not provide any treatment for parents. The effectiveness of EMDR might improve when an active parental treatment component would be added [177, 240].

Despite the mentioned possible limitations, this study represents the largest RCT up-to-date investigating the effectiveness of EMDR in children with medically related subthreshold PTSD after hospitalization.

Conclusion

In children with medically related subthreshold PTSD, EMDR and CAU performed similarly well at reducing PTSD symptoms. However, the present study provides some indication for the effectiveness of EMDR in reducing BII phobia, depression and sleep problems. No firm conclusions can be drawn from these findings since results changed during additional analyses. Comparable studies should be done to support the implementation of EMDR as an evidence-based therapy for BII phobia, depression and sleep problems after paediatric hospitalization.

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Disclosure statement

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CHAPTER 7

Long-term effectiveness of eye movement desensitization and reprocessing in children and adolescents with medically related subthreshold post-traumatic stress disorder: a randomized controlled trial

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Abstract

Aims

Medical procedures and hospitalizations can be experienced as traumatic and can lead to post-traumatic stress reactions. Eye movement desensitization and reprocessing (EMDR) shows promising results but very few long-term studies have been published. Therefore, our aim was to test the long-term (8 months post-treatment) effectiveness of EMDR in children and adolescents with medically related subthreshold post-traumatic stress disorder (PTSD).

Methods and results

Seventy-four children (including 39 with congenital or acquired heart disease) aged 4-15 (*M*=9.6 years) with subthreshold PTSD after previous hospitalization were included into a parallel group randomized controlled trial. Participants were randomized to EMDR (*n*=37) or care-as-usual (CAU; *n*=37; medical care only). The primary outcome was PTSD symptoms of the child. Secondary outcomes were symptoms of depression and blood-injection-injury (BII) phobia, sleep problems, and health-related quality of life (HrQoL) of the child. Assessments of all outcomes were planned at baseline and 8 weeks and 8 months after the start of EMDR/CAU. We hypothesized that the EMDR group would show significantly more improvements on all outcomes over time. Both groups showed improvements over time on child's symptoms of PTSD (only parent report), depression, BII phobia, sleep problems and most HrQoL subscales. GEE analyses showed no significant differences between the EMDR group (n_{T2}=33, n_{T3}=30) and the CAU group (n_{T2}=35, n_{T3}=32) on the primary outcome. One superior effect of EMDR over time was found for reducing parent-reported BII phobia of the child.

Conclusion

EMDR did not perform better than CAU in reducing subthreshold PTSD up to 8 months post-treatment in previously hospitalized children. Possible explanations and clinical implications are discussed.

Implications for practice

- This study provides preliminary evidence for the use of eye movement desensitization and reprocessing (EMDR) for blood-injection-injury phobia symptoms in children and adolescents after hospitalization
- EMDR may be more effective for post-traumatic stress disorder (PTSD) symptoms when symptom severity is high
- The effectiveness of EMDR for children and adolescents with full diagnostic PTSD after various medically related potentially traumatic events should be studied in the future

Introduction

Exposure to medical care is common during childhood and adolescence, especially for children and adolescents with congenital heart disease (ConHD) [241]. Medical care involves a variety of potentially traumatic events, such as painful diagnostics or medical treatments, surgical interventions, hospitalizations, life-threatening diagnoses, and separation of children from their caregivers. Subsequently, some children develop impairing emotional and behavioural difficulties, including post-traumatic stress [23]. The long-term prevalence of post-traumatic stress disorder (PTSD) in children with ConHD is approximately 29% and roughly 11% after injury [61, 111]. Even more children (up to 38%) develop impairing symptoms of PTSD without meeting all criteria for a diagnostic disorder, called subthreshold PTSD [22]. Subthreshold PTSD is associated with long-lasting impairment comparable to full diagnostic PTSD and accounts for a substantial future PTSD burden [38, 242, 243]. Next to PTSD symptoms, 9-18% of adolescents with ConHD and 7-13% of critical ill children develop clinically relevant depressive symptoms [48, 49, 59]. Furthermore, it has been found that 31% of children with ConHD show significant medical fears [244]. Children with acquired heart disease also show more depressive and anxiety problems than children from the general population [245]. Decreased health-related quality of life (HrQoL) is experienced in 25-60% of children with a ConHD and in up to 43% of children after paediatric intensive care unit admission [246, 247]. Sleep problems are also frequent, reported in up to 86% of children with common medical conditions and 79% of children with ConHD [52, 248].

Attuned psychosocial interventions should be offered to reduce the wide diversity of symptoms. Meta-analyses show that eye movement desensitization and reprocessing (EMDR) is an effective psychotherapy to reduce PTSD symptoms in adults [70, 71]. EMDR has also been found to be effective in reducing depression, anxiety, and sleep problems, and in improving quality of life in adults [69, 221]. During EMDR, the vividness and emotional intensity of a distressing memory is reduced by concentrating on that memory while simultaneously engaging in bilateral stimulation (typically horizontal eye movements). See the recent review of Landin-Romero et al. [81] for more information on possible underlying mechanisms of action. While there has been a great deal of research interest in EMDR, studies into its effectiveness for children are underrepresented. Furthermore, only few studies have documented long-term benefits of EMDR for children. Of the 11 available controlled studies into EMDR for children only three documented $\geq$6

months post-treatment follow-ups. All three studies found positive improvements to be maintained at 6-12 months follow-up [67, 78, 249]. To the best of our knowledge, only one other randomized-controlled trial studied EMDR in a sample of children (aged 6-12 years) with medically related trauma [78]. All participants in this study (*n*=27) had experienced a motor vehicle accident and initially met two or more PTSD criteria. They were randomly assigned to either EMDR or a wait-list control group. Again, the study found that improvements of PTSD symptoms were maintained at 12-month follow-up.

However, there are still gaps in the scientific literature on EMDR for children. The effectiveness of EMDR for children with cardiovascular disease has not been studied before. Furthermore, no other previous study has focused on children with subthreshold PTSD when evaluating the effectiveness of EMDR, even though it has been reported that children with subthreshold PTSD responded better to psychological treatment than those with PTSD[75]. Considering secondary prevention, investigating treatments for the use of subthreshold levels of mental disorders is very important. The current RCT is the first to evaluate the effectiveness of EMDR focusing on children with subthreshold PTSD after hospitalization at a paediatric cardiology department or following emergency department (ED) admission. This article specifically aims to investigate the long-term (8 months post-treatment) effectiveness of EMDR on reducing subthreshold PTSD (primary outcome), depression, BII phobia, and sleep problems, and improving HrQOL following hospitalization. The short-term results of our RCT were published recently and showed superior effects of EMDR on symptoms of BII phobia, depression and sleep problems of the child [250]. The aim of the present article was to investigate whether the positive effects of EMDR would maintain over time.

Methods

The present study was a single-blinded RCT with two parallel groups comparing EMDR and care-as-usual (CAU). After written informed consent (from parents/guardians and children $\geq$12 years) and a positive screening for subthreshold PTSD, participating children were randomized using a 1:1 allocation ratio. A detailed version of the study protocol has previously been published [155]. The study was approved by the Medical Ethics Committee of the Erasmus Medical Centre in the Netherlands, registered in the Dutch Trial Register (NTR5801), and designed

conform the CONSORT guidelines (Supplementary information) [251]. The investigation conforms with the principles outlined in the Declaration of Helsinki [252].

Participants

Participants were continuously recruited from July 2016 until May 2018. Participants were recruited mainly at the Erasmus MC Sophia children's hospital (paediatrics division and paediatric cardiology division) and the Maasstad hospital (paediatrics division) in Rotterdam, the Netherlands. Additional participants were recruited at the paediatric cardiology division of the Radboud UMC Nijmegen (RUMC), and nationally through the Dutch Association for patients with a congenital heart defect (*Patiëntenvereniging Aangeboren Hartafwijkingen*, *PAH*) and the Dutch non-profit organization Heartchild Foundation (*Stichting Hartekind*). We expected medium effects on PTSD symptoms based on a meta-analysis [73]. A sample size of 78 participants was aimed to reach sufficient power [155].

Participating children were 4-15 years old and had been hospitalized at least 4 weeks but no more than 5 years ago for at least one night. The amount of psychological reactions in children might differ after acute versus chronic medical events [22, 253]. To encompass both groups we included children who had been hospitalized 1) at a paediatric cardiology department due to a congenital or acquired heart defect or 2) after consultation at an ED due to acute injury or illness. Information on hospitalizations (number, data, length, and reason) was retrieved from the medical record by the research psychologist after possible participants were selected by the participating departments. For children included by the RUMC, PAH and Heartchild foundation, parent-report was used. We included children who experienced single and multiple hospitalizations with possible additional medical procedures.

Exclusion criteria were: (1) intellectual disability (IQ<70) as assessed by previous standardized test or evaluated by a clinician; (2) parental inability to read or write Dutch; (3) diagnosis of a chronic illness for the ED subgroup; (4) previous successful treatment for medically related PTSD; and (5) current psychological treatment.

Procedure

After having provided written informed consent, children and their parents completed a baseline measurement. The main goal of this measurement was to screen children for present post-traumatic stress symptoms using the Children's Responses to Trauma Inventory (CRTI) [184]. Children who (1) fulfilled at least two of the three DSM-IV (Diagnostic and Statistical Manual of Mental Disorder, 4th edition) PTSD symptom criteria (i.e. re-experience, avoidance or hyperarousal) measured by the CRTI and/or (2) had an above average score (i.e. >60th percentile) on the CRTI were invited for a semi-structured interview using the Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA) [186]. For children aged 4-7 we used the PTSD module of the Diagnostic Infant and Preschool Assessment (DIPA) [187]. The interview was scheduled as soon as possible after the baseline assessment was completed. The purpose of the interview was to divide children into having subthreshold or full diagnostic PTSD. Children were defined as having subthreshold PTSD when they met at least one CRTI criterion (by child and/or parent report) but did not meet all criteria for a full diagnostic PTSD during the interview. Only children with subthreshold PTSD were enrolled in the randomization. Children with full diagnostic PTSD were excluded from the study and were referred for psychosocial care.

Blinding & randomization

Stratified block randomization was performed by an independent research psychologist with 4 randomizations per block using opaque envelopes. The number of blocks was only known by the independent research psychologist. We stratified by trauma type (i.e. children who experienced a one-time hospitalization vs. children who experienced $\geq$2 hospitalizations or an additional medical procedure next to an one-time hospitalization [155]) and age. Four fixed blocks (trauma type 1/age 4-11; trauma type 1/age 12-15; trauma type 2/age 4-11; trauma type 2/age 12-15) were used. Participants and therapists could not be blinded due to the nature of EMDR. However, the research psychologist and research assistants performing all measurements and the treating physician were blinded of group allocation (they had no access to files containing this information, nor were they informed). Participants were instructed to not share their group allocation with the research team nor treating physician. To plan post-treatment measurements, the independent research psychologist provided a start date for both groups falling within 2 weeks after the interview (for the EMDR group this was the date of the intake and for the CAU group a random date was picked).

Measures

Parents and children (≥6 years of age) were asked to fill out online questionnaires (while thinking about a medical event the child experienced). Children aged 6-15 years filled out the same questionnaires. All questionnaires have adequate psychometric properties and Dutch normative data. Questionnaires were filled out at home at baseline and during two follow-up measurements that were planned 8 weeks and 8 months after the start of EMDR/CAU. Study data were collected and managed using GemsTracker [254].

Post-traumatic stress symptoms (primary outcome)

The Dutch version of the Children's Responses to Trauma Inventory (CRTI) [184] provides a reliable and valid self-report (for ages 8-18) and parent-report (for ages 4-18) measure of the DSM-IV-TR PTSD symptoms. It contains 24 PTSD items divided into three symptom clusters of PTSD (intrusion, avoidance, and hyperarousal). The PTSD total score can range from 17 to 85, with a higher score indicating more problems. Internal consistency was .75, .90, and .88 for self-report and .87, .92, and .90 for parent-report at T1, T2 and T3, respectively (Cronbach's α).

Additionally, semi-structured interviews were administered (only to participants meeting at least one of the two CRTI criteria mentioned before) to exclude children with a full diagnostic PTSD. The interview scores were not used for statistical analyses. We used the Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA) [186] for all participants aged 8-15 and the PTSD module of the DIPA [187] for all parents of participants aged 4-7. The interviews were administered by the research psychologist (trained in both instruments) at the Erasmus MC Sophia Children's Hospital.

Symptoms of depression (secondary outcome)

The Dutch Children's Depression Inventory 2 (CDI-2; 8-21 years)[190] has a parent version with 17 items on a 4-point Likert scale and a child version with 28 items on a 3-point Likert scale. The range of the total score of all items is 0 to 51 for parent report and 0 to 56 for child report. A higher score indicates more problems. Internal consistency was .81, .86, and .85 for self-report and .82, .84, and .86 for parent-report at T1, T2, and T3, respectively (Cronbach's α).

Symptoms of blood-injection-injury phobia (secondary outcome)

The BII subscale of the Screen for Child Anxiety Related Emotional Disorders (SCARED-NL; 7-19 years) [255] was used to measure child-report and parent-report of symptoms of BII phobia of the child. The BII subscale consists of 7 items and its total score ranges from 0 to 14 with a higher score indicating more problems. Internal consistency was .74, .69, and .73 for child-report and .71, .76, and .74 for parent-report at T1, T2, and T3, respectively (Cronbach's α).

Sleep problems (secondary outcome)

Children filled out the Dutch Sleep Self Report (SSR; 23 items; 7-12 years) [226] and parents filled out the parallel parent version called Child Sleep Habits Questionnaire (CSHQ; 35 items; 4-10 years)[194]. Maximum total scores are 69 for the SSR and 99 for the CSHQ. Again, a higher score indicates more sleep problems. Internal consistency was .73, .80, and .81 for the SSR and .81, .83, and .82 for the CSHQ at T1, T2, and T3, respectively (Cronbach's α).

Health-related quality of life (secondary outcome)

The TNO-AZL Questionnaires for Children's Health-Related Quality of Life (TACQOL; 8-15 years) provides a reliable and valid description of health-related quality of life [192]. Based on the 63 items, seven subscales can be computed, namely: body, motor, autonomy, cognition, social, positive emotions, and negative emotions. In contrast to the other questionnaires used, a higher score on the TACQOL subscales indicates better HrQoL. Cronbach's α on most subscales ranged from .66-.81, .62-.82, and .66-.83 for self-report and from .62-.88, .66-.90, and .74-.92 for parent report at T1, T2, and T3, respectively. The only poor to inadequate internal consistencies were found for the subscale autonomy: Cronbach's α was .66, .62, and .32 for self-report and .59, .52, and .44 for parent report at T1, T2, and T3, respectively.

Demographics

Demographic information was gathered with the general scale of the Rotterdam's Quality of Life Interview [256]. Furthermore, we checked for the experience of non-medical stressful life events using the life events scale of the Cognitive Emotion Regulation Questionnaire [156].

Intervention

The intervention was provided using the Dutch version of the standard EMDR

protocol for children [202]. Young children or children with pre-verbal memories were treated with the modified protocol by Lovett [203, 204]. In accordance to the standard protocol, children could make a drawing of their distressing medical experiences during therapy to facilitate a mental representation of the memory. All EMDR sessions took place at the Erasmus MC Sophia Children's Hospital in Rotterdam, the Netherlands, and were provided by five licensed and experienced clinical psychologists. Sessions were planned once a week and lasted approximately 50 minutes. Parents were allowed to be present during the sessions when the child agreed on this with the therapist, but were instructed not to interfere with the session. EMDR treatment was completed when Subjective Units of Distress (SUDs) of all selected memories regarding the medical trauma were zero. Only when this was impossible, EMDR treatment was ended when positive cognitions were established (rated by the child) and child, parents and therapist agreed that PTSD symptoms had sufficiently decreased. Therapists reported all details and dates to the independent researcher who documented this in protected files.

Children in the CAU (care-as-usual control) group also received standard medical care and standard study-related procedures (psychological screening and interview). They did not receive EMDR or any other form of psychotherapy.

Treatment integrity

Treatment integrity was ensured by providing regular supervision by an EMDR Europe consultant (licensed EMDR supervisor) and by rating all videotaped or documented sessions of 10 randomly chosen children (27%) as to adherence to the protocol. Rating was done by a research psychologist trained in the EMDR protocol and by two trained Master students in psychology (supervised by the aforementioned research psychologist) using an EMDR-specific treatment integrity checklist (16 items). A total score ranging from 0-16 can be computed from the checklist with a higher score indicating higher protocol adherence. All total scores given independently by all three raters were ranging between 13 and 16, indicating high agreement between the raters and high treatment integrity.

Statistical analyses

We used t-tests and χ^2-tests where appropriate to test differences in baseline characteristics between the EMDR and CAU groups.

We conducted Generalized Estimating Equations (GEE) with an unstructured correlation matrix to examine the effect of the intervention on all outcomes. The GEE analysis accounted for all assessments and were performed using intention-to-treat principles. Every outcome was analyzed separately. We included time of the assessments in every GEE analyses and added the interaction between group (EMDR vs. CAU) to test for the effects of the intervention. *Wald* χ^2 tests indicated whether the interactions were significant. If interactions were significant, we conducted subsequent analyses in which we included age, gender and whether the child had experienced ≥1 other non-medical stressful life event as covariates. For explorative analyses, we ran the same GEE analyses again separated by group (cardio vs. ED).

P-values of < 0.05 were considered significant. Cohen's *d* effect sizes were computed as the interaction effect of group by time multiplied by the number of weeks at the endpoint divided by the pooled standard deviations of the outcomes at T1 [227]. GEE accommodates missing data. SPSS version 24.0 was used for all statistical analyses [257].

Results

General characteristics

We randomized 74 children to the EMDR (*n*=37) and CAU (*n*=37) group (see **figure 1**). There were no significant differences between both groups on demographic baseline variables (see **table 1**). The average number of EMDR sessions received was *M*=3.53 (*SD*=1.90; range 1-9). Every child in the EMDR group was treated for at least one medically related distressing memory. The follow-up assessments took place M_{T2}=9.75 (*SD*=2.28) weeks and M_{T3}=8.15 (*SD*=.57) months after the start of EMDR/CAU. The time between baseline and follow-up assessments was not different for both groups. Two participants of the CAU group reported the start of mental health care after the 8 weeks follow-up. No study-related adverse events were communicated.

Long-term effectiveness of EMDR

Primary outcome

Child report: The interaction of group by time was not significant for PTSD symptoms reported by the child (see **table 2**). The improvement over time was also not significant for child-reported PTSD symptoms (*b*=-0.02, *p*=.641).

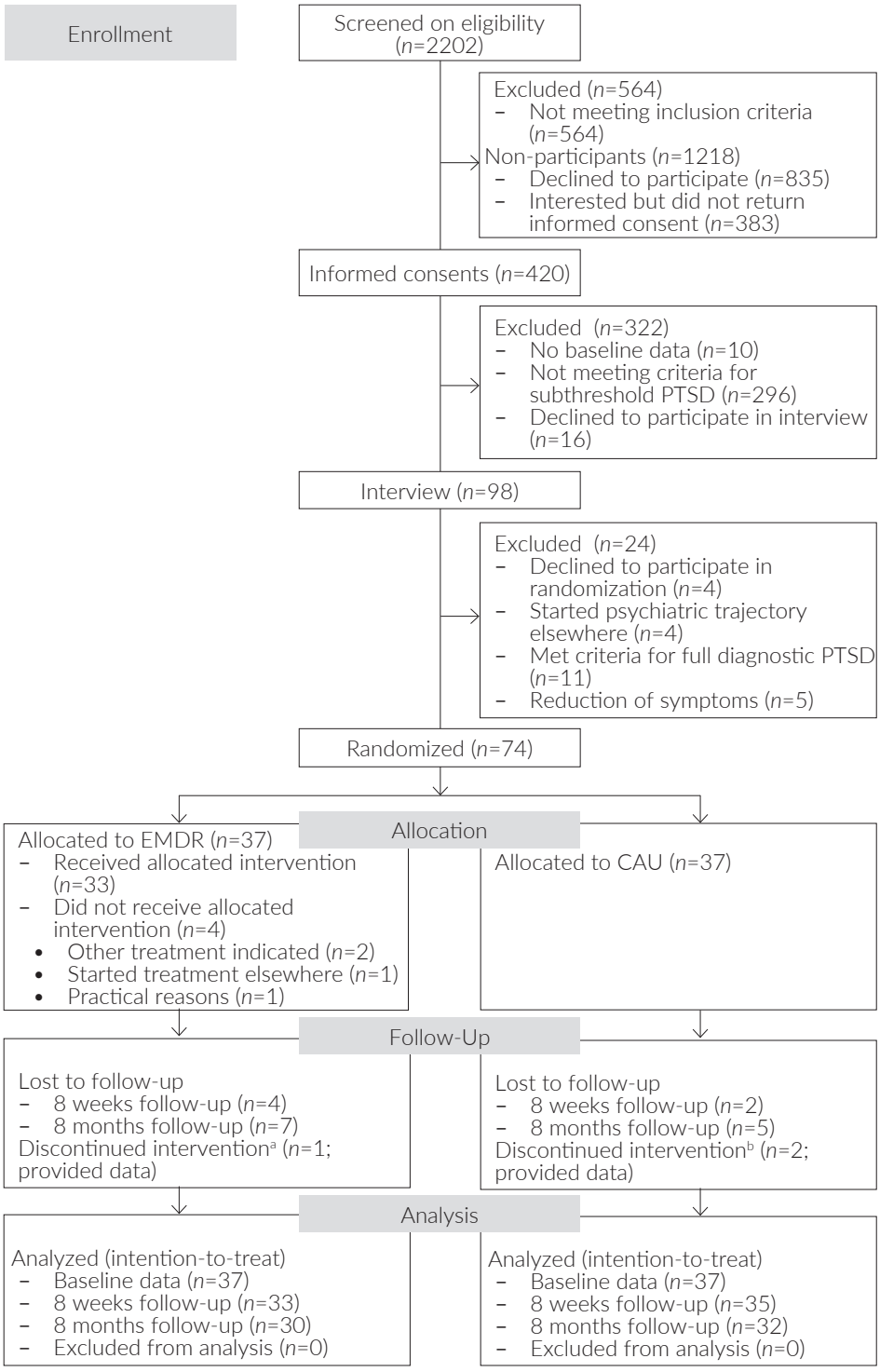
Enrollment
Screened on eligibility (n=2202)
Excluded (n=564)
– Not meeting inclusion criteria (n=564)
Non-participants (n=1218)
– Declined to participate (n=835)
– Interested but did not return informed consent (n=383)
Informed consents (n=420)
Excluded (n=322)
– No baseline data (n=10)
– Not meeting criteria for subthreshold PTSD (n=296)
– Declined to participate in interview (n=16)
Interview (n=98)
Excluded (n=24)
– Declined to participate in randomization (n=4)
– Started psychiatric trajectory elsewhere (n=4)
– Met criteria for full diagnostic PTSD (n=11)
– Reduction of symptoms (n=5)
Randomized (n=74)
Allocation
Allocated to EMDR (n=37)
– Received allocated intervention (n=33)
– Did not receive allocated intervention (n=4)
• Other treatment indicated (n=2)
• Started treatment elsewhere (n=1)
• Practical reasons (n=1)
Allocated to CAU (n=37)
Follow-Up
Lost to follow-up
– 8 weeks follow-up (n=4)
– 8 months follow-up (n=7)
Discontinued intervention[a] (n=1; provided data)
Lost to follow-up
– 8 weeks follow-up (n=2)
– 8 months follow-up (n=5)
Discontinued intervention[b] (n=2; provided data)
Analysis
Analyzed (intention-to-treat)
– Baseline data (n=37)
– 8 weeks follow-up (n=33)
– 8 months follow-up (n=30)
– Excluded from analysis (n=0)
Analyzed (intention-to-treat)
– Baseline data (n=37)
– 8 weeks follow-up (n=35)
– 8 months follow-up (n=32)
– Excluded from analysis (n=0)

Figure 1. (left) CONSORT flow chart.
*[a]Did not show up for last sessions and did not answer to calls nor e-mails. [b]Two participants of the CAU group started mental health services after T2. Participation rate: 100/(total non-participants + informed consents)*informed consents.*

Parent report: The interaction of group by time was not significant for parent-reported PTSD symptoms of the child neither (see **table 2**). However, the improvement of child PTSD symptoms over time reported by parents was significant (*b*=-0.20, *p*=.000).

Secondary outcomes

Child report: There were no significant interactions of group by time for any of the secondary child-report outcomes (see **table 2**). Both groups showed improvements on the secondary outcomes over time: depressive symptoms (*b*=-0.06, *p*=.000), symptoms of BII phobia (*b*=-0.05, *p*=.000), sleep problems (*b*=-0.04, *p*=.020), HrQoL-body (*b*=0.07, *p*=.000), HrQoL-Motor (*b*=0.03, *p*=.022), HrQoL-Autonomy (*b*=0.02, *p*=.034), HrQoL-Cognitive (*b*=0.04, *p*=.004), HrQoL-Positive Emotions (*b*=0.03, *p*=.000), and HrQoL-Negative Emotions (*b*=0.02, *p*=.004). The improvement over time was not significant for child-reported HrQoL-Social (*b*=0.03, *p*=.053).

Parent-report: One interaction of group by time was significant for parent-report (see **table 2**). That is, EMDR was more effective than CAU in reducing parent-reported BII-phobia of the child. This interaction was still significant when controlling for age, gender, and other non-medical stressful life events (*b*=-0.03, *p*=.033). Furthermore, both groups showed improvements on the following secondary outcomes over time: depressive symptoms (*b*=-0.04, *p*=.009), symptoms of BII phobia (*b*=-0.03, *p*=.000), sleep problems (*b*=-0.07, *p*=.000), HrQoL-body (*b*=0.03, *p*=.037), HrQoL-Cognitive (*b*=0.03, *p*=.045), HrQoL-Social (*b*=0.03, *p*=.001), and HrQoL-Negative Emotions (*b*=0.03, *p*=.000). The improvement over time was not significant for parent-reported HrQoL-Motor (*b*=0.02, *p*=.083), HrQoL-Autonomy (*b*=0.01, *p*=.108), and HrQoL-Positive Emotions (*b*=0.00, *p*=.543).

Explorative analyses

One interaction of group by time was significant when running the GEE analyses by group. For the cardiology group, EMDR was more effective than CAU in reducing parent-reported BII-phobia of the child (*b*=-0.06, *p*=.000). The same interaction was not significant for the ED group (*b*=-0.00, *p*=.854).

Table 1. Baseline demographics.

	N	Total	EMDR group *n*=37	CAU group *n*=37	χ^2 ***or t value***	***P-value***
Child						
Age in years, M ± SD	74	9.6 ± 2.9	9.8 ± 2.7	9.4 ± 3.1	-0.52	0.60
Gender - male, n (%)	74	49 (66.2)	25 (67.6)	24 (64.9)	0.06	0.81
Ethnicity, n (%)	72				3.20	0.20
Dutch		59 (81.9)	32 (88.9)	27 (75.0)		
Other Western		4 (5.6)	2 (5.6)	2 (5.6)		
Non-Western		9 (12.5)	2 (5.6)	7 (19.4)		
Prior non-medical stressful life event, n (%)	67				0.03	0.86
Yes		55 (82.1)	29 (82.9)	26 (81.3)		
No		12 (17.9)	6 (17.1)	6 (18.8)		
Parental						
Education, n (%)	74				0.36	0.84
High		41 (55.4)	21 (56.8)	20 (54.1)		
Medium		30 (40.5)	15 (40.5)	15 (40.5)		
Low		3 (4.1)	1 (2.7)	2 (5.4)		
Medical						
Department, n (%);	74				0.05	0.82
Cardiology		39 (52.7)	19 (51.4)	20 (54.1)		
Emergency unit		35 (47.3)	18 (48.6)	17 (45.9)		
Trauma Type, n (%)	74				0.32	0.57
I – Single PTME		16 (21.6)	9 (24.3)	7 (18.9)		
II – Multiple PTMEs		58 (78.4)	28 (75.7)	30 (81.1)		
No. of hospitalizations, M ± SD	71	4.01 ± 4.00	4.5 ± 4.4	3.6 ± 3.5	-0.98	0.33
Length of hospitalization(s) in days, M ± SD	59	28.14 ± 47.23	31.7 ± 54.9	24.2 ± 37.6	-0.61	0.55
Time since last medical event in years, M ± SD	71	1.76 ± 1.42	1.7 ± 1.5	1.8 ± 1.4	0.27	0.79
Type of medical event, n (%)	74				0.45	0.93
Heart Disease		39 (52.7)	19 (51.4)	20 (54.1)		
Accident (motor-vehicle)		7 (9.5)	3 (8.1)	4 (10.8)		
Accident (other)		14 (18.9)	7 (18.9)	7 (18.9)		
Acute illness		14 (18.9)	8 (21.6)	6 (16.2)		

χ^2 tests were used for categorical variables. T-tests were used for continuous variables. M, mean; no., number; PTME, potentially traumatic medical event; SD, standard deviation.

Discussion

The present RCT examined the long-term effectiveness of EMDR on PTSD symptoms and other psychological complaints in children with medically related subthreshold PTSD. The results show that most outcomes improved over time with one significant difference between the EMDR and CAU group.

We found preliminary evidence that EMDR was significantly superior than CAU in reducing parent-reported symptoms of children's BII-phobia. It is possible that this was a random finding. However, it is supported by earlier research that has found EMDR to be effective in reducing dental phobia [232, 233]. This could have high clinical relevance as phobic people tend to avoid the source of their fear. Consequently, children with symptoms of BII-phobia might avoid medical treatment. This is especially concerning considering the necessity of continuous medical checkups for children affected by a heart disease. By reducing BII phobia symptoms, EMDR contributes to medically necessary adherence. Future research is needed before validated statements can be made. This is also true considering the fact that we only found a superior long-term effect for parent-reported BII-phobia of the child. On self-report, both the EMDR and the CAU group showed improvement. Nevertheless, it has been argued that parent report might identify recovery from anxiety symptoms better than child report [258]. Unfortunately, we could not control for parental psychopathology, which has been found to influence parent report of the child's mental health, as we did not measure parental psychopathology [259]. Our results regarding the effectiveness of EMDR in treating BII phobia symptoms warrants further research in this area. Especially as the effect of EMDR on BII phobia seemed to be present in the cardiology group only.

Our results that EMDR was not superior than CAU in reducing symptoms of PTSD, depression, and sleep problems and in improving HrQoL over time are not in line with earlier studies with ≥6 months post-treatment follow-ups [67, 78, 249]. In our view, there are five major possible explanations for this. **First**, CAU did not represent standard medical care in this study as all participants received detailed information about possible reactions to a potentially traumatic medical event (through an information letter), a psychological screening (i.e. questionnaires), an interview about PTSD symptoms with a psychologist and a conversation together with their parents about the nature of their PTSD symptoms after the interview.

Table 2. Means and standard deviations for child- and parent-reported outcomes at T1, T2 and T3, and interaction effects of group by time.

	EMDR		
	T1 *n*=37	**T2** *n*=33	**T3** *n*=30
Child report			
CRTI PTSD score	45.00 ± 9.17	32.00 ± 11.80	29.97 ± 10.93
CDI-2 total score	11.23 ± 6.04	6.17 ± 5.27	6.18 ± 5.22
SCARED BII	6.31 ± 3.23	4.30 ± 2.83	3.75 ± 2.40
SSR	38.63 ± 6.48	33.80 ± 6.04	33.57 ± 7.24
TACQOL Body	22.54 ± 5.13	25.80 ± 4.06	25.07 ± 5.19
TACQOL Motor	27.14 ± 5.74	29.83 ± 3.71	27.86 ± 4.63
TACQOL Auto	30.26 ± 2.59	30.97 ± 2.28	30.75 ± 1.67
TACQOL Cognit	25.63 ± 6.01	27.00 ± 4.91	28.46 ± 4.16
TACQOL Social	27.11 ± 5.37	29.17 ± 3.33	28.43 ± 3.48
TACQOL EmPos	12.26 ± 2.66	14.17 ± 2.17	13.57 ± 3.00
TACQOL EmNeg	11.54 ± 2.85	13.20 ± 2.16	13.25 ± 2.65
Parent report			
CRTI PTSD score	44.51 ± 10.80	32.94 ± 10.44	29.37 ± 9.04
CDI-2 total score	17.59 ± 6.42	12.06 ± 6.03	12.17 ± 6.75
SCARED BII	5.38 ± 3.06	4.52 ± 3.05	2.97 ± 2.08
CSHQ	51.14 ± 8.61	46.12 ± 8.20	44.48 ± 7.13
TACQOL Body	24.16 ± 4.46	25.50 ± 4.05	26.62 ± 4.19
TACQOL Motor	27.51 ± 4.26	29.47 ± 3.15	29.45 ± 2.44
TACQOL Auto	29.57 ± 2.74	30.34 ± 2.16	30.07 ± 2.20
TACQOL Cognit	25.22 ± 4.80	26.06 ± 5.51	28.69 ± 4.38
TACQOL Social	26.76 ± 3.52	28.88 ± 3.37	29.38 ± 2.88
TACQOL EmPos	13.24 ± 3.03	14.66 ± 2.16	14.07 ± 3.06
TACQOL EmNeg	9.92 ± 3.30	12.06 ± 2.85	12.52 ± 2.08

Data are represented as mean ± standard deviation.

CAU, care-as-usual; CDI-2, Children's Depression Inventory 2; CI, confidence interval; CRTI, Children's Responses to Trauma Inventory; CSHQ, Child Sleep Habits Questionnaire; PTSD, post-traumatic stress disorder; SCARED BII, BII subscale of the Screen for Child Anxiety Related Emotional Disorders; SSR, Sleep Self Report; TACQOL, TNO-AZL Questionnaires for Children's Health-Related Quality of Life.

[a]*GEE analyses. Interaction of group by time.*

[b]*GEE analyses. P-values indicates level of significance of the group by time interaction. *Significant.*

[c]*Cohen's d*

CAU			GEE analyses		
T1 *n*=37	**T2** *n*=35	**T3** *n*=32	***B***[a]	***p***[b]	**Effect size**[c] **[95% CI]**
44.37 ± 8.32	31.54 ± 11.76	30.77 ± 10.75	-.10	.26	-.37 [-.85, .12]
9.03 ± 6.38	7.07 ± 6.55	6.58 ± 6.21	-.05	.06	-.25 [-.73, .23]
5.16 ± 3.12	4.37 ± 3.20	3.15 ± 3.43	-.00	.85	-.03 [-.51, .45]
35.41 ± 4.92	34.59 ± 6.80	33.04 ± 5.71	.05	.21	.30 [-.19, .78]
22.44 ± 6.04	23.56 ± 5.89	26.96 ± 5.71	-.06	.06	-.36 [-.84, .13]
28.00 ± 4.23	28.78 ± 3.75	30.42 ± 2.16	-.05	.09	-.31 [-.79, .18]
30.59 ± 2.86	30.85 ± 2.43	31.62 ± 0.75	-.02	.28	-.19 [-.67, .30]
24.78 ± 6.03	25.63 ± 6.45	26.27 ± 5.70	.01	.76	.05 [-.43, .53]
28.63 ± 4.32	28.52 ± 3.94	29.69 ± 3.51	.00	.86	.03 [-.45, .51]
12.56 ± 3.02	13.04 ± 2.93	14.35 ± 2.04	-.01	.66	-.08 [-.56, .40]
11.53 ± 3.13	11.78 ± 3.07	12.38 ± 3.06	.02	.31	.18 [-.30, .66]
43.46 ± 9.78	35.43 ± 12.58	32.19 ± 10.77	-.03	.56	-.11 [-.57, .34]
14.65 ± 6.63	12.14 ± 7.20	11.63 ± 6.92	-.00	.95	-.01 [-.47, .45]
4.49 ± 3.05	4.17 ± 3.48	4.16 ± 3.38	-.03	.01*	-.36 [-.82, .11]
48.76 ± 7.96	47.35 ± 8.15	46.56 ± 8.50	-.05	.15	-.20 [-.66, .26]
24.46 ± 4.72	25.73 ± 4.43	25.78 ± 4.99	.03	.30	.19 [-.27, .64]
28.76 ± 3.83	29.48 ± 3.62	28.75 ± 4.25	.04	.06	.34 [-.12, .80]
30.08 ± 2.55	30.24 ± 2.36	30.59 ± 2.15	.00	.93	.01 [-.44, .47]
25.65 ± 5.49	26.67 ± 6.17	25.97 ± 5.92	.06	.06	.36 [-.10, .82]
28.41 ± 3.63	28.36 ± 4.60	29.13 ± 3.83	.02	.21	.19 [-.27, .65]
13.70 ± 2.73	13.85 ± 2.95	14.22 ± 2.57	-.00	.78	-.04 [-.49, .42]
10.54 ± 3.01	11.42 ± 2.84	11.59 ± 3.04	.02	.10	.26 [-.20, .72]

Trauma-related symptoms were thereby acknowledged, validated, and normalized. This is not part of standard medical care in the Netherlands. It has been found earlier that merely participating in a psychological study and/or receiving psychoeducation can improve mental health [228, 260, 261]. **Second**, the average PTSD symptom scores appear lower in our sample (age 4-15) compared to the sample of De Roos et al. [67] who also used the CRTI to measure PTSD symptoms in treatment-seeking youth (age 8-18) following single-incident trauma. It is possible that EMDR shows its superior effects only when symptom severity is high, whereas a brief trauma-focused psychoeducational intervention might be equally effective when symptom severity is moderate. This is in line with research into online interventions based on cognitive behavioural therapy that found improvements and usefulness primarily in children and adults with high initial PTSD symptom levels following medical events [262-264]. **Third**, it is likely that participants of both groups were more motivated than non-participants to address psychosocial needs and seek help, which might have washed out differences between the EMDR and CAU group on the long run. Furthermore, more than half of all participants had at least one parent with a high educational level. Together with professional psychological attention, motivation and cognitive skills might have led to improvements in the CAU group. **Fourth**, although our sample size of 74 children was close to the aimed 78 participants, perhaps we would have found significant group differences with a larger sample size. **Fifth**, most outcome variables improved over time regardless of the group. Therefore, it might be possible that our study showed natural improvements without any study-related effects. However, children were included into the study on average almost 2 years after their last medical event and still showed subthreshold levels of PTSD at baseline. Therefore, the chances seem small that the significant improvements are unrelated to the study.

Strengths & Limitations

While this study is the first to evaluate the effectiveness of EMDR in a relatively large sample of children with medically related subthreshold PTSD recruited throughout the Netherlands, including a broad age range, multi-informant outcomes, high treatment integrity, and single-blind randomization, some limitations must be considered. **First**, it is possible that some participants in the CAU group might have arranged psychosocial treatment for themselves during the study period. However, participants were asked friendly to communicate any contact with a mental health specialist during the study period. Two children of the CAU group started EMDR elsewhere between both follow-up assessments. **Second**, we did not measure parental mental health nor did parents

receive treatment. Research suggests that parental mental health is a strong predictor for child PTSD symptoms and that involving parents in the treatment of their child might be beneficial [169, 240, 265, 266]. **Third**, it must be noted that the used self-report questionnaires were not validated for children aged 6 and 7 years old. However, our main aim was to compare changes between the EMDR and CAU group over time (and not to make comparisons to the normative data). It is still possible that their responses were biased because parents helped them to fill out the questionnaires. **Fourth**, families with a low educational level were underrepresented in this study which might limit generalizability of the findings. **Fifth**, participation rate was low in our sample (26%, see figure 1) which may limit generalizability of our findings. **Sixth**, it was not the scope of the article to explore whether severity of the heart condition is related to treatment outcome. This could be relevant for future studies. **Finally**, this study is the first RCT investigating the effectiveness of EMDR specifically for children with medically related subthreshold PTSD. It is unclear to which extent our findings are generalizable to other kind of traumas or to children with full diagnostic PTSD.

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Conflict of Interest

none declared

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

CHAPTER 8

General discussion

Scars remind us where we've been -
they don't have to dictate where we are going

Joe Mantegna

PART I: PSYCHOLOGICAL OUTCOMES AFTER PEDIATRIC HOSPITALIZATION

Children and adolescents experiencing physical illness or injury are often exposed to potentially traumatic medical events. Medical events, such as hospitalizations and medical procedures, can lead to posttraumatic stress reactions and mental health problems in children and their parents [267]. Hospitalizations and medical procedures are especially common after a diagnosis of congenital heart disease (ConHD). Pediatric patients with ConHD overall experience longer hospitalizations and more medical procedures compared to other pediatric patients [268]. 76% of all pediatric hospitalizations for ConHD include a minor or major medical procedure. Consequently, an important aim of this thesis was to examine medically related posttraumatic stress reactions in children with ConHD and their parents.

Main findings

In **chapter 2**, we reviewed the scarce literature on medically related posttraumatic stress in children with (congenital) heart disease. Based on relevant key words (corresponding to posttraumatic stress disorder and congenital heart disease) our literature search identified only five studies with a focus on posttraumatic stress in children and adolescents with a heart disease. Only four of these studies used standardized measurements. Three of the five reviewed studies included children with a congenital heart disease. The prevalence rates for PTSD measured with standardized instruments ranged from 12-31%. These rates are comparable to those of children with other chronic physical illnesses and also adults with ConHD [118, 147]. Furthermore, our findings showed an elevated risk for PTSD in children with ConHD compared to lifetime prevalence rates of 0.4-9% in representative general population samples of children and adolescents [33, 34]. Interestingly, two reviewed studies discovered elevated PTSD prevalence rates many years (13.7 $\pm$ 2.48 & 7.3 $\pm$ 7.3 years) after the potentially traumatic medical event [111, 112]. However, both studies were cross-sectional which makes evaluations over time of PTSD onset and symptom course over the years impossible. Furthermore, two reviewed studies also reported prevalence rates of subthreshold PTSD in children with a heart disease using standardized measurements [110, 112]. These rates were 12% (experiencing some DSM-IV PTSD symptoms) and 14% (meeting two of the three DSM-IV PTSD symptom criteria). All reviewed studies were very

heterogeneous regarding age, type of heart disease, instruments used, and time elapsed since the medical event. More systematic research in this area is highly needed in order to draw more firm conclusions. Nevertheless, we can conclude that children with ConHD undergoing surgery are at risk of developing PTSD symptoms. The results of our review clearly underline a need for screening for PTSD symptoms in children and adolescents with ConHD.

In **chapter 3**, we reviewed 23 studies regarding mental health problems of parents of children with ConHD. Results showed that parents, especially mothers, have an elevated risk for mental health problems, including psychological distress, anxiety, depression, somatization, hopelessness, and posttraumatic stress symptoms. Psychological distress (i.e. experiencing symptoms of a mental disorder) was found in 30-80% of parents following hospitalization of their child [124]. After diagnosis of ConHD, PTSD was present in up to 88% of mothers and up to 66% of fathers [128]. After cardiac surgery, 16.4% of mothers and 13.3% of fathers were found to have PTSD in a study by Helfricht, Latal, Fischer, Tomaske, and Landolt [132] and 19% of parents were found to have PTSD in another study by Farley et al. [136]. These prevalence rates of PTSD are clearly elevated compared to PTSD prevalence rates in adults from the general population [144, 269, 270].

Symptoms of PTSD, anxiety, and depression were reported mainly at time of the diagnosis and in the immediate weeks and months after cardiac surgery. Contradictory results were found regarding the few long-term ($\geq$1 year after diagnosis/surgery) studies. Two studies showed persistent parental psychological distress, especially in mothers with an avoidant attachment style [122, 142], while another study showed that mental health problems (e.g. anxiety) declined to normative levels 12-50 months post-surgery [143]. Evidently, more research is needed to understand the long-term course of mental health problems in parents of children with ConHD. It is without doubt that parents of children with ConHD face various stressful periods often resulting in elevated symptoms of mental disorders, such as PTSD. This is especially concerning when we consider the fact that parental posttraumatic stress reactions following the child's trauma are associated with child PTSD symptoms [253, 271]. Therefore, we also recommended parental mental health screening.

In **chapter 4**, we report on our screening of a large baseline cohort of children with a heart disease and children with acute physical illness or injury (serving as a

possible control group) who had been hospitalized. Half of all participating children had been hospitalized after consultation at a pediatric cardiology department (due to a congenital or acquired heart disease) and the other half had been hospitalized after consultation at an emergency department (due to acute illness or injury). This screening formed the first step of our RCT (which is described more in detail in part II of this thesis). 420 children aged 4-15 years (*M*=9.33; *SD*=3.18) were willing to participate in the baseline screening and data of 399 of them could be analyzed.

Combined prevalence rates (i.e. symptoms disclosed by either child and/or parent report) revealed that 26% of the participating children showed elevated medically related PTSD symptoms and 31% showed elevated depressive symptoms. We also investigated child-reported anxiety symptoms. The most present anxiety symptoms were situational phobia (25%), social phobia (21%), and BII phobia (15%). The results of our study are generally in line with other studies with pediatric samples [22, 272, 273]. However, Davydow, Richardson, Zatzick, and Katon [59] reviewed psychological outcomes after pediatric critical illness and found comparable prevalence rates of clinically significant PTSD symptoms (10-28%), but found lower prevalence rates of significant depressive symptoms (7-13%). It might be possible that the prevalence of depressive symptoms was somewhat overestimated in our sample. Considering the low participation rate (24%), we cannot rule out that especially distressed children participated in our study and were therefore overrepresented. Although, in a study of adolescents with inflammatory bowel disease (IBD) with a comparable participation rate (29%), similar levels of depressive symptoms (30%) were found [272].

Next to prevalence rates, we were interested in the role of trauma type. Illness and injury can encompass single (e.g. one acute hospitalization after an accident), but also multiple (e.g. multiple hospitalizations because of a ConHD) potentially traumatic events. We included 115 children (29%) with type I trauma (i.e. single hospitalization) and 284 children (71%) with type II trauma (i.e. $\geq$2 hospitalizations or at least one additional invasive medical procedure next to a single hospitalization). The combined (based on child and/or parent report) prevalence rates of PTSD symptoms and depressive symptoms were significantly higher after type II trauma compared to type I trauma. Based on child report only, no significant differences were found between type I and type II trauma regarding any prevalence rates. Parents, on the other hand, reported more elevated PTSD symptoms of the child after type II than type I trauma. This difference between child and parent report

might be due to the fact that 63% of the children included with type II trauma were children with a heart disease and 83% of the children with type I trauma were children hospitalized via the ED because of acute illness of injury. It has been suggested that chronic illness (here heart disease) of the child can be experienced as more threatening to parents than to children themselves [253]. Parents might realize the longitudinal impact of living with a chronic illness more than children. In addition, it has been found earlier that parents' own PTSD symptoms are associated with their report of child's PTSD symptoms [165]. We could not perform statistical analyses on this relationship as parental PTSD symptoms were not measured.

In line with the above, trauma type appeared to be a risk factor for child PTSD symptoms only for parent report (not for child report). Furthermore, the strongest risk factor for child PTSD symptoms (by child and parent report) was parental stress. This is in line with earlier studies of similar aged children after accidental trauma or pediatric injury [151, 166]. This is alarming considering that up to 80% of parents of children with a ConHD can experience distress (chapter 3). Family functioning was not associated with child PTSD symptoms in our sample. While not expected, this finding is in line with another study that found family functioning to be associated with parental PTSD symptoms, but not child PTSD symptoms after unintentional pediatric injury [167]. However, our finding might also be due to the fact that we used the general functioning subscale of the Family Assessment Device (FAD). Another study found a significant association between PTSD and family functioning in adolescent cancer survivors only on the subscales problem solving, affective responsiveness, and affective involvement of the FAD [274]. Another risk factor for PTSD symptoms in our study was low level of parental education, which was related to higher parent-reported PTSD symptoms of the child. We found no significant child (age, gender) or objective medical (length and time since last hospitalization, cardio vs. ED) risk factors for child PTSD symptoms. In sum, our baseline cohort study found heightened prevalence rates of symptoms of PTSD, depression and anxiety in previously hospitalized children. The strongest risk factor for medically related PTSD symptoms of the child was parental stress. Medically related trauma type and low level of parental education appeared to be risk factors of parent-reported symptoms of PTSD of the child.

Clinical implications

Part I of this thesis underlines the elevated risk for children and their parents of developing posttraumatic stress reactions after pediatric hospitalization. In line with other studies into mental health screening after pediatric injury or families of children with complex ConHD, we recommend structural mental health screening in pediatric health care settings [246, 275]. The guideline on PTSD of the National Institute for Health and Care Excellence (NICE) suggests active monitoring (which has also been called watchful waiting) of PTSD symptoms in children, young people and adults in the acute phase after a PTE [65]. Active monitoring implies regular monitoring of posttraumatic stress reactions. However, implementing a psychosocial screening routine into pediatric health care settings has been shown to be complex [276, 277]. The challenge is to incorporate mental health screening as efficient and cost-effective as possible into busy medical health care. Therefore, we recommend that in future research a decision tree should be developed and studied in order to organize the best fitted type and intensity of monitoring for different pediatric populations.

Collaborative care is a multidisciplinary model where health care professionals work together in a team, integrating physical and mental health [278]. Possibly, stigmas could be minimized when mental health professionals are part of the health care team from the beginning. By applying such a model, on-site screening could be introduced as a routine part of health care. Face-to-face mental health screening integrated within medical care and done by an involved health-care provider has been suggested to reach higher feasibility [279, 280]. This is in line with our study where web-based screening introduced by an external researcher yielded low participation rates (chapter 4). Participation rates might have been higher when screening was introduced by an involved health-care provider. Furthermore, research suggests that screening should be systematically presented as a routine part of outpatient medical follow-up visits [281]. This might be feasible with chronically ill children, but children who are hospitalized for acute illnesses or minor injuries might not have any planned follow-up appointments in the hospital. Therefore, computerized screening or screening apps, introduced during hospitalization, can be useful. In the Netherlands (and also at the Erasmus Medical Center), various attempts have already been made to implement web-based screening [e.g. 282]. The clinical utility and efficiency of a screening might be improved when questionnaires are brief, reliable, easy, and encompass somewhat illness-specific questions [283]. A

computerized system applying software algorithms to select optimal questions could be an option to organize screening as efficient as possible [e.g. 284]. Clearly, the optimal timing, the amount, and the type of instruments that should be used warrant further research.

Based on this thesis we make the following recommendations:

- We recommend to develop an evidence-based regular mental health screening process for assessments during and after all pediatric hospitalizations (directed by a decision tree) including PTSD symptoms, depression, anxiety, sleep problems, and quality of life
- Parental stress during and after hospitalization of a child should be limited as much as possible and parents should receive adequate support. Especially parents with a low educational level and parents of children who experience multiple hospitalizations should receive extra attention from a dedicated (mental) health specialist with expertise in this field.

PART II: EFFECTIVENESS OF EMDR AFTER PEDIATRIC HOSPITALIZATION

Despite the evidence of medically related posttraumatic stress reactions in children and parents, research into psychosocial interventions in this field is still very scarce. EMDR has shown promising results in a few RCTs that included children who experienced mainly non-medical trauma (such as (sexual) abuse and (natural) disasters) [73, 74]. At the start of our study, no RCT had yet specifically focused on the effectiveness of EMDR for medically related subthreshold PTSD in children. Subthreshold PTSD (i.e. having significant PTSD symptoms below the threshold for a full diagnostic PTSD) is known to be associated with similar impairment and distress as a full diagnostic PTSD [38]. The three studies that have investigated the effects of EMDR in pediatric medical samples only included children who had experienced a traffic accident [76-78]. The RCT described in this thesis was the first to test the effectiveness of EMDR for children with medically-related subthreshold PTSD after hospitalization for illness or injury.

Main findings

In **chapter 5**, we described the design of our RCT to evaluate the effectiveness of EMDR for children and adolescents with medically related subthreshold PTSD. Our goal was to randomize children who had been hospitalized and reported subthreshold PTSD during the baseline assessment of our RCT into two groups: EMDR or care-as-usual (CAU; medical care only). Our main aim was to evaluate the short and long-term effectiveness of EMDR for children with medically related subthreshold PTSD.

In **Chapters 6**, the short-term effectiveness of EMDR is described (i.e. *M*=9.7 weeks after the start of EMDR/CAU). Children in both groups improved significantly on all outcomes from baseline to short-term follow-up. This might be explained by the fact that participants in both groups (also the CAU group) engaged in a psychological screening and an interview with a psychologist. Research participation alone and repeatedly filling out questionnaires can lead to changes in cognitions, emotions, and behavior [228]. Eliciting awareness and acknowledging medically related psychological problems during our research might have been sufficient to improve symptoms in our sample. Our finding that EMDR was not superior to CAU in reducing PTSD symptoms is in contrast to earlier research into the effectiveness of EMDR for children [73, 74]. However, no previous study has specifically examined the effectiveness of EMDR for medically related subthreshold PTSD. Earlier research suggests EMDR to be effective for children with full diagnostic PTSD, but it might not be of added therapeutic value for medically-related subthreshold PTSD in addition to a careful mental health screening.

In our study, EMDR did have an added value in reducing child-reported symptoms of blood-injection-injury (BII) phobia and depression, and child-, and parent-reported sleep problems of the child. These findings are in line with previous research, showing that EMDR can be effective in improving depression in children and adolescents [67] and dental phobia and sleep quality in adults [221, 232]. By reducing symptoms of BII phobia and depression, EMDR can be beneficial for medical adherence as phobic and depressed patients tend to avoid medical treatment [234, 285]. We recommend additional research to confirm our findings supporting the value of EMDR in treating BII phobia, depression, and sleep problems in children and adolescents after hospitalization.

In **chapter 7**, we explored the long-term effectiveness of EMDR in children and adolescents with medically related subthreshold PTSD (i.e. *M*=8.2 months after the start of EMDR/CAU). There was one superior effect of EMDR found. Namely, parent-reported symptoms of BII phobia of the child reduced significantly more in the EMDR group compared to the CAU group. Again, this finding is in line with previous research and might be of high clinical relevance to medical adherence. Interestingly, EMDR was superior to CAU in reducing *child*-reported BII phobia symptoms at short-term (see chapter 6), but *parent*-reported BII phobia of the child at long-term. Clearly, the use of EMDR for BII phobia symptoms in children and adolescents warrants future research.

We did not find any superior effects of EMDR on subthreshold PTSD, symptoms of depression, sleep problems, and HrQoL at long-term follow-up. This is in contrast to other long-term (≥6 months post-treatment) studies regarding a variety of childhood traumas [67, 78, 249]. There are various possible explanations. As mentioned earlier, participation in the baseline screening might have led to acknowledgment, validation, and normalization of psychological symptoms and thereby might have been therapeutic in itself. Furthermore, it is possible that EMDR might be more effective when (PTSD) symptom severity is high. We only included children with subthreshold PTSD (aiming on secondary prevention). Another explanation for the very few significant differences in treatment effect between EMDR and CAU could be the low participation rate, possibly resulting in more highly motivated participants. Additionally, improvements could be due to natural remission over time. However, this is unlikely as children were included up to 5 years (*M*=1.76) after their last medical event and still met criteria for subthreshold PTSD.

Limitations of our RCT

The limitations of our RCT have been described in the Discussion sections of this thesis. The most important are mentioned again below:
Though our sample was larger than samples used in earlier RCTs evaluating the effectiveness of EMDR for children, we did not reach full power (sample size of 74 instead of the aimed 78). Furthermore, the participation rate was low during the screening assessment (24%) and families with a low educational level were underrepresented in our sample. Generalizability of the findings is therefore limited. Moreover, we did not measure parental mental health nor did parents receive psychotherapy.

Initial PTSD in parents is related to poorer recovery from PTSD in the child and involving parents in the treatment of their child might be beneficial [240, 253, 265].

Clinical implications

Mental health screening has limited value without adequate psychosocial follow-up care. Children with ConHD and their parents report a need for psychosocial care [62]. However, the referral rate of pediatricians to mental health services is low and limited engagement of patients can persist [286, 287]. Specific beliefs or stigmas regarding mental health care and structural constraints (e.g. costs, time burden) can limit actual use of mental health care [288]. Integrating mental health care into pediatric health care settings is therefore crucial to improve the rates of children that receive the needed psychosocial care in time [289, 290].

The results of our RCT (described in part II of this thesis) suggest that EMDR might not be necessary to treat subthreshold PTSD reactions to potentially traumatic medical events. Future research should examine which patients should be provided with EMDR. It has been found that impairment increases with rising number of PTSD symptoms in adults [39, 291]. Therefore, the intensity and/or frequency of symptoms might be more relevant than the diagnostic status when developing a decision tree for screening and treating mental health problems [292]. A stepped-care model, ensuring that people receive care according to their needs, might facilitate treatment engagement and efficiency [293].

Stepped-care model

In line with the results of our study, it has been suggested that screening and subsequent psychosocial interventions should be administered using a stepped-care approach [294]. The first step of this approach implies a brief mental health screening for all children/families who enter pediatric health care settings (see part I of this thesis). Brief rescreening about 4-6 weeks afterwards might be useful to account for possible natural remission of symptoms (in line with active monitoring) [279]. The second step is to identify those children at risk for, or suffering from, elevated mental health problems (e.g. posttraumatic stress reactions) and offer them a more extended screening and low-intensive interventions as secondary prevention [295-297]. These (online) interventions might be introduced by mental

health professionals who are part of the primary care setting and should promote coping skills, social support, and information on possible symptoms through psychoeducation. Third, children who experience severe distress should be referred for more intensive psychotherapy (e.g. EMDR).

Comparable to the stepped-care model, Kazak [298] developed the Pediatric Psychosocial Preventative Health Model (PPPHM) for assessing and treating children and their families in pediatric health care settings. This model is based on allocating children into universal, targeted and clinical services based on their risk status and level of need (see **figure 1**). Future research should explore whether EMDR should only be used as a clinical treatment for those at the top of the pyramid.

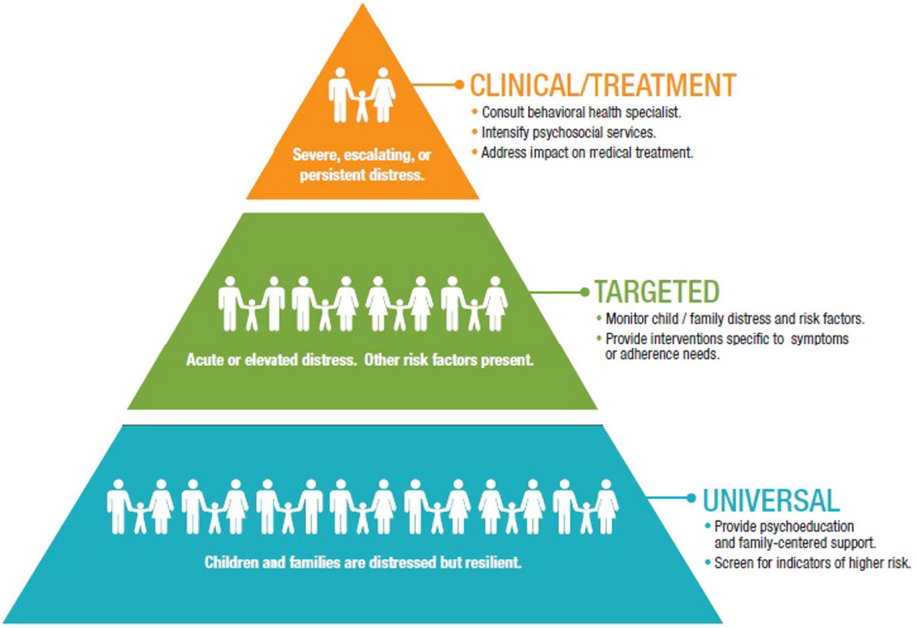

Figure 1. Pediatric Psychosocial Preventative Health Model.

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FUTURE DIRECTIONS

Research into PTSD after potentially traumatic medical events is a fast-growing area of study in PTSD research [299]. However, only 6.4% of PTSD literature is dedicated to children and adolescents [299]. As many psychiatric problems originate during childhood and adolescence, future research should focus more on children (especially regarding PTME's) [300].

We recommend to integrate pediatric mental health screening into medical health care systems to make it realistically feasible and cost-effective. Short but psychometrically adequate questionnaires (preferable integrated online or into an app with incorporated scoring to limit time investment) are necessary and are being developed. Future research should design and test the sensitivity and specificity of such short mental health screening questionnaires in children experiencing physical illness or injury.

The results of our RCT showed no superiority of EMDR compared to standard medical care (with additional psychological screening) on reducing subthreshold PTSD. Children with more severe PTSD symptoms may benefit more from EMDR [73, 74]. Children with subthreshold PTSD might benefit sufficiently from active monitoring and/or brief interventions. Future research into trauma-focused psychotherapies should include both, children with moderate and severe PTSD symptoms, and compare both groups.

Specific recommendations for future research

- Elaborate an evidence-based decision tree which indicates the optimal timing and intensity of mental health screening and interventions after pediatric hospitalization
- Develop short but reliable & valid online mental health instruments for ill or injured children
- Further investigate the effectiveness of EMDR for BII phobia in children
- Establish evidence-based interventions for children and adolescents with moderate medically related PTSD symptoms
- Identify predictors for EMDR treatment success in children and adolescents
- Explore possible cut-offs (e.g. symptom severity or level of impairment) to indicate which children should be provided with more intensive psychotherapy (such as EMDR)
- Evaluate the cost-effectiveness of a psychosocial stepped-care model in pediatric medical health care settings

APPENDICES

Summary

Medical procedures and hospitalizations are commonly occurring potentially traumatic experiences (PTE's) during childhood and adolescence. These experiences can result in subthreshold posttraumatic stress symptoms or even a diagnosis of posttraumatic stress disorder (PTSD). Furthermore, PTE's frequently lead to symptoms of anxiety and depression, sleep problems, and lower health-related quality of life (HRQoL). Eye Movement Desensitization and Reprocessing (EMDR) is an innovative trauma-focused intervention aiming to reduce (medically related) PTSD symptoms and associated problems (e.g. anxiety, depression, sleep problems, and lower HRQoL). During EMDR, the vividness and intensity of a traumatic memory can be decreased by engaging in bilateral stimulation (e.g. horizontal eye movements) while thinking about a distressing event.

This thesis describes the psychological consequences of pediatric hospitalizations (part I) and a randomized controlled trial (RCT) that investigated the effectiveness of EMDR for children and adolescents with medically related subthreshold PTSD (part II). **Chapter 1,** the general introduction, presents detailed information on the background and aims of the present thesis.

We included a large group of children with a congenital heart disease in our RCT since these children often experience potentially traumatic medical events (PTME's). In this context, we first reviewed the literature on medically related posttraumatic stress in children with a (congenital) heart disease in **Chapter 2**. A lot of children born with a heart defect need surgery or catheterization early in life and lifelong checkups with their cardiologist. Since mortality has decreased drastically over the last three decades, greater attention has been drawn to the psychosocial impact of invasive medical procedures and living with a chronic illness. The reviewed literature suggests that a range of 12-31% of the children meets PTSD criteria after cardiac surgery and a range of 12-14% meets some, but not all, DSM-IV PTSD symptom criteria. These prevalence rates are comparable to those of children with other pediatric conditions than ConHD. In the international literature, early mental health screening in children with heart diseases is recommended.

Chapter 3 represents a review on mental health problems of parents of children with ConHD. This review indicated that parents of children with ConHD, especially mothers, have an increased risk for symptoms of PTSD, anxiety, depression,

somatization, and hopelessness. Parental distress has been reported to be present in 30-80% of the parents. Prevalence rates of PTSD in parents were found to be especially high during the immediate post-diagnosis (up to 88%) and post-surgery (up to 19%) periods. More research is needed to determine the long-term course of mental health problems in these parents. As parental posttraumatic stress reactions are associated with child PTSD symptoms, mental health screening and psychosocial support for parents of children with ConHD is recommended.

Chapter 4 describes the baseline results of the cohort of our RCT, consisting of 399 children aged 4-15 years who had been hospitalized for illness or injury in Dutch hospitals. Medically related elevated PTSD symptoms (i.e. above the cut-off for an above average score) were present in 26% of our sample, based on combined child and/or parent report. Parents reported elevated PTSD symptoms significantly more often in children with medically related trauma type II (24%) than trauma type I (15%). Elevated depressive symptoms were present in 31% of our sample according to combined child and/or parent report. Situational phobia (25%), social phobia (21%), and BII phobia (15%) were the most frequently mentioned anxiety symptoms, according to child report.

Using multiple regression analyses, we found that parental stress was significantly associated with a higher level of child- and parent-reported PTSD symptoms of the child. Trauma type and parental education were significantly associated with parent-reported (but not child-reported) PTSD symptoms of the child. Based on our findings, we recommended standardized screening for psychosocial problems after pediatric illness or injury. Based on our findings, extra attention should be paid to children with medically related trauma type II whose parents experience stress and have a low educational level. This underscores the importance of reducing parental stress within hospital settings.

In **Chapter 5** we elaborated upon the study design of our RCT testing the effectiveness of EMDR for children with medically related subthreshold PTSD (trial registration NTR5801). We included children who had undergone a one-time hospitalization or repeated hospitalization up to maximally five years ago. Children who had been hospitalized for minimally one night for acute illnesses/injuries (via the emergency department) or for a heart condition (via a pediatric cardiology department) were included. For this RCT, participating children and their parents first took part in a psychosocial screening by completing standardized

questionnaires. Those with an above average PTSD score and/or those who met 2 of the 3 symptom criteria for a DSM-IV PTSD diagnosis by child and/or parent report were invited for a semi structured interview. Afterwards, only children with subthreshold PTSD were randomly assigned to EMDR or CAU (medical care only). The main outcome measure of the RCT was PTSD symptoms. Secondary outcomes were anxiety, depression, sleep problems, and HRQoL. Children showing full diagnostic PTSD were excluded from the study and referred for direct treatment. Follow-up measurements were planned eight weeks and eight months after the start of EMDR/CAU.

Chapter 6 presents the short-term results of our RCT (*M*=9.7 weeks after the start of EMDR/CAU). Intention-to-treat analyses showed that both groups (EMDR *n*=37; CAU *n*=37) improved significantly on all outcomes. EMDR was not superior in reducing subthreshold PTSD compared to CAU. However, the EMDR group showed significantly more improvements regarding child-reported symptoms of BII phobia and depression, and child- and parent-reported sleep problems of the child. Treatment effect was not associated with medically related trauma type (I vs. II) or hospital department (ED vs. cardiology). Interestingly, the effect of EMDR in reducing child-reported symptoms of depression and sleep problems were larger the longer ago the last medical event happened. Furthermore, EMDR was rated positively by participating parents and children. Our result that EMDR was not superior to CAU in reducing subthreshold PTSD may be related to the psychoeducational components of the study (study information letter, psychosocial questionnaires, conversation with a psychologist). The CAU group may have made progress as a result of this. It may also be that EMDR was less effective due to the subthreshold nature of PTSD symptoms.

In **Chapter 7**, we provided the long-term results of our RCT (*M*=8.2 months after the start of EMDR/CAU). Also on the long-term, EMDR was not superior in reducing subthreshold PTSD compared to CAU. On the long-term, EMDR was only superior in reducing parent-reported BII-phobia symptoms of the child. Improvements in depressive symptoms, sleep problems and HRQoL did not differ significantly between the EMDR and CAU group at long-term. The information letter, questionnaires, and interview might have resulted in increased awareness, validation and normalization of symptoms for all participating children and their parents. This might have been sufficient to improve symptoms in children with subthreshold PTSD. EMDR might be more useful for children with more severe PTSD symptoms.

In **Chapter 8**, the general discussion, the main findings are discussed, future directions for scientific research are elaborated, and clinical implications are evaluated. Part I of this thesis clearly underlines that children and adolescents (and their parents) undergoing hospitalizations are at risk for developing a variety of mental health problems, such as PTSD symptoms. Therefore, regular (online) mental health screening should be implemented into pediatric health care settings. More research is needed to determine the optimal timing, amount, and type of instruments that should be used. Part II of this thesis shows that EMDR had benefits at short-term on symptoms of BII phobia and depression and sleep problems. On the long-term, EMDR was still effective in treating BII phobia. No superior effects of EMDR on subthreshold PTSD symptoms were found on the short- and long-term.

Considering our findings, we conclude that for the treatment of medically related *subthreshold* PTSD EMDR might not be necessary. However, EMDR has been proven effective for children with full diagnostic PTSD in earlier studies. Future research is needed to examine which patients should be provided with EMDR. Psychoeducational interventions and regular screening might be sufficient for children and adolescents with moderate symptom severity. More research is needed to explore the efficiency of a stepped-care model within pediatric health care.

Samenvatting

Medische procedures en ziekenhuisopnames zijn veel voorkomende, potentieel traumatische ervaringen (PTE's) tijdens de kindertijd en adolescentie. Deze ervaringen kunnen resulteren in partiële posttraumatische stresssymptomen of zelfs een diagnose van posttraumatische stressstoornis (PTSS). Bovendien leiden PTE's vaak tot symptomen van angst en depressie, slaapproblemen en een lagere gezondheidsgerelateerde kwaliteit van leven (HRQoL). EMDR is een innovatieve traumagerichte interventie die gericht is op het verminderen van (medisch gerelateerde) PTSS symptomen en bijbehorende problemen (bijv. angst, depressie, slaapproblemen en lagere HRQoL). Tijdens EMDR kan de levendigheid en intensiteit van een traumatische herinnering worden verminderd door bilaterale stimulatie (bijv. horizontale oogbewegingen) tijdens het denken aan een verontrustende gebeurtenis.

Dit proefschrift beschrijft de psychologische gevolgen van pediatrische ziekenhuisopnames (deel I), en een gerandomiseerde gecontroleerde studie die de effectiviteit van EMDR onderzocht voor kinderen en adolescenten met medisch gerelateerde partiële PTSS (deel II). **Hoofdstuk** 1, de algemene inleiding, geeft meer gedetailleerde informatie over de achtergrond en doelstellingen van dit proefschrift.

We hebben een grote groep kinderen met een aangeboren hartafwijking in onze RCT opgenomen, aangezien deze kinderen vaak potentieel traumatische medische ervaringen (PTME's) meemaken. In deze context hebben we eerst de literatuur over medisch gerelateerde posttraumatische stress bij kinderen met een (aangeboren) hartafwijking bestudeerd in **Hoofdstuk 2**. Een groot deel van de kinderen die met een hartafwijking wordt geboren heeft op jonge leeftijd een operatie of katheterisatie en levenslange controle bij hun cardioloog nodig. Terwijl de mortaliteit de afgelopen drie decennia drastisch is afgenomen, is er meer aandacht gekomen voor de psychosociale impact van invasieve medische procedures en het leven met een chronische ziekte. De bestudeerde literatuur suggereert dat 12-31% van de kinderen voldoet aan de criteria voor PTSS na een hartoperatie en dat 12-14% voldoet aan enkele, maar niet alle, DSM-IV PTSS symptoomcriteria. Deze prevalentiecijfers zijn vergelijkbaar met die van kinderen met andere lichamelijke aandoeningen dan een aangeboren hartafwijking. In de internationale literatuur wordt vroege screening van de mentale gezondheid bij kinderen met hartaandoeningen aanbevolen.

Hoofdstuk 3 geeft een overzicht van geestelijke gezondheidsproblemen van ouders van kinderen met een aangeboren hartafwijking. Dit review gaf aan dat ouders, vooral moeders, van kinderen met een aangeboren hartafwijking een verhoogd risico hebben op symptomen van PTSS, angst, depressie, somatisatie en hopeloosheid. Ouderlijk onwelbevinden werd gemeld bij 30-80% van de ouders. De prevalentiecijfers van PTSS bij ouders bleken bijzonder hoog te zijn tijdens de periode onmiddellijk na de diagnose (tot 88%) en na een operatie (tot 19%). Er is meer onderzoek nodig om het beloop van psychische problemen bij deze ouders op de lange termijn vast te stellen. Aangezien posttraumatische stressreacties van ouders verband houden met PTSS symptomen bij kinderen, wordt screening op de geestelijke gezondheid en psychosociale ondersteuning voor ouders van kinderen met aangeboren hartafwijking aanbevolen.

Hoofdstuk 4 beschrijft de baseline resultaten van het cohort van onze RCT, bestaande uit 399 kinderen van 4-15 jaar die in een Nederlands ziekenhuis zijn opgenomen geweest vanwege ziekte of letsel. Medisch gerelateerde verhoogde PTSS symptomen (d.w.z. boven de cut-off voor een bovengemiddelde score) waren aanwezig in 26% van onze steekproef, gebaseerd op de gecombineerde kind- en/of ouderrapportage. Ouders rapporteerden significant vaker verhoogde PTSS symptomen bij kinderen met medisch gerelateerd trauma type II (24%) dan bij trauma type I (15%). Verhoogde depressieve symptomen waren aanwezig in 31% van onze steekproef volgens de gecombineerde kind- en/of ouderrapportage. Situationele fobie (25%), sociale fobie (21%) en medische fobie (15%) waren volgens kindrapportage de meest vaak voorkomende angstsymptomen.

Met behulp van meervoudige regressieanalyses ontdekten we dat ouderlijke stress significant geassocieerd was met een hoger niveau van PTSS symptomen bij het kind op grond van kind- en/of ouderrapportage. Trauma type en ouderlijk opleidingsniveau waren significant geassocieerd met ouderrapportage (maar niet kindrapportage) van PTSS symptomen van het kind. Op basis van deze resultaten hebben we gestandaardiseerde screening van psychosociale problemen na pediatrische ziekte of letsel aanbevolen. Op basis van onze bevindingen dient extra aandacht te worden besteed aan kinderen met medisch gerelateerd trauma type II van wie de ouders stress ervaren en die een laag opleidingsniveau hebben. Dit onderstreept het belang van het verminderen van ouderlijke stress binnen ziekenhuisomgevingen.

In **Hoofdstuk 5** hebben we de onderzoeksopzet van onze RCT naar de effectiviteit van EMDR voor kinderen met medisch gerelateerde partiële PTSS beschreven (trial registratie NTR5801). We includeerden kinderen die tot maximaal vijf jaar geleden een eenmalige ziekenhuisopname of herhaalde ziekenhuisopname hadden ondergaan. Kinderen die minimaal één nacht in een ziekenhuis opgenomen waren geweest vanwege een acute ziekte of verwonding (afdeling spoedeisende hulp) of vanwege een hartafwijking (kindercardiologie) mochten meedoen. Voor deze RCT hebben deelnemende kinderen en hun ouders eerst deelgenomen aan een psychosociale screening doormiddel van het invullen van gestandaardiseerde vragenlijsten. Degenen met een bovengemiddelde PTSS-score en/of degenen die voldeden aan 2 van de 3 symptoomcriteria voor een DSM-IV PTSS diagnose, werden uitgenodigd voor een semigestructureerd interview. Daarna werden alleen de kinderen met een partiële PTSS willekeurig toegewezen aan EMDR of CAU (alleen medische zorg). De belangrijkste uitkomstmaat van onze RCT was PTSS symptomen. Secundaire uitkomsten waren angst, depressie, slaapproblemen en gezondheidsgerelateerde kwaliteit van leven. Kinderen met volledig diagnostische PTSS werden uitgesloten van de studie en verwezen voor directe behandeling. Follow-up metingen waren acht weken en acht maanden na de start van EMDR / CAU gepland.

Hoofdstuk 6 geeft de korte termijn resultaten van onze RCT (*M* = 9,7 weken na de start van EMDR/CAU) weer. Intention-to-treat-analyses toonden aan dat beide groepen (EMDR *n* = 37; CAU *n* = 37) significant verbeterden op alle uitkomsten. EMDR was niet superieur in het verminderen van partiële PTSS vergeleken met CAU. De EMDR groep vertoonde echter significant meer verbeteringen wat betreft door het kind gerapporteerde symptomen van medische fobie en depressie, en door kind en ouder gerapporteerde slaapproblemen van het kind. Het behandeleffect was niet geassocieerd met medisch gerelateerd trauma type (I vs. II) of ziekenhuisafdeling (SEH vs. cardiologie). Interessant is dat het effect van EMDR bij het verminderen van door kinderen gerapporteerde symptomen van depressie en slaapproblemen groter was naarmate de laatste medische gebeurtenis langer geleden plaatsvond. Bovendien werd EMDR positief beoordeeld door deelnemende ouders en kinderen. Ons resultaat dat EMDR niet superieur was aan CAU in het verminderen van partiële PTSS kan te maken hebben met de psycho-educatieve componenten van de studie (studie informatiebrief, psychosociale vragenlijsten, gesprek met een psycholoog). Mogelijk boekte de CAU groep hierdoor vooruitgang. Ook kan het zijn dat EMDR minder effect sorteerde vanwege de partiële aard van de PTSS-symptomen.

In **Hoofdstuk 7** werden we de lange termijn resultaten van onze RCT weergegeven (*M* = 8,2 maanden na de start van EMDR/CAU). Ook op de lange termijn was EMDR niet superieur in het verminderen van partiële PTSS vergeleken met CAU. Op de langere termijn was EMDR alleen superieur in het verminderen van de door ouders gerapporteerde symptomen van medische fobie van het kind. Verbeteringen in depressieve symptomen, slaapproblemen en gezondheidsgerelateerde kwaliteit van leven verschilden op de lange termijn niet significant tussen de EMDR en CAU groep. De informatiebrief, vragenlijsten en het interview hebben mogelijk geleid tot bewustwording, validatie en normalisatie van symptomen voor alle deelnemende kinderen en hun ouders. Dit zou voldoende kunnen zijn geweest om de symptomen bij kinderen met partiële PTSS te verbeteren. EMDR is wellicht nuttiger voor kinderen met ernstigere PTSS-symptomen.

In **Hoofdstuk 8**, de algemene discussie, worden de belangrijkste bevindingen besproken, toekomstige richtingen voor wetenschappelijk onderzoek uitgewerkt en klinische implicaties geëvalueerd. Deel I van dit proefschrift onderstreept duidelijk dat kinderen en adolescenten (en hun ouders) die in het ziekenhuis zijn opgenomen geweest, het risico lopen om een verscheidenheid aan psychische problemen te ontwikkelen, zoals PTSS symptomen. Daarom moet regelmatige (online) screening van geestelijke gezondheid worden geïmplementeerd in pediatrische gezondheidszorginstellingen. Er is meer onderzoek nodig om de optimale timing, hoeveelheid en type instrumenten te bepalen die moeten worden gebruikt. Deel II van dit proefschrift laat zien dat EMDR op korte termijn voordelen had bij symptomen van medische fobie en depressie en slaapproblemen. Op de lange termijn was EMDR nog steeds effectief bij de behandeling van medische fobie. Er werden geen superieure effecten van EMDR op partiële PTSS symptomen gevonden op korte en lange termijn.

Gezien onze bevindingen concluderen we dat EMDR voor de behandeling van medisch gerelateerde *partiële* PTSS misschien niet nodig is. In eerdere onderzoeken is EMDR echter effectief gebleken bij kinderen met volledig diagnostische PTSS. Toekomstig onderzoek is nodig om te onderzoeken welke patiënten EMDR moeten krijgen. Psycho-educatieve interventies en regelmatige screening zijn misschien voldoende voor kinderen en adolescenten met matig ernstige symptomen. Er is meer onderzoek nodig om de efficiëntie van een stepped-care model binnen de pediatrische gezondheidszorg te verkennen.

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Publications

Meentken MG, van Beynum IM, Legerstee JS, Helbing WA, & Utens EMWJ (2017). Medically Related Post-traumatic Stress in Children and Adolescents with Congenital Heart Defects.
Frontiers in Pediatrics 5:20,
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Kolaitis GA, **Meentken MG**, & Utens EMWJ (2017) Mental Health Problems in Parents of Children with Congenital Heart Disease.
Frontiers in Pediatrics 5:102,
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Meentken MG, van Beynum IM, Aendekerk EWC, Legerstee JS, El Marroun H, van der Ende J, Lindauer RJL, Hillegers MHJ, Moll HA, Helbing WA, & Utens EMWJ (2018). Eye movement desensitization and reprocessing (EMDR) in children and adolescents with subthreshold PTSD after medically related trauma: design of a randomized controlled trial.
European Journal of Psychotraumatology, 9:1,
doi: 10.1080/20008198.2018.1536287

van der Mheen M, **Meentken MG**, van Beynum IM, van der Ende J, van Galen E, Zirar A, Aendekerk EWC, van den Adel TPL, Bogers AJJC, McCusker CG, Hillegers MHJ, Helbing WA, & Utens EMWJ (2019). CHIP-Family intervention to improve the psychosocial wellbeing of young children with congenital heart disease and their families: results of a randomized controlled trial.
Cardiology in the Young, 29:9
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Cooper DK, Bachem R, **Meentken MG**, & Perez Barrios AG (2020). Cumulative lifetime adversity and depression among a national sample of U.S. Latinx immigrants: Within-group differences in risk and protective factors using data from the HCHS/SOL sociocultural ancillary study.
Journal of Latinx Psychology, 8:3,
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European Journal of Psychotraumatology, 11:1,
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Meentken MG, van der Mheen M, van Beynum IM, Aendekerk EWC, Legerstee JS, van der Ende J, del Canho R, Lindauer RJL, Hillegers MHJ, Helbing WA, Moll HA & Utens EMWJ (2021). Long-term effectiveness of eye movement desensitization and reprocessing in children and adolescents with medically related subthreshold post-traumatic stress disorder: a randomized controlled trial.
European Journal of Cardiovascular Nursing,
doi:10.1093/eurjcn/zvaa006

Meentken MG, van der Ende J, del Canho R, van Beynum IM, Aendekerk EWC, Legerstee JS, Lindauer RJL, Hillegers MHJ, Helbing WA, Moll HA, & Utens EMWJ (2021). Psychological outcomes after pediatric hospitalization: the role of trauma type.
Children's Health Care,
doi: 10.1080/02739615.2021.1890077

PhD Portfolio

General information	
Name PhD student:	Maya Meentken
Erasmus MC Department:	Child and Adolescent Psychiatry/Psychology
PhD period:	January 2016 – October 2019
Promotors:	Prof. E.M.W.J. Utens, prof. M.H.J. Hillegers
Supervisor:	prof. W.A. Helbing,
Research school:	Prof. E.M.W.J. Utens NIHES

1. Training program	Year	Workload
General courses		
Basic course on Regulations and Organization for clinical investigators (BROK)	2016	1.00 ECTS
Patient Oriented Research (CPO) course	2016	0.30 ECTS
Scientific Integrity	2017	0.30 ECTS
Biomedical English Writing and Communication	2017/2018	3.00 ECTS
Specific courses		
Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA)	2016	0.30 ECTS
Diagnostic Infant and Preschool Assessment (DIPA)	2016	0.15 ECTS
EndNote, PubMed and other databases	2016	1.00 ECTS
LimeSurvery & GemsTracker	2016	0.30 ECTS
EMDR training	2016	0.50 ECTS
Congenital Heart Disease Part I	2017	0.50 ECTS
Basic course on SPSS	2017	1.00 ECTS
Repeated Measurements	2018	1.40 ECTS
Missing Values in Clinical Research	2018	1.40 ECTS
Workshop Presenting Skills for junior researchers	2018	1.00 ECTS
Workshop Stress Management	2018	1.00 ECTS
Workshop Photoshop, Illustrator & InDesign	2018	0.45 ECTS
Hands-on Training: Getting your PhD done	2019	0.30 ECTS

Seminars and workshops

Research Work Meetings KJPP (*incl. 1 oral presentation*)	2016-2019	1.00 ECTS
Clinical & Research Meetings KJPP (*incl. 2 oral presentations*)	2016-2019	1.00 ECTS
Sophia Research Days (*incl. 1 oral presentation*)	2016-2019	1.00 ECTS
Erasmus PhD-days	2016-2019	1.00 ECTS
Colloquia KJPP (*incl. 1 oral presentation*)	2016-2019	0.50 ECTS
Young Talent Day Young@Heart Community	2016	0.30 ECTS
Meetings pediatric cardiologists Erasmus MC (*incl. 2 oral presentations*)	2016	0.30 ECTS
Meeting pediatric cardiologists Radboud UMC (*incl. 1 oral presentation*)	2017	0.15 ECTS
Get-together days Stichting Hartekind (*incl. 2 oral presentations*)	2018-2019	0.50 ECTS
KJPP Scientific Cafés (*incl. 1 oral presentation*)	2017-2019	0.50 ECTS

(Inter)national conferences

17th EMDR Europe conference, The Hague, the Netherlands (*attending*)	2016	1.00 ECTS
PPN-NL symposium, Utrecht, the Netherlands (*attending*)	2016	0.30 ECTS
AEPC conference, Rotterdam, the Netherlands (*attending*)	2016	1.00 ECTS
Symposium Major Milestones in child & adolescent psychiatry (*attending*)	2017	0.30 ECTS
VGCT Najaarscongres, Eindhoven, the Netherlands (*oral presentation*)	2017	1.00 ECTS
AEPC conference, Leicester, U.K. (*oral presentation*)	2018	1.00 ECTS
11th National EMDR congres, Utrecht, the Netherlands (*oral presentation*)	2018	1.00 ECTS
EPPC conference, Ghent, Belgium (*oral presentation*)	2018	1.00 ECTS
34th ISTSS Annual Meeting, Washington, U.S. (*poster presentation*)	2018	1.00 ECTS
12th National EMDR congres, Utrecht, the Netherlands (*oral presentation*)	2018	1.00 ECTS

16th ESTSS conference, Rotterdam, the Netherlands (*oral presentation*)	2019	1.00 ECTS
20th EMDR Europe conference, Krakow, Poland (*poster presentation*)	2019	1.00 ECTS
14th ICCAP conference, Londen, U.K. (*oral presentation*)	2019	1.00 ECTS
2nd WASAD congres, Würzburg, Germany (*oral presentation*)	2019	1.00 ECTS
PPN-NL symposium, Utrecht, the Netherlands *(attending)*	2019	0.30 ECTS

2. Teaching

Supervising research internships

Faezeh Moallemzadeh (no thesis)	2016-2017	1.00 ECTS
Leonie Wigman, Title thesis: '*PTSS-symptomen in kinderen met een medisch gerelateerd trauma: studie naar de relatie met depressie- en angstsymptomen en de invloed van familie functioneren'*	2016-2017	1.50 ECTS
Renée Ran – Title thesis: '*Posttraumatische stress bij kinderen met een medisch gerelateerd trauma: de rol van de cognitieve emotieregulatie'*	2017	1.50 ECTS
Sofie Koomen – Title thesis: '*The influence of family functioning and self-perception on PTSD-symptoms in children aged 12-16 with a medical-related trauma'*	2017	1.50 ECTS
Jolie Vullinghs (no thesis)	2017	1.00 ECTS
Kim Kentin – Title thesis: '*Verminderde kwaliteit van leven bij kinderen met posttraumatische stresssymptomen na een medische traumatische gebeurtenis'*	2017-2018	1.50 ECTS
Sabina Khan (no thesis)	2017	1.00 ECTS
Ruo Yi Ly – Title thesis: '*De relatie tussen ouderlijke last en posttraumatische stress symptomen bij kinderen na een medisch gerelateerd trauma'*	2017-2018	1.50 ECTS
Janine de Bruijn – Title thesis: '*De invloed van copingsstijlen op de wederkerige relatie tussen PTSS-symptomen en slaapverstoring'*	2018	1.50 ECTS

Nader Malekzadeh (no thesis)	2018-2019	1.00 ECTS
Sarah Tell – Title thesis: 'Medische fobie bij kinderen met een medisch gerelateerd trauma: de invloed van ouderlijke stress'	2018-2019	1.50 ECTS
Priscilla Grootjes – Title thesis: 'De relatie tussen ouderlijke stress en de PTSS-symptomen bij kinderen met een medisch trauma; gemedieerd door het niet-adaptieve copingsgedrag van het kind'	2019	0.50 ECTS

Other teaching activities

Skills education (vaardigheden onderwijs), Medical Faculty Erasmus MC	2017-2019	1.30 ECTS
Writing a systematic review, medical students, Erasmus MC	2018-2019	2.00 ECTS

ECTS=European Credit Transfer and Accumulation System (1 ECTS represents 28 hours)

Abbreviations

AIP	Adaptive information processing
BII-phobia	Blood-injection-injury phobia
CAU	Care-as-usual
ConHD/CHD	Congenital heart disease
DSM-IV/V	Diagnostic and Statistical Manual of Mental Disorders, 4th edition/5th edition
ED	Emergency Department
EMDR	Eye Movement Desensitization and Reprocessing
FCC	Family-centered care
HRQoL	Health-related quality of life
PICU	Pediatric Intensive Care Unit
PMTS	Pediatric medical traumatic stress
PTE	Potentially traumatic event
PTME	Potentially traumatic medical event
PTSD	Posttraumatic stress disorder
PTSS	Posttraumatic stress symptoms
RCT	Randomized controlled trial
TF-CBT	Trauma-focused cognitive behavioral therapy
WHO	World Health Organization