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Psychological Aspects of Anesthesia in Children

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Psychological Aspects of Anesthesia in Children

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'The way that can be spoken of
Is not the constant way;
The name that can be named
Is not the constant name.' (*Tao Te Ching*, 1)
道可道，非常道。名可名，非常名。

Chapter 1

General Introduction

PSYCHOLOGICAL ASPECTS OF ANESTHESIA IN CHILDREN

Perioperative behavior and postoperative pain incidence and importance

One of the important aims of pediatric anesthesia is to shepherd each child through the surgical procedure with the least possible mental and physical stress. Since its emergence in the 1940's, the field of pediatric anesthesia has reached a high level of sophistication, with many novel anesthetic agents, locoregional techniques and patient monitoring tools that have been developed. Over the past two decades, the interest in the child's perioperative behavior (anxiety, emergence delirium, postoperative behavior changes) within the field of pediatric anesthesia has increased considerably[1-3]. Correspondingly, the relevance of identifying vulnerable children, who are at elevated risk for such problems is beyond dispute[3]. What seems to be lacking still, however, is research into psychological aspects in this field, such as the influence of pre-existing emotional/behavioral problems on the child's perioperative behavior. Children's emotional/behavioral problems that are already present before induction of anesthesia might have a considerable impact on the child's psychological and somatic recovery and also on postoperative pain. Therefore, in this thesis emotional/behavioral problems will be studied as clinically relevant factors for the medical treatment of children being operated upon.

In the past decades, an increasing body of information was accumulated about children's perioperative behavior. Preoperative anxiety in children was shown to be associated with emergence delirium, negative postoperative behavior changes and sleeping problems[4,5]. Incidences up to 75% of children with significant anxiety at induction of anesthesia have been reported[1,2,6,7]. The incidence of emergence delirium in children varies between 2 - 80%, depending on the used assessment procedures and the diagnostic criteria[8-10]. Also negative postoperative behavior changes (such as separation anxiety, general anxiety, eating disturbances, apathy/withdrawal, sleep anxiety and aggression towards authority) are commonly seen in children after surgery with reported percentages between 24% and 73%[6,11].

Moreover increased perioperative anxiety is also associated with neuroendocrine changes (*e.g.* higher serum levels of cortisol, adrenocorticotropic hormone, epinephrine, natural killer cell activity)[12,13]. This interferes with wound healing and is related to postoperative immunosuppression.

Additionally, it is well established that increased children's preoperative anxiety is associated with higher postoperative pain scores[5,14]. Furthermore, postoperative pain at home is often underestimated and undertreated in children[15] with reported incidences of significant pain up to more than 50% the first days after surgery[15]. A negative maladaptive perioperative experience might also interfere with future medical contacts[6,16,17], in the sense of anxious reactions to hospital equipment, medical procedures or non-adherence to medical (follow-up) consultations or treatment.

Finally, the child's state anxiety will challenge the social and communicative skills of the whole anesthesia team[2].

Preoperative preparation of children

Nowadays, when preparing children for a surgical procedure, a lot of attention is paid to preventing and alleviating preoperative anxiety during induction of anesthesia. Still, more than 75% of children are very anxious at induction[1,7,18], notwithstanding pharmacological treatments that are available[19] to reduce anxiety, including midazolam, clonidine[19], and dexmedetomidine[20-22]. Of note, children do not necessarily need premedication or they (especially toddlers) may even react adversely to it[6,19,23-25].

Many non-pharmacological interventions have been developed to reduce children's preoperative anxiety[26] such as streamed video clips[27], cartoon distraction[28], computer preparation[29], web-based preparation[30], music therapy[31], clown doctors[32,33] and parental presence at induction[26]. Also extensive psychological-behavioral programs[1,26,34,35] (including: distraction, video modelling, education, involving and coaching of parents, no excessive parental reassurance of the child, exposure /shaping of the child using an induction mask and support by a psychologist)[34,35] have proven their efficacy. Recently, researchers stated that[36] shaping/exposure by using an induction mask and distraction by parents significantly reduced the child's anxiety at induction. So, parental presence appeared to be helpful. A recent Cochrane report, however, showed that parental presence at induction was not useful in reducing children's anxiety at induction of anesthesia[26]. Nowadays, also modern tools such as virtual reality are available to reduce children's anxiety. However, their efficacy has to be established.

Considering the above, more attention should be paid to identification of children at risk for perioperative emotional/behavioral problems[18,37,38] in order to optimize children's preparation for surgery. Preparation of children towards a surgical intervention under anesthesia is a very complex matter.

In the remainder of this chapter we will make a distinction between:

- the period prior to the induction of anesthesia, focusing on preoperative anxiety;
- the period after surgery, focusing on emergence delirium, postoperative behavioral changes and sleep problems and postoperative pain at home.

Hereafter, the overall aim and the outline of the thesis will be described.

A. PERIOD PRIOR TO THE INDUCTION OF ANESTHESIA: PREOPERATIVE ANXIETY IN CHILDREN AND PARENTAL INVOLVEMENT

Children's preoperative anxiety and distress behavior was studied by Chorney *et al*[39]. They filmed children during their walk from the holding area towards the operating theatre and during induction of anesthesia. In a majority of children the following behaviors were observed: 1) crying or screaming (28.1 %); 2) verbal and nonverbal resistance (53.6 %); 3) negative verbal emotional expressions (8.6 %). Acute distress behavior is especially seen in very young children (less than 3 years old). In comparison to adults, children show higher levels of preoperative anxiety and express their anxiety in a very marked or explicit behavioral sense[2,39]. Unlike adults, children often try to escape the anesthetic induction in up to 30% of cases[39]. The child's state anxiety peaks at induction and steadily declines in the postoperative period [37].

1. Child specific predictors

Several predictors of child preoperative anxiety can be identified:

1) age of the child: children between 1-5 years are more at risk[7];
2) low level of cognitive development[1];
3) higher trait anxiety[40,41];
4) a passive coping style[6,42];
5) previous bad experience with medical encounters[7,16];
6) emotional/behavioral problems were found to be predictive for anxiety at induction in a small sample of adolescents[43];
7) parental anxiety[7,44].

2. Assessment tools for preoperative anxiety

The assessment of the child's state anxiety remains a challenge[2]. Kain *et al* published the modified Yale Perioperative Anxiety Scale (mYPAS) which was designed for researchers to assess child's state anxiety in the preoperative period from the holding area onwards to the induction of anesthesia. The mYPAS is a well validated tool for use in children aged between 2 – 12 years, with good to excellent psychometric characteristics. It consists of five behavioral domains: activity, emotional expressivity, state of arousal, vocalization and use of parents[45]. The mYPAS can be considered nowadays as the *Gold Standard* to measure state anxiety at induction of anesthesia in children. However, it requires training, is time-consuming, was not devised for parental completion and is difficult to incorporate in daily practice. Another very often used tool is the Induction Compliance Checklist (ICC)[46]. This is, however, a rather limited tool; it aims to assess state anxiety at induction by observing compliance of the child. Compliance and state anxiety, however, are different concepts[47].

An easy-to-use tool for the assessment of preoperative anxiety is not available yet. It has been recommended that good anxiety assessment and management should be incorporated as a cornerstone of Family-centered Pediatric Perioperative Care[14,48]. There is a need for an easy-to-use anxiety assessment tool, which requires no training and is suited for a broad age-range, including non-verbal young children. In order to incorporate anxiety assessment into Family-centered Pediatric Perioperative Care[14,48] it is important that not only anesthesiologists but also parents can quickly complete such a tool in a busy clinical setting. An advantage of letting parents complete a Visual Analogue Scale (VAS), is that it requires them to focus on and be aware of their children's anxiety level.

Therefore, in the present thesis, a VAS to assess perioperative anxiety in children was investigated. With the VAS we aim to assess state anxiety throughout the entire perioperative period for children from a broad age-range, including young non-verbal children[14].

Perioperative parental involvement

Not only children but also parents may find the surgery of their child a stressful experience[49]. Parents may become very anxious when their child undergoes a surgical intervention under anesthesia[50]. This is reflected by physiological changes such as increased heart rate, heart rate variability, blood pressure and skin conductance[51,52]. Parents are also often very motivated to be present at induction[49,53]. Several studies have shown that parents with a high desire to be present at the anesthesia induction of their child are very anxious[49,53]. High levels of parental state and trait anxiety (situational anxiety and a more general anxiety disposition) have been identified as important risk factors for children's preoperative anxiety[6,7,11,49]. Parental anxiety may even intensify the child's perioperative state anxiety[49]. Therefore, it is of utmost importance to prepare parents to decrease parental anxiety, when they accompany their child during induction of anesthesia. Preparing parents may also increase their feeling of self-efficacy and trust in their role in the operating room[54]. This can help to decrease their children's anxiety at induction.

B. PERIOD AFTER SURGERY: EMERGENCE DELIRIUM, POSTOPERATIVE BEHAVIORAL CHANGES, SLEEP PROBLEMS AND POSTOPERATIVE PAIN AT HOME.

Emergence delirium

1. Definition

Emergence Delirium (ED) has been defined as: *a disturbance in a child's awareness of and attention to his or her environment with disorientation and perceptual alterations including hypersensitivity to stimuli and hyper-active motor behavior in the immediate post-anesthesia period*[8,10]. The incidence of ED in children varies widely between 2 - 80%, depending on the assessment system and the anesthetic technique used[8-10]. It most often occurs during awakening from anesthesia in the Post Anesthesia Care Unit (PACU)[40,55]. Although ED is mostly of short duration, it should not be underestimated for the following reasons: possible physical hazards for children (i.e. injury surgical wound repair), elevated anxiety in children and parents, extra workload for nurses (constant supervision) and professional feeling of guilt for the healthcare provider[8] resulting from seeing the child agitated.

2. Predictors

The following risk factors for ED[55] can be distinguished:

1) preschool age[56];
2) higher incidence for ear nose throat and eye surgery[40,57];
3) anesthesia related factors (new inhalation anesthetics: sevoflurane & desflurane give rise to a higher incidence)[9,58];
4) experience of previous surgery[59];
5) state anxiety child / parent[60];
6) psychological factors in relation to the child (i.e. low adaptability to novel situations)[59].

Furthermore, it should be stated that some of the predictors which contribute to preoperative anxiety are the same for ED, which implies that there may be a common underlying psychological cause.

3. Assessment tools

Sikich *et al*[8] published the Pediatric Anesthesia Emergence Delirium scale (PAED), a well validated scale with good intra-observer reliability, internal consistency and with a cut-off value to establish ED. Nevertheless, it is extremely complicated to assess behavior during awakening from anesthesia, since anxiety, pain, discomfort and ED are interrelated and can easily be confused[60,61].

Postoperative behavioral changes and sleep problems

Undergoing anesthesia and surgery can have a profound impact on the psychological well-being of the child, with negative postoperative behavioral changes and changes in sleep pattern (problems falling asleep, staying asleep and waking up crying) as a consequence[5,6,11,62,63]. Among the changes that may occur in children after undergoing anesthesia are changes in sensory processing. Sensory processing is how children perceive, modulate and self-regulate sensory information (auditory, visual, tactile, vestibular and oral) and how it might influence their behavior (attention, arousal, affect and action). Therefore in this thesis we studied sensory processing.

In previous research the following predictors were found to be associated with maladaptive postoperative behavioral functioning at home

1) preoperative state anxiety, distress[1,4-6,60];
2) younger age[6];
3) inhibited temperament[64,65];
4) pre-existing internalizing problems (anxious/depressed and somatic problems) and quality of previous medical contacts[2,6,11,65];
5) parental factors such as parental state/trait anxiety, cultural aspects, socio-economic status and level of education[6,11,62,66].

However, to the best of our knowledge, changes in in sensory processing have not been investigated in this context before. Therefore, we investigated pre- to postoperative changes in sensory processing, since insight in these changes might be a useful contribution to explain observed postoperative behavioral changes.

To evaluate the sensory processing skills of young children we used the Infant Toddler Sensory Profile ($ITSP_{6\text{-}36}$)[67]. It assesses different aspects of sensory processing skills and modulating sensory input of toddlers and covers 5 processing sections: 1. auditory; 2. visual; 3. tactile; 4. vestibular; 5. oral sensory.

Furthermore, sleep problems in children in pain conditions often occurs after surgery. However, sleep problems have not been thoroughly investigated despite the fact that they are very common[5,63,68]. There is no wide variety of validated assessment tools regarding the assessment of postoperative sleep problems in children[68]. Therefore, in our study we used some of the questions of the Posthospitalization Behavior Questionnaire (PHBQ)[69] related to sleep problems.

Pain after surgery at home

1. Prevalence of postoperative pain in children

Significant postoperative pain has been reported to occur in up to 80% of all children[15,62,70]. A possible explanation for this phenomenon is that nowadays pediatric surgery is often performed on a day-case basis[71]. Consequently, parents become responsible for their child's pain management at home. Research shows that postoperative pain management by parents for children at home is often insufficient[15].

2. Predictors of postoperative pain in children

Parents are quite capable to recognize their child's pain. However, several predictors influence parental pain management of their child[62,72,73] and children's postoperative pain at home[15] such as:

- parental personality characteristics;
- parental anxiety;
- parental level of education;
- cultural factors;
- parental misconceptions[62,72,73].

Parents can have the following misconceptions about pain medication[74]:

1) 52% believe that analgesics are addictive;
2) 73% have concerns about side effects;
3) 37% even believe that analgesics work better the less often children receive them[75]. Parents often do not expect that their child can have a persistent level of pain[76].

Among child-related factors influencing children's postoperative pain are:

- children's higher levels of preoperative anxiety[5,14];
- children's postoperative pain anxiety[77];
- children's refusal to take the medication[78].

Finally, ineffective medication and hospital related organizational system factors, such as insufficient information at discharge and poor communication from health care professionals[15], may contribute to children's postoperative pain.

3. Assessment tools

As far as we know, the only well validated assessment tool for parents to rate their children's pain at home is the Parents' Postoperative Pain Measure (PPPM)[79], developed for children aged from 1 to 12 years. The PPPM has been recommended [68] and it is proven that the PPPM has a good specificity (80%) and sensitivity (88%) to detect children with postoperative pain[79].

RATIONALE

As outlined in the previous sections, several aspects of children's perioperative behavior have been studied so far: preoperative situational state anxiety, ED, postoperative maladaptive behavior changes and pain. Important associations between these variables were found, showing that the child's state anxiety at induction might be related to ED, postoperative pain and negative postoperative behavioral changes[4].

Still, there are important gaps in the current knowledge about these perioperative behaviors, gaps which provide the rationale for this study. Firstly, most studies focus on prevention or control of preoperative anxiety and do not focus on identifying vulnerable children regarding maladaptive perioperative behavior. Secondly, there is insufficient knowledge regarding children's pre-existing emotional/behavioral problems in relation to these perioperative behaviors (anxiety, ED, changes in sensory processing) and postoperative pain. Therefore, we wanted to study these associations. Furthermore assessing pre-existing emotional/behavioral problems with an assessment tool like the CBCL might create an opportunity to tailor anxiety reducing strategies to the specific needs of each child. Thirdly, the study of changes in sensory processing might create a new opportunity for understanding postoperative behavioral changes in children.

Moreover, it would be relevant to study the overall impact of predictors of perioperative and postoperative behaviors. So far, predictors of these behaviors have mostly been studied separately.

Indeed a pilot study in adolescents[43] showed that pre-existing preoperative emotional/behavioral problems were predictive for state anxiety during induction. The same authors further concluded in another study that specific child factors like pre-existing internalizing problems (anxious/depressed and somatic problems) predicted maladaptive postoperative behavior (general postoperative anxiety)[65].

For this reason we hypothesized that pre-operative emotional/behavioral problems as assessed with the Child Behavior Checklist (CBCL)[80,81], a well validated international tool, could be associated with different aspects of perioperative behavior. Broadening our understanding of predictors of perioperative anxiety should make it possible to identify children at risk and may create an opportunity to optimize the children's psychological preparation for surgery.

A final motivation for this study is the fact that the role of the parents in assessing and managing children's preoperative anxiety has received scant attention. We consider it to be important that parents become aware that their child is significantly anxious and that their child will consequently be more vulnerable to postoperative maladaptive behavior and higher pain scores. So far, studies focusing on children's preoperative anxiety mainly focused on health care professionals, without an explicit role for the parents. Parents should be involved in the preparation of their child but they should also receive adequate information (such as audiovisual aids) which in turn would lead to less parental state anxiety.

Therefore, we considered it of interest to investigate an easy-to-use tool to assess children's state anxiety during induction of anesthesia, which can be completed by both parents and anesthesiologists without the need for training and which is also useful in the non-verbal younger age group of children.

AIMS

The overall aim of this thesis is to gain greater understanding of psychological aspects of anesthesia in children. The sub-aims include: 1) to examine associations between pre-existing emotional/behavioral problems in children and specific children's peri- and postoperative behaviors; 2) to explore the validity of a new, easy-to-use anxiety assessment tool at induction of anesthesia; 3) to explore the usefulness of an audio-visual tool for decreasing parental anxiety at induction of anesthesia.

RESEARCH QUESTIONS

The main research questions of this thesis considering preoperative anxiety are threefold:

1. Do preoperative emotional/behavioral problems predict anxiety during induction and ED after anesthesia in children undergoing elective day-care surgery?

2. Does the Visual Analogue Scale completed during induction of anesthesia (VAS-I) represent a valid instrument for measuring the child's state anxiety during induction and what are optimal cut-off values on the VAS-I to distinguish between anxious and non-anxious children?
3. What is the impact of audiovisual aid (AVA) on parental state anxiety and the child's compliance and anxiety at induction of anesthesia?

Regarding postoperative behavioral changes and postoperative pain the research questions are twofold:

1. Are there any pre- to postoperative changes in sensory processing in toddlers after pediatric anesthesia using the validated Infant/Toddler Sensory Profile ($ITSP_{6\text{-}36}$) and is it possible to identify predictors of these changes?
2. What is the degree of postoperative pain and postoperative sleep problems found in children aged between 1.5 and 5 years old undergoing adenotonsillectomy and what is the influence of children's preoperative emotional/behavioral problems on postoperative pain?

THE STRUCTURE OF THE PRESENT THESIS

In chapter 2 we examine the predictive value of the child's emotional/behavioral problems as to their level of anxiety at induction of anesthesia and ED at awakening in the PACU. Chapter 3 provides evidence for the usefulness of a VAS to assess anxiety at induction by parents and anesthesiologists. In chapter 4 we investigate the specific influence of preoperative information towards parents, provided by means of an audio-visual tool, on parental state anxiety at induction of their child's anesthesia. In chapter 5 we look into pre- to postoperative changes in infants' sensory processing up to two weeks after surgery and further study the specific influence of emotional/behavioral problems on these changes. In chapter 6 we study the influence of the child's emotional/behavioral problems on postoperative pain. Finally chapter 7 will provide a general discussion of the results of this present dissertation.

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'What cannot be seen is called evanescent;
What cannot be heard is called rarefied;
What cannot be touched is called minute.' (*Tao Te Ching*, 14)
视之不见，名曰夷；听之不闻，名曰希；搏之不得，名曰微。

Chapter 2

Does the Child Behavior Checklist predict levels of preoperative anxiety at anesthetic induction and postoperative emergence delirium? A prospective cohort study.

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ABSTRACT

Background: Preoperative anxiety at induction and postoperative emergence delirium (ED) in children are associated with postoperative behavioral changes and adjustment disorders. This study's aim is to assess the value of the Child Behavior Checklist (CBCL) score in order to predict anxiety during induction and emergence delirium after anesthesia in children undergoing elective day-care surgery.

Methods: Anxiety at induction, assessed by the modified Yale Preoperative Anxiety Scale (mYPAS), was studied as outcome in 401 children (60.1% male, age range: 1.5 – 16 years). For 343 of these children (59.8 % male, age range: 1.5 – 16 years) ED could be investigated postoperatively, as assessed by the Pediatric Anesthesia Emergence Delirium scale (PAED). Demographic data, healthcare contacts, anesthesia and surgical data were registered. Preoperative emotional/behavioral problems, during the 6 months prior to surgery, were assessed by the CBCL. Hierarchical, multiple regression was used to test whether anxiety and ED could be predicted by CBCL scores.

Results: Children with a higher CBCL score on preoperative internalizing problems (e.g. anxious/depression) showed preoperative more anxiety at induction (P=0.003). A higher CBCL score on preoperative emotional/behavioral problems was not associated with ED.

Conclusions: The CBCL predicted anxiety at induction but not ED.

Keywords: Anxiety, Children, Emergence Delirium, Perioperative Care, Psychological Tests, Surgery

Key messages

- Anxiety at induction and emergence delirium (ED) are important issues in pediatric anesthesia
- This study tested the value of the Child Behavior Checklist (CBCL) as a tool to predict anxiety at induction and ED in a large prospective cohort of children undergoing elective surgery.
  The CBCL predicted anxiety at induction but not ED

INTRODUCTION

Anxiety at induction of anesthesia in children is inevitably a cause of important stress,[1-3] linked to increased pain and higher analgesic requirements[4-6]. Earlier studies suggest that anxiety at induction, emergence delirium (ED) and postoperative behavioral problems might be connected[7-9]. Children between 1 and 5 years of age are the most vulnerable group in developing anxiety at induction[10-12]. Parental anxiety seems an important factor for preoperative anxiety in children[1,13,14]. Fortier *et al*[15] used, among other tools, the Child Behavior Checklist (CBCL) and found that internalizing behavior was predictive for anxiety at induction, in adolescents.

The identification of children at risk for increased anxiety at induction may create an opportunity to tailor pharmacological and psychological support towards their individual needs. Thus postoperative consequences such as ED and behavioral maladjustment might be reduced or prevented. Moreover, preoperative assessment can be a tool for the anesthesiologist to explain to parents perioperative behavioral problems. Until now no studies have been performed to validate an assessment tool in order to identify children at increased risk for preoperative anxiety. This study aims to fill this gap by studying the value of the CBCL, an internationally well-known standardized assessment tool,[16,17] in predicting anxiety at induction and ED in children undergoing elective surgery.

In this study we hypothesized that:1. higher scores on emotional/behavioral problems in children undergoing elective day-care surgery, as measured with the CBCL, are of predictive value for higher levels of anxiety at induction (assessed with the modified Yale Preoperative Anxiety Scale; mYPAS), and 2. that higher scores on emotional/behavioral problems in these children, as measured with the CBCL, are of predictive value for ED (assessed with the Pediatric Anesthesia Emergence Delirium scale; PAED).

MATERIALS AND METHODS

This prospective observational cohort study was conducted at the Queen Paola Children's Hospital in Antwerp, Belgium, with approval from the Institutional Review Board (B009201213439) and in accordance with the Declaration of Helsinki and the STROBE statement for observational studies.

Inclusion and exclusion criteria: Eligible were all consecutive patients undergoing day-care surgery, aged between 1.5 – 16 years who met the following inclusion criteria: 1. an American Society of Anesthesiologists (ASA) physical status I-II; 2. written informed consent of parents and of children aged ≥ 10 years obtained on the day of surgery; 3. parents with good understanding of Dutch language; 4. without premedication; 5. one parent present during induction. Children with known intellectual disability, suspect of malignant hyperthermia and ASA physical status higher than II were excluded.

Anesthesia procedure: all children received a standardized preparation and an informative preoperative video film just before entering the operating theatre. The anesthetic procedure was left to the discretion of the seven participating pediatric anesthesiologists in charge. All inductions were performed by inhalation of sevoflurane 8 vol.% in 50% oxygen without nitrous oxide. General anesthesia was maintained with sevoflurane and if appropriate a laryngeal mask airway (LMA) or endotracheal tube (ETT) was inserted. Intra-operative pain management included: 1. opioids (fentanyl, pethidine); 2. non-steroidal anti-inflammatory drugs (NSAID's). If necessary, children received regional anesthesia and the intravenous (IV) use of α_2- adrenergic agonist (clonidine) was noted because it can influence the occurrence of ED[18]. For postoperative pain management children received paracetamol IV (20 mg. kg^{-1}). At the end of surgery the inhalation agent was discontinued, the children were extubated awake and transferred to the Post Anesthesia Care Unit (PACU) for further observation.

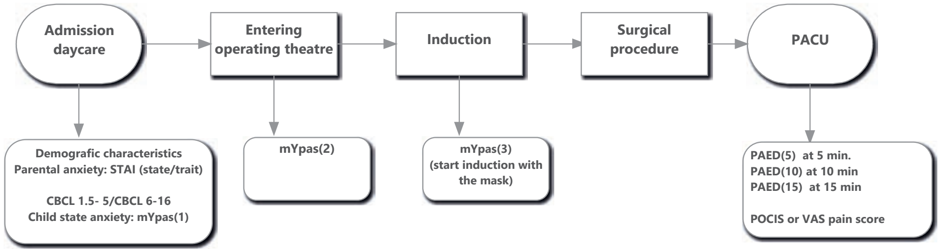
Assessment procedure (Figure 1)

Demographical/medical data were collected on the day of admission (standardized interview performed by a research nurse). The surgical procedures were dichotomized into Ear Nose Throat surgery (ENT) *versus* other, because ED is more common in ENT surgery[18]. Parental education (PE) used as an indicator of socioeconomic status (SES), was classified into three categories (1. no education, elementary school; 2. secondary school; 3. higher education or university).

Predictive assessment tools

Preoperative emotional/behavioral problems during the past 6 months were assessed by the CBCL (Appendix 1) completed by parents prior to surgery[16,17,19]. The CBCL contains respectively 100 (CBCL $1^{1/2}$ – 5 years of age) and 113 (CBCL 6 – 18 years of age) problem items. Each item can be scored by answering either: 1. not true; 2. somewhat or sometimes true; 3. very true or often true. Summary scores on internalizing problems (withdrawn, somatic complaints and anxious/depressed), externalizing problems (rule-breaking and aggressive behavior) and a total problem score were computed. A higher

Figure 1 Flowchart diagram of different moments during assessment



Parental anxiety (Spielberger's State-Trait Anxiety Inventory); CBCL = Child Behavior Checklist/1,5-5 and 6-18 as assessed by the accompanying mother or father; mYPAS = modified Yale Preoperative Anxiety scale at [mYPAS(1)], holding area,[mYPAS(2)] at entrance of the operating theatre and at [mYPAS(3)], induction with mask; PACU, Postoperative Care Unit; PAED = Pediatric Anesthesia Emergence Delirium scale at 5 min. [PAED(5)], 10 min. [PAED(10)] and 15 min. [PAED(15)]; POCIS = Pain Observation Scale for Young Children; VAS = Visual Analogue Score

score indicates more problems. A good validity and reliability for the Dutch version has been confirmed[20]. For all children, the accompanying parent was asked to complete the CBCL.

Parental anxiety was measured with the internationally acknowledged Spielberger State – Trait Anxiety Inventory (STAI) on admission[21] using its two parts: state anxiety (current emotional state) and trait anxiety (general anxiety disposition). The STAI has been validated for a Dutch speaking population[22].

Outcome variables

State anxiety at induction was assessed by the modified Yale Preoperative Anxiety Scale (mYPAS),[23] a structured observational instrument to measure anxiety in the holding area and at induction (Appendix 2). It consists of five domains: activity, emotional expressivity, state of arousal, vocalization and use of parents. These domains have a good to excellent psychometric properties. Adjusted scores range from 23 to 100, with higher scores indicating greater anxiety at induction. The mYPAS was completed at three moments: on admission [mYPAS(1)], in the holding area just before entering the operating theatre [mYPAS(2)] and finally at induction [mYPAS(3)]. All measurements were carried out by three independent observers who received standardized instructions and training in using the mYPAS.

ED was assessed using the Pediatric Anesthesia Emergence Delirium Scale (PAED)[24]. By summing the scores at 5 min [PAED(5)], 10 min [PAED(10)] and 15 min [PAED(15)] the total score is computed [PAED sum scores]. The PAED is a well-validated instrument for ED with a good internal consistency and reliability (Appendix 3). At all three moments two nurses completed the PAED in the PACU.

Since pain is considered a confounding factor in the ED assessment, it was rated by the Pain Observation Scale for young Children (POCIS)[25] in children aged ≤ 4 year and a Visual Analogue Scale (VAS)[26] in children ≥ 5. Both forms were measured by the PACU nurse. Children with at least moderate pain (POCIS score or a VAS score higher than 3) were removed from the final analysis (Figure 2).

Statistical analysis

A power analysis for multiple regression (GPOWER version 3.1.2) showed that with a power of 0.90 and an alpha of < 0.05, using 15 possible predictors, a total sample size of 171 was sufficient to detect a medium effect size (Cohen's f^2= 0.15). Subsequently our final sample (N.=343) was sufficiently large enough to adequately test the hypothesis that R^2 is different from zero.

Baseline child and parental characteristics such as demographic data and psychological assessment were displayed as means ± standard deviations (continuous data) or as percentages (categorical data). Normality was checked by using a Kolmogorov-Smirnov (K-S) test with Lilliefors significance correction for normal distribution.

To test whether the child's anxiety and ED changed across time, the mYPAS and PAED scores, respectively, were compared at the different time points using Friedman's two-way ANOVA.

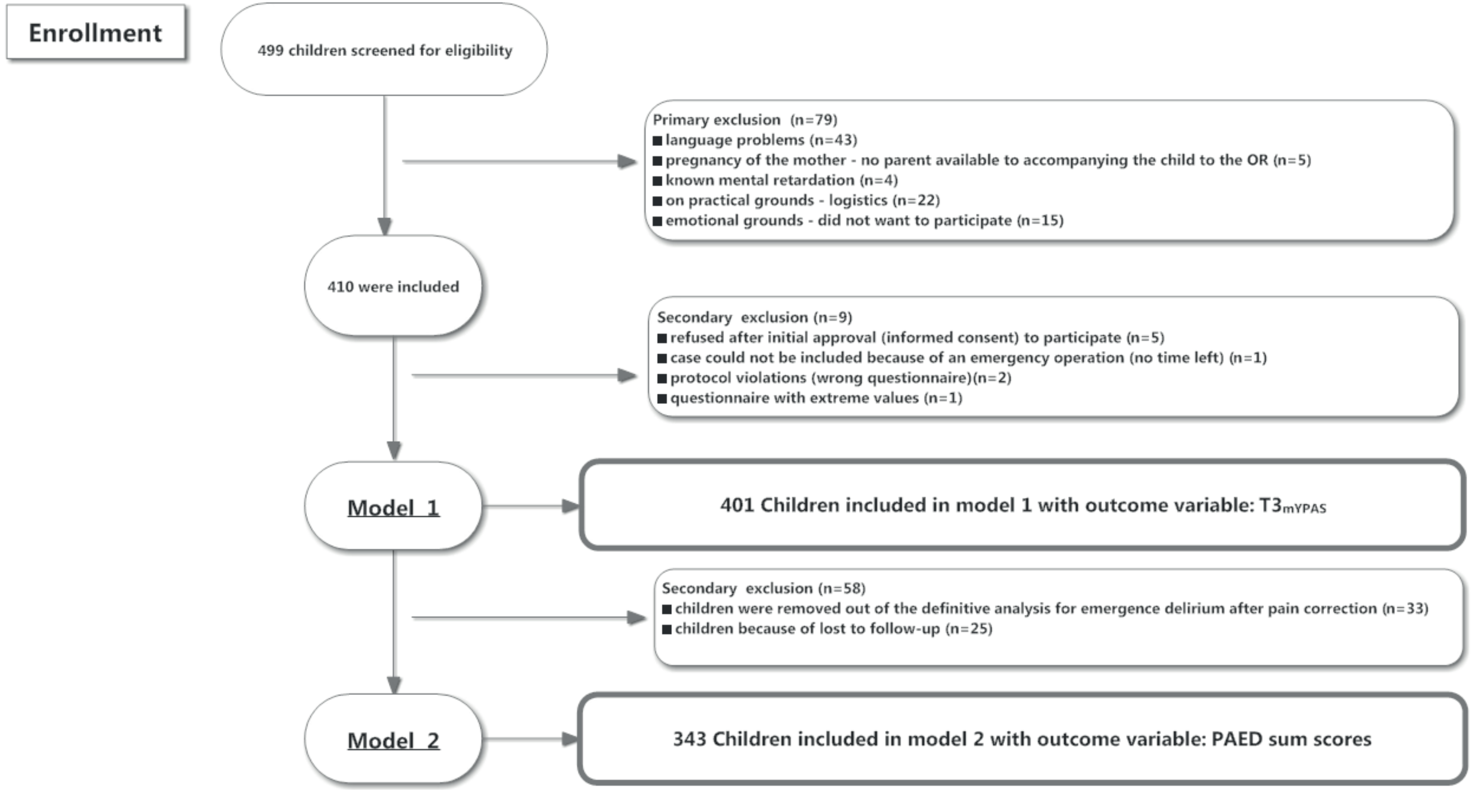
To analyze differences in parental state and trait anxiety between mothers and fathers and, whether there were differences in parental anxiety according to the child's age, *t*-tests were used.

To test for significant associations between all predictors and outcome variables (assumption of multicollinearity, r ≥ .8) a Pearson correlation matrix and also the variance inflation factor (VIF) and tolerance statistics were computed.

Main analyses

Two hierarchical, multiple regression models (forced entry) were constructed: one to explain anxiety at induction (model 1) and the other to explain ED (model 2). In model 1,

Figure 2 ● Flowchart inclusion of patient inclusion in model 1 and model 2



Model 1: hierarchical multiple linear regression – outcome: child anxiety at induction [mYPAS(3)]
Model 2: hierarchical multiple linear regression – outcome: emergence delirium – PAED = Pediatric Anesthesia Emergence Delirium Scale: PAED sum scores = PAED(5) + PAED(10) + PAED(15)
OR = operating room

with [mYPAS(3)] as the dependent variable, the following predictor variables were first entered into the model: 1. child's age; 2. child's gender; 3. previous experience of the child with anesthesia; 4. the child's state anxiety as assessed on admission [mYPAS(1)]; 5. parental state anxiety; 6. parental trait anxiety; 7. PE; 8. previous parental experience with accompanying a child to induction; 9. parental gender. Afterwards the CBCL summary scores for internalizing problems and for externalizing problems were added to the model. Using raw scores to test how much of the variance in anxiety at induction was explained by these CBCL summary scores, after controlling the other variables.

Similarly, in model 2, with sum scores of PAED as the dependent variable, the predictor variables were entered into two blocks. First, variables 1 to 3 and 5 to 8 as mentioned above for model 1 were entered in model 2, as well as three additional variables; 9. type of surgical procedure (ENT versus other types); 10. use of α_2-adrenergic agonist (clonidine); 11. anxiety at induction (i.e. the outcome variable of model 1). Second, CBCL - internalizing and externalizing problems, were added to the model. R^2 and R^2 change values were calculated to assess how much of the variance in anxiety at induction and ED can be explained by the model after adjusting for other variables.

All analyses were performed with IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.

P-values of <0.05 were considered statistically significant.

RESULTS

Patient sample

From January 2011 to February 2012, 499 children were approached. Data of 401 patients were included in model 1 (anxiety during induction) and 343 of them could also be analyzed in model 2 (ED) (Figure 2). Sixty percent was male (mean age: 5.9 years), approximately 40% underwent ENT procedures and for about 55%, it was their first anesthetic experience (Table I).

The child's state anxiety increased significantly from [mYPAS(1)] over [mYPAS(2)] to [mYPAS(3)] (P< 0.0001). The PAED scores at different time points decreased significantly over time (P<0.0001).

Table I Characteristics of the children and accompanying parent

	Children			**Accompanying Parent**	
	Child model 1	**Child model 2**		**Parent model 1**	**Parent model 2**
N.=401	N.=401	N.=343		N. =401	N.=343
demographic data					
gender boy	241 (60.1%)	205 (59.8%)	gender mother	305 (76.1%)	261(76.1%)
age,[a] months	70.2 ± 40.7	70.3 ± 40.9	parental age,[a] (y)	35,4 ± 6.3	35.4 ± 6.4
weight,[a] kg	22.5 ± 11.9	22.4 ± 11.9			
number of siblings			PE [b]		
≥ 1	329 (82%)	284 (82.7%)	PE 1	34 (8.5%)	30 (8.7%)
			PE 2	176 (43.9%)	146 (42.6%)
			PE 3	161 (40.1%)	143 (41.7%)
			missing values	30 (7.5%)	24 (7%)
child nationality			parental nationality		
Belgian	383 (95.5%)	331 (96.5%)	Belgian	367 (91.5%)	319 (93%)
other	18 (4.5%)	12 (3.5%)	other	31 (7.8%)	21 (6.1%)
			Missing values	3 (0.7%)	3 (0.9%)
surgical procedure					
adenotonsillectomy	153 (38.2%)	128 (37.3%)			
T-tube	43 (10.7%)	31 (9.0%)			
dental surgery	64 (16.0%)	62 (18.1%)			
general surgery	36 (9.0%)	31 (9.0%)			
urology	63 (15.7%)	54 (15.7)			
ophthalmology	13 (3.2%)	10 (2.9%)			
gastroenterology	3 (0.7%)	3 (0.9%)			
orthopaedic surgery	26 (6.5%)	24 (7.0%)			
ASA [c] 1	378 (94.3%)	324 (94.5%)			
ASA [c] 2	23 (5.7%)	19 (4.5%)			
first anesthetic experience	220 (54.9%)	190 (55.4%)			
Sevoflurane Vol. % [a]		3.3 (0.4)			
α_2-receptor agonist (clonidine)		132 (38.5%)			
intra-operative use of opioids		330 (96.2%			
use of IV paracetamol		335 (97.7%)			
use of NSAID [d]		142 (41.4%)			
locoregional anesthesia		52 (15.2%)			
psychological assessment					
child state anxiety [b,e]			parental anxiety [a,f]		
mYPAS(1)	28 ± 8	28 ± 8	state anxiety	38 ± 11	38 ± 10

Table I Characteristics of the children and accompanying parent (continued)

	Children			Accompanying Parent	
	Child model 1	Child model 2		Parent model 1	Parent model 2
mYPAS(2)	38 ± 18	38 ± 17	trait anxiety	34 ± 8	34 ± 8
mYPAS(3)	50 ± 27	50 ± 26			
			parental experience at induction	207 (51.8%)	177 (51.6%)
PAED scale [b,g]					
PAED(5)		12 ± 2			
PAED(10)		9 ± 3			
PAED(15)		6 ± 7			
PAED $_{\text{sum scores}}$		27 ± 7			
CBCL assessment [a,h]					
internalising problems	7.7 ± 6.6	7.7 ± 6.5			
externalizing problems	8.9 ± 7.2	8.9 ± 7.3			
(one accompanying parent report, 76% mothers)					

Model 1: hierarchical multiple linear regression – outcome: child anxiety at induction [mYPAS(3)]; Model 2: hierarchical multiple linear regression – outcome: emergence delirium (Pediatric Anesthesia Emergence Delirium Scale (PAED): PAED sum scores = PAED(5) + PAED(10) + PAED(15); data are expressed as N. (%); [a]data are expressed as mean with ± SD; [b]PE, parental education: PE 1 (no education or primary school), PE 2 (high school), PE 3 (further studies or university); [c]ASA, American Society of Anesthesiologists; [d]NSAID, non steroidal anti-inflammatory drugs; [e]mYPAS, modified Yale Preoperative Anxiety scale at [mYPAS(1)], holding area, [mYPAS(2)] at entrance of the operating theatre and at [mYPAS(3)], induction with mask; [f]parental anxiety (Spielberger's State-Trait Anxiety Inventory); [g]PAED, Pediatric Anesthesia Emergence Delirium scale at PAED(5), PAED(10) and PAED(15) and PAED sum scores = PAED(5) + PAED(10) + PAED(15) ; CBCL, [h]Child Behavior Checklist/1,5-5 and 6-18 as assessed by the accompanying mother or father.

Parental state anxiety was higher in accompanying mothers than in accompanying fathers ($P=0.006$) whereas no difference between the parents was found in trait anxiety ($P>0.05$).

In parents of children aged 1.5 to 5 years, state anxiety was higher (N.=249, Mean =39, SD ± 9.7) than in parents of children aged ≥ 6 (N.=150, Mean =35, SD ± 10.2)($P=0.007$).

Univariate analyses showed significant associations between the separate predictors CBCL-internalizing and externalizing problems, younger age, state anxiety on admission, parental state anxiety and children's anxiety at induction (Table II).

Furthermore, five predictors were significantly associated with ED [PAED sum scores]: younger age, the child's first anesthetic, externalizing behavior, anxiety at induction and ENT surgery.

Table II Univariate associations between predictor variables and of the child's anxiety during induction respectively emergence delirium

	Model 1	**Model 2**
prediction variables	**mYPAS(3)** [a]	**PAED sum scores** [b]
Child characteristics		
1. child age (m)	0.43**	-0.25**
2. child gender	0.05	0.06
3. first anesthetic	-0.09	-0.17**
4. preoperative internalizing problems [c]	0.16**	0.03
5. preoperative externalizing problems [c]	0.16**	0.14**
6. [mYPAS(1)] [a]	0.38**	_
7. [mYPAS(3)] [a]	_	0.15**
Parental characteristics		
1. gender accompanying parent	-0.02	0.02
2. previous experience	0.04	0.08
3. state anxiety [d]	0.14**	0.07
4. trait anxiety [d]	0.08	0.00
5. PE [e]	-0.08	0.01
procedure		
1. dichotomy ENT [f] *versus* other surgery	_	0.14**
2. use of α_2- adrenergic agonist (clonidine)	_	0.03

Pearson correlation coefficients: *P<0.05. **P<0.01 (2-tailed); [a] mYPAS, modified Yale Preoperative Anxiety scale at [mYPAS(1)], holding area and at [mYPAS(3)], induction with mask; [b] PAED sum scores, Pediatric Anesthesia Emergence Delirium Scale (PAED) sum scores = PAED(5) + PAED(10) + PAED(15); [c] Child Behavior Checklist/1,5-5 and 6-18 as assessed by the accompanying mother or father; [d] parental anxiety (Spielberger's State-Trait anxiety Inventory); [e] PE, Parental education; [f] ENT, ear-nose-throat surgery.

Multiple regression models

Prediction of child's anxiety during induction (mYPAS(3), model 1, N.=401, Table III)

Preoperative internalizing problems, the child's age, mYPAS(1) and parental education were significant predictors of anxiety at induction (P=0.003). CBCL internalizing problems significantly predicted anxiety during induction, after controlling for the other predictors. One SD difference on the internalizing problem score is associated with a 0.19 SD difference in mean at [mYPAS(3)]. Overall, this model explains 33% of the variance of anxiety at induction as measured with mYPAS.

Prediction of ED (PAED sum scores, model 2, N.=343, Table IV)

Table III ● Predictors of the child's anxiety during anesthetic induction: results of the final multiple regression model

	Anxiety at induction as measured with mYPAS [mYPAS(3)]						
	Model 1						
Variable	Step 1	*B*	β	Step 2	*B*	β	95% CI for *B*
constant		36.96**			39.78**		[21.42 - 58.14]
child age		-0.25**	-0.37**		-0.26**	-0.39**	[-0.33, - 0.20]
child gender		2.81	0.05		3.02	0.06	[-1.71, 7.76]
first anesthetic		-1.60	-0.03		-1.93	-0.04	[-7.23, 3.38]
[mYPAS(1)] [a]		1.19**	0.35**		1.17**	0.34**	[0.87, 1.47]
parental state anxiety [b]		0.03	0.01		0.00	0.00	[-0.26,0.28]
parental trait anxiety [b]		0.17	0.05		0.07	0.02	[-0.26, 0.39]
PE [c]		-4.00	-0.10*		-4.00	-0.10*	[-7.55, -.36]
previous parental experience		-0.62	0.12		-0.43	-0.01	[-5.60, 4.75]
gender parent		-3.07	-0.05		-3.25	-0.05	[-8.88, 2.15]
preoperative internalizing problems [d]					0.81*	0.19**	[0.33, 1.29]
preoperative externalizing problems [d]					-0.31	-0.08	[-0.75, 0.13]
R^2		.31			.33		
F		17.86**			5.76**		
ΔR^2					.022		
ΔF					12.10		

Note. N.=401. CI = confidence interval. *P<0.05; **P≤0.001. [a][mYPAS(1)] modified Yale preoperative anxiety scale in the holding area; [b]parental anxiety (Spielberger's State-Trait anxiety Inventory); [c]PE, Parental education; [d]preoperative internalizing and externalizing problems - Child Behavior Checklist/1,5-5 and 6-18 as assessed by the accompanying mother or father.

After adjustment for confounders, no association was found between CBCL internalizing, externalizing behavior and ED. Younger age of the child and the first experience with anesthesia were significant predictors of ED. Overall, approximately one tenth of the variance in emergence delirium could be explained by the variables included in the model (R^2 =0.11).

DISCUSSION

This study examined whether CBCL scores, reflecting emotional/behavioral problems during the last 6 months prior to surgery, were predictive of anxiety during induction of anesthesia and of ED in children admitted for day-care surgery. Internalizing problems were indeed significant predictors of anxiety at induction, as were the child's age, parental education and child's state anxiety on admission. Younger age also significantly

Table IV Prediction of postoperative emergence delirium: results of the final linear regression model

	ED at induction as measured with PAED sum scores						
	Model 2						
Variable	Step 1	*B*	β	Step 2	*B*	β	95% CI for *B*
constant		26.63**			25.96**		[19.91, 32.01]
child age		-0.03*	-0.16*		-0.02*	-0.14*	[-0.05, -0.00]
child gender		1.04	0.07		0.93	0.07	[-0.63, 2.49]
first anesthetic		-1.90*	-0.14*		-1.84*	-0.13*	[-3.56, -0.13]
parental state anxiety [a]		0.04	-0.05		-0.04	0.06	[-0.05, 0.13]
parental trait anxiety [a]		-0.02	-0.02		-0.05	-0.06	[-0.16, 0.06]
PE [b]		0.17	0.02		0.31	0.03	[-0.86, 1.48]
previous parental experience		-0.41	-0.03		-0.45	-0.03	[-2.15, 1.26]
gender accompanying parent		-0.08	-0.00		-0.01	-0.00	[-1.81, 1.80]
dichotomy ENT [c] *versus* other surgery		1.53 †	0.11 †		1.52 †	0.11 †	[-.09, 3.01]
use of α_2-adrenergic agonist (clonidine)		0.60	0.04		0.66	0.05	[-0.88, 2.19]
[mYPAS(3)] [d]		0.01	0.05		0.01	0.05	[-0.02, 0.05]
preoperative internalizing problems [e]					-0.01	-0.01	[-0.17, 0.14]
preoperative externalizing problems [e]					0.12 †	0.12 †	[-0.02, 0.26]
R^2		.10			.11		
F		3.03**			1.85		
ΔR^2					.01		
ΔF					1.18		

Note. N.=343. CI = confidence interval. *P<0.05; **P<0.01; †P≤0.1. Sum scores Pediatric Anesthesia Emergence Delirium (PAED) scale = PAED(5) + PAED(10) + PAED(15); [a]parental anxiety (Spielberger's State-Trait anxiety Inventory); [b]PE, Parental education; [c]ENT, ear-nose-throat surgery; [d][mYPAS(3)], modified Yale preoperative anxiety scale at induction; [e]preoperative internalizing and externalizing problems - Child Behavior Checklist/1,5-5 and 6-18 as assessed by the accompanying mother or father.

predicted ED (consistent with earlier findings[18,24]) as did the first anesthetic experience. ED could not be predicted by preoperative emotional/behavioral problems of the child.

Prediction of anxiety during induction

CBCL internalizing problems significantly predicted anxiety at induction. This is in line with the results of a pilot study in adolescents[15]. Also consistent with previous findings, age appeared to be an important risk factor for anxiety at induction[10,11]. Furthermore, anxious behavior already expressed on admission in the holding area [mYPAS(1)], was strongly associated with anxiety at induction. This is consistent with studies documenting that behavior in the direct preoperative period predicted anxiety at induction[2,3,6,27,28].

Finally, parental education appeared to be a factor that influenced anxiety at induction: children of parents with higher education were less anxious. For that matter, it is well-known from previous studies that emotional/behavioral problems (assessed by the CBCL) are associated with parental SES[29,30].

Not all factors included in our model indeed appeared to be predictors of anxiety at induction. In contrast to internalizing problems, externalizing problems did not show up as a predictor of anxiety at induction in our final model 1. Although literature demonstrated that externalizing and internalizing scores are moderately correlated[16,17].

Furthermore, in contrast with earlier findings,[11,30] parental state anxiety was not an independent risk factor for anxiety at induction. Fathers reported less state anxiety compared to mothers, yet no parental gender effect was found. Parental anxiety was higher in parents of children younger than five years than in parents with older children – an outcome that corresponds to preceding findings[31]. However, as Davidson *et al.*[10] pointed out, the child-parental interaction cannot be reflected by taking only parental anxiety into account.

Children undergoing anesthesia display a wide range of distress and non-distress behavior[2] The mYPAS only measures state anxiety[23]. Presumably it is easier to assess anxious behavior at induction in younger children, since they express their anxiety more openly (e.g. by crying) compared to older children, in whom anxiety may be less visible. Rather these older children might not express it openly but tend to keep it to themselves or pretend to be brave.

From a methodological perspective, it is worthwhile mentioning that anxiety and ED were considered as psychological constructs on a continuum. Therefore we used no cut-off scores and we performed multiple rather than logistic regression. Moreover, it is still subject of debate which cut-off value should be used to dichotomize anxiety levels or diagnose ED[32.]

Prediction of ED

The child's age and first experience with anesthesia were found to be independent predictors of ED, which is in line with previous research[33,34]. In contrast with earlier studies[4,7,35] preoperative anxiety was not a significant predictor for ED in the multivariate regression. This may be explained by the use of different non-validated assessment tools for measuring ED in these earlier studies. In line with the proposals of Locatelli *et al*[36], the present study measured ED with a validated tool, and children with at least moderate pain were excluded from the final analysis to leave out a confounding influence of postoperative pain. Moreover our results are conform to recent findings by Bortone *et al*[37]. Although not statistically significant, there was a trend (P=0.1) towards an increased risk for ED in children with more externalizing problems. An explanation might be that children who are more prone to acting out their behavior, might be more prone to ED. This could be a topic for future research. ED seems to be very limited in time with almost complete disappearance after 15 minutes, which is consistent with earlier findings[35].

A univariate analysis confirmed an association between ENT and ED – consistent with previous reports[8,34] – but this was not sustained in multivariate regression, although it was nearly significant (P =0.06). No association was found with α_2-adrenergic agonist (clonidine) and ED which is in accordance with previous findings[8,18,34].

Strengths and limitations of the study

The strengths of this prospective study include: the large sample size and the use of standardized assessment tools at defined time points. A well-validated screening instrument (CBCL) was used to screen emotional/behavioral problems of children during the preceding 6 months period[16,17]. Another advantage of the CBCL is that it covers a wide range of emotional/behavioral problems and a broad age range (1.5 to 18 years). The broad range of surgical procedures is both an advantage as well as a limitation. Another limitation is that there was no preoperative family visit with the anesthesiologist before the day of surgery.

To what extent the use of only one parent having filled out the CBCL may have influenced our results, is unknown. It would be better to use a multi-informant approach (both parents or even a caregiver or teacher), so that multi-informant information can be combined for the final analysis. For practical reasons it was impossible to organize this in our setting. Having the CBCL completed on the day of surgery could have influenced the accompanying parents' perception and their ratings as to the child's typical behavior.

The anesthesia protocol could not be standardized due to the wide range of surgical procedures, which may have generated biases. This may also have contributed to our findings that the CBCL did not predict ED. For future research it is recommended to investigate the present research questions using more homogenous prospective patient samples and more standardized anesthetic procedures.

CONCLUSIONS

This study has focused attention on the complex relationships between emotional/behavioral functioning of a child and anxiety at induction of anesthesia and emergence delirium. Our data provide a strong body of evidence that CBCL scores *per se* can predict anxiety at induction. Not only is the assessment of anxiety in the direct preoperative period important, but also pre-existing perioperative emotional/behavioral problems related to anxious behavior should be considered. In addition to internalizing problems during the last 6 months prior to surgery, younger age of the child, lower parental education status and anxious behavior on admission are significant predictors of anxiety during anesthetic induction.

Thus the CBCL can provide anesthesiologists insight into the anxiety that the child will experience during induction. It may serve as tool to tailor the anesthesia procedure to the individual needs of emotionally vulnerable children undergoing surgery. As to clinical implications: the CBCL is easy to deliver, takes only 15 minutes to complete. However, in a busy clinical setting, this may be a burden for both the staff and parents. Future research should focus on implementing the CBCL as a tool to screen for preoperative anxiety, by delivering and scoring it in the preoperative period at home, online, in an adequately protected and anonymous web-based area.

APPENDIX 1

The modified Yale Preoperative Anxiety Scale

Activity

1. Looking around, curious, playing with toys, reading (or other age-appropriate behavior); moves around holding area/treatment room to get toys or to go to parent; may move toward operating room equipment
2. Not exploring or playing, may look down, fidget with hands, or suck thumb (blanket); may sit close to parent while waiting, or play has a definite manic quality
3. Moving from toy to parent in unfocused manner, non-activity-derived movements; frenetic/frenzied movement or play; squirming, moving on table; may push mask away or cling to parent
4. Actively trying to get away, pushes with feet and arms, may move whole body; in waiting room, running around unfocused, not looking at toys, will not separate from parent, desperate clinging

Vocalizations

1. Reading (nonvocalizing appropriate to activity), asking questions, making comments, babbling, laughing, readily answers questions but may be generally quiet; child too young to talk in social situations or too engrossed in play to respond
2. Responding to adults but whispers, "baby talk,"only head nodding
3. Quiet, no sounds or responses to adults
4. Whimpering, moaning, groaning, silently crying
5. Crying or may be screaming "no"
6. Crying, screaming loudly, sustained (audible through mask)

Emotional expressivity

1. Manifestly happy, smiling, or concentrating onplay
2. Neutral, no visible expression on face
3. Worried (sad) to frightened, sad, worried, or tearful eyes
4. Distressed, crying, extreme upset, may have wide eyes

State of apparent arousal

1. Alert, looks around occasionally, notices or watches what anesthesiologist does (could be relaxed)
2. Withdrawn, sitting still and quiet, may be sucking on thumb or have face turned into adult
3. Vigilant, looking quickly all around, may startle to sounds, eyes wide, body tense

4. Panicked whimpering, may be crying or pushing others away, turns away

Use of parents

1. Busy playing, sitting idle, or engaged in age appropriate behavior and doesn't need parent; may interact with parent if parent initiates the interaction
2. Reaches out to parent (approaches parent and speaks to otherwise silent parent), seeks and accepts comfort, may lean against parent
3. Looks to parent quietly, apparently watches actions, doesn't seek contact or comfort, accepts it if offered or clings to parent
4. Keeps parent at distance or may actively withdraw from parent, may push parent away or desperately clinging to parent and not let parent go

APPENDIX 2

The Pediatric Anesthesia Emergence Delirium (PAED) scale

1. The child makes eye contact with the caregiver.
2. The child's actions are purposeful.
3. The child is aware of his/her surroundings.
4. The child is restless.
5. The child is inconsolable.

Items 1, 2, and 3 are reversed scored as follows: 4 = not at all, 3 = just a little, 2 = quite a bit, 1 = very much, 0 = extremely. Items 4 and 5 are scored as follows: 0 = not at all, 1 just a little, 2 = quite a bit, 3 = very much, 4 = extremely.

The scores of each item are summed to obtain a total score

APPENDIX 3

The Child Behavior Checklist (CBCL)

Sample of 5 selected items (question)

1. Afraid to try new things 0 – 1 – 2
2. Demands must be met immediately 0 – 1 – 2
3. inattentive, easily distracted 0 – 1 – 2
4. Temper trantrums or hot temper 0 – 1 – 2
5. Wants a lot of attention 0 – 1 – 2

Each item can be scored by answering either: 0 = not true; 1 = Somewhat or Sometimes True; 2 Very True or Often True

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Editorial on our findings

Evaluation and treatment of preoperative anxiety in children: are we doing what we should do?

Gomez-Rios MA.

Minerva Anestesiol. 2015;81(2):113-5.

'Exterminate learning and there will no longer be worries.
Between yea and nay
How much difference is there?
Between good and evil
How great is the distance?' (*Tao Te Ching*, 20)
绝学无忧，唯之与阿，相去几何？善之与恶，相去若何？

Chapter 3

A Visual Analogue Scale to assess anxiety in children during anesthesia induction (VAS-I): results supporting its validity in a sample of day care surgery patients

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What is already known

- Children's preoperative state anxiety is positively associated with postoperative pain and with postoperative behavior changes.

What this article adds

- A Visual Analogue Scale to assess anxiety at induction is easy to use and may be helpful for parental assessment of their child's anxiety during induction of anesthesia.

ABSTRACT

Background: The modified Yale Preoperative Anxiety Scale is widely used to assess children's anxiety during induction of anesthesia, but requires training and its administration is time-consuming. A Visual Analogue Scale, in contrast, requires no training, is easy-to-use and quickly completed.

Aim: To provide preliminary support for a Visual Analogue Scale to assess anxiety during induction of anesthesia and to determine cut-offs to distinguish between anxious and non-anxious children.

Methods: Four hundred one children (1.5 – 16 years) scheduled for daytime surgery were included. Children's anxiety during induction was rated by parents and anesthesiologists on a Visual Analogue Scale and by a trained observer on the modified Yale Preoperative Anxiety Scale. Psychometric properties assessed were: 1. concurrent validity (correlations between parents' and anesthesiologists' Visual Analogue Scale and modified Yale Preoperative Anxiety Scale scores); 2. construct validity (differences between subgroups according to the children's age and the parents' anxiety as assessed by the State – Trait Anxiety Inventory); 3. cross-informant agreement using Bland-Altman analysis; 4. determine cut-offs to distinguish between anxious and non-anxious children (reference: modified Yale Preoperative Anxiety Scale ≥ 30).

Results: Correlations between parents' and anesthesiologists' Visual Analogue Scale on the one hand and modified Yale Preoperative Anxiety Scale scores on the other were strong (0.68 and 0.73 respectively). Visual Analogue Scale scores were higher for children ≤ 5 years compared to children aged ≥ 6. Visual Analogue Scale scores of children of high-anxious parents were higher than those of low-anxious parents. The mean difference between parents' and anesthesiologists' Visual Analogue Scale scores was 3.6, with 95% limits of agreement [-56.1 to 63.3]. To classify anxious children, cut-offs for parents (≥ 37 mm) and anesthesiologists (≥ 30 mm) were established.

Conclusions: The present data provide preliminary data for the validity of a Visual Analogue Scale to assess children's anxiety during induction.

Keywords: Anesthesia, Child, Anxiety, Psychometrics, Pain Measurement, Visual Analogue Scale

INTRODUCTION

Preoperative anxiety is an important problem in children undergoing anesthesia[1,2]. It has been associated with emergence delirium and postoperative behavioral changes[3,4]. The highest state anxiety levels during the entire perioperative period are seen at the moment of induction[2,5]. Children with high levels of preoperative state anxiety are assigned higher postoperative pain scores and require more analgesics, both in hospital and at home[5-8]. Furthermore, stressful and anxious experiences may compromise future medical contacts[9].

Children's preoperative anxiety at induction is often assessed with the modified Yale Preoperative Anxiety Scale (m-YPAS)[10-12], which is a well validated tool widely used in research. However, the m-YPAS has some major drawbacks for clinical practice: it should be administered by trained raters, and is lengthy and therefore time consuming.

Visual Analogue Scales (VAS) are widely employed to assess both general anxiety[13] and pre- and postoperative anxiety[14,15]. In contrast to the m-YPAS, they require no training, are simple and not time consuming. Bringuier *et al*[7] previously validated a perioperative VAS for anxiety, for use in children aged 7 – 16 years. Previous research has failed to investigate whether this VAS is also valid to assess perioperative anxiety for younger children. It is important to fill this knowledge gap, bearing in mind that very young children commonly exhibit more overt anxious behavior compared to older children[2,12,16].

Given that anxiety peaks during induction, it would seem best to assess the anxiety level at that moment. By rating anxiety during induction, parents and anesthesiologists focus their attention on the child's anxiety. Consequently, postoperative behavior and pain management could be tailored to the child's needs. This requires a valid, easy-to-use assessment instrument for use by parents and anesthesiologists.

Therefore, the aim of this study was to obtain preliminary evidence for the validity of the VAS-anxiety (VAS-I) for use by anesthesiologists (VAS-IA) and parents (VAS-IP) in children over a broad age range (1.5 – 16 yrs) during induction of anesthesia. More specifically, we aimed to investigate concurrent validity (by assessing correlations between the VAS-IP and VAS-IA, on the one hand, and m-YPAS scores on the other hand) and construct validity (by analyzing differences between subgroups according to the children's age and the parents' anxiety). Furthermore, we aimed to assess cross-informant agreement between VAS-IP and VAS-IA scores and to establish cut-offs for the VAS-IP and VAS-IA to distinguish between anxious children and non-anxious children, with the m-YPAS as reference standard.

MATERIALS AND METHODS

Design and setting

This study was conducted at the Queen Paola Children's Hospital in Antwerp, Belgium, with approval from the Institutional Review Board (B009201213439) and in accordance with the Declaration of Helsinki and reported following the STROBE statement for observational studies. The data gathering was part of a larger prospective cohort study[12].

Inclusion and exclusion criteria[12]

Children between the ages of 1.5 – 16 years who underwent daytime surgery between January 2011 and February 2012 and were accompanied by a parent during induction were eligible. Further inclusion criteria were as follows: 1. an American Society of Anesthesiologists physical status I-II; 2. written informed consent of parents and of children aged ≥ 10 years obtained on the day of surgery; 3. parents with a good understanding of the Dutch language; and 4. no premedication. Children with known intellectual disabilities and those suspected of having malignant hyperthermia were excluded.

All parents and children received a standard information brochure and watched an instructive video on the anesthesia procedure immediately prior to entering the operating theatre. Upon admission, the accompanying parent's demographics were registered, and parental anxiety was assessed with Spielberger's State – Trait Anxiety Inventory (STAI)[17]. A cut-off value of ≥ 46 on the state subscale of the STAI was used to distinguish between low and high parental state anxiety[18]. The STAI has been validated for the Dutch population[19].

Seven pediatric anesthesiologists participated in the study. All inductions were performed via sevoflurane inhalation, which is standard practice in our hospital.

Child anxiety assessment during induction

The child's anxiety during induction was rated by: 1. completion of the VAS-I during anesthesia induction by the attending pediatric anesthesiologist and accompanying parent (VAS-IA, VAS-IP, respectively); 2. completion of the m-YPAS during induction by one of three trained raters.

Both the VAS-IP and VAS-IA consist of a 100-mm horizontal line with two extremes, '*not anxious*' (left) and '*very anxious*' (right), on which the parent or anesthesiologist marks the point that represents their perception of the child's anxiety. An independent researcher determined the score by measuring the distance in millimeters from the left-hand extreme to the marked point (Figure 1).

Figure 1 ● Visual Analogue Scale Anxiety during Induction (VAS-I).

The m-YPAS[10] is a structured observational instrument to measure anxiety both in the holding area and during induction. It consists of five domains: activity, emotional expressivity, state of arousal, vocalization and use of parents (children seek support by parents), each with 4 or 6 items. The single summary score ranges from 23 to 100 and is obtained by summating the partial weights of each category. The m-YPAS has good to excellent psychometric properties, as documented by Kain and co-workers[10]. The authors reported good inter- and intra-observer agreement (κ statistics ranging between 0.63 and 0.90), high concurrent validity (correlation with the STAI for children: coefficient r = 0.79), and high construct validity of the instrument. To identify anxious children, they determined a cut-off value of 30[2].

Statistical analysis

Parental and child demographic characteristics and psychological scores are presented as means and standard deviations, as medians with interquartile range or as numbers and percentages (categorical data).

We set out to describe the concurrent validity of the VAS-I, which involves comparing a new measure to an existing, valid measure. Therefore we assessed correlations between on the one hand both the VAS-IP and VAS-IA and on the other hand the m-YPAS, using Pearson's correlation coefficients and two-tailed tests of significance (H_0:population correlation coefficient zero). According to Cohen's criteria[20], correlations of 0.10 - 0.29 are considered small, 0.30 – 0.49 medium and above 0.50 large.

Construct validity can be understood as the extent to which an instrument measures the construct or concept that it is designed to measure. This can be established by studying whether the instrument is sensitive to differences between subgroups that are known to score differently from each other (referred to as known-groups validity). To this aim we created two subgroups according to the children's age [1.5 – 5 yrs vs. 6 – 16 yrs] and parents' anxiety level [cut-off value of ≥ 46 on the state subscale of the STAI]. Based on literature[2,12], it was hypothesized that younger children and children of anxious parents would score higher on the VAS-I. For these analyses, Mann-Whitney *U* tests were used.

Then we determined cross-informant agreement, which reflects the strength between ratings of two different types of raters on an instrument. The agreement between parents and anesthesiologists was analyzed using a Bland-Altman plot (showing the mean difference and the 95% limits of agreement).

Lastly, receiver operating characteristic (ROC) curves were calculated to determine cut-offs on the VAS-IP and VAS-IA to distinguish between anxious and non-anxious children, with the m-YPAS as reference (cut-of value on m-YPAS ≥ 30). The optimal cut-offs on the ROC for the VAS-IP and VAS-IA were chosen according to the Youden index method, which means that we choose the point of the ROC-curve as a cut-off where the equation "sensitivity + specificity – 1" is maximal.

All analyses were conducted with IBM SPSS Statistics for Windows, Version 19.0 (Armonk, NY, USA; IBM Corp.) and MedCalc Statistical Software version 14.12.0 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2014).

RESULTS

During the study period 410 children were approached. Of these, 9 children could not be included, due to practical or logistic reasons (n = 4) or refusal after initial approval (n = 5). The final sample consisted of 401 children, with a mean age of almost 6 years and a male predominance (60%). Approximately 76% of the accompanying parents were mothers, and 52% had previous experience with induction (Table 1). Four hundred parents completed a VAS-IP and the seven attending anesthesiologists made 397 VAS-IA assessments. Table 2 presents scores on the VAS-IA, VAS-IP and m-YPAS, broken down for the child's age category and parental anxiety level.

Concurrent validity

Strong positive correlations were found between the VAS-IP and m-YPAS (N = 400; r = .67; *P* = .000) and between the VAS-IA and m-YPAS (N = 397; r = 0.79; *P* =.000).

Table 1 Characteristics of the children and accompanying parent(s) during induction

	Children		**Accompanying parents**
	N. =401		N. =401
demographic data		**demographic data**	
sex, male	241 (60.1%)	sex, mother	305 (76.1%)
age, months	70.2 ± 41	parental age (yrs)	35.4 ± 6
native Belgian	383 (95.5%)	native Belgian	367 (91.5%)
		education	
		no education / primary school	34 (8.5%)
		high school	176 (43.9%)
		further studies / university	161 (40.1%)
		missing values	30 (7.5%)
		previous experience with induction	207 (51.8%)
surgical procedure			
adenotonsillectomy	153 (38.2%)		
dental surgery	64 (16.0%)		
urology	63 (15.7%)		
T-tube	43 (10.7%)		
general surgery	36 (9.0%)		
orthopedic surgery	26 (6.5%)		
ophthalmology	13 (3.2%)		
gastroenterology	3 (0.7%)		
[a]ASA 1	378 (94.3%)		
[a]ASA 2	23 (5.7%)		
		[b]**anxiety assessment,**	
		STAI - state anxiety	37.8 ± 11
		STAI - trait anxiety	34.4 ± 8

Data are expressed as means with ± standard deviationsRO or as numbers (percentages); [a]ASA, American Society of Anesthesiologists; [b]STAI, Parental anxiety (Spielberger's State-Trait Anxiety Inventory) – state subscale.

Construct validity

VAS-I scores in relation to age group

The VAS-IP scores assigned to younger children (1.5 – 5 yrs) were higher than the scores assigned to older children (6 – 16 yrs) (medians of 44.5 versus 25.0 respectively; P = 0.0005). This held for the VAS-IA scores as well (medians of 45.0 versus 10.0; $P < .0001$) (Table 2).

Table 2 ● Assessments of children's state anxiety during induction

	All Children	**Aged 1.5 –5 yrs.**	**Aged 6–16 yrs.**
	N. = 401	N. = 250	N. = 151
[a]m-YPAS	40.0 [28.3-73.3]	50.0 [31.7-86.7]	28.0 [23.3-46.7]
[b]VAS-IP	40.0 [9.25-44.0]	44.5 [15.0-73.0]	25.0 [5.0-55.5]
[c]VAS-IA	20.0 [6.0-75.0]	45.0 [10.0-81.0]	10.0 [2.5-28.5]
	Non-anxious parents	**Anxious parents**	
	[d]STAI state subscale < 46	**[d]STAI state subscale ≥ 46**	
	N. = 314	N. = 86	
[a]m-YPAS	37.0 [28.3-73.3]	47.5 [33.3-76.7]	
[b]VAS-IP	30.0 [8.0-63.0]	57.0 [23.5-84.5]	
[c]VAS-IA	18.0 [6.0-70.0]	35.0 [10.0-83.0]	

Data are expressed as medians with interquartile range (IQR); [a]mYPAS, modified Yale Preoperative Anxiety scale during induction with mask; [b]VAS-IP, Visual Analogue Scale Anxiety during Induction by parents; [c] VAS-IA, Visual Analogue Scale Anxiety during Induction by the anesthesiologist; [d]STAI, Parental anxiety (Spielberger's State-Trait Anxiety Inventory) – state subscale.

VAS-I scores in relation to parental anxiety level

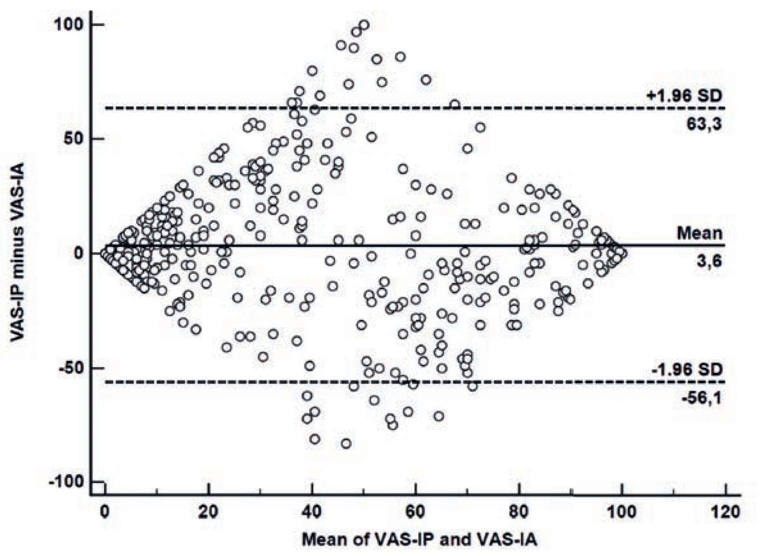
Based on their STAI state scores, 86 (21.5%) parents were classified as high-anxious (mean STAI score = 53 ± 6), and 314 (78.5%) as low-anxious (mean STAI score = 34 ± 6).

The VAS-IP ratings for children of high-anxious parents were higher than those for children of low-anxious parents (medians of 57.0 versus 30.0; $P = 0.0006$). This pattern was also found for the anesthesiologists' scores (medians of 35.0 versus 18.0; $P = 0.024$) (Table 2).

Cross-informant agreement

To determine the agreement between the parents' and the anesthesiologists' ratings of the children's anxiety, a Bland-Altman plot was constructed (Figure 2). In this graphical method, the differences between the two scores (i.e. the VAS-IP and VAS-IA) are plotted against the averages of the two scores. As shown, the mean difference between the VAS-IP and the VAS-IA is 3.6 (standard deviation = 30.5), the VAS-IP being the highest on average. The 95% limits of agreement between the two ratings ranged from -56.1 to 63.3. There seemed to be no obvious pattern of agreement over the range of the measurements.

Figure 2 Cross-informant agreement

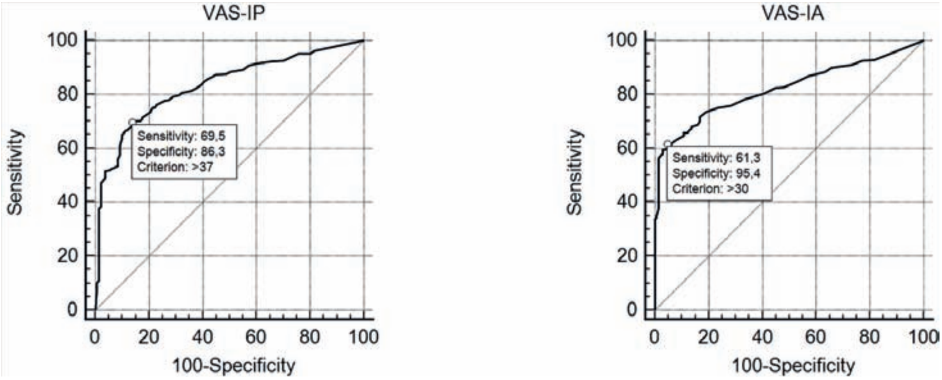


Bland-Altman plot showing the mean difference and the 95% limits of agreement. VAS-IP, Visual Analogue Scale Anxiety during Induction by parents; VAS-IA, Visual Analogue Scale Anxiety during Induction by anesthesiologists

Cut-offs on the VAS-IP and VAS-IA

As assessed with the m-YPAS, 269 children (67.2%) were anxious during induction. The sensitivity and specificity of the VAS-IP and VAS-IA for predicting anxiety were assessed using an ROC analysis in order to identify the optimal cut-offs. The *ROC curve analysis for parents* (VAS-IP: area under the curve [AUC] = 0.83; [95% CI: 0.79-0.87], *P* = 0.000) (*Figure* 3) identified a score of > 37 mm on the VAS-IP as the cut-off to distinguish between anxious and non-anxious children. For this cut-off, the sensitivity (true positive rate) was 70%, and the specificity (true negative rate) was 86%, with negative predictive value of 58% and a positive predictive value of 91%. The *ROC analysis for anesthesiologists* (VAS-IA: AUC = 0.82; [95% CI: 0.78-0.86], *P* = 0.000) identified a VAS-IA score > 30 mm as cut-off, with a sensitivity of 61%, a specificity of 95%, a negative predictive value of 54% and a positive predictive value of 95%.

Figure 3 ● Cut-points on the VAS-IP and VAS-IA to distinguish between anxious and non-anxious children using the m-YPAS as reference (cut-off value on m-YPAS ≥ 30).



Comparison of receiver operating characteristic (ROC) curves for VAS-IP and VAS-IA for sensitivity (true-positive rate) and 100-specificity (false-positive rate)

DISCUSSION

The results of this study provide preliminary data supporting the validity of the VAS-I to detect perioperative anxiety during anesthesia induction. This is of clinical importance, since children's perioperative anxiety has been associated with emergence delirium and post-hospital behavior changes. Moreover, perioperative anxiety is a crucial component of postoperative pain management [4,6,7]. In spite of this, the issue is significantly under-appreciated[4].

To assess the concurrent validity of the VAS-I, we compared the VAS-I to the m-YPAS. The results were encouraging, in that strong correlations were found both between the VAS-IA and the m-YPAS and between the VAS-IP and the m-YPAS. In a previous study investigators found that an anxiety VAS in the *holding area* could not satisfactorily predict a child's anxiety during induction as measured with the m-YPAS[14]. In contrast, we found a strong correlation between the VAS-I and the m-YPAS. This suggests that induction might be the best time to assess a child's anxiety. Indeed, children's state anxiety peaks during induction[2,8,11,12,16].

Construct validity of the VAS-I was considered in relation to a child's age group and parental anxiety. It is well established that a child's anxiety state as measured with the m-YPAS at induction is higher in toddlers and very young children when compared to older children and adolescents[2,12,16]. We hypothesized that the same pattern could be found in our sample, using the VAS-I. Our findings confirmed this hypothesis: VAS-I scores were higher in the children aged up to 5 years compared to the children aged 6 to 16 years. This may be interpreted as a first indication of the construct validity of the scale. Moreover, this suggests that the VAS-I could be useful for a much broader age range (1.5 to 16 years) than previously reported[7], thus including the children who are too young to verbalize their emotions. Secondly, in a previous research study, parental anxiety was found to be associated with higher child anxiety during induction[2,12]. This study confirmed that high-anxious parents reported higher scores on the VAS-IP as compared to low-anxious parents, which further supports the construct validity of the VAS-I. The simultaneously obtained anesthesiologists' ratings on the VAS-IA and m-YPAS scores were also higher for children of high-anxious parents than for children with low-anxious parents, indicating that this finding does not reflect a reporter bias on the side of the parents. The correlation between our findings and previously established patterns is supportive of the construct validity of our scale.

Analysis of cross-informant agreement showed that the mean difference between the VAS-I ratings of parents and anesthesiologists was quite small (3.6 on a 100-point scale), while there was no strong relationship between the difference and the magnitude of the ratings.

To assess the sensitivity and specificity of the VAS-I for predicting anxiety, an ROC analysis was performed. This analysis identified optimal cut-offs of 37 mm for the VAS-IP and 30 mm for the VAS-IA. Establishing cut-offs is important from a clinical perspective, as they permit identification of children with high anxiety levels during induction. Further studies are required in different settings and with different populations to establish the accuracy and appropriateness of these cut-offs.

We suggest that it is worthwhile for parents to complete the VAS-I. Other rating systems, such as the Pediatric Anesthesia Behavior score[11], do not require a parental rating. Having parents rate their child's anxiety levels potentially makes them more aware of their child's vulnerability. This strategy fits well with the concept of family-centered pediatric perioperative care based on collaboration between patients, families and health care professionals and the involvement of parents in the care of their child[21]. Anxiety management is an important component in this approach. Once it is known that a child has shown high perioperative anxiety, both the anesthesiologists and the parents will be aware that the child is at risk for higher postoperative pain levels[6,11]. Completing the VAS enables the anesthesiologists and parents to focus their attention towards more vulnerable, highly anxious children. In a busy surgical day-care center, it may be more feasible to complete the easy and quick VAS-IA and VAS-IP than the time-consuming m-YPAS.

The strengths of this study include the large sample size, broad age range, and a wide variety of surgical procedures. Some limitations of the study need to be addressed. The VAS-I was tested in a single institution on a specific population and this study does not prove validity with respect to its use in a wider context. Also, none of the children received premedication and all inductions were performed by inhalation. It is unknown to what extent this approach could have influenced the results. From a more general point of view, validation of a new scale is a complex matter because it requires information concerning reliability (inter-rater, intra-rater, test-retest and internal consistency) and validity (content, construct and criterion related). In this study, not all different forms of validity have yet been tested, therefore future research is needed to confirm the validity of the VAS-I. Furthermore, no analyses of reliability were carried out. It would have been interesting, for example, to gain insight in the intra-rater reliability, but this fell outside the scope of the study.

CONCLUSIONS

The data of this study provide some indication for the validity of the VAS-IP and VAS-IA to assess children's state anxiety during induction. These assessments take only a few seconds to complete and their results can be incorporated into global patient management.

DISCLOSURES

1. Ethical approval: Approval from the ZNA Middelheim Institutional Review Board (B009201213439), Lindendreef 1, 2020 Antwerp, Belgium.
2. Funding: This study was funded by institutional means.
3. Conflict of interest: The authors declare no conflicts of interest.

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'One who knows does not speak; one who speaks does not know.
Block the openings;
Shut the doors.
Blunt the sharpness;
Untangle the knots;
Soften the glare;
Let your wheels move only along old ruts.
This is known as mysterious sameness.' (Tao Te Ching, 56)

知者不言，言者不知。塞其兑，闭其门，挫其锐，解其分，和其光，同其尘，是谓玄同。

Chapter 4

Audiovisual aid viewing immediately before paediatric induction moderates the accompanying parents' anxiety

Johan Berghmans, Frank Weber, Candyce van Akoleyen, Elisabeth Utens, Peter Adriaenssens, Jan Klein. and Dirk Himpe.

Pediatr Anesth. 2012 Apr;22(4):386-92.

ABSTRACT

Background: Parents accompanying their child during induction of anaesthesia experience stress. The impact of audiovisual aid (AVA) on parental state anxiety and assessment of the child's anxiety at induction has been studied previously but needs closer scrutiny.

Methods: One hundred and twenty parents whose children were scheduled for day-care surgery entered this randomized, controlled study. The intervention group (n = 60) was exposed to an audiovisual aid in the holding area. Parental anxiety was measured with the Spielberger State-Trait Anxiety Inventory (STAI) and the Amsterdam Preoperative Anxiety and Information Scale (APAIS) at three time points: 1. on admission [T1]; 2. in the holding area just before entering the operating theatre [T2]; 3. after leaving [T3]. Additionally, at [T3] both the parent and attending anaesthetist evaluated the child's anxiety using a Visual Analogue Scale (VAS). The anaesthetist also filled out the Induction Compliance Checklist (ICC).

Results: On the state anxiety subscale APAIS parental anxiety at T2 ($P = 0.015$) and T3 ($P = 0.009$) was lower in the AVA-intervention group than in the control group. Correlation coefficients between VAS-ICC as measured by anaesthetist and parents differed significantly between the intervention and control group.

Conclusions: Preoperative AVA shown to parents immediately before induction moderates the increase in anxiety associated with the anaesthetic induction of their child. Present results suggest that behavioral characteristics seem better predictors of child anxiety during induction than anxiety ratings *per se* and that anesthesiologists are better in predicting child anxiety during induction than parents.

Keywords: Induction of anaesthesia; Age, Child; Education; Ambulatory, Outpatient

INTRODUCTION

Both children and their accompanying parents experience preoperative fear and anxiety[1-5]. The state anxiety of the accompanying parent – including apprehension, nervousness and worry – can increase the child's anxiety at induction of anaesthesia[6,7]. Since levels of preoperative anxiety in children are known to induce adverse postoperative phenomena, namely emergence delirium and postoperative behavioural changes[8], one should also try to decrease state anxiety of the accompanying parent by providing adequate information about the anaesthetic procedure[9]. A preoperative audiovisual aid (AVA) shown at the right time may be a useful tool in reducing parental anxiety and have a positive influence on the level of their child's anxiety both prior to and during anaesthetic induction[10-12]. Parents who are anxious at induction are significantly more likely to consider their child as upset[13]. Recent findings demonstrated that attending paediatric anaesthetists can more accurately predict the child's anxiety than mothers[14].

The primary aim of this randomized trial was to assess whether or not an AVA shown to accompanying parents just before anaesthesia would have a positive impact on parental state anxiety until after induction. Our hypothesis was that AVA would reduce parental state anxiety. Secondary areas of the study were the impact of AVA on parental assessment of the child's anxiety during induction and a comparison of their assessment with that of the anaesthetist.

METHODS

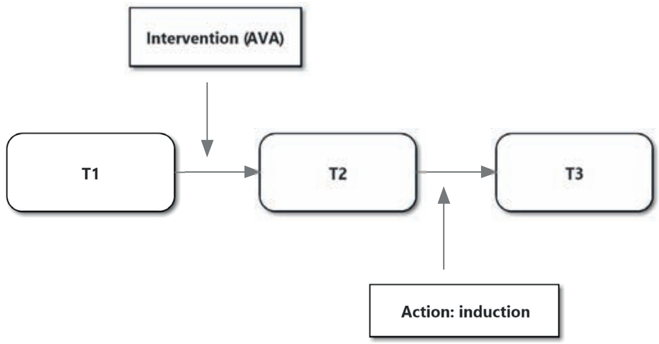
Enrolment and data collection

After approval for this randomized, controlled, single-blind study from the local ethics committee (Ref: 009/OG031/E.C. Approval N° 3541) parents of children planned for day-care surgery in the Queen Paola Children's Hospital in Antwerp were approached to take part in this study. Of the 129 parents approached, 120 parents gave their written informed consent. The study, registered at http://www.controlled-trials.com/ISRCTN66030835, was conducted in accordance with the Declaration of Helsinki and the CONSORT guidelines. The parents were informed about the hospital admission and the anaesthesia procedure. Only the parents of children between the ages of 6 months to 16 years old, with an American Society of Anesthesiologists (ASA) class 1 or 2 status, were included in the study. By picking a computer-generated randomly numbered envelope parents were assigned to either the intervention group or the control group. Demographic data of parents and children were collected. No premedication was administered.

Assessment procedure

Anxiety of the accompanying parent was measured with the Spielberger State-Trait Anxiety Inventory (STAI)[15,16] and the Amsterdam Preoperative Anxiety and Information Scale (APAIS)[17] at three time points: 1. on admission [T1]; 2. in the holding area just before entering the operating theatre [T2]; 3. after leaving [T3]. After the first assessment [T1] the accompanying parent and child were conveyed to a child-friendly holding area for 10 minutes just before entering the operating theatre. The intervention group then received the AVA-intervention. Immediately after seeing the AVA and just before entering the operating theatre, the second assessment [T2] was performed. Thereafter the child and the accompanying parent entered the theatre where inhalation induction was commenced. The third measurement [T3] was completed immediately after induction. At this moment, parents were also asked to estimate their child's anxiety at induction by using a Visual Analogue Scale (VAS) marking two extremes: *not anxious at all - very anxious*. The seven blinded anaesthetists in this study assessed the children's anxiety using an Induction Compliance Checklist (ICC) (Figure 1) as well as a VAS.

Figure 1 Flow diagram of the different time points in relation to the intervention (AVA) and induction



Intervention

The intervention group (including children) was exposed to the 4-minute AVA, a video recorded at the day-care unit, the holding area and the operating theatre of our hospital. It portrays the fairytale-like journey of a little boy and his cuddly bear 'mister Dragon', travelling to *Greenland* (which resembles our operating theatre) together with his mum. This video – conceptually based on McEwen's video[11] – is intended to model what parent and child will experience during the whole procedure. It shows the admission to the day-care, the entrance to the operating theatre and the child undergoing an inhalation induction. The end sequence reveals the boy leaving the hospital together with his parents.

Finally, parents were invited to fill in a short additional questionnaire, consisting of four general VAS items for both groups and one extra intervention group VAS item, in order to assess their general satisfaction level and the quality of the provided preoperative information (Table 6).

Parental anxiety assessment tools

The internationally often applied STAI[15], which has been validated for the Dutch population[16]. It consists of two parts: the state anxiety measures the current emotional state; the trait anxiety estimates the subject's disposition to anxiety in general. Each part consists of 20 items, on which respondents are asked to evaluate themselves on a 4-point scale. The total score ranges between 20 and 80. A cut-off value of ≥ 46 on the state subscale of STAI was used to make a dichotomy between: 1. anxious; 2. not or slightly anxious parents[17,18].

The APAIS[17] – a validated self-report instrument – measures the preoperative anxiety level and the need for information of the attending parent on a 6-item scale. Every item can be scored on a Likert scale ranging from 1 to 5. The anxiety part, which correlates (r = 0.74) strongly with the state part of the STAI, has been validated for the Dutch population and for parents of paediatric surgery patients[19]. A cut-off value of ≥ 13 on the state subscale of APAIS was used to dichotomize levels of parental anxiety[17].

Child anxiety assessment tools

The ICC[20], in this study considered as a surrogate outcome for the assessment of anxiety[1,21], was developed to rate the child's behaviour during the induction of anaesthesia. It consists of 11 items indicating the level of compliance of the child at induction stratified into three categories: 1. perfect induction (ICC = 0); 2. moderate compliance (ICC = 1-3); 3. poor compliance (ICC ≥ 4)[22]. A perfect induction (that is to say without exhibition of negative behaviour, fear or anxiety) is scored as 0. The total score reflects a summation of scores on the categories checked and ranges from 0 to 10.

The ICC displays an excellent inter- and intraobserver reliability interclass: r > 0.995.

The level of a child's anxiety experienced at induction was also estimated by applying a VAS – a widely employed scale to assess general anxiety[23] and preoperative anxiety[14], showing a 100mm horizontal line indicating two behavioural extremes.

Statistical analysis

An a priori power analysis was performed using GPOWER (version 3.1.2, Franz Faul, Universität Kiel, Germany). Based on previous studies a criterion of 10% difference was used in mean state anxiety as clinically significant[9-11]. To reach a power of 80% with an effect size of 0.8 one hundred and twenty parents were included.

All data are displayed as means ± SD or median with interquartile range when data distribution was skewed using a D'Agostino-Pearson test for normal distribution. A Friedman one-way ANOVA was utilized to test the groups on changes over time and a Bonferroni corrected multiple Mann-Whitney *U*-test was employed to compare both groups at different time points. A *P*-value of < 0.05 was statistically significant. The correlation between non-parametric data was determined by means of the Spearman correlation coefficient. Statistical analysis was performed using MedCalc, version 11.3, (MedCalc Software plc, Mariakerke, Belgium).

RESULTS

At T1 no significant differences were found between the baseline demographics in the two groups (Table 1). In most cases mothers accompanied their children into one of two similar operating theatres, both staffed with a nurse, an anaesthetist and a research assistant. The most frequent procedures were urology (31.7%) in the control group and Ear Nose Throat (ENT) (35%) in the intervention group. There was no statistical difference relating to all procedures in the two groups.

Table 2 shows parental anxiety as measured with STAI and APAIS at different time points (T1, T2 and T3) with a Friedman one-way ANOVA and Intergroup Bonferroni corrected multiple Mann-Whitney *U*-tests. STAI-scores increased over time, with a significant increase at T3 compared to T1 and T2 in both control ($P < 0.05$) and intervention group ($P < 0.05$). By contrast, when using the APAIS-state subscale, parental anxiety at T3 only increased in the control group ($P < 0.05$).

At T2 and T3 intergroup-comparisons demonstrated significant differences between the intervention and control group, showing less anxiety in the intervention group in both STAI and APAIS.

Table 1 Demographics and types of surgery

	Intervention group (n = 60)	Control group (n = 60)
gender parent (M/F %)[1]	10/90	18.3/81.7
age parent (years)[2]	35.0 (31-39)	31.5 (28-38)
gender child (M/F %)[1]	65/35	78.3/21.7
age child (years)[2]	4.5 (2-7)	3 (1-7.5)
mother tongue[1]		
Dutch	43 (71.7)	41 (68.3)
other	17 (28.3)	19 (31.7)
Surgical service[1]		
maxillofacial	6 (10)	8 (13.3)
gastroenterology	11 (18.3)	13 (21.7)
urology	9 (15)	19 (31.7)
general surgery	9 (15)	2 (3.3)
orthopedic surgery	2 (3.3)	1 (1.7)
ENT	21 (35)	17 (28.3)
ophthalmology	1 (1.7)	
missing data	1 (1.7)	
previous anesthetic[1]	20 (33.3)	20 (33.3)

[1]Data are expressed as *n* (%).
[2]Data are expressed as median with interquartile ranges shown in parentheses.
ENT, ear nose and throat.

Table 2 Measurements of parental anxiety at different time points

		Intervention group (n = 60)	Control group (n=60)	*P value*
STAI/S	T1	38.6 (35.9-41.2)	41.9 (39.4-44.4)	0.08
	T2	38.3 (35.5-41.2)	43.6 (41-46.3)	0.008*
	T3	41.5 (38-44.7)†	46.5 (43.5-49.5)†	0.024*
STAI/T	T1	34.7 (32.5-36.9)	37.6 (35.3-39.9)	0.06
APAIS/S	T1	10 (9.0-10.8)	10.8 (9.9-11.7)	0.25
	T2	9.2 (8.3-10.1)	10.9 (9.9—11.8)	0.015*
	T3	9.4 (8.5-10.4)	11.4 (10.3-12.4)†	0.009*
APAIS/I	T1	7.4 (7.1-7.8)	7.2 (6.7-7.6)	0.37
	T2	7.3 (6.8-7.7)	7.2 (6.8-7.7)	0.82
	T3	7.0 (6.5-7.5)	7.0 (6.4-7.5)	0.97

STAI/S, State-Trait Anxiety Inventory/state; STAI/T, State-Trait Anxiety Inventory/trait.
APAIS/S, Amsterdam Preoperative Anxiety and Information Scale/state.
APAIS/I, Amsterdam Preoperative Anxiety and Information Scale/information.
Data are expressed as mean with 95% confidence intervals for the mean in parentheses.
*$P < 0.05$ as determined with a Mann-Whitney *U*-test.
†$P < 0.05$ as determined with a Friedman one-way ANOVA vs T1, T2.

For further analysis, parents were dichotomized into two groups: 1. not or slightly anxious; 2. very anxious parents (Table 3). Cut-off values were ≥ 46 on state anxiety subscale of STAI and ≥ 13 on APAIS. Intergroup comparison as to proportions of anxious parents showed on the STAI a nearly significant trend (p = 0.06) and on the APAIS anxiety subscale a significant (*P* = 0.01) intergroup difference at T3. These intergroup comparisons, demonstrated on both instruments that the proportion of anxious parents was lower in the intervention group.

Table 3 ● Number of anxious parents as assessed with the state anxiety subscale of STAI/S and APAIS/S

	Intervention group	Control group		Intervention group	Control group	
	STAI/S	**STAI/S**	**P *value***	**APAIS/S**	**APAIS/S**	**P *value***
T1	15 (25%)	17 (28.3%)	0.8	16 (26.7%)	20 (33.3)	0.6
T2	12 (20%)	22 (36.7%)	0.07	11 (18.3%)	21 (35%)	0.06
T3	19 (30%)	30 (50%)	0.06	12 (20%)	26 (43.3%)	0.01*

STAI/S, State-Trait Anxiety Inventory/state with a cut-off value ≥ 46.
APAIS/S, Amsterdam Preoperative Anxiety and Information Scale/state with a cut-off value ≥ 13.
data are expressed as n (%)
*$P < 0.05$ as determined with a Chi-square test for intergroup comparison of two proportions

Table 4 shows the assessment of the child's anxiety at induction by VAS scores of the accompanying parent (VAS_p) and the anaesthetist (VAS_a). Significant differences were found between VAS_p and VAS_a in both the control (*P* = 0.05) and intervention group (*P* = 0.029), with the anesthesiologist rating the child's level of anxiety as lower in both groups.

Table 4 ● Anxiety scores of the child at induction measured with a VAS

	VAS_p	VAS_a	*P* value
Intervention group (n = 60)	48 (28-64)	20 (8-41)	0.03*
Control group (n = 60)	50 (42-73)	45 (19-68)	0.05*
P Value**	0.32	0.14	

Data are expressed as median score with 95% confidence intervals for the median shown in parentheses.
VAS_p, visual analogue scale parents; VAS_a, visual analogue scale anaesthetist.
*$P \leq 0.05$ comparison between VAS_p and VAS_a in the intervention and control group as determined with a Mann-Whitney *U*-test.
**$P > 0.1$ intergroup comparison of VAS_a and VAS_p in the intervention and control group as determined with a Mann-Whitney *U*-test.

Table 5 displays the results obtained by the ICC; no difference was found between the two groups.

Table 5 Induction Compliance Checklist (ICC) results

	Intervention group (n = 60)	Control group (n = 60)
Perfect induction	30 (50)	23 (38.3)
Moderate compliance	19 (31.7)	21 (35)
Poor compliance	11 (18.3)	16 (26.7)

Data are expressed as *n* (%).
Perfect induction: ICC = 0; Moderate compliance: ICC = 1-3; Poor compliance: ICC ≥ 4.
P = 0.17 between both groups as determined with Mann-Whitney U-test.

By means of a Spearman Rank a very high correlation was found between ICC and VAS_a in the intervention ($r = 0.89$; $P < 0.0001$) and in the control group ($r = 0.82$; $P < 0.0001$). These correlation coefficients were not significantly different ($P = 0.16$).

A less strong medium correlation could be demonstrated between ICC and VAS_p in the intervention ($r = 0.44$; $P = 0.0004$) and in the control group ($r = 0.37$; $P = 0.0037$). These correlation coefficients were not significantly different ($P = 0.65$). By contrast, correlation coefficients between anaesthetist and parent significantly differed in the intervention ($P < 0.0001$) and control group ($P < 0.0001$).

The VAS scores of the additional questions did not differ significantly between groups (Table 6).

Table 6 Additionally asked VAS questions

	Intervention group (n =60)	Control group (n=60)	*P* value
VAS 1:	87 (76-97)	83 (53-99)	0.39
VAS 2:	96 (85-99)	98 (91-100)	0.07
VAS 3:	97 (89-100)	99 (89-100)	0.96
VAS 4:	95 (88-98)	97 (86-100)	0.45
VAS 5:	95(81-99)	n/a	

VAS, visual analogue scale; AVA, audiovisual aid.
Data are expressed as median with interquartile ranges shown in parentheses.
P value as determined with a Mann-Whitney *U*-test.
n/a, not applicable
VAS 1 Are you satisfied about the given information in connection to the anaesthesia?
VAS 2 Were you really motivated to be present at the induction of anaesthesia?
VAS 3 Do you believe that your presence was useful for your child?
VAS 4 Are you satisfied with the course of the procedure?
VAS 5 Do you think AVA was useful for your preparation of anaesthesia?

DISCUSSION

The main finding from this study is that an AVA shown to parents immediately before induction moderates the increase in anxiety associated with the anaesthetic induction of their child.

The anxiety subscale of APAIS showed an increase of anxiety after induction in the control group but not in the intervention group. This result was not found in on the STAI-state anxiety subscale. Intergroup comparisons at different time points revealed significant differences at T2 and T3 between both groups with lesser levels of anxiety in the intervention group.

Considering the real-life threatening nature of entering the operating theatre, it is psychologically natural and logical that the parental levels of stress increase at this very moment in both groups[2,3]. This could explain why no significant decrease in anxiety was seen in the intervention group at T2. Parents experience their child's loss of consciousness and separation after induction as the moment of greatest stress which is reflected by an increase in anxiety after induction in both groups[2,4,24]. However, this increase was less pronounced in the intervention group; a non-significant trend shows that the number of anxious parents in both questionnaires decreased in the intervention group just after viewing the AVA, a result not seen in the control group. Considering all above findings AVA is a useful tool in preparing parents, this in accordance with previous findings[9-12].

The secondary aims focus on the assessment of the child's anxiety by the anaesthetist and parent. Previous findings demonstrated that parents judging themselves to be upset at induction were significantly more likely to consider their child as upset[13]. The present study, however, shows that a difference in parental state anxiety does not influence the way parents evaluate their child's anxiety at induction. Previous findings[14] showed that attending paediatric anaesthetists are better in predicting the child's anxiety at induction. Furthermore those findings did not show a correlation between the parental prediction and the actual anxiety of the child at induction. More overt anxiety behavioural signs than usual will be expressed by the child at the very moment of induction which may be easily recognised by the parent[14]. This could explain why a medium correlation was found between ICC and VAS_p. This suggests that anxiety assessment based on overt behavioural characteristics as mentioned in the ICC seems better to predict the level of anxiety and this is consistent with previous findings[14,21]. Our assumption that behavioral characteristics (ICC) seem better predictors of the level of anxiety at induction applies even better to anaesthetists in our study. This is in line with previous studies which also point to the fact that the anaesthetist may be better equipped to notice the behavioural characteristics of anxiety at induction[14].

Finally, parents in this study were very motivated to be present at induction and strongly believed their presence was useful[4,24]. They were also very satisfied with the course of the procedure this in accordance with previous findings. Both groups were equally satisfied about the given information and the intervention group rated the AVA as very useful which is in accordance with previous findings[9,11]. A possible explanation as to why no difference was found between satisfaction levels in the two groups may be that both groups had already received sufficient general written information[5].

Limitations of the study

When viewing the results of parental levels of anxiety at T1 on the STAI, one sees that bias levels were almost reached, with control parents having higher levels of anxiety at baseline. This may have an impact on the interpretation. Anxious people may react more anxiously in stressful situations, which may in part explain the differences found at T2 and T3. By contrast, state anxiety measured with APAIS did not reach bias level at T1.

Although the ICC assesses a child's anxiety, fear and negative behaviour during induction, it is not an anxiety measurement *per se*[1,20,21]. It should be noted that the anxiety VAS, a subjective assessment of the child's anxiety, and the ICC measure different items. The fact that the same anaesthetist completed both the VAS_a and the ICC may have introduced a so-called informant bias, thus these results should be interpreted carefully.

The clinical significance of our findings should be tailored in the knowledge that preparing parents and their children towards anaesthesia is a complex matter with many interactions. AVA is only one method that could beneficially influence state anxiety of parents and their children for anaesthesia.

CONCLUSIONS

Viewing AVA moderates parental increase in state anxiety towards their child's anaesthetic induction. Present results also suggest that behavioural characteristics seem better predictors of a child's anxiety during induction than anxiety ratings *per se* and that anesthesiologists are better in predicting a child's anxiety during induction than parents.

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'As a thing the way is
Shadowy, indistinct.
Indistinct and shadowy,
Yet within it is an image;
Shadowy and indistinct,
Yet within it is a substance.
Dim and dark,
Yet within it is an essence.
This essence is quite genuine
And within it is something that can be tested.' (*Tao Te Ching*, 21)

道之为物，唯恍唯惚。忽兮恍兮，其中有象；恍兮忽兮，其中有物。窈兮冥兮，其中有精；其精甚真，其中有信。

Chapter 5

Changes in sensory processing after anesthesia in toddlers

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What is already known about this topic

- Postoperative behavioral problems are very common in pediatric anesthesia;
- Pre-existing emotional/behavioral problems might be associated with postoperative behavioral problems.

What is new in this article

- Sensory processing in toddlers changes after day-care surgery;
- Changes in sensory processing may be influenced by pre-existent emotional/behavioral problems;
- The generalizability of our findings should be assessed in future studies in pediatric populations of different age-ranges, undergoing different procedures.

ABSTRACT

Background: Anesthesia and surgery may influence toddlers' sensory processing and consequently postoperative adjustment and behavior.

This is the first study to: 1. test pre- to postoperative changes in sensory processing after pediatric anesthesia using the validated Infant/Toddler-Sensory Profile for 7-36 months ($ITSP_{7-36}$); 2. identify putative predictors of these changes.

Methods: This prospective cohort study included 70 healthy boys (ASA I & II), aged 18-30 months, who underwent circumcision for religious reasons**.** Exclusion: boys with prior surgery and known developmental delay.

Primary outcome: Changes in sensory processing from the day of admission to day 14 postoperatively. The accompanying parent completed the $ITSP_{7-36}$. Putative predictors: 1. child's preoperative emotional/behavioral problems; 2. child's state anxiety at induction; 3. postoperative pain at home. All children received standardized anesthesia and pain management.

Results: For 45 boys, assessments were completed at both time points. Significant changes in sensory processing (mean $ITSP_{7-36}$ scores) were found on: low registration (47.5 to 49.8; p = .015), sensory sensitivity (45.2 to 48.0; p = .011), sensation avoiding (48.2 to 51.3; p = .010), low threshold (93.4 to 99.4; p = .007), auditory processing (39.3 to 43.3; p = .000) and tactile processing (53.9 to 58.4; p = .002). Higher scores on emotional/behavioral problems predicted changes on sensory processing.

Conclusions: Sensory processing of these toddlers had changed after anesthesia. Children with more pre-existent emotional/behavioral problems are more vulnerable to these changes.

Keywords: Anesthesiology, Anxiety, Infant, Postoperative Pain, Problem Behavior, Sensation

INTRODUCTION

Postoperative behavioral changes in preschool children are very common after surgery under anesthesia, with incidence rates ranging from 80.4% at day one postoperatively, to 32% four weeks after discharge and still 16% after three months[1-3]. The psychological impact of these changes cannot be ignored as in a minority of cases they may last even longer, from several months[1] to even more than a year[4]. Furthermore there are indications that young children are more vulnerable to such changes than are older children[1,4,5].

Research has shown a relationship between children's perioperative anxiety, emergence agitation and/or emergence delirium and postoperative pain on the one hand and postoperative behavioral changes on the other hand[1,3,6]. It may be that changes in sensory processing contribute to postoperative behavioral changes as well. Sensory processing encompasses the way toddlers perceive, modulate, integrate and self-regulate sensory information, and also how this sensory processing influences the toddlers arousal, attention, affect and action. In this way, a change in sensory processing might influence postoperative behavior changes, since sensory processing has an impact on the child's ability to learn and to show adaptive social functioning at home and e.g. to participate in play[7,8].

Furthermore, we postulate that several variables, which have been demonstrated to predict postoperative behavioral changes, may also influence young children's postoperative sensory processing. Previous studies showed that higher scores on preoperative emotional/behavioral problems (such as anxiety, depressive symptoms) are associated with higher levels of children's anxiety at induction[9,10]. We hypothesize that: 1) pre- to postoperative changes in sensory processing will occur after pediatric surgery under anesthesia; 2) that pre- and perioperative emotional/behavioral problems, especially anxiety during induction, and postoperative pain will change a child's sensory processing.

In this field of research, hardly any studies have focused on sensory processing in toddlers. The novelty of the present study lies in the identification of toddlers' changes in sensory processing after surgery under anesthesia and as such the impact on postoperative behavior, using a validated questionnaire that specifically targets this age group.

This study aims to: a. test pre- to postoperative changes in sensory processing, assessed by the ITSP$_{7-36}$, 14 days after a surgical day care procedure under anesthesia in children aged between 18 – 30 months; b. test whether changes in sensory processing are associated with: 1. the children's preoperative emotional/behavioral problems; 2. the children's state anxiety at induction; 3. postoperative pain at home.

MATERIALS AND METHODS

This prospective observational cohort study was conducted at the Queen Paola Children's Hospital in Antwerp, Belgium between April 2012 and April 2014, with approval from the Institutional Review Board (B009; OG031 E.C. approval N° 3952). It was part of a larger trial (www.trialregister.nl / NTR 3306), and was conducted in accordance with the Declaration of Helsinki, the APA ethical standards and reported following the STROBE statement for observational studies.

Inclusion criteria

Boys aged between 18-30 months, undergoing circumcision because of religious reasons in day care treatment; written informed consent; an American Society of Anesthesiologists (ASA) physical status I-II; no premedication (which is standard practice in our hospital); parents with a satisfactory written understanding of Dutch language; one parent present during induction.

Exclusion criteria

Known developmental delay, prior surgery under anesthesia.

Demographical/medical data

Collected on the day of admission by a research nurse. Socioeconomic status (SES) was categorized, by parental highest educational level into: 1. no education, elementary school; 2. secondary school; 3. higher education or university. Data were compared to Belgian population references[11].

Anesthesia procedure

All parents and children received standardized preoperative information. The anesthesia procedure was also standardized. In line with standard practice in our hospital, all inductions were performed by inhalation of sevoflurane 8 vol.% in 50% oxygen without nitrous oxide. A laryngeal mask was inserted and the child was assisted until breathing spontaneously. Anesthesia was maintained with sevoflurane 2.5 vol.%. Intraoperative pain management included: 1. a penile block with Levobupivacaine 2.5%; 2. opioids (pethidine 1.0 mg/kg IV); 3. a non-steroidal anti-inflammatory drug (NSAID) (ketorolac 0.5mg/kg IV) and 4. ondansetron (0.1 mg /kg) for post-operative nausea and vomiting (PONV) management. For in-hospital postoperative pain management each child received paracetamol IV (20 mg. kg^{-1}). At the end of surgery the inhalation agent was discontinued and the child was transferred to the Post Anesthesia Care Unit (PACU) and afterwards again to the ward were they stayed at least for 2 hours before discharge.

The parents received a written instruction for postoperative pain management at home stating that oral acetaminophen 60mg/kg divided in 4 doses should be given for 3 days. Adherence to this regimen on day 1 was recorded.

Assessment tools and assessment moments (Fig. 1)

Main outcome variable

The $ITSP_{7-36}$[12] was developed to assess sensory processing skills of babies and toddlers between 7 and 36 months old. Sensory processing is defined as the capacity of the central nervous system for processing and modulating sensory input. The ITSP consists of 48 structured questions (response categories: 1 = almost always to 5 = almost never) and 2 open questions, resulting in a sensory processing summary covering 5 processing sections: 1. auditory (reaction to sound, noise, voices); 2. visual (reaction to anything that can be seen); 3. tactile (reaction to touching of the skin); 4. vestibular (reaction to movement); 5. oral sensory (reaction to touch, taste and smell).

In addition, 4 independent quadrant scores can be calculated: 1. weak registration (consciousness/ awareness to different sensory stimuli); 2. sensation seeking (seeking more intense sensory experiences); 3. sensory sensitivity (ability to notice sensory stimuli); 4. sensory avoiding (to counteract/avoid or control sensory stimuli). Finally a low threshold score is derived from the summation of quadrant 3 and 4.

Lower scores on the quadrant scores (i.e. scores below the reference range for healthy peers) indicate higher frequencies of these behaviors than in 'healthy' children, whereas higher scores indicate the opposite.

However, caution is warranted not to interpret ITSP concepts as problematic by definition; rather sensory processing should be regarded as a general concept describing a continuum of sensory experiences in children. Consequently when a child scores higher or lower *than others,* it simply means that the child shows behaviors (listed in the sections or quadrant groupings) more or less frequent than peers from the general population[13].

Test- retest reliability of the ITSP is acceptable for the quadrant scores (r = .74) and for sensory processing (r = .84), internal consistency ranges from acceptable to good (Cronbach's α = .70 to .86). In a systematic review of assessments of sensory processing the ITSP is being recommended because of sound psychometric properties and excellent content validity.[8] It was translated in Dutch[14].

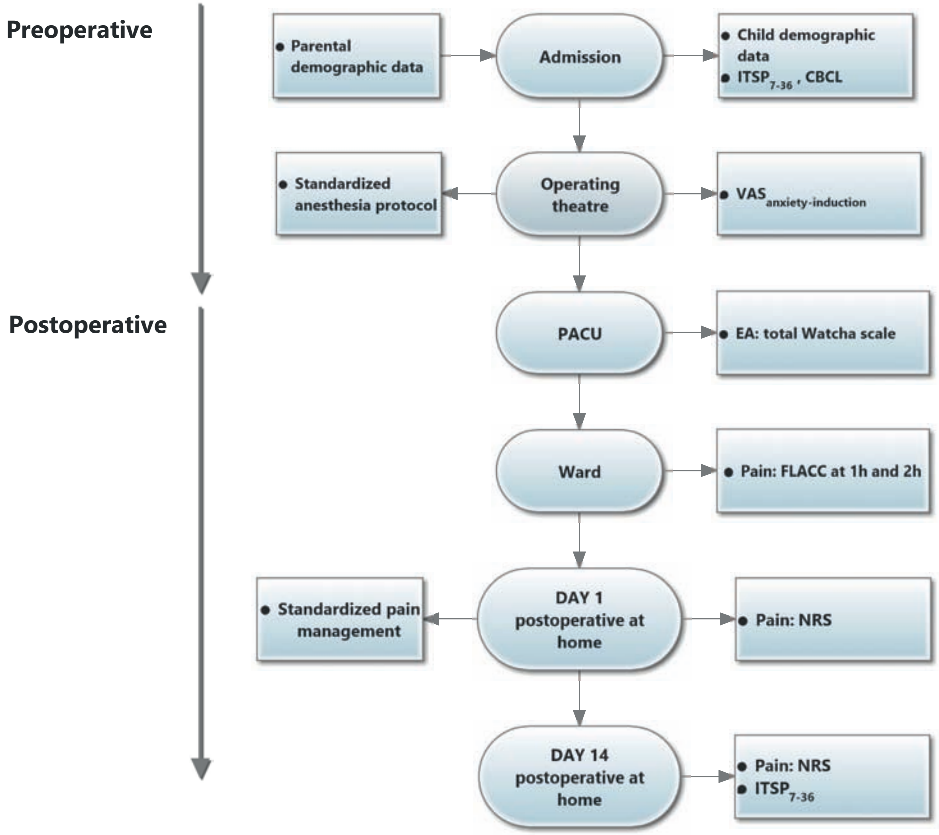
In this study the $ITPS_{7\text{-}36}$ was completed by the accompanying parent preoperatively at admission [T1] and postoperatively at day 14 [T14] (Fig. 1).

Predictor variables

The Child Behavior Checklist 1½-5 (CBCL/1½-5)[15], an internationally widely used and validated parent-report, was completed by the accompanying parent prior to surgery at [T1] to assess emotional/behavioral problems during the past 2 months (Fig. 1). It consists of 100 problem items (response-categories: 1. not true; 2. somewhat or sometimes true; 3. very true or often true). Summary scores on the Internalizing scale (Emotionally Reactive, Anxious/Depressed, Somatic Complaints, Withdrawn), Externalizing scale (Attention Problems and Aggressive Behavior), Sleep Problems and a Total Problems scale were computed. Higher scores indicate more problems. Good validity and reliability for the Dutch version have been reported[16].

The attending pediatric anesthesiologist completed a Visual Analogue Scale ($VAS_{anxiety\text{-}induction}$) to assess the child's anxiety level at induction. This scale consists of a 100 mm horizontal line, with the two ends representing the opposite, extreme limits 'absolutely no anxiety' and 'extreme anxiety', respectively. It has been used and was preliminarily validated for assessing a child's anxiety preoperatively[17].

Figure 1 Flowchart diagram of the different moments during assessment



$ITSP_{7\text{-}36}$, Infant/Toddler Sensory Profile 7-36 months as assessed by the accompanying mother or father
CBCL, Behavior Checklist 1½-5 as assessed by the accompanying mother or father
$VAS_{anxiety\text{-}anesthesiologist}$, Visual Analogue Scale anxiety at induction as assessed by the attending anesthesiologist
EA - Watcha, Emergence Agitation as assessed by a Post Anesthesia Care Unit (PACU) nurse
FLACC, Face Legs Activity, Cry and Consolability scale
NRS, Numerical Rating Scale

Emergence agitation (EA) was assessed postoperatively by a PACU nurse using the Watcha scale, which consists of 4 items: 1. calm; 2. crying, but consolable; 3. crying, not consolable; 4. agitated, kicking with arms and legs. A Watcha sum score was calculated, based on the scores at 5, 10, 15, and 20 minutes after awakening and a mean sum > 2 was considered to reflect the presence of EA. The scale is easy to use and has a high overall sensitivity and specificity[18].

The Face, Legs, Activity, Cry, Consolability (FLACC)[19] measures pain intensity. The FLACC has good interrater reliability and validity for use in the postoperative phase[19]. The FLACC was filled in 1 and 2 hours after surgery, on the ward by an independent nurse.

The child's postoperative pain at home was assessed with a Numerical Rating Scale (NRS)[20] At day 1 after discharge the research nurse called the parents to register the parents' rating of the child's pain (score-range: 0-10; question: how much pain did your child experience on average after surgery?). This was repeated at day 14, (score-range: 0-10; question: how much pain did your child experience on average during the past 14 days). NRS scores < 4 are considered to indicate no or mild pain; ≥ 4 to indicate moderate to serious pain[21].

Statistical analysis

A power calculation based on pre- to postoperative changes in sensory processing, as assessed 14 days after surgery, showed that, to detect a difference on the $ITSP_{7\text{-}36}$ low threshold score corresponding to an effect size of 0.5, a total sample size of 44 would be needed (GPOWER version 3.1.2) with a power of 0.90 and an alpha of 0.05.

All data are presented as mean ± standard deviation for continuous data, as percentages for categorical data or as median with IQR. Normal distribution was indicated by two characteristics (skewness and kurtosis) and was further confirmed/validated by Kolmogorov-Smirnov tests.

Paired Student's t tests were performed to analyze differences in $ITSP_{7\text{-}36}$ scores between [T1] and [T14] on: 1. sensory processing section scores; 2. quadrant scores; 3. low threshold score.

We first did a univariate linear regression analysis to estimate the associations between changes in sensory processing over time and three variables: 1) children's preoperative emotional/behavioral problems, 2) children's state anxiety at induction and 3) postoperative pain at home. The $ITSP_{7\text{-}36}$ scales that showed statistically significant differences over time (i.e., between T1 and T14) were used as dependent variables.

Next, multivariable linear regression (forced entry method) was used to analyze whether the changes in sensory processing (again restricted to those ITSP scales that showed significant change over time) could be explained by the predictor variables mentioned above. To avoid multicollinearity issues (assessed by variance inflation factors), predictor variables that correlated highly with other predictors were excluded from the regression analyses. Predictors were accepted into the model if their contribution to the model was statistically significant ($p < 0.05$). The standardized regression coefficients, which express the strength of each predictor in the regression equation, and explained variance (R^2) are presented. Linearity and homoscedasticity were tested by looking at the plots of standardized predicted values against the standardized residuals. Independence of residuals was checked with the Durbin-Watson statistic.

All analyses were performed with IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. p-value of < 0.05 was considered statistically significant.

RESULTS

Of the 117 eligible children, 32 had to be excluded. The remaining 85 were invited to participate, 70 of whom accepted (response rate 82 %, Fig. 2). The children's mean age was 22.8 months (± 4.5 SD) (Table 1). For 25 (35.7%) children, data were missing at T14, because telephone contact was not possible or parents did not complete the $ITSP_{7\text{-}36}$, neither after a second telephone reminder. Thus for 45 children both pre- and postoperative data (T1 and T14) were available.

On the basis of the Watcha score, 22.7% of all 70 participants (n = 15; 4 missing values) could be categorized as having EA during the first 20 minutes after awakening (Table I).

Figure 2 Flowchart inclusion and exclusion of children

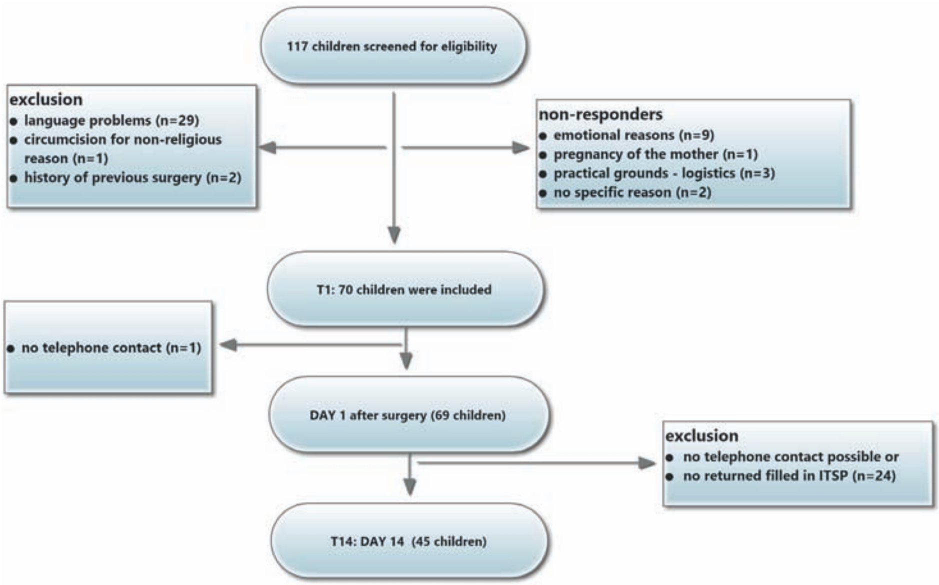


Table I Demographic and psychological assessment of the children and accompanying parent.

	Children with complete assessments at 2 time points (n = 45)	All children included (n = 70)
Children		
Age (months)	23 ± 4.0	22.8 ± 4.5
Weight	12.7 ± 2.3	12.8 ± 2.3
[a]ASA I	42 (93.3%)	63 (90%)
Born prematurely	4 (8.9%)	4 (5.7%)
Number of siblings ≥ 1	37 (82.2%)	58 (82.6%)
Prior hospitalizations	12 (26.7%)	19 (26.1%)
Nationality		
Belgium	37 (82.2%)	57 (81.4%)
other	8 (17.8%)	13 (18.6%)
[b]CBCL		
Internalizing problems	8.8 ± 7.3	8.7 ± 6.8
Externalizing problems	12.0 ± 6.4	11.6 ± 6.6
Total problems	31.9 ± 20.3	31.8 ± 18.9
[c]Anxiety at induction ($VAS_{anxiety-induction}$)	60.5 ± 29.2	65.5 ± 27.6
[d]Emergence delirium (Watcha score > 2)	10 (23.8%)	15 (22.7%)
(4 missing values)		
[e]In hospital postoperative pain (FLACC score)	0 (0 – 0)	0 (0 – 0)
[f]Pain at home (NRS)		
postoperative day 1	4 (0 – 6)	3 (2 – 6)
postoperative day 14	3 (0 – 7)	
Prescribed pain medication adherence	23 (51.1%)	40 (57.1%)
Parents		
Gender of accompanying parent (% male)	30 (66.7%)	44 (62.9%)
[g]Highest educational level	11 (24.4%)	17 (24.3%)
	28 (62.2%)	42 (60%)
	6 (13.3%)	11 (15.7%)

Data are expressed as mean ± SD or as median with IQR or as number (%). [a]ASA, American Society of Anesthesiologists; [b]CBCL, Child Behavior Checklist 1½-5 (Internalizing, Externalizing and Total Problems); [c]Child Anxiety at induction: $VAS_{anxiety-induction}$, Visual Analogue Scale anxiety; [d]Emergence delirium – total Watcha score was obtained by summing the scores at 5 min, 10 min, 15 min and 20 min after awakening; [e]In hospital postoperative pain: FLACC = Face, Legs, Activity, Cry, Consolability scale, sum score (1 hour + 2 hour) ; [f]Pain at home: NRS = Numeric Rating Scale at postoperative day 1 and day 14; [g]Highest educational level: 1. no education, elementary school; 2. secondary school; 3. higher education or university - [reference values for the Belgian population: level 1 = 13.9%; level 2 = 56.2%; level 3 = 29.9%].

Postoperative pain scores

One child had been assigned a score > 3 on the FLACC scale (n = 70). Parents of 49.3% (n = 35) of the children considered the child's postoperative pain moderate to serious at day 1, as assessed with the NRS. At day 14, 48.9% (n = 22) of parents reported that the overall pain experienced the past 14 days by their child was moderate to serious. Prescribed pain medication at day 1 at home was given conform instructions by 57.1% (n = 40) of parents.

The parent who accompanied the child during induction of anesthesia was the father in almost two third (62.9%) of the cases.

Pre- postoperative changes sensory processing

Paired Student's t tests showed statistically significant differences between $ITSP_{7\text{-}36}$ mean scores on T1 and T14 for the sections auditory and tactile processing, indicating that children postoperatively have significantly sharper, more sensitive, strong and alert auditory and tactile information processes (Table II). On the 'visual processing' and 'vestibular processing' sections of the $ITSP_{7\text{-}36}$, the children's scores increased slightly over time, but these changes were not statistically significant. Except for the sensation seeking quadrant, all quadrant scores increased significantly over time.

Table II Pre- to postoperative changes on the Infant/Toddler Sensory Profile

	T1 (n = 45)	**T 14** (n =45)	**mean DIFF**	**P value**	**ES**
Sensory processing section					
Auditory processing	39.3 (± 4.9)	43.3 (± 4.5)	+4.0 [2.5, 5.7]	.000**	0.77
Visual processing	22.0 (± 4.2)	22.4 (± 3.9)	+.36 [.9, 1.6]	.57	
Tactile processing	53.9 (± 9.0)	58.4 (± 7.8)	+4.5 [1.8, 7.0]	.002**	0.50
Vestibular processing	20.1 (± 3.5)	20.3 (± 3.6)	+.2 [.8, 1.1]	.75	
Oral sensory processing	29.2 (± 4.3)	28.0 (± 4.2)	-1.2 [-.5, 2.8]	.18	
Quadrant grid					
Quadrant 1 - Low registration	47.5 (± 6.4)	49.8 (± 3.6)	+2.3 [.5, 4.1*	.015*	0.38
Quadrant 2 - Sensation seeking	35.9 (± 8.3)	36.2 (± 8.0)	+.3 [-2.1, 2.7]	.82	
Quadrant 3 - Sensory sensitivity	45.2 (± 7.1)	48.0 (± 5.8)	+2.8 [.7, 4,9]	.011*	0.40
Quadrant 4 – Sensation avoiding	48.2 (± 7.2)	51.3 (± 7.4)	+3.1 [.8, 5.5]	.010*	0.40
Low Threshold (combined quadrant 3+4 score)	93.4 (± 13.5)	99.4 (± 12.4)	+6.0 [1.7, 10.1]	.007**	0.42

Data are expressed as mean (± SD) or as mean [95% CI]; T1 = baseline measure; T14 = measure at day 14 postoperative; mean DIFF: mean difference. Paired T- tests between quadrant scores at T1 and T14 and sensory processing section at T1 and T14. *P < 0.05; **P < 0.01 as determined with a paired T- test. ES: effect size (Cohen's d): 0.2 (small); 0.5 (medium); 0.8 (large) has been calculated using the formula: d = mean DIFF/SD.

Results of the univariate regression analyses showed that the CBCL Total Problems score and the CBCL Internalizing Problems score were statistically significant predictors of changes in sensory processing over time (standardized regression coefficients between .29 and .43). This holds for all ITSP sensory processing sections and all quadrant grids, except for the association between Internalizing Problems and auditory processing (Table III). There were no statistically significant associations between CBCL Externalizing Problems, the child's anxiety at induction, and postoperative pain at home, and changes in ITSP scores.

Table III Pre- to postoperative changes on quadrant and sensory processing sections of the Infant Toddler/Sensory Profile - univariate regression models

	ΔaudP	**ΔtactP**	**ΔQ. 1**	**ΔQ. 3**	**ΔQ. 4**	**ΔQ.LT**
Internalizing problems	.21 (.16)	.37 (.013)*	.33 (.028)*	.43 (.003)**	.29 (.046)*	.38 (.01)*
Externalizing problems	.24 (.119)	.28 (.061)	.28 (.065)	.25 (.097)	.19 (.215)	.23 (.126)
Total problems	.29 (.047)*	.38 (.011)*	.39 (.008)**	.43 (.003)**	.30 (.046)*	.38 (.01)*
$VAS_{anxiety\text{-}induction}$	.06 (.703)	.24 (.107)	-.023 (.88)	.23 (.122)	.16 (.286)	.21 (.169)
NRS postoperative day 1	.09 (.567)	.11 (.477)	.06 (.681)	.09 (.577)	.00 (.987)	.05 (.773)
NRS postoperative day 14	.04 (.777)	-.04 (.787)	-.23 (.146)	.11 (.500)	-.06 (.701)	.02 (.908)

Data are expressed as: standardized regression coefficients (P value); *P < 0.05; **P < 0.01.
Dependent variables from the Infant/Toddler Sensory Profile (ITSP) : Δaudp = Difference Auditory processing = [Auditory processing T14] – [Auditory processing T1]; Δtactp = Difference Tactile processing = [Tactile processing T14] – [Tactile processing T1]; ΔQ. 1 = Difference quadrant 1 = [quadrant 1 T14] – [quadrant 1 T1]; ΔQ. 3 = Difference quadrant 3 = [quadrant 3 T14] – [quadrant 3 T1]; ΔQ. 4 = Difference quadrant 4 = [quadrant 4 T14] – [quadrant 4 T1]; ΔQ.LT = Difference low threshold = [quadrant 3+4 T14] – [quadrant 3+4 T1];.
Independent variables: Child Behavior Checklist 1½-5 as assessed by the accompanying mother or father, Internalizing, Externalizing and Total problems; $VAS_{anxiety\text{-}induction}$: Child anxiety at induction = Visual Analogue Scale anxiety at induction; NRS = Numeric Rating Scale at postoperative day 1 and day 14.

In the multivariate regression analyses, the NRS pain score at day 1, the CBCL Internalizing problems score and the CBCL Externalizing problems score were left out, for reasons of multicollinearity. So, the following predictor variables were considered: 1) CBCL Total problems score; 2) anxiety at induction, and 3) postoperative assessment of pain during the past 14 days. The analyses revealed that the changes over time on the ITSP were related to higher scores on preoperative CBCL total problems score (Table IV). Anxiety at induction and – with one expection - postoperative pain at 2 weeks did not make a statistically significant contribution to explaining the changes in sensory processing. Between 9% and 25% of the variance of the ITSP dimensions was explained by preoperative emotional/behavioral problems (and postoperative pain).

Table IV Results of the multivariable regression models

	ΔaudP	ΔtactP	ΔQ. 1	ΔQ. 3	ΔQ. 4	ΔQ.LT
CBCL – total problems	.298(.047)*	.377(.011)*	.459(.002)**	.427(.003)**	.299(.046)*	.382(.010)*
Anxiety at induction ($VAS_{anesthesiologist}$)						
Postoperative pain (NRS day 14)			-.314(.03)*			
Variance explained (R^2)	.089(.047)*	.142(.011)*	.254(.003)**	.182(.003)**	.089(.046)*	.146(.010)*

Data are expressed by: standardized regression coefficient (P value); model R^2 (P value); P value: *P < 0.05.; **P < 0.01. Independent variables: 1.CBCL – preoperative Total problems, Child Behavior Checklist 1½-5; 2. The child's anxiety at induction with a Visual Analogue Scale - $VAS_{anesthesiologist}$; 3. Postoperative pain scores by a Numerical Rating Scale (NRS) at day 14. **Dependent variables from the Infant/Toddler Sensory Profile ($ITSP_{7-36}$):** Δaudp = Difference Auditory processing = [Auditory processing T14] – [Auditory processing T1]; Δtactp = Difference Tactile processing = [Tactile processing T14] – [Tactile processing T1]; ΔQ. 1 = Difference quadrant 1 = [quadrant 1 T14] – [quadrant 1 T1]; ΔQ. 3 = Difference quadrant 3 = [quadrant 3 T14] – [quadrant 3 T1]; ΔQ. 4 = Difference quadrant 4 = [quadrant 4 T14] – [quadrant 4 T1]; ΔQ.LT = Difference low threshold = [quadrant 3+4 T14] – [quadrant 3+4 T1].

DISCUSSION

The present study found evidence for significant pre- to postoperative changes in sensory processing of children undergoing circumcision. Analysis showed significant changes on different quadrants (low registration, sensory sensitivity, sensation avoiding and low threshold) and on auditory and tactile processing two weeks after surgery. Postoperatively less distinct behaviors were seen in response to auditory and tactile stimuli. From a clinical point of view these sensory processing changes can have a considerable psychological impact by influencing the toddlers' daily functioning and as such are clinically relevant. Preoperative emotional/behavioral problems significantly predicted pre- to postoperative changes in sensory processing.

The higher postoperative scores on low registration, sensory sensitivity, sensation avoiding, and low threshold indicate that, compared to their pre-operative situation, in some situations the children *miss less* information. Otherwise stated: they *detect more information* (i.e. show less behavior associated with 'low registration': e.g. touch or loud talk is not needed to get the child's attention). In other situations however, they *detect less* (i.e. show less behavior reflecting 'sensory sensitivity', e.g. do not startle from noise), and are *less bothered by input* (i.e. show less 'sensation avoiding', e.g. do not resist cuddling). These divergent findings can be explained by the fact that the quadrants cover different domains of sensory processing and behaviours belonging to these diverging domains, whereas they all fall under the overarching umbrella of the concept 'sensory processing'. In other words, generally speaking, children may for instance react strongly to auditory stimuli (by avoiding), and at the same time react less strongly to motion stimuli. And furthermore, a child may react differently to the same stimuli in different situations (e.g. an alarming ringtone while playing at home versus while lying in bed in-hospital).

Overall, our findings on the pre- to postoperative changes in sensory processing indicate that postoperatively after circumcision, in most situations, these boys after having undergone circumcision under anesthesia react less strongly to sensory input. Such behaviour could be interpreted as withdrawn or passive. However, these sensory processing changes (reflected by higher scores on the ITSP) do not necessarily imply more problematic behavior. When children are less conscious or less aware of sensory stimuli, they may be less sensitive and less alert to information. This could have been the case for the children in this study, since quadrant scores on sensation sensitivity, sensation avoiding, and the low threshold score were higher in the post-operative period. These sensory processing changes (as reflected by higher scores) could give rise to under-responsive behavior which could be explained through habituation after the surgical experience.

Clinical relevance. The findings mentioned above are of *clinical relevance*, since changes in sensory processing (e.g. less alert detection of auditory/visual information) can influence the child's ability to show adaptive social functioning at home. The fact that toddlers can be under-responsive (more withdrawn, more passive, less sensitive and alert) after surgery, constitutes important information which a clinician should convey to parents. Importantly, some children seem more vulnerable to these sensory processing changes, especially children with pre-existent preoperative emotional/behavioral problems.

When interpreting the results of this study, it needs to be kept in mind that this is a rather unexplored field of study using the ITSP and that the surgery was minor, elective and performed voluntarily for religious reasons (which may have resulted in informant bias, perhaps underestimating children's behavioral changes). Despite the surgery being 'minor', we nonetheless found significant changes in sensory processing. Therefore we think that our results are to be considered as a first signal that changes in sensory processing may occur, even after mild anesthesia. To what extent changes in sensory processing will occur after more serious or repetitive surgeries, with more and longer anesthesia and whether these changes persist into the long-term is a worthy area of investigation for future studies.

We found that the changes in the ITSP scores were associated with preexisting emotional/behavioral problems. This could be explained by the fact that children with more emotional/behavioral problems (especially Internalizing; emotionally reactive, anxious/

depressed, somatic complaints, withdrawn) have more behavior inhibition[22]. These children tend to be more calm, withdrawn and in general react less strongly to different experiences. This is consistent with the findings of Fortier *et al*,[23] who reported that individual child emotional/behavioral problems as assessed with the CBCL were predictive for changes in postoperative behavior.

Although pain has been identified as a strong risk factor of postoperative problematic behavior,[3,5] in this study no clear associations were found between pain and pre- to postoperative changes in sensory processing. This may be partly explained by the nature of pain instrument used in this study (i.e., the NRS). This short instrument was chosen to minimize the burden to the parents. However, it is a global rating scale, which may have influenced the sensitivity to detect changes. In hospital the children were assigned very low pain scores. However at home almost 50% of the children were perceived to have moderate to serious pain, both at day 1 and day 14 after discharge. Nevertheless, 40% of the parents did not adhere to the prescribed medication regimen. Others have reported similar findings[24,25]. Moreover, the religious significance of male circumcision may have contributed to a different parental attitude concerning pain medication. A study indeed found that parents were likely to consider pain as something that is inseparably linked to Calvinistic values[26] The cultural background might explain the relatively high proportion of fathers present at induction and this may have influenced the ratings by parents.

Besides pain, also the child's state anxiety has been reported as a factor explaining postoperative behavioral changes[4,6]. Overall, in this study, the regression coefficients did not reach the level of statistical significance. This may be partly explained by the fact that measuring state anxiety at induction in very young children is very difficult[17].

Strengths and limitations

Strengths: This study is innovative since it is the first investigating: a) pre- to postoperative changes in sensory processing in a *homogeneous* group of toddlers, using a well-validated questionnaire, the ITSP, and b) preoperative children's emotional/behavioral problems as a significant predictor, using the internationally well-known CBCL.

Limitations

This was a single center study with drop-outs at day 14 postoperatively. To what extent selection bias may have influenced our results is unknown. Furthermore, it seems that parents with low education were overrepresented compared to national statistics for Belgium (24.4% in this study vs 13.9 % the general population)[11]. The children, boys only, underwent minor, elective surgery (circumcision for religious reasons), these factors may have affected our results. Furthermore, parents completed both the CBCL and the $ITSP_{6\text{-}36}$ which may have affected the associations – this phenomenon where the same respondent completes several measures is known as *common method variance*[27]. It would be desirable if future studies would use a multi-informant approach (both parents as independent informants).

CONCLUSIONS

Our findings demonstrate that following surgery boys (18-30 months) reacted less sensitively, less strong (less alert) to sensory input, suggesting higher thresholds and more habituation. Future research should address: how long these changes in sensory processing last, how they affect postoperative behavior in toddlers, whether larger changes in sensory processing occur after more serious surgeries requiring longer anesthesia, and whether there are gender differences in sensory processing changes after pediatric surgery.

Preoperative emotional/behavioral problems predicted pre-to-postoperative changes in sensory processing. Anesthesiologists should be aware that children with current emotional/behavioral problems are more vulnerable to postoperative changes in sensory processing.

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‘Therefore a weapon that is strong will not vanquish;
A tree that is strong will suffer the axe.
The strong and big takes the lower position,
The supple and weak takes the higher position.’ (*Tao Te Ching*, 76)
是以兵强则不胜，木强则共。强大处下，柔弱处上。

Chapter 6

Association between children's emotional/behavioral problems before adenotonsillectomy and postoperative pain scores at home

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What is already known

- Having Internalizing problems is associated with higher state anxiety at anesthesia induction
- Higher state anxiety is associated with higher postoperative pain scores and behavioral changes.

What this article adds

- Preoperative internalizing problems and high parental need for information are independently associated with higher postoperative pain scores at home in children after adenotonsillectomy.
- Screening for these problems can help to identify vulnerable children and adapt the postoperative analgesic strategy accordingly.

ABSTRACT

Background: Children undergoing adenotonsillectomy are at risk of severe postoperative pain and sleep problems. Little is known about the specific child risk factors for these problems.

Aims: To assess the occurrence of postoperative pain, sleep problems and medication adherence and assess the influence of internalizing and externalizing problems on postoperative pain.

Methods: This prospective cohort study included 160 children, aged 1.5 – 5 years undergoing day-care adenotonsillectomy. Parents rated their child's pain with the Parents' Postoperative Pain Measure and their child's sleep problems with Vernon's Post Hospital Behavioral Questionnaire during the first 3 days and at day 10 postoperatively. Emotional/behavioral problems (i.e., internalizing and externalizing behaviors) during the past 2 months were assessed using the Child Behavior Checklist. Regression analysis was used to assess whether children's pain intensity at home was associated with internalizing/externalizing problems, after controlling for age, preoperative child state anxiety, parental state anxiety, parental need for information and socioeconomic status.

Results: Applying a threshold of ≥ 6 on the Parents' Postoperative Pain Measure the incidence of moderate to severe pain was 57.6% at day 1, 53.5% at day 2, 35.4% at day 3, and 4.8% at day 10. During the first 3 postoperative nights 37.1 % of the children woke up. Internalizing problems (β=. 343; *P*=.001) and parental need for information (β=.207; *P*=.011) were independently associated with higher pain scores at home during the first 3 days (R^2= .225).

Conclusions: Following adenotonsillectomy, children often experienced moderate to severe pain and sleep problems during the first 3 days at home. Preoperative internalizing problems and parental need for information were independently associated with increased pain at home. Screening for these problems can help to identify vulnerable children and adapt the perioperative analgesic strategy accordingly (which includes preparation, information and prescription of pain analgesics).

Keywords: Anesthesia, Anxiety, Child, Pain Postoperative, Risk Factors, Tonsillectomy

INTRODUCTION

Inadequate postoperative analgesia for children following day-care surgery is a major issue[1-3]. Adenotonsillectomy is a procedure after which children may experience much pain, as well as functional limitations and sleep problems for more than one week[4]. This may be the result of poor pain management as many parents do not to expect protracted postoperative pain[4]. Furthermore, parents often have misconceptions about pain medication, although they are able to recognize and assess their child's pain[5]. Alternatively, the prescribed analgesic regimen could be inadequate, refused by the child (bad taste, opposition) and parents may have received insufficient information[1,5]. Finally, parental anxiety, which seems to be related to preoperative need for information[3,6,7], socio-economic status[3] and cultural factors[1] are also known predictors of the children's pain levels[3].

Surprisingly little is published about specific child factors in relation to postoperative pain. What is known is that children often refuse to take pain medication, e.g. because it scares them, because it tastes bad, or swallowing is painful[1]. Furthermore, increased perioperative situational anxiety, which is more often seen in younger children[8,9], has been associated with higher postoperative pain scores[7,10]. In addition, children's pre-existing emotional/behavioral problems (specifically internalizing problems) are associated with children's situational anxiety during induction[9].

It is still unknown to what extent children's preoperative factors contribute to their postoperative pain experience after discharge. More knowledge on this issue would enable us to attune perioperative care and especially pain management at home towards individual needs.

Apart from postoperative pain, children have often sleep problems following surgery[10]. Sleep problems have not been thoroughly investigated so far, although a recent consensus statement for core outcome domains and measures for pediatric acute and chronic/recurrent pain in clinical trials recommended this[11].

Aims of this study: 1. to assess the level of postoperative pain in hospital, pain medication adherence at home, as well as pain and sleep problems at home in children aged 1.5 to 5 years undergoing adenotonsillectomy, during the first three days and at day ten after discharge; and 2. to assess whether emotional/behavioral functioning is related to postoperative pain during the first three days after discharge.

METHODS

This was a prospective observational cohort study in young children (and their parents) undergoing adenotonsillectomy at the Queen Paola Children's Hospital in Antwerp (Belgium) between April 2013 and January 2016.

This observational study was registered at http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=3955 , and is reported following the STROBE statement and performed conform the Declaration of Helsinki. It was approved by the local Institutional Review Board (approval N°4157 B009201317117).

Inclusion/exclusion

All children aged 1.5 – 5 years undergoing day-care adenotonsillectomy were eligible. The following inclusion criteria applied: 1. written informed consent of parents; 2. American Society of Anesthesiologists (ASA) physical status I-II; 3. parents having a good understanding of Dutch language.

Excluded were: children with known developmental delay, children with a Body Mass Index above the 95th percentile for children of the same age and sex, and children who had a subsequent bleeding requiring re-intervention.

Parents received information at the preoperative Ear, Nose and Throat surgery consultation and informed consent was obtained by a research nurse on the day of surgery.

Demographic and medical data

On the day of admission demographical/medical data were collected by a research nurse. Parental education served as an indicator of socioeconomic status[12] classified into: 1. elementary school; 2. secondary school; 3. higher education or university.

Surgical technique

A common conventional cold dissection followed by bipolar diathermy for hemostasis was used.

Anesthesia procedure

All children and parents received a standardized preparation including a preoperative educational video. One parent was present during induction of anesthesia (parents chose themselves who would accompany the child) and no premedication was given - as is common practice at the Queen Paola Children's Hospital. The anesthesia management consisted of: 1. inhalation induction with sevoflurane 8 vol.% in a fresh gas flow of

6/8 liters/minute with a fractional inspired oxygen concentration (FiO_2) of 50% in air; 2. maintenance with sevoflurane: end-tidal concentration of 2.5-3 vol.% in FiO_2 of 50%; 3. opioids (fentanyl – Fentanyl-Janssen®: two mcg/kg and if necessary additionally pethidine – Pethidine®: 0.5 mg/kg, IV); 4. α_2 - adrenergic agonist (clonidine – Catapressan®: two mcg/kg, IV); 5. dexamethasone – Aacidexam-Aspen®: 0.15 mg/kg. IV; 6. Ondansetron – Ondansetron-Fresenius Kabi®: 0.1 mg/kg, IV; 7. fluid administration of Hartmann-solution (10 ml/kg/h, during surgery); 8. if necessary the muscle relaxant atracurium – Tracrium® (0.5 mg/kg, IV) was administered. During anesthesia ECG, O_2-saturation, *end-tidal* CO2, inhalation gas concentration, non-invasive blood pressure measurement (5 min. interval) were monitored.

For descriptive purposes intra-hospital postoperative pain management was assessed and it consisted of paracetamol (20 mg/kg, IV) and ketorolac - Taradyl® (0.5 mg/kg, IV). Intra-hospital postoperative rescue pain management consisted of tramadolhydrochloride - Tramadol HCL® 2 mg/kg, IV.

All children were extubated while being awake, transferred to the Post Anesthesia Care Unit and thereafter to the ward for 6 hours before discharge home.

Description of pain management at home

The parents received oral and written standardized pain management instructions with the recommendation to strictly adhere to prescribed regimen for the first three days. The regimen consisted of oral paracetamol – Perdolan® (syrup 15 mg/kg four times a day) and oral Ibuprofen – Nurofen® (syrup 5 mg/kg four times a day) 'by the clock'. Parents were asked to register medication adherence in a diary during the first three days and again at day 10. Good adherence was defined as having administered at least 16 of the 24 prescribed pain medications during the first three postoperative days.

On day 1, day 3 and day 10 a research nurse contacted the parents by phone and the parents were encouraged to ask questions whenever needed.

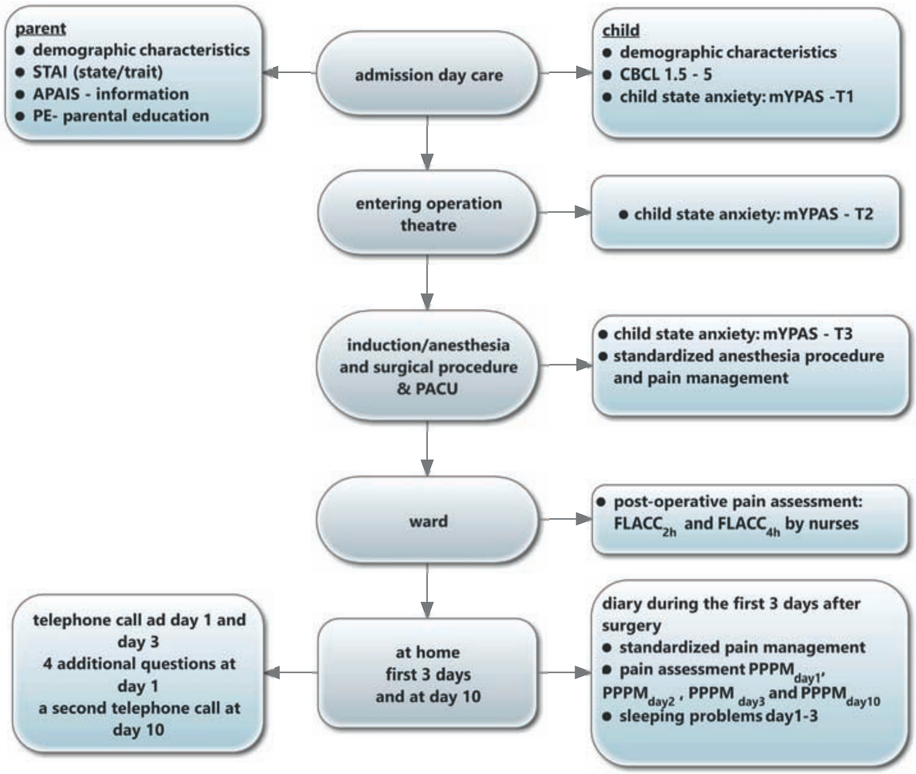
At day 1, the research nurse asked: 1. Are you satisfied with the information about post-operative care?; 2. Are you worried about your child's general well-being?; 3. Do you have any questions regarding your child's pain management?; 4. Did your child vomit or feel nauseated?

Assessment tools

Child pain assessment tools (see Figure 1)

Pain in hospital was assessed by a nurse at 2 hours and 4 hours postoperatively using the Face, Legs, Activity, Cry and Consolability (FLACC) scale. This scale has an excellent inter-rater reliability and validity in the postoperative phase[11,13]. By adding the scores at 2 hours and 4 hours a $FLACC_{sum\text{-}score}$ was computed.

Figure 1 ● Flowchart diagram of the different moments of assessment



STAI: Spielberger's State-Trait Anxiety Inventory; APAIS-info, Amsterdam Perioperative Anxiety Information scale – information part; CBCL/1$^{1/2}$-5: Child Behavior Checklist; mYPAS: modified Yale Preoperative Anxiety scale; FLACC: Face, Leg, Activity, Cry, Consolability scale; PPPM: Parents' Postoperative Pain Measure.

Pain at home was measured using the 15-item Parents' Postoperative Pain Measure (PPPM)[14], a recommended tool[11] validated for children aged from 1 to 12 years. The total score of this observational checklist ranges from 0 to 15. The PPPM has good specificity (80%) and sensitivity (88%) to detect children with postoperative pain. The internal consistency as reflected by Cronbach's alpha was 0.88 at day 1 postoperatively. Clinically significant pain has been defined as a PPPM score ≥ 6 (each day)[14].

On the day of surgery, a research nurse instructed the parents how to use the PPPM and asked them to complete it every evening during the first three days and at day 10 postoperatively. A mean PPPM score [mean-score $PPPM_{1-3}$] was calculated based on the separate PPPM scores during the first three days.

Postoperative sleep problems

During the first three days postoperatively and at day 10, parents answered four questions about their child's potential sleep problems based on Vernon's Post Hospital Behavioral Questionnaire (PHBQ)[15]. Questions addressed whether the child made a fuss about going to sleep, was afraid of the dark, had trouble getting asleep, and woke up at night. The responses (five response categories) were dichotomized into: sleep problems or no sleep problems.

Other child assessment tools

Emotional/behavioral problems of the child during the past two months were assessed, in hospital prior to surgery by the accompanying parent, using the internationally well-validated Child Behavior Checklist (CBCL/$1^{1/2}$-5)[16]. The CBCL/$1^{1/2}$-5 consists of 100 problem items (response categories 1-3). Summary scores on internalizing problems (subscales: emotionally reactive, anxious/depressed, withdrawn, somatic complaints), externalizing problems (subscales: attention problems and aggressive behavior), and a total problem score were calculated. Higher scores indicate more emotional/behavioral problems. Good validity and reliability of the CBCL/$1^{1/2}$-5 have been confirmed for the Dutch-translated version.

A trained research nurse completed the modified Yale Preoperative Anxiety Scale (mYPAS)[17] at three moments: 1. on admission (mYPAS-T1); 2. in the holding area (mYPAS-T2); 3. during induction (mYPAS-T3). This structured observational instrument assesses five domains: activity, emotional expressivity, state of arousal, vocalization and use of parents (number of items 4 or 6). It has good-to- excellent reliability and validity. Kain *et al*[17] reported that the instrument has: 1. good inter- and intra-observer agreement (κ statistics ranged between 0.63 and 0.90); 2. high concurrent validity ($r = 0.79$ with the STAI for children); and 3. high construct validity. A mean summary score [$mYPAS_{mean}$] was calculated from the scores for the three measurement moments.

Parental assessment tools

Parents completed the Spielberger's State Trait Anxiety Inventory[18] to assess their own state anxiety (current situational state) and trait anxiety (general disposition to anxiety). The Dutch-translated version has been validated[18].

Parents' attitude towards receiving information was assessed with two items of the Amsterdam Preoperative Anxiety Information Scale (APAIS)[19]: 1. I would like to know as much as possible about the anesthetic; 2. I would like to know as much as possible about the procedure. A summary score was based on scores on both items (each with response categories on a 5-point Likert scale). A score between 2 – 4 means no/little information need; 5 – 7 average information need and scores between 8 – 10 a high information need [19]. A score ≥ 5 is interpreted as having a positive attitude towards receiving information.

Statistical analysis

Baseline demographic and psychological data of children and parents are presented as means ± standard deviations (for continuous data), as median with interquartile range or as percentages (for categorical data). Skewness and kurtosis indicated that the data were normally distributed. This was further checked by Kolmogorov-Smirnov tests and Q-Q plots.

An a priori power analysis for multiple regression (mean-score $PPPM_{1-3}$ as outcome parameter) was performed using GPOWER version 3.1.9.2., based on a fixed model (model parameters are fixed or non-random quantities). This analysis showed that 147 children were needed to detect a medium effect size, (reflected by Cohen's $f^2 = 0.15$), with a power of 0.9 and an α of 0.05, using 10 predictors. Allowing for approximately 10% loss to follow-up, a sample size of 160 was considered sufficiently large for this study's aims.

Linear regression analyses

Univariate linear regression was initially conducted to identity variables individually associated with increased pain at home. The mean $PPPM_{1-3}$ score was used as dependent variable. Based on their theoretical relevance from previous publications, the following independent variables were considered: child's age, parental state anxiety, parental trait anxiety, parental need for information, parental education (recoded into dummy variables), child's state anxiety, preoperative internalizing problems (CBCL), preoperative externalizing problems (CBCL) and preoperative total problems (CBCL).

After that, a multiple regression model was constructed to assess whether internalizing and externalizing problems explained pain at home. To avoid multicollinearity issues, independent variables that correlated highly with other independent variables were excluded from the regression analyses. This implies that the CBCL total problems score (which highly correlated with both internalizing and externalizing problems) and parental trait anxiety (which highly correlated with parental state anxiety) were excluded. The remaining independent variables were entered into two blocks. First, the following variables already mentioned above were entered into the model: child's age, child's state anxiety, parental state anxiety, parental need for information, and parental education. Second, internalizing/externalizing problems of the CBCL were added to see what these variables add to the strength of the model, after the previous variables had been controlled for.

All analyses were performed with IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.

RESULTS

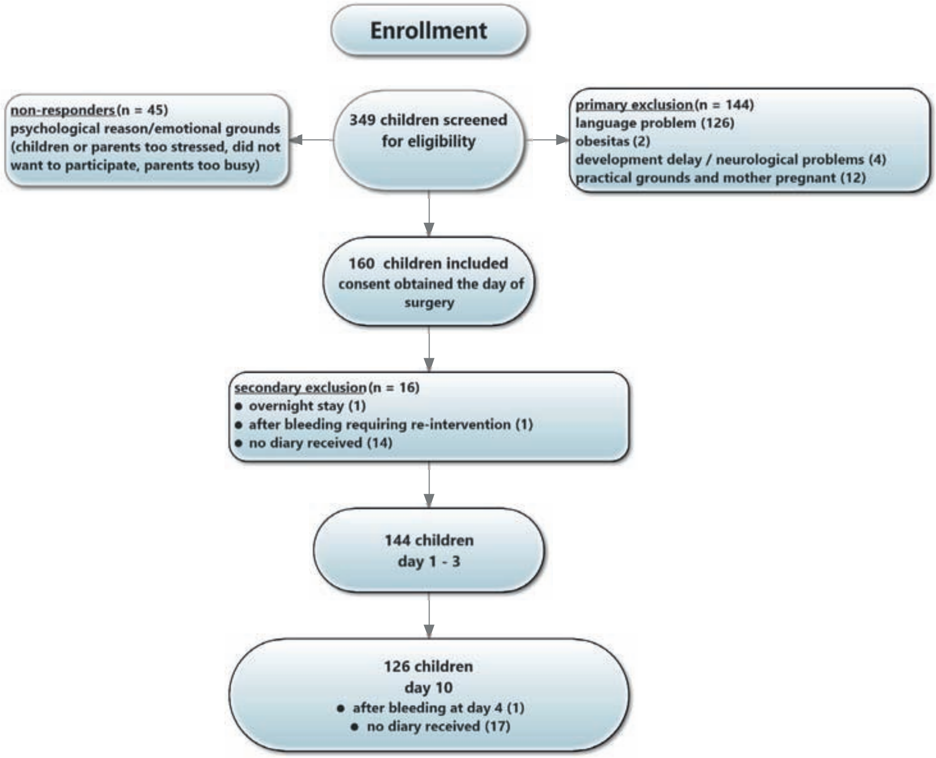
A total of 349 eligible children-parent pairs were screened. Of these, over one third (n = 126) was excluded due to insufficient knowledge of Dutch, while another 18 children had to be excluded for other reasons (obesity, developmental delay and logistic grounds). Of the remaining 205 children, 45 children and parents refused to participate for emotional or practical reasons (parents too busy, children or parents too stressed), corresponding to a response rate of 78%. One child was excluded because of bleeding requiring re-intervention and another stayed overnight. Of the remaining 158 children, the data of 14 children had to be removed from the analyses after three days, as no diaries were received.

Eventually, complete data of 144 children were available for final analysis up to three days. Unless indicated otherwise, the analyses described below refer to those 144 children.

At day 10, complete data were available for 126 (78.8%) children (see exclusion details in Figure 2).

The mean age was 46.4 months (SD ± 11.2); nearly half (49%) were boys; and 107 (74.8%) were accompanied by the mother at induction (Table 1). One hundred seventeen parents (81.3%) had a positive attitude towards receiving information (score APAIS ≥ 5) and 58 (41%) had a high information need (score APAIS ≥ 8). Furthermore, at day 1 postoperatively, 130 (90.3%) parents reported they were satisfied with the information about postoperative accompaniment. Nine (6.3%) parents reported they were worried about the child's general wellbeing at home and 8 (5.9%) parents had some additional questions regarding their child's pain management.

Figure 2 ● Flowchart of patient inclusion



Pain scores

In-hospital pain

The FLACC scores at 2 hours postoperatively in the ward (median = 0, IQR 0-0) reflected no to mild pain (FLACC score ≤ 3) in 137 children (95.1%) and moderate pain in 7 children (4.9%). The FLACC scores (median = 0, IQR 0-0) 4 hours after leaving the Post Anesthesia Care Unit reflected no to mild pain in 134 children (95.7%), moderate pain in 5 (3.6%) and severe pain in 1 child (0.7%).

Primary outcome: pain at home

Mean PPPM scores decreased over time from 6.5 at day 1 to 1.0 at day 10, consistent with a decrease of postoperative pain intensity over time (Table 2). At day 1, 57.6% of the children had moderate to severe pain versus 4.8% at day 10.

Table 1 Characteristics of the children and the parent complete cases after 3 days postoperatively (n = 144)

	Children	Accompanying Parent	
demographic data			
gender boy	71 (49.3%)	gender mother	107 (74.3%)
age, months'	46.4 ± 11.2	parental age, (y)	33.3 ± 5.7
weight, kg	16.5 ± 2.9	parental nationality Belgian	133 (92.6%)
number of siblings ≥ 1	119 (82.6%)		
psychological variables			
[a]CBCL/1$^{1/2}$-5		[b]parental education	
Internalizing problems	10.3 ± 8.3	PE 1	28 (19.4%)
Externalizing problems	11.4 ± 7.1	PE 2	86 (59.7%)
Sleep problems	2.5 ± 2.6	PE 3	30 (20.8%)
Total problems	33 ± 21.4		
[c]child state anxiety		[d]parental anxiety	
mYPAS-T1	30.7 ± 8.0	state anxiety	42.4 ± 10.1
mYPAS-T2	42.2 ± 17.6	trait anxiety	34.8 ± 8.4
mYPAS-T3	51.6 ± 25.5		
$mYPAS_{mean}$	41.5 ± 14.5	[e]APAIS-info	6.7 ± 2.2
		APAIS 2 – 4	27 (18.8%
		APAIS 5 – 7	59 (40.9%)
		APAIS 8 – 10	58 (40.3%)
[f]pain in hospital			
$FLACC_{sum\text{-}score}$	0 (0 – 0)		
additional opioid pain medication			
during anesthesia			
paracetamol IV	144 (100%)		
ketorolac IV	144 (100%)		
pethidine IV	132 (82.5%)		
after anesthesia: tramadol IV	13 (8.1%)		
at home			
nausea/vomiting day 1 at home	6 (4.2%)	information satisfaction	130 (90.3%)
[g]medication adherence day 1-3	36 (25.2%)		

Data are expressed as N. (%); as mean with ± SD or as mean and IQR; [a]CBCL/1$^{1/2}$-5: Child Behavior Checklist as assessed by the accompanying parent (internalizing, externalizing, sleep- and total problems); [b]PE, parental education: PE 1 (no education or primary school), PE 2 (high school), PE 3 (further studies or university); [c]child state anxiety: modified Yale Preoperative Anxiety scale (mYPAS) at [mYPAS-T1] holding area, at [mYPAS-T2] entrance of the operating theatre and at [mYPAS-T3] during induction, mean summary score $mYPAS_{mean}$ = [mYPAS-T1 + mYPAS-T2 + mYPAS-T3]/3; [d]parental anxiety: Spielberger's State – Trait Anxiety Inventory; [e]APAIS – info, Amsterdam Perioperative Anxiety Information scale – information part; [f]$FLACC_{sum\text{-}score}$; Face, Leg, Activity, Cry, Consolability scale; [g]medication adherence (dichotomized using a cut-off value of 75% of max. allowed number of pain medication at home during the first 3 days postoperative)

Adherence to pain management at home

Prescribed pain medication at home was given according to instructions by only 25.2% (n = 36) of parents during the first three days after surgery. (Table 1)

Sleep problems after surgery

On day 1, 52 (36%) children woke up at night versus 20 (16%) at day 10 (Table 2). On day 1, 21 (15%) children resisted going to sleep and 16 (11%) had trouble falling asleep. At day 10 these problems had almost completely disappeared.

Table 2 ● Postoperative pain scores and sleep problems at home

Primary outcome	**Day 1**	**Day 2**	**Day 3**	**Day 10**	
Pain at home	**$PPPM_{day1}$**	**$PPPM_{day2}$**	**$PPPM_{day3}$**	**$PPPM_{day10}$**	**$PPPM_{day1-3}$**
Mean (± SD)	6.48 ± 3.87	6.11 ± 4.18	4.51 ± 4.22	1.06 ± 2.47	5.7 ± 3.7
N (%) score ≥ 6	83 (57.6%)	77 (53.5%)	51 (35.4%)	6 (4.8%)	

Secondary outcome	**Day 1**	**Day2**	**Day 3**	**Day 10**
Sleep problems				
Making a fuss about going to sleep at night	21 (14.6%)	20 (14%)	21 (14.6%)	6 (4.7%)
Being afraid of the dark	4 (2.8 %)	7 (4.9%)	4 (2.8%)	1 (0.8%)
Having trouble getting to sleep at night	16 (11.1%)	22 (15.3%)	26 (18%)	5 (3.9%)
Waking up at night	52 (36.1%)	57 (39.9%)	52 (36.1%)	20 (15.8%)

Data are expressed as N. (%); as mean with ± SD. **Primary outcome: pain at home 1. PPPM**: Parents' Post-operative Pain Measure at day 1, ($PPPM_{day1}$), day 2 ($PPPM_{day2}$), day 3 ($PPPM_{day3}$) (n = 144); day 10 ($PPPM_{day10}$) (n = 126) and mean score $PPPM_{day1-3}$ = ($PPPM_{day1}$ + $PPPM_{day2}$ + $PPPM_{day3}$)/3; **Secondary outcome: sleep problems** – after dichotomizing (more problems vs. no problems). Parents had 5 answers options: a. much less; b. less; c. the same; d. more; e. much more as normal. For questions 1 & 2 and 3 the results were dichotomized by having no sleep problems (a + b + c) or having sleep problems (d + e). Regarding question 4 the results were dichotomized by having no sleep problems (c + d + e) or having sleep problems (a + b): number and % present more problems

Univariate regression model

Positive associations were found between the children's level of pain on $PPPM_{1-3}$ and respectively: 1. CBCL internalizing, externalizing, and total problems; 2. parental state anxiety; 3. parental need for information. Standardized regression coefficients ranged from 0.227 to 0.368 (Table 3).

Multiple regression model

In first-block analysis, the multiple regression model explained 9.7% of the variance (P = .028). Parental state anxiety and parental need for information (APAIS-info) were independently associated with pain scores at home ($PPPM_{1-3}$) (Table 4).

Table 3 Univariate regression model explaining the child's postoperative pain during the first 3 days at home

	Postoperative pain during the first 3 days at home
	mean scores [a]PPPM 1-3
child's age	-.033 (.069)
[b]parent state anxiety	.237 (.004)
[b]parent trait anxiety	.066 (.432)
[c]APAIS – info	.227 (.006)
[d]parental education 1	-.073 (.385)
[d]parental education 3	.009 (.910)
[e]$mYPAS_{mean}$	-.024 (.777)
[f]preoperative internalizing problems (CBCL)	.368 (.000)
[f]preoperative externalizing problems (CBCL)	.255 (.002)
[f]preoperative total problems (CBCL)	.359 (.000)

Data are expressed as standardized regression coefficients; (P- value).
[a]mean scores PPPM1-3: Parents' Postoperative Pain Measure [PPPM1-3 = day 1 + day 2 + day 3]/3; [b]Parent state/trait anxiety, Spielberger's State – Trait Anxiety Inventory; [c]APAIS-info, Amsterdam Perioperative Anxiety Information scale – information part; [d]Parental education recoded in three dummy variables: Parental education recoded 1 = no education, elementary school; Parental education 2 (reference) = secondary school; Parental education 3 = higher education or university; [e]mYPASmean: mean child state anxiety as assessed with the modified Yale Preoperative Anxiety scale (mYPAS), mean scores mYPASmean = [mYPAS(1) + mYPAS(2) + mYPAS(3)]/3; [f]preoperative internalizing/externalizing/total problems, Child Behavior Checklist List (CBCL).

In the second-block analysis, we entered the CBCL internalizing and externalizing problems scores into the regression model. Preoperative internalizing and externalizing problems explain postoperative pain above and beyond the other variables. In the final model, internalizing problems and parental need for information were independently associated with pain scores at home ($PPPM_{1-3}$). A difference of respectively 0.34 SD and 0.21 SD on the $PPPM_{1-3}$ score was associated with 1 SD difference on internalizing problems and parental need for information. Overall, this model explained 22.5% ($P = .000$) of the variance of pain scores at home.

DISCUSSION

More than 50% of children in this study had moderate to severe pain during the first three days after adenotonsillectomy, which is consistent with previous research[2,4]. On day 10, 3.8% of children still experienced moderate to severe pain. Furthermore, parents reported sleep problems for almost 40% of the children during the first three postoperative days at home.

Table 4 ● Multiple regression model – associations with the child's postoperative pain as assessed with the Parents' Postoperative Pain Measure during the first 3 days at home ($PPPM_{1-3}$)

	Postoperative pain $PPPM_{1-3}$ (n = 144)							
	Model step 1				**Model step 2**			
Variable	unstandardized B	95% CI for B	standardized β	*P-value*	unstandardized B	95% CI for B	standardized β	*P-value*
Constant	.841	[-4.02, 5.70]		.733	1.523	[-3.10, 6.15]		.516
child's age	.001	[-.055, .057]	.004	.966	-.012	[-.065, .041]	-.037	.647
[a]parent state anxiety	.076	[.014, .138]	.209	.017	.039	[-.021, .099]	.107	.202
[b]APAIS-info	.290	[.006, .573]	.173	.046	.347	[.081, .613]	.207	.011
[c]parental education 1	-.945	[-2.50, .614]	-.102	.233	-.928	[-2.38, .529]	-.100	.210
[c]parental education 3	.259	[-1.26, 1.78]	.029	.736	.633	[-.797, 2.06]	.070	.383
[d]$mYPAS_{mean}$	-.006	[-.049, .038]	-.022	.800	-.026	[-.067, .015]	-.102	.215
[f]preoperative internalizing problems					.152	[.063, .242]	.343	.001
[f]preoperative externalizing problems					.03	[-.072, .132]	.058	.557

Dependent variable: mean scores PPPM1-3: Parents' Postoperative Pain Measure [PPPM1-3 = day 1 + day 2 + day 3]/3;

Model step 1. Predictor variables: 1. Child age; 2. [a]Parent state and trait anxiety with, Spielberger's State-Trait Anxiety Inventory; 3. [b]APAIS-info, Amsterdam Perioperative Anxiety Information scale – information part; 4. [c]Parental education recoded in three dummy variables: Parental education recoded 1 = no education, elementary school; Parental education 2 (reference) = secondary school; Parental education 3 = higher education or university; 5. [d]$mYPAS_{mean}$: mean child state anxiety as assessed with the modified Yale Preoperative Anxiety scale (mYPAS), mean scores $mYPAS_{mean}$ = [mYPAS(1) + mYPAS(2) + mYPAS(3)]/3;

Model step 2. All predictor variables of model 1 + [g]preoperative internalizing/externalizing problems, Child Behavior Checklist (CBCL/$1^{1/2}$-5).

Note: model 1 ($R^2 = .097$; $P = .028$) and model 2 ($R^2 = .225$; $P = .000$); $\Delta R^2 = .128$

Pre-existing internalizing problems (emotionally reactive, anxious/depressed, withdrawn, somatic complaints) were independently associated with higher pain scores during the first three postoperative days after adenotonsillectomy. This finding remained even after controlling for the child's age, the child's state anxiety, parental state anxiety and parental education. In addition, parental need for information was also associated with pain scores at home.

The finding that children's preoperative internalizing problems were associated with higher pain scores at home suggests that children showing anxiety/depression, withdrawn behavior, somatic complaints and emotional reactiveness, are at high risk for increased postoperative pain experience. This is consistent with previous studies in which higher levels of internalizing problems were associated with recurrent abdominal pain[20] and headache in children[21]. On the other hand, an earlier study in children undergoing tonsillectomy found no association between preoperative CBCL scores and postoperative pain, which may be related to the small study size (n = 43)[22].

Furthermore, parents with a higher need for information reported more postoperative pain for their children. A majority of parents (81%) had a positive attitude towards receiving information, 40% had a high need for information (APAIS ≥ 8) and a vast majority (92 %) seemed to be satisfied with the information given. The finding that higher parental state anxiety was related to a higher parental need for information is consistent with literature[6,19].

Remarkably, only one quarter of the parents adhered to the prescribed pain management, consistent with previous findings[2,4]. Our results may indicate that parents can recognize their child's pain but do not give pain medication accordingly. Although a majority of parents were satisfied with the information provided, it may have been too general and not attuned to what parents needed to know about the importance of adherence to the medication regimen. Still, their knowledge on this issue, including the side effects of the medication, was not assessed. Future research should unravel why parents would not adhere to a pain medication regimen for their child.

In this study, many of the children showed postoperative sleep problems, which is consistent with previous findings[10]. From a clinical perspective it is important to inform parents that these postoperative sleep problems may occur.

Several strengths of this study deserve mention. We included a large sample of children in a vulnerable age category (1.5 to 5 years). Furthermore, anesthetic and pain management was standardized, both in-hospital and at home. Lastly, internationally validated instruments such as the FLACC and PPPM were used, as advocated by PedIMMPACT[11] recommendations. Still, some limitations regarding pain assessment in young non-verbal children should be addressed. Firstly, psychological traits might have an impact on assessment tools' pain outcomes as compared to how they affect the patients' actual experience of pain. Secondly, the validity of pain assessment tools in children under the age of five is poor and children's pain self-report should be preferred[11,23]. Furthermore, although parents might be reliable as assessors, they may tend to overestimate the severity of the child's pain[23].

On the other hand, this is a single centre study, which implies that it may have limited generalizability. Then, as the study used information from a single informant (a parent), it may be vulnerable to common method variance[24]. Since one informant competed the questionnaires, scores may be biased (e.g. if a parent "overestimates" the child anxiety, he/she will presumably do so on all questionnaires, which may elevate correlations just by the fact that one informant completed them).

Furthermore, it is not known to what extent other parental characteristics, such as parental stress and pain catastrophizing thoughts, could have influenced the results.

As this study shows, children with internalizing problems are at risk for higher pain at home after day-care adenotonsillectomy and are at risk for sleep problems. Moreover, children who undergo a medical procedure might be at risk for developing post-traumatic stress symptoms[25]. This should be investigated in children with prolonged postoperative pain and in children with more emotional problems, since posttraumatic stress symptoms may harm psychosocial functioning.

In conclusion, the take-home messages of this study are: 1. including some form of psychological screening in the preoperative evaluation of children can be beneficial as pre-existing internalizing problems are a risk factor for higher postoperative pain at home; 2. providing parents with specific information regarding their child's pain management at home is essential to enhance adherence to the prescribed medication regimen.

DISCLOSURES

1. Ethical approval: Approval from the ZNA Middelheim Institutional Review Board (B009; OG031 E.C. approval N° 4157 B009201317117), Lindendreef 1, 2020 Antwerp, Belgium.
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3. Conflict of interest: Dr F. Verhulst published the Dutch translations of ASEBA from which he receives remuneration. Dr F. Veyckemans is section editor for Pediatric Anesthesia. The other authors have no conflict of interest.

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'Without stirring abroad
One can know the whole world;
Without looking out of the window
One can see the way of heaven.
The further one goes
The less one knows.' (*Tao Te Ching*, 47)
不出户知天下；不闚牖见天道。其出弥远，其知弥少。

Chapter 7

General discussion

GENERAL DISCUSSION

In this general discussion, from an overall view, we will discuss the main findings of this PhD thesis, set out the limitations of the studies executed and discuss implications of the present findings both for research as well as for clinical practice.

The content of this PhD thesis covers two settings: the pre- and postoperative setting.

Regarding the preoperative setting, the aims of this thesis were:

1. to explore associations between children's emotional/behavioral problems, as assessed with the Child Behavior Checklist (CBCL), and their anxiety during induction of anesthesia, when undergoing elective day-care surgery;

2. to validate a new, easy-to-use anxiety assessment tool during induction of anesthesia;

3. to evaluate the usefulness of an audio-visual aid to decrease parental state anxiety.

Considering the postoperative setting, this thesis focused on associations between children's emotional/behavioral problems and: 1. emergence delirium (ED) at awakening; 2. changes in sensory processing as assessed with the Infant/Toddler Sensory Profile ($ITSP_{6-36}$) two weeks after surgery for circumcision; 3. pain at home after adenotonsillectomy.

Following this line of thought, the next sections will discuss the findings of this thesis: first focusing on the period prior to surgery, then on the period after surgery.

PERIOD PRIOR TO THE INDUCTION OF ANESTHESIA: PREOPERATIVE ANXIETY IN CHILDREN AND PARENTAL INVOLVEMENT

In the first study (chapter 2) we focused on the association between children's pre-existing emotional/behavioral problems and their state anxiety during induction. In 401 children admitted for day-care surgery, we examined whether the scores on the CBCL[1,2] – a well-validated parent report assessing emotional/behavioral problems during the 6 months prior to surgery – were associated with anxiety during induction, as assessed by trained research nurses using the modified Yale Preoperative Anxiety Scale (mYPAS)[3]. Our main findings showed that internalizing problems prior to surgery were significantly associated with anxiety at induction, as were the child's state anxiety on admission in the hospital, the child's age and the level of parental education (PE). Externalizing problems were not associated with anxiety at induction. Similar results were obtained by Fortier *et al.*[4] in a pilot study with adolescents, showing that internalizing problems as assessed by the CBCL were predictive for anxious behavior during induction.

It is interesting to compare our findings to those of Davidson *et al.*[5], who aimed to assess risk factors for anxiety at induction, using a cohort study of 1,224 children aged 3 – 12 years. Their analysis identified younger age, behavioral problems during previous health care attendance, duration of the procedure and parental anxiety as risk factors for anxiety during induction of anesthesia. They also studied the influence of pre-existing emotional/behavioral problems. To measure emotional/behavioral problems, they did not use the CBCL, but instead a question that the parents had to answer with a simple 'yes' or 'no'. In contrast to our results and those of Fortier *et al*., Davidson *et al.* did not find evidence for an effect of pre-existing emotional/behavioral problems on the child's anxiety during induction. The discrepant results may be explained by the different assessment tools used. The method of Davidson *et al.* has not been psychometrically established so far. Furthermore, our model explained 33% of the variance in the children's anxiety at induction, whereas that of Davidson *et al.* explained only 5.3%.

In literature, children's behavior in the direct preoperative period has been reported to be associated with children's state anxiety at induction[6-10]. In our study anxious behavior on admission in the holding area (measured with the mYPAS by independent research nurses) was strongly associated with anxiety at induction. This indicates that the use of a preoperative screening tool may give valuable information to anesthesiologists, since this can create an opportunity to attune the preparation of children during induction of anesthesia to their psychological needs.

Our results showed that the younger the age of the child, the higher the risk for anxiety at induction. This is indeed in line with previous findings[5,11]. However, assessing children's state anxiety during induction is a complex matter; older children and adolescents may show socially desirable behavior and may be inhibited to express themselves openly. This is one of the reasons why it has been recommended to use the parent report CBCL[4], because a screening tool regarding preoperative emotional/behavioral problems seems more suited as a screening tool than state anxiety scores on the mYPAS provided by health care workers (nurses, anesthesiologists).

Next, our study showed that children of parents with a high educational level were less anxious at induction than children from parents with a lower education level (in research parental education is often used as indicator for socio-economic status[12]). A possible explanation for our finding is that in general children of parents of a lower socio-economic status tend to have more emotional/behavioral problems[13,14]. In addition, another possible explanation might be that highly educated parents may have more facilities to provide their children with specific informative tools for psychological preparation, which could be anxiety-reducing for their children.

In contrast to the extensive study by Davidson *et al*. and earlier studies[5,11,14,15], our study found that parental state anxiety was not an independent risk factor for children's anxiety at induction. To measure parental state anxiety at admission both Davidson *et al*. and our research team used the Spielberger's State Trait Anxiety Inventory (STAI)[16], which is considered the *Gold Standard*. However, we used the STAI in our regression model whereas Davidson *et al*. used the parents' scores on a global Visual Analogue Scale just after induction in their regression model. This may explain the discrepancy between our results and those of Davidson *et al*. Apart from all this, we do support their view that the overall child-parental interaction is much broader than *only* parental anxiety during induction and that 'the relationship between the child's and the parent's anxiety is probably complex with bidirectional influences'. This may also explain the equivocal findings reported in the literature regarding the impact of parental anxiety on the children's anxiety at induction.

Another relevant finding of our study was that parents of younger children compared to those of older children had higher levels of state anxiety during induction. Furthermore, in comparison to mothers, fathers revealed less state anxiety during induction than mothers, although no difference in trait anxiety between fathers and mothers was found. Both findings are in line with a previous study[17].

Considering our main outcomes above, we recommend to introduce psychological screening (by means of the CBCL) in perioperative care, together with an assessment of the child's anxiety in the direct preoperative period using the structured mYPAS (by trained nurses).

Several methods exist to measure children's anxiety. Chapter 3 presents the results of our study into the validity of the newly developed Visual Analogue Scale during induction (VAS-I) to assess anxiety in children. This instrument was meant to be completed by the child's parents. This has the advantage that the parents will feel that they are involved in the medical procedure and taking care for their child, which might consequently have a beneficial effect on parental knowledge[18], as to providing medical care and providing adequate pain medication for their children at home. It also fits well with the philosophy of Family-centered Pediatric Perioperative Care[10].

The VAS-I was developed with the aim of measuring anxiety during induction, considering that children's state anxiety increases during the entire preoperative period and peaks during induction[10,11]. This is the moment when children exhibit more overt anxious behavior. Therefore, the induction of anesthesia can be considered the best time to assess the child's state anxiety. One earlier study demonstrated that preoperative VAS child anxiety assessments in the holding area by accompanying mothers were inaccurate predictors of their child's anxiety during induction[19].

Only two assessment tools[7] are currently available to assess the child's state anxiety in the perioperative period. The mYPAS, regarded as the *Gold Standard* in research[3], is a well-validated and reliable tool but needs training of the raters and is time-consuming. Therefore it may not be feasible to use the mYPAS in a busy clinical setting. The second scale, the Induction Compliance Checklist (ICC)[20] can be used as a measure for the child's anxiety during induction of anesthesia (chapter 4). The ICC has excellent inter-and intra-observer reliability but its validity has never been established. A further disadvantage is that both scales cannot be used by parents. More recently developed tools like the Pediatric Anesthesia Behavior score[21] and the Children's Perioperative Multidimensional Anxiety Scale (CPMAS)[22] neither include an evaluation by the parents. The VAS-I scale, proposed and investigated in our present study, has the advantage that it can be used in children across a broad age-range (1 – 16 years), including nonverbal children (i.e., infants or toddlers who are too young to speak). Previous research has been much more limited in using a narrower age-range (7 – 16 years)[23].

In chapter 3 we present preliminary evidence regarding the validity of the VAS-I tool. To our knowledge, global, brief anxiety rating scales have not been validated before for use during induction of anesthesia in children. As to concurrent validity, our findings showed strong correlations between the VAS-I and mYPAS. For construct validity it is important that an assessment tool (in this case the VAS-I) is sensitive to known group differences. It was hypothesized that VAS-I ratings of parents and anesthesiologists would be higher in younger children (1.5 – 5 years) than in older children (6 – 16 years) and higher in high-anxious parents than in low-anxious parents. Consistent with these hypotheses, our results showed that: 1) the VAS-I scores of both parents and anesthesiologists were higher for younger children than for older children; 2) VAS-I scores were higher for children of high-anxious parents than for children of low-anxious parents. This latter result was not only found while considering the VAS-I scores of the parents (in this case, 'shared informant bias' possibly played a role, as the parents rated both their own and their child's anxiety), but also while looking at the VAS-I scores of the anesthesiologists. Moreover, parent ratings (VAS-IP) were significantly higher than the anesthesiologists' ratings (VAS-IA). This is in line with our findings described in chapter 4, also showing that the parental VAS-I anxiety assessment scores were higher than anesthesiologists' ratings. Finally, in our study optimal cut-offs were identified for the VAS-IP (37 mm) and VAS-IA (30 mm) in order to identify anxious children as identified by the mYPAS (cut-off value ≥ 30) during induction.

Considering our findings, the VAS-I provides an opportunity to incorporate anxiety assessment and management in a busy daily perioperative clinical practice. Parents can easily complete it and it requires no training. Our evidence-based cut-off points will need to be confirmed in future research. If the VAS-I is further validated, than more children at risk for perioperative anxiety can be detected. Also, the use of the VAS-I could be instructive for parents to pay extra attention to anxiety. It should be explained to parents that children with higher state anxiety during induction are at risk for more postoperative pain[23,24].

So far, this discussion has mainly focused on the child's anxiety. However, more attention should also be devoted to the parents' anxiety. After all, parents accompanying their child during induction of anesthesia tend to become very anxious[15,25,26]. Their state anxiety increases towards the anesthetic induction, when their child will lose consciousness and parents will be separated from their child after induction[17,25,26]. Chapter 4 presents the results of a randomized controlled trial (RCT) into the effects of an audio visual aid (AVA) to reduce the accompanying parents' anxiety during the induction of anesthesia of their child. In this trial, the level of parental state anxiety increased during the entire period in the operating theatre up to the moment of the child's induction, in both intervention and control groups. From a psychological point of view this seems natural and logical considering the precarious situation of the child. Our results are in line with previous findings, showing increases in parental heartrate and skin conductance[26,27] during induction of anesthesia of their child. Although parents may become very anxious, they can be very motivated to be present during the induction and our findings showed that parents strongly believe their presence is very useful for their child. This is consistent with earlier studies[17,25]. Surprisingly, in our study parents from both the control and the AVA intervention group were equally satisfied about the procedure and the information received. It should be mentioned that besides the AVA in the intervention group, both groups also received extended general written information[28].

Although, as said above, parental state anxiety increased in both groups, this increase was significantly less in the intervention group, indicating that AVA seems a useful tool in preparing parents. This finding is in accordance with earlier findings in literature[29-32]. However, two more recent studies[33,34] could not show a beneficial effect of visual aids on parental state anxiety. Still, one of these studies found that a preoperative video DVD could enhance parents' participation on how to actively support their child and also had a positive effect on the child postoperative pain (children aged 3 – 10 years) during one-day surgery[33], while the other study demonstrated an improved parental self-efficacy about their role in the OR[34].

In addition, our results showed no differences in child's state anxiety at induction (as rated by the parents and the anesthesiologists using the VAS-I) between the AVA and control group. Put otherwise, the small but significant favorable effect of the AVA on parental state anxiety was not paralleled by a favorable effect on the child's state anxiety during induction, which is in line with the two above-mentioned studies[33,34].

In conclusion, our study showed that AVA had a favorable influence on parental state anxiety. Therefore it can be recommended to use AVA for preparing parents towards anesthesia of their child. Unfortunately, AVA had no beneficial effect on the child's anxiety. In a sense, this is not surprising because, as already mentioned, there are probably complex bidirectional influences in the relationship between the child's and the parent's anxiety. Next to that, even if parental anxiety decreases, it is still the child who has to face the realistic danger of surgery. From an evolutionary survival perspective, it is logical and natural that anxiety increases in the face of acute realistic, imminent danger. To reduce the children's state anxiety we recommend to develop additional interventions, specifically targeted at the child's anxiety (see the section 'Implications and recommendation for future research' below).

PERIOD AFTER SURGERY: EMERGENCE DELIRIUM, SENSORY PROCESSING CHANGES, POSTOPERATIVE PAIN AT HOME AND SLEEP PROBLEMS

In chapter 2 we examined the possible predictive power of parent reported pre-existing emotional/behavioral problems in children for Emergence Delirium (ED) at awakening from anesthesia as assessed by nurses with the well validated PAED scale. This was done in a sample of 343 children undergoing elective day-care surgery. So far, this topic had not been investigated thoroughly. An earlier study of 521 children aged 3 – 7 years, using a temperament scale, demonstrated a univariate association between children's temperament (low adaptability) and ED[35]. In the multivariate analysis, only Ear Nose Throat (ENT) surgery, time to awakening and the use of isoflurane as inhalational anesthetic appeared to be independent risk factors for ED. Furthermore, in other studies state anxiety in children was demonstrated to be associated with ED[24,36-38].

In line with earlier findings, we demonstrated in our final multivariate model that the child's age and its first experience with anesthesia were independently associated with ED. We did not find an association between pre-existing emotional/behavioral problems and ED (on PAED scores), nor between child's state anxiety and ED. As already mentioned, this last finding is in contrast with earlier studies[24,36-38].

Several reasons might explain why we did not find an association between pre-existing emotional/behavioral problems and ED. In general, it is clear that ED is a very complex phenomenon, influenced by psychological, medical and social putative risk factors[39-41]. Related to this, the assessment of ED at awakening from anesthesia (like the assessment of all behaviors in children awakening from anesthesia) remains challenging[37,42-44]. ED can be measured, but all instruments available for this purpose have their limitations. For example, it is difficult to distinguish ED from pain due to overlaps between the PAED scale and pain assessment tools[42,43,45]. In this respect, a recent retrospective analysis of observational studies posed that making no eye contact and unawareness of the surroundings characterized ED in children, whereas crying, abnormal facial expression, and inconsolability indicated pain[45].

However, there were several strengths to the approach that we used. The present study assessed ED with a validated tool and in the final analysis, children with moderate and severe pain were excluded to control for the confounding influence of postoperative pain. Furthermore, we considered ED as psychological construct on a continuum (using continuous scores) rather than dichotomizing it into two categories (by using a cut-off score: ED yes or no). This may be considered an advantage, as dichotomization results in loss of information. Apart from that, it is still a matter of debate which cut-off value should actually be used to dichotomize ED[46].

In chapter 5 we studied changes in sensory processing after anesthesia in toddlers. This is a clinically relevant issue, because changes in sensory processing influence the toddlers' arousal, attention, affect and behavioral actions. Consequently changes in sensory processing can contribute to postoperative behavioral changes.

Sensory processing after anesthesia and its relation to emotional/behavioral problems is an unexplored field. In a group of 45 boys aged between 18 – 30 months, circumcised for religious reasons, we studied pre- to postoperative changes in sensory processing, using the ITSP[47,48], and we investigated if preoperative children's emotional/behavioral problems were associated with these sensory processing changes. To the best of our knowledge, this is the first study to look at changes in sensory processing following pediatric anesthesia, using a structured instrument to assess sensory processing.

Significant changes were found on low registration, sensation avoiding and low threshold and on auditory and tactile processing, which can be considered clinically relevant: our study showed that following surgery children reacted less sensitively to sensory input (e.g. less alert detection of auditory/tactile information). Changes in sensory processing might give rise to under-responsive behavior. Such behavior could be interpreted as withdrawn or passive, which seems consistent with earlier findings showing that apathy and withdrawal besides separation anxiety are common in children after having undergone surgery[49,50]. This increase of under-responsive behavior could affect the toddlers' daily social functioning. This is an unexplored domain and should be unraveled further in future research.

Interestingly, pre- to postoperative sensory processing changes were associated with pre-existing emotional/behavioral problems. As already noted above, changes in sensory processing and postoperative behavior changes are different though clinically related concepts. For this reason it is worthwhile to mention the results of Fortier *et al*.[50], which showed that internalizing problems were associated with maladaptive postoperative behavior. Fortier's study was the first to investigate pre-existing emotional/behavioral problems, assessed by the CBCL, as predictors for maladaptive postoperative behavior. Noteworthy, earlier studies already demonstrated that children with more internalizing problems tend to have more behavior inhibition[51]. In general, these children tend to be more calm and withdrawn. Further research is needed to unravel these complex patterns.

We investigated whether pre- to postoperative changes in sensory processing were related to postoperative pain because pain is a strong risk factor of postoperative problematic behavior[52,53]. We did not, however, find such a relationship. This may be due to the religious reasons for the circumcision and also to of the relative small study sample. In our study almost 50% of the children had moderate to serious pain on day one postoperatively, which is conform previous findings[54,55]. Only 40% of the parents did adhere to the prescribed medication for their child and this is line with previous findings[56-58]. The modest adherence to pain medication may be explained by the fact that the children underwent circumcision for religious reasons[59], which may have contributed to both parental pain assessment and their attitude towards the child's pain medication.

Finally, in this study the child's state anxiety (assessed with the VAS-I) was not associated with changes in sensory processing. The relation between sensory processing, anxiety and pain needs to be investigated further, using larger samples with more serious procedures (requiring longer anesthesia) and more long-term follow-up assessments.

Next to emergence delirium and sensory processing changes, pain was one of the postoperative/anesthesia outcomes that this thesis was interested in. In chapter 7, we studied postoperative pain at home and sleep problems in children who had undergone surgery. An observational study was performed in 160 children aged 1.5 – 5 years undergoing adenotonsillectomy, to evaluate postoperative pain levels and sleep problems at home and to test whether emotional/behavioral problems were predictive for postoperative pain up to three days after surgery. Of the participating children, 50% had moderate to severe pain and this is consistent with previous research[56,60]. Only 25.2% of parents adhered to the prescribed pain medication for their child at home. Previous findings also showed that compliance with prescribed pain medication following surgery was suboptimal[56,60]. Both findings closely resemble our results obtained in the group of boys who were circumcised, as described in chapter 5.

In our study of children who underwent adenotonsillectomy, pre-existing internalizing problems and parental need for information were associated with higher children's pain scores at home during the first postoperative three days. A plausible explanation for the relationship we found may be that children with more internalizing problems are more anxious, which has been shown to be related to higher pain scores[23,24]. These children also react more emotionally and have more somatic complaints which may further explain their vulnerability. In contrast, another study with a relatively small sample (n = 43) of children undergoing tonsillectomy found no association between preoperative CBCL scores (internalizing/externalizing and total emotional/behavioral problems) and postoperative pain[61]. At present, there is still insufficient good-quality evidence to draw strong conclusions about the influence of pre-existing internalizing problems on postoperative pain. Although not specifically related to postoperative pain, it could be interesting in this context to mention that previous studies associated higher levels of internalizing problems with recurrent abdominal pain[62] and headache in children[63].

Parents reported close to 40% postoperative sleep problems for children at home, which is consistent with previous findings in large sample of 241 children undergoing adenotonsillectomy[24]. This study showed that anxious children had a higher incidence of postoperative sleep problems. Importantly, the relationship between pre-existing emotional/behavioral problems and postoperative sleep problems in children needs to be investigated further.

A higher parental need for information as assessed with the APAIS was associated with higher postoperative pain scores in their children. Reasons for this association are speculative, but a potential explanation may be found in the parent's anxiety. That is, parental need for information was related to higher parental state anxiety (which is consistent with the literature[64,65]) and parental state anxiety was (univariately) associated with the child's postoperative pain scores (which also fits with earlier findings[11,66]).

CONCLUSIONS OF THIS PhD PROJECT

Previous evidence had already shown that perioperative anxiety was probably associated with ED, postoperative maladaptive behavior and higher postoperative pain intensity scores[36].

The present thesis provided additional evidence that pre-existing emotional/behavioral problems (as assessed by the CBCL) during the six months prior to surgery were associated with the child's preoperative state anxiety, ED, changes in sensory processing and postoperative pain at home. More specifically, the studies of the present thesis show that:

1. children's preoperative internalizing problems as assessed by the accompanying parent at admission prior to surgery are associated with children's state anxiety at induction as assessed by the mYPAS;
2. children's preoperative externalizing problems are associated with ED assessed by the PAED scale, whereas internalizing problems are not;
3. children's preoperative total emotional/behavioral problems are associated with pre- to postoperative changes in sensory processing;
4. after adenotonsillectomy children's preoperative internalizing problems are associated with postoperative pain intensity scores as assessed with the PPPM during the first three days at home.

Our findings show evidence that preoperative screening with a standardized tool such as the CBCL helps us focus on children at risk for perioperative maladaptive psychological and physical outcomes (such as anxiety, ED, sensory processing changes and pain) in order to improve perioperative health care management. This should lead to a more individualized approach in preoperative preparation of children based on their specific vulnerability and could also support health care workers to pay more attention to children at risk.

This thesis also presented preliminary data supporting the validity of a VAS-I to be completed by parents and anesthesiologists, in order to assess children's anxiety during induction of anesthesia. It is important to have an easy-to-use tool, which requires no training and can be quickly completed. This allows parents to be involved and become aware of their child's anxiety level and vulnerability.

We concluded that an Audio Visual Aid (AVA), shown to parents immediately prior to their child's anesthetic induction, reduced parental state anxiety. Considering the fact that parents become very anxious during the anesthetic induction of their child, it is essential that the whole preparation should not only be directed towards the child, but also towards the accompanying parents. If the parents' anxiety can be reduced, this will strengthen their ability to cope with their own feelings as well as with their child's feelings of anxiety during induction. However, in our study the AVA did not influence the child's state anxiety and compliance during induction. Therefore, we recommend that, when psychologically preparing the parents, specific psycho-education is provided to them offering (communication) tools and strategies on how to decrease children's anxiety and how to cope with the stressful situation.

In conclusion, our studies contribute to understanding children's perioperative behavior and parents' involvement in their child's preparation and anxiety management.

STRENGTHS AND LIMITATIONS

The studies presented in this thesis have several strengths. Firstly, they include relatively large prospective observational cohorts varying from 70 to 401 children in several age groups ranging from 1.5 years up to 16 years which enhances generalizability.

Secondly, further strengths are that throughout the studies we made use of international well-validated assessment tools like the CBCL[1,2], $ITSP_{6\text{-}36}$[47], mYPAS[3], ICC[20], PAED[67] scale, Spielberger's STAI[16], APAIS[64], PPPM[68,69] and the FLACC[70] scale among others, at well-defined time-points. The two latter pain scales are in fact recommended by Core Outcome Domains and Measures for Pediatric Acute and Chronic/Recurrent Pain Clinical Trials (PedIMMPACT)[71], which also strongly advocates assessment of sleep problems. Apart from the validated state anxiety assessment tools (mYPAS and ICC) in children, we provided some evidence for the validity of a new global general state anxiety assessment tool, the VAS-I.

There are several limitations to this study that need to be mentioned. In our study groups all children underwent minor day-care surgery and did not receive any premedication, all anesthetic inductions were performed by inhalation, and the studies were performed in a single center. There was also an overrepresentation of parents with low education status.

It also should be kept in mind that there are a few limitations concerning some of the scales that we used. The mYPAS might not be suited for the use in very young children (≤ 2 years), nor for adolescents (> 12 years) whereas the ICC rather assesses the child's compliance during induction[8,20,72].

Regarding the parental PPPM assessment, parental psychological traits (such as state/trait anxiety, stress and pain catastrophizing thoughts) may have an impact on the assessment. Furthermore, it must be kept in mind that parents tend to overestimate the severity of the child's pain[73], which is why children's pain self-report would be preferred[71,73].

When analyzing ED with the PAED scale it has become clear that instead of using all the PAED scale items, maybe only those now considered as ED-specific[42,43] (*no eye contact*, *no purposeful action*, and *no awareness of surroundings*) should be used.

Furthermore, in general, when using the CBCL to obtain an assessment of the child's emotional/behavioral problems, it is often proposed to use a multi-informant approach (such as both parents, a caregiver or teacher) instead of a single informant, as was used in this thesis' studies. The CBCL was completed on the day of surgery which could have biased the parents' perception and their ratings as to the child's typical behavior.

Finally, we should also pay attention to the so-called *common method variance*[74] – the same respondent completing multiple measures. In other words, having one informant completing questionnaires (as in our studies), may have biased the obtained scores. Parents, for instance, who tend to rate higher CBCL scores might also do the same when rating the PPPM or the STAI. This might lead to inflated associations.

IMPLICATIONS AND RECOMMENDATIONS FOR CLINICAL PRACTICE

The results of this thesis underline the importance of an individualized approach and preoperative screening of children in their perioperative period. Healthcare workers should be aware of an increased vulnerability in children with higher scores on pre-existing emotional/behavioral problems. Preoperative preparation should not consist of a uniform method, rather it should be seen as an individualized program tailored in a more holistic approach[18]. In an ideal situation it would be essential to screen for psychological vulnerability, which was shown in our studies to be related to children's maladaptive perioperative and postoperative behavior (perioperative state anxiety, ED, postoperative maladaptive behavior and postoperative pain intensity). This makes it possible to prioritize extensive behavioral preparation programs, which are effective[10,75], to the most vulnerable children.

This thesis gives additional evidence that higher emotional/behavioral CBCL problem scores are associated with difficult perioperative behavior. So the CBCL proved to be a clinically significant and useful screening tool in this context. For future clinical use, we recommend that these screenings ought to be organized in an anonymous online safe web-based connection at home.

As concerns the assessment of the child's anxiety during the perioperative period, we recommend to perform this assessment during the process of induction, the point at which the highest child state anxiety is measured during the whole perioperative period[5,11]. To this end, we propose that parents and anesthesiologists apply the user-friendly VAS-I. The information thus obtained on the child's anxiety, and consequently its vulnerability, can be discussed with the parents.

Regarding the preparation of their child towards the surgical procedure, our AVA study showed that parents should be encouraged to be involved and could benefit from receiving specific information, to reduce their state anxiety. We recommend additional tools to reduce children's preoperative anxiety, such as an innovative, age-attuned Virtual Reality Exposure[76] (see further below).

With reference to the child's pain management at home, this thesis demonstrated high pain scores in children at home[54,56,60] and insufficient parental adherence to the prescribed medication regimen[55,56]. Accordingly postoperative care should be enhanced by better follow-up consisting of clear instructions to parents and online assessment of postsurgical pain by the parents. This could be supplemented by automatic text messages that remind parents when to administer medication, by giving parents direct access to an email address for questions, and the availability of liaison nurses who can be contacted for advice.

If all these recommendations (psychological screening for the child's vulnerability, the child's anxiety assessment and parental involvement) will be adopted, it will bring us closer to the ideal of Family-centered Pediatric Perioperative Care[18]. This thesis showed that children with existing internalizing problems as well as their and their parents' level of anxiety should receive more attention from healthcare workers, who in turn also ought to realize that these individual aspects have to be incorporated into a flexible perioperative health care delivery system.

DIRECTIONS FOR FUTURE RESEARCH

Considering the above, the question remains how to fit all our recommendations into a busy clinical practice in times when economic and financial matters have become prominent in healthcare decision making. It is in this light that the following suggestions for future research should be read.

In the previous section, we emphasized the value of preoperative psychological screening of children scheduled for surgery. Considering our findings and the psychometric qualities of the CBCL, with availability of translations and normative data for different countries (which is useful for patients from different ethnic minorities), we recommend the CBCL for this purpose. Since the CBCL takes about 15 minutes to complete, it can be useful to provide the questionnaire via a secured internet site to parents and also its parallel version for teenagers, the Youth Self Report, for youth aged 11 – 17 years. If this is not feasible, we consider it worthwhile to investigate the usefulness of the Brief Problem Monitor[77], a short form of the CBCL (19 items only) to screen for emotional/behavioral problems[78]. Further research could also pave the way to establish specific cut-off values for the CBCL to distinguish between vulnerable and less vulnerable children prior to surgery, which would make the CBCL more clinically applicable.

In this thesis we recommended the VAS-I as a tool to assess children's anxiety during induction. We provided preliminary evidence on the validity of this instrument. However, further research is needed to establish the psychometric properties of the VAS-I more extensively.

Future investigation should also be directed towards the efficacy of integrating anxiety management into clinical practice and towards the improvement of pain management for children at home. Interventions to improve parental pain medication adherence should be developed and tested on their efficacy.

Furthermore, we consider it relevant to examine a possible association between preexisting child's emotional/behavioral problems and persistent postsurgical pain. In this study, pain measurements were restricted to up to 10 days after surgery. It has been recognized that children who undergo a surgical procedure are at risk of developing posttraumatic stress symptoms[79] and chronic pain[80,81]. This is, however, still an understudied area. There is evidence to suggest that preoperative pain[82,83], postoperative pain intensity[83-85], child pain coping efficacy[86] and parental pain catastrophizing thoughts[87,88] are predictors of persistent postsurgical pain in children. However, the impact of children's pre-existing emotional/behavioral problems on persistent postsurgical pain has not been studied so far.

According to the results presented in this thesis, an AVA seems to be a useful tool to reduce parents' anxiety as to their child's surgery. Future research should focus on developing innovative tools for preparing children and parents for surgery, such as online videos/games[89,90] or web-based interventions[90-92]. Certainly worth mentioning here is a new preparation tool, namely Virtual Reality Exposure. In an ongoing study[76] at the Erasmus MC-Sophia, the perioperative process is simulated by means of an interactive Virtual Reality tool. Using Virtual Reality Exposure may reduce anxiety surrounding surgery, and enhance coping mechanisms and self-efficacy of both child and parent. Other tools like chat groups and skype sessions guided by and under supervision of trained and experienced hospital staff may also facilitate the psychological preparation of children and their parents and should be further investigated.

Postoperative maladaptive behavior is still very common. For example, a study by Power and co-workers[53], using a cohort of children aged 2 – 12 years who underwent general surgery, urology or ear, nose and throat surgery, documented that up to 80% of the children exhibited problematic behavior. In most cases, postoperative maladaptive behavior is examined by using the Post Hospitalization Behavior Questionnaire[93], of which the validity and reliability is questionable[94]. In this context, the ITSP might break new grounds in perceiving how changes in sensory processing influence postoperative behavior in toddlers and children. This should be investigated using larger, multicenter samples, using different age ranges and more serious types of surgery. Longitudinal studies with a longer-term follow-up are necessary (e.g. to study bidirectional relationships between parameters over time).

As a final thought, this dissertation was necessarily limited in scope. It did not focus on the influence of characteristics such as the child's temperament, the quality of parent-child attachment (in families from different cultures), nor the child's intelligence on peri- and postoperative behavior. To our knowledge, this has not yet been studied before. Nor did this study consider the behavior of healthcare workers (nurses and anesthesiologists). This is a delicate issue, because certain specific behaviors (for example, reassuring comments, empathy, apologies, and criticism) might actually increase stress/anxiety in the child and parent[95,96]. To avoid possibly anxiety-inducing behaviors, more attention should be given to training and collaboration of healthcare workers (for example to promote more distracting behavior, humor, and nonprocedural talk)[95,97]. It is our opinion that all these issues should be further explored in studies covering psychological aspects of anesthesia in children.

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Summary

Samenvatting

SUMMARY

The **overall aim** of the present thesis is to attain a better insight into different psychological aspects related to anesthesia in children. The **specific aims** include: firstly, the examination of associations between pre-existing emotional/behavioral problems in children and children's specific peri- and postoperative behaviors, including anxiety during induction, emergence delirium, changes in sensory processing and pain at home; secondly, the exploration of the validity of a new, easy-to-use anxiety assessment tool at induction of anesthesia; thirdly, the assessment of the usefulness of an audio-visual tool for decreasing parental anxiety at induction of anesthesia of their child.

In **chapter 1**, the introduction, we describe previous research into psychological aspects related to anesthesia in children, which forms the background for the present PhD thesis. In recent years, there has been an increased interest in the child's perioperative behaviors, that is to say, anxiety which may be related to emergence delirium, postoperative emotions, behavior changes, and postoperative pain. Most studies, however, focused on the prevention or regulation of preoperative anxiety and other maladaptive perioperative behaviors, and not so much on identifying children at risk for these problems. So, there is still insufficient knowledge regarding the associations between children's pre-existing emotional/behavioral problems and perioperative behaviors and postoperative pain.

The role of the parents in assessing and managing children's preoperative anxiety has also received scant attention so far. Studies focused mainly on children's preoperative anxiety, but less on parental anxiety and stress. Parental anxiety and stress can increase due to their child's surgery, which in turn can increase children's preoperative anxiety. For this reason, parents should receive adequate information (using audiovisual aids as well as other tools) and should also be involved in the preparation of their child, since this can reduce parental state anxiety and in turn might have a beneficial effect on the child's preoperative state anxiety. Finally, in previous studies, children's preoperative anxiety was mostly rated by health care professionals. However, it is also important to incorporate parents in anxiety ratings and management. This will make them aware of their children's anxiety level.

Chapter 2 presents a study of associations between preoperative anxiety in children during induction (in a sample of 401 children aged between 1.5 – 16 years undergoing elective day-care surgery) and pre-existing emotional/behavioral problems, during the 6 months prior to surgery, as assessed by the Child Behavior Checklist (CBCL). Anxiety at induction was assessed by the modified Yale Preoperative Anxiety Scale (m-YPAS). This

study demonstrated that children with higher preoperative CBCL internalizing scores, showed more anxiety at induction of anesthesia. Additionally, this study investigated associations between pre-existing emotional/behavioral problems and emergence delirium as assessed by the Pediatric Anesthesia Emergence Delirium scale (PAED), in a subsample of 343 children. Children's internalizing problems were not related to emergence delirium, whereas in contrast externalizing problems were univariately associated with emergence delirium but this association was not withheld in the multivariate analysis. Concluding, preoperative CBCL scores predicted anxiety at induction but not emergence delirium.

Chapter 3 presents preliminary support for the validity of a Visual Analogue Scale to assess anxiety in children during induction of anesthesia (VAS-I), as completed by parents and anesthesiologists. Using a sample of 401 children aged between 1.5 and 16 years, accompanied by their a parent, the VAS-I was compared to the *gold standard*, namely the m-YPAS. The m-YPAS is widely used to assess children's anxiety during induction of anesthesia. However, completing the m-YPAS requires training and its administration is time-consuming. Results demonstrated that the concurrent validity of the VAS-I (correlations between parents' and anesthesiologists' scores on the VAS-I and m-YPAS) was strong. Furthermore, VAS-I scores were higher for children ≤ 5 years compared to children aged ≥ 6. VAS-I scores of children of high-anxious parents were higher than those of low-anxious parents. These last findings support the construct validity of the VAS-I. Analysis of cross-informant agreement showed that the mean difference between the VAS-I ratings of parents and anesthesiologists was quite small. To classify anxious children, specific cut-offs for parents and anesthesiologists were determined. Overall, our results regarding the validity of the VAS-I are promising, suggesting that the VAS-I is a valuable, easy-to-use tool to assess children's anxiety during induction of anesthesia. However, different forms of validity and reliability have to be investigated in larger samples.

Chapter 4 describes an RCT in a sample of 120 parents of children scheduled for day-care surgery testing the effects of an audiovisual aid (AVA) on parental state anxiety and on the child's anxiety at induction. The intervention group (n = 60) was exposed to the AVA in the holding area whereas the control group (n = 60) was not. The Spielberger's State-Trait Anxiety Inventory (STAI) and the Amsterdam Preoperative Anxiety and Information Scale (APAIS) were used to assess parental state anxiety at three time points: 1. on admission; 2. in the holding area just before entering the operating theatre; 3. after leaving the operating theatre. The child's state anxiety during induction was assessed by a VAS-I (see chapter 3) and the Induction Compliance Checklist (ICC). The results of our study demonstrated that parental state anxiety was lower in the intervention group compared to the control group at the last two time points. After induction, the child's anxiety-rating given by the anesthesiologists was significantly lower than the same ratings done by the parents, in both the intervention and control group. In conclusion, preoperative AVA shown to parents immediately before induction moderates the increase in anxiety associated with the anesthetic induction of their child.

In **chapter 5** we described changes in sensory processing after anesthesia in toddlers. We studied a prospective cohort, consisting of 70 healthy boys, aged 18-30 months, who underwent circumcision for religious reasons. The aims of this study were: 1. to assess pre- to postoperative changes in sensory processing after anesthesia at day 14 postoperatively using the Infant/Toddler-Sensory Profile for 7-36 months ($ITSP_{7\text{-}36}$); 2. to identify putative predictors of these pre- to postoperative changes in sensory processing, including the child's preoperative CBCL emotional/behavioral problems, the child's state anxiety at induction, and postoperative pain at home. Accompanying parents completed the $ITSP_{7\text{-}36}$ and the CBCL. This study showed significant changes in sensory processing on: 1. low registration (consciousness/awareness to different sensory stimuli); 2. sensory sensitivity (ability to notice sensory stimuli); 3. sensation avoiding (to counteract/avoid or control sensory stimuli); 4. low threshold (score is derived from the summation of 2 and 3). auditory processing (reaction to sound, noise, voices) and tactile processing (reaction to touching of the skin). Higher scores on CBCL scores were associated with changes on sensory processing. It can be concluded from this study that sensory processing had changed after anesthesia. From a clinical point of view, these are important findings, as these sensory processing changes can influence young children's daily functioning.

In **chapter 6** we studied the occurrence of postoperative pain, sleep problems, and medication adherence in children at home after adenotonsillectomy. This prospective cohort study, which included 160 children, aged 1.5 – 5 years, undergoing day-care adenotonsillectomy, further investigated the influence of pre-existing emotional/behavioral problems (assessed by the CBCL) on postoperative pain. The child's pain intensity at home was assessed by parents using the Parents' Postoperative Pain Measure (PPPM) and the child's sleep problems with Vernon's Post Hospital Behavioral Questionnaire, during the first 3 days and at day 10 postoperatively. The results of this study showed that following adenotonsillectomy 49% of the children experienced moderate to severe pain during the first 3 days at home and that parental pain medication adherence is poor. Sleep problems occurred in 37% of the children during the first three postoperative nights. Regression analysis revealed that higher scores on preoperative internalizing problems were associated with increased pain during the first 3 days at home, after controlling for age, preoperative child state anxiety, parental state anxiety, parental need for information, and socioeconomic status. Furthermore, higher parental need for information was also an independent risk factor for increased pain at home. So, one of the key findings from this study is that screening for preoperative emotional/behavioral problems could be helpful to identify children at risk for higher pain scores and that this offers the opportunity to adapt the perioperative analgesic strategy accordingly (which includes preparation, information and prescription of pain analgesics).

Finally, in **chapter 7,** the general discussion, the main findings of this research were discussed.

In conclusion, this PhD thesis shows that:

1. children's internalizing problems prior to surgery are associated with their state anxiety at induction;
2. children's internalizing/externalizing problems are not associated with emergence delirium;
3. children's emotional/behavioral problems are associated with postoperative changes in sensory processing;
4. children's internalizing problems are associated with higher postoperative pain intensity scores at home after adenotonsillectomy;
5. preliminary data support the validity of a VAS-I, as completed by parents and anesthesiologists. The VAS-I can be used to assess children's anxiety during induction of anesthesia. We consider it important to have an easy-to-use tool, which requires no training and can be completed quickly;
6. an audiovisual aid, shown to parents, immediately prior to their child's anesthetic induction, reduced parental state anxiety, but did not have a positive influence on the child's state anxiety during induction.

Overall we conclude that our studies contribute to the understanding of children's perioperative behavior and parents' involvement in their child's preparation and anxiety management.

Clinical implications for practice

Our results underline the importance of an individualized approach to the preoperative preparation of children and highlight the clinical relevance of preoperative psychological screening of children. Healthcare workers should be aware of an increased risk for maladaptive perioperative and postoperative behavior in children with higher scores on state anxiety and pre-existing emotional/behavioral problems. For this reason, we also recommend to incorporate anxiety assessment into daily clinical practice. Identifying children based on these risks makes it possible to attune preparation to the specific needs of each child. Furthermore, parents should be encouraged to be involved in preparing their child for surgery, when needed. Postoperative care should also be enhanced by follow-up contact with parents in order to improve parental adherence to the prescribed pain medication for their child.

Directions for future research

For future research we recommend to further investigate the association between emotional/behavior problems and persistent postsurgical pain, bearing in mind that in this study pain measurements were restricted to up to 10 days after surgery. Additionally, the efficacy of integrating anxiety management into clinical practice and of improving pain management for children at home should be studied further. Moreover, interventions to improve parental pain medication adherence should be developed and tested for their efficacy. Furthermore, research towards innovative tools for preparing children and parents for surgery, such as online videos/games, web-based interventions and Virtual Reality Exposure should be encouraged. Finally, by focusing on specific variables, this PhD thesis, consequently limited in scope, could not go into the influence of other characteristics, such as the child's temperament, the quality of parent-child attachment, the child's intelligence, and the behavior and attitude of healthcare workers, on children's peri- and postoperative behavior. These are new avenues to be explored by future studies covering psychological aspects of anesthesia in children.

SAMENVATTING

De **algemene doelstelling** van dit proefschrift is een beter inzicht te verkrijgen in verschillende psychologische aspecten van anesthesie bij kinderen. De **specifieke doelstellingen** omvatten: ten eerste, het onderzoeken van mogelijke associaties tussen al reeds bestaande emotionele/gedragsproblemen bij kinderen en het specifiek peri- en postoperatief gedrag van kinderen, waaronder angst tijdens de inductie, postoperatief delirium, veranderingen in sensorische prikkelverwerking en pijn thuis; ten tweede, onderzoek naar de validiteit van een nieuw, makkelijk bruikbaar evaluatie-instrument om angst bij inductie van anesthesie te meten; ten derde, de beoordeling van de waarde van een audiovisuele video voor het verminderen van angst bij de ouders tijdens inductie van anesthesie bij hun kind.

In **hoofdstuk 1**, de inleiding, beschrijven we voorgaand onderzoek naar de psychologische aspecten gerelateerd aan anesthesie bij kinderen. Deze vormen de achtergrond van dit promotieonderzoek. In de afgelopen jaren is de interesse in het perioperatieve gedrag van het kind aanzienlijk toegenomen, dat wil zeggen, angst die gerelateerd kan zijn aan emergence delirium, postoperatieve emoties, gedragsveranderingen en postoperatieve pijn. De meeste studies richten zich echter op de preventie of behandeling van preoperatieve angst en ander maladaptief perioperatief gedrag, en minder op de identificatie van kinderen met een verhoogd risico op deze problemen. Zo is er is nog steeds onvoldoende kennis over de verbanden tussen bestaande emotionele/gedragsproblemen van kinderen en perioperatief gedrag en postoperatieve pijn.

Ook de rol van de ouders bij het beoordelen en beheersen van preoperatieve angst bij hun kind kreeg nauwelijks aandacht. De studies waren voornamelijk gericht op preoperatieve angst bij kinderen, en minder op de angst en stress bij de ouders. Angst en stress bij de ouders kunnen echter toenemen vanwege de operatie van hun kind, die op hun beurt de preoperatieve angst van het kind kunnen doen toenemen. Daarom zouden ouders adequate informatie moeten krijgen (met gebruik van audiovisuele video's alsook andere hulpmiddelen) en zouden ze ook betrokken moeten worden bij het voorbereiden van hun kind op de operatie, aangezien dit de ouderlijke situationele angst kan verminderen en op zijn beurt een gunstig effect kan hebben op de preoperatieve situationele angst van het kind. Ten slotte werd in voorgaande studies de preoperatieve angst van het kind meestal beoordeeld door professionals werkend in de gezondheidszorg. Het is echter ook belangrijk om ouders te betrekken bij de beoordeling en het beheersen van angst. Dit zal hen meer bewust maken van het angstniveau van hun kind.

Hoofdstuk 2 bestudeert de mogelijke associaties tussen preoperatieve angst tijdens inductie bij kinderen (in een steekproef van 401 kinderen tussen 1,5 - 16 jaar die een electieve dagbehandeling ondergaan) en gedurende de 6 maanden voorafgaand aan de operatie reeds aanwezige emotionele/gedragsproblemen, zoals beoordeeld met de Child Behavior Checklist (CBCL). De angst tijdens de inductie werd beoordeeld door middel van de modified Yale Preoperative Anxiety Scale (m-YPAS). Deze studie toonde aan dat kinderen met hogere preoperatieve CBCL-scores op internaliserende problemen, meer angst toonden bij inductie van anesthesie. Daarnaast onderzocht deze studie de associaties tussen reeds aanwezige emotionele/gedragsproblemen en postoperatief delirium gebruikmakend van de Pediatric Anesthesia Emergence Delirium-schaal (PAED) in een steekproef van 343 kinderen. Internaliserende problemen bij kinderen waren niet gerelateerd aan emergence delirium. Externaliserende problemen waren daarentegen univariaat met postoperatief delirium geassocieerd, hoewel deze associatie in de multivariate analyse niet werd gevonden. Concluderend toont dit onderzoek aan dat de preoperatieve CBCL-scores angst tijdens de inductie wel voorspellen, maar postoperatief delirium niet.

Hoofdstuk 3 presenteert de resultaten van een eerste validiteitsonderzoek van een Visuele Analoge Schaal voor angst (VAS-I) bruikbaar tijdens inductie van anesthesie bij kinderen, gemeten door ouders en anesthesiologen. In deze studie, uitgevoerd bij 401 kinderen tussen 1,5 - 16 jaar en hun begeleidende ouder, werd de VAS-I vergeleken met de *gouden standaard*, namelijk de m-YPAS, die veelal wordt gebruikt in onderzoek om angst bij kinderen te meten tijdens inductie van anesthesie. Het gebruik van de m-YPAS vereist echter training en de uitvoering is tijdrovend. De resultaten toonden aan dat de concurrent validiteit (correlaties tussen scores van ouders en anesthesiologen op de VAS-I en m-YPAS) sterk was. Bovendien waren de VAS-I scores hoger voor kinderen ≤ 5 jaar in vergelijking met kinderen ≥ 6 jaar oud en ook de VAS-I scores van kinderen van uitgesproken angstige ouders waren hoger dan die van ouders met lage angst. Deze laatste bevinding ondersteunt de constructvaliditeit van de VAS-I. Analyse van cross-informant overeenkomst toonde aan dat het gemiddelde verschil tussen de VAS-I scores van ouders en anesthesiologen vrij klein was. Om angstige kinderen te classificeren, werden specifieke afkappunten voor ouders en anesthesiologen bepaald. Over het algemeen zijn onze resultaten met betrekking tot de validiteit van de VAS-I veelbelovend hetgeen erop wijst dat de VAS-I een betrouwbaar en gemakkelijk te gebruiken instrument is om de angst van kinderen tijdens inductie van anesthesie te beoordelen. Verschillende vormen van validiteits- en betrouwbaarheidsanalyses moeten echter onderzocht worden in grotere steekproeven.

Hoofdstuk 4 beschrijft een RCT naar de effectiviteit van een audiovisueel hulpmiddel (AVA) in een steekproef van 120 ouders waarvan de kinderen waren ingepland voor een dagbehandeling onder narcose. Zowel de ouderlijke situationele angst als de angst van het kind tijdens inductie werden beoordeeld. De interventiegroep (n = 60) werd blootgesteld aan de AVA in de voorbereidingsruimte; de controlegroep (n = 60) niet. De Spielberger's State-Trait Anxiety Inventory (STAI) en de Amsterdam Preoperative Anxiety and Information Scale (APAIS) werden gebruikt om de situationele angst van de ouders op drie tijdstippen te beoordelen: 1. bij opname; 2. in de wachtruimte vlak voor het betreden van de operatiekamer; 3. na het verlaten van de operatiekamer. De situationele angst van het kind tijdens de inductie werd beoordeeld met een VAS-I en de Induction Compliance Checklist (ICC). De resultaten van onze studie toonden aan dat ouderlijke situationele angst in de interventiegroep lager was dan die in de controlegroep tijdens de laatste twee tijdstippen. Na inductie was de angstmeting van het kind door de anesthesiologen significant lager dan dezelfde beoordelingen gemeten door de ouders, zowel in de interventie- als in de controlegroep. Als besluit kan gesteld worden dat een voorbereidende AVA die getoond wordt aan ouders net voor inductie de toename matigt van de angst geassocieerd met de anesthesie-inductie van hun kind.

In **hoofdstuk 5** bespreken we veranderingen in sensorische prikkelverwerking na anesthesie bij peuters. In een prospectief cohort bestudeerden we 70 gezonde jongens van 18-30 maanden oud, die om religieuze redenen besnijdenis ondergingen. De doelstellingen van deze studie waren: 1. het beoordelen van pre-tot postoperatieve veranderingen in sensorische prikkelverwerking na anesthesie, bepaald met behulp van de Infant/Toddler-Sensory Profile for 7-36 months ($ITSP_{7-36}$) tot 14 dagen na de operatie; 2. het identificeren van vermoedelijke voorspellers van deze veranderingen, waaronder de preoperatieve emotionele/gedragsproblemen van het kind (gemeten met de CBCL), de situationele angst bij kinderen tijdens inductie en de postoperatieve pijn thuis. De begeleidende ouders vulden de $ITSP_{7-36}$ en de CBCL in. Deze studie toonde significante veranderingen in sensorische prikkelverwerking aan in de zin van: 1. lage registratie (bewustzijn/besef hebben van verschillende sensorische prikkels); 2. sensorische gevoeligheid (het vermogen om sensorische prikkels waar te nemen); 3. sensatie vermijdend (het tegenwerken/vermijden of controleren van sensorische prikkels); 4. lage drempel (de score wordt afgeleid van de som van 2 en 3); 5. auditieve verwerking (reactie op geluid, lawaai, stemmen) en tactiele verwerking (reactie op het aanraken van de huid). Hogere scores op CBCL-problemen waren geassocieerd met de veranderingen in sensorische prikkelverwerking. Besluitend toont deze studie aan dat de sensorische prikkelverwerking veranderd was na de anesthesie. Vanuit klinisch perspectief zijn deze bevindingen belangrijk aangezien deze veranderingen in sensorische prikkelverwerking het dagelijks functioneren van jonge kinderen kan beïnvloeden.

In **hoofdstuk 6** bestudeerden we het voorkomen van postoperatieve pijn, slaapproblemen en therapietrouw bij kinderen thuis na adenotonsillectomie. Deze prospectieve cohortstudie bevatte 160 kinderen tussen de 1,5 en 5 jaar oud, die tijdens een dagbehandeling een adenotonsillectomie ondergingen. Verder onderzochten we de invloed van reeds preëxistente emotionele/gedragsproblemen (beoordeeld door de CBCL) op postoperatieve pijn. De pijnintensiteit thuis bij het kind werd beoordeeld door de ouders met behulp van de Parents' Postoperative Pain Measure (PPPM) en de slaapproblemen van het kind met Vernon's Post Hospital Behavioral Questionnaire en dit tijdens de eerste 3 dagen en op dag 10 na de operatie.

De resultaten van deze studie toonden aan dat 49% van de kinderen na de adenotonsillectomie de eerste 3 dagen thuis matige tot ernstige pijn ervaren en dat de ouderlijke therapietrouw slecht is. Slaapproblemen traden op bij 37% van de kinderen tijdens de eerste drie postoperatieve nachten. Regressieanalyse toonde aan dat hogere scores op preoperatieve internaliserende problemen geassocieerd waren met meer pijn gedurende de eerste 3 dagen thuis, na te het hebben gecontroleerd voor leeftijd, preoperatieve situationele angst van het kind, ouderlijke situationele angst, ouderlijke behoefte aan informatie en socio-economische status. Een van de belangrijkste bevindingen van deze studie is dat het screenen van preoperatieve emotionele/gedragsproblemen nuttig kan zijn om kinderen te identificeren die een hoger risico lopen op hogere pijnscores en de mogelijkheid biedt om het perioperatieve pijnbeleid aan te passen (waaronder voorbereiding, informatie en het voorschrijven van pijnanalgetica).

Ten slotte werden in **hoofdstuk 7**, de algemene discussie, de belangrijkste bevindingen van dit onderzoek besproken. Besluitend toont dit proefschrift het volgende aan:

1. internaliserende problemen bij kinderen voorafgaand aan de operatie zijn geassocieerd met hun angst tijdens inductie;
2. internaliserende/externaliserende problemen bij kinderen zijn niet geassocieerd met postoperatief delirium;
3. emotionele/gedragsproblemen van kinderen zijn geassocieerd met postoperatieve veranderingen in sensorische prikkelverwerking;
4. internaliserende problemen bij kinderen zijn geassocieerd met hogere postoperatieve pijnintensiteit scores thuis na adenotonsillectomie;
5. voorlopige data ondersteunen de validiteit van een VAS-I, zoals gemeten door ouders en anesthesiologen. De VAS-I kan worden gebruikt om de angst van kinderen vast te stellen tijdens inductie van anesthesie. We beschouwen het als belangrijk om een eenvoudig te gebruiken meetinstrument te hebben, dat geen training vereist en snel kan worden uitgevoerd;

6. een audiovisueel hulpmiddel, dat onmiddellijk voorafgaand aan de narcose van hun kind wordt getoond aan de ouders, vermindert de de situationele angst bij de ouder, maar heeft geen positieve invloed op de situationele angst van het kind tijdens de inductie.

Over het algemeen besluiten we dat onze studies hebben bijdragen tot een beter begrip van het perioperatieve gedrag van kinderen en het belang van de betrokkenheid van ouders bij de voorbereiding van hun kind en het beheersen van angst.

Klinische implicaties voor de praktijk. Onze resultaten onderschrijven het belang van een geïndividualiseerde aanpak en ondersteunen het gegeven dat een preoperatieve psychologische screening bij kinderen klinisch relevant is.

Gezondheidszorgmedewerkers moeten zich bewust zijn van een verhoogd risico op maladaptief perioperatief en postoperatief gedrag bij kinderen met hogere situationele angstscores en reeds preëxistente emotionele/gedragsproblemen. Om deze reden raden we ook aan om angstevaluatie op te nemen in de dagelijkse klinische praktijk. Het identificeren van kinderen op basis van deze risico's kan het mogelijk maken om de voorbereiding af te stemmen op de specifieke behoeften van elk kind. Bovendien zouden ouders aangemoedigd moeten worden om betrokken te zijn bij de voorbereiding van de operatie van hun kind indien nodig. Postoperatieve zorg zou ook moeten worden verbeterd door een betere follow-up van de ouders om de ouderlijke therapietrouw van het voorgeschreven pijnmedicijn voor hun kind te verhogen.

Aanbevelingen voor toekomstig onderzoek

Voor de toekomst raden we aan om verder onderzoek uit te voeren naar de associatie tussen emotionele/gedragsproblemen en aanhoudende post-chirurgische pijn. De pijnmetingen in deze studie waren beperkt tot 10 dagen na de operatie. Wij bevelen dan ook studies met een lange follow-up duur aan. Bovendien moet de effectiviteit van het integreren van angstmetingen in de klinische praktijk en de verbetering van pijnbestrijding voor kinderen thuis verder worden onderzocht. Daarnaast moeten interventies ter verbetering van de ouderlijke therapietrouw worden ontwikkeld en getest op hun werkzaamheid. Daarenboven dient men ook verder onderzoek aan te moedigen naar innovatieve hulpmiddelen voor de voorbereiding van kinderen en ouders op chirurgie, zoals online video's/games, web-gebaseerde interventies en virtual reality-toepassingen. Ten slotte, aangezien dit promotieonderzoek zich richtte op specifieke variabelen en daardoor gelimiteerd werd in omvang, kon ze niet ingaan op de invloed van andere kenmerken op het peri- en postoperatieve gedrag van kinderen, zoals het temperament van het kind, de kwaliteit van de gehechtheid tussen ouder en kind, de intelligentie van het kind, en het gedrag en de houding van de gezondheidszorgmedewerkers. Dit zijn nieuwe wegen die moeten worden verkend door toekomstige studies psychologische aspecten van anesthesie bij kinderen.

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Ik heb geluk in het leven!

CURRICULUM VITAE

Personal Details

Surname	Berghmans
First name	Johan Maria Armand
Date / place of birth	12 April 1965, Mortsel, Antwerp (Belgium)
Marital status	Married to Mewis Edith
Children	Amaury, Alexander, Olivier & Caroline

Catholic University Leuven

June 1991	GP Medical Science Degree
July 1993	Electrocardiography for GPs Certificate

Current Job

Since 2001: Supervising Anesthesiologist at the Department of Anesthesia & Reanimation, ZNA Middelheim - Queen Paola Children's Hospital, Antwerp (Belgium)
2015: Accreditation Internship Supervisor Training in Anesthesiology - ZNA Middelheim, Antwerp

Work Experience / Expert Training

March 2000 – December 2000: Fellowship Pediatric Anesthesiology at Erasmus MC - Sophia Children's Hospital, Rotterdam (the Netherlands)
April 2000: Accreditation Medical Expert in Anesthesia & Reanimation
April 1995 – March 2000: Trainee – Anesthesia & Reanimation, AZ Middelheim Antwerp
September 1997 – August 1998 Trainee Anesthesia & Reanimation, Prof. P. Coriat, Groupe Hospitalier Pitié-Salpêtrière, Paris (France)
Expertise in transthoracic echocardiography, Groupe Hospitalier Pitié-Salpêtrière
Trainee – Échocardiographie, Hôpital Gilles de Corbeil, Corbeil-Essonnes (France)
September 1993 – August 1994: Trainee – GP, Certificate GP Medical Science Training
August 1991 – July 1993: Trainee – Internal Diseases Department, Virga Jesse Hospital, Hasselt (Belgium)

Job Related Activities

December 2016: elected member medical council ZNA Middelheim
February 2015 – present: Board member of the Belgian Pediatric Pain Association (BePPa)
April 2014 – September 2018: President of the Belgian Association for Paediatric Anaesthesiology (BAPA), Vice-President 2012 -2014
2014 – 2007: representative member BAPA in the office of the Belgian Society for Anesthesia & Reanimation (BSAR)

PHD PORTFOLIO

Name PhD student: Johan M.A. Berghmans
PhD period: 2011 - 2019
Erasmus MC Department: Sophia – Kinder- en Jeugd Psychiatrie/Psychologie
Promotors: prof. dr. F.C. Verhulst, prof. dr. E.M.W.J. Utens
Supervisor: Mr. Dr. M.J. Poley

GENERAL COURSES		ECTS
NIHES Rotterdam (Erasmus Winter Progamme)		
2010	Introduction to Clinical Research	0.7
2010	Biostatistics for Clinicians	0.7
2013	Multiple Linear Regression Analysis	1.4
2014	Pharmaco-Epidemiology and drug Safety	1.4
2014	Principles of Epidemiologic Data-Analysis	0.7
2014	Advanced Analysis of Prognosis Studies	0.7
2015	Survival Analysis for clinicians	1.4
BROK (Basiscursus Regelgeving Klinisch Onderzoek)		
2012	Certification	1.4
2016	Re-certification	0.2
Erasmus MC		
2015	Research Integrity	0.3
Erasmus MC – Medical Library		
2013	EndNote course	0.1
2012	Course Systematic Literature search	0.1
European Society of Anaesthesiology (ESA)		
2014	Masterclass in Scientific Writing	0.9
2018	**Meta-Analysis Workshop Biostat (London)**	0.9
Specific courses Antwerp Management school		
2016	Clinical Leadership Program	1.4

Seminars and workshops		ECTS
2018	Medbook UIA	0.1
2018	Train the Trainer – U Gent & KU Leuven	0.2
2017	Train training supervisors KU Leuven	0.2

2017	Oratie prof. Dr E.M.W.J Utens	0.1
2016	Train training supervisors KU Leuven	0.1
2016	Train de Trainer MSG UGent (2 sessies)	0.3
2016	Practical Workshop (Giving Effective Feedback to Trainees) 0.1 (London – ESA Congress)	

Presentations and lectures		**ECTS**
2010	Best free paper competition, Congress of the European Society for Paediatric Anaesthesiology (ESPA) Berlin, Germany	1.4
2010	Belgian Association for Paediatric Anaesthesiology (BAPA), Sectie Kinderanesthesie(SKA), Eindhoven	1.0
2010	12th Children's Anesthesia Symposium Wilhelmina Kinderziekenhuis in Utrecht	1.0
2011	Postgraduate meeting Bruges	0,3
2012	First Pain Symposium at ZNA Antwerp	1.4
2012	Postgraduate: UZ Leuven	0.3
2013	Postgraduate: LOK Child Psychiatry	0.3
2013	Autumn Symposium Pediatrics ZNA - Queen Paola Children's Hospital	1.0
2014	Jaarlijks congres Belgische Vereniging Kindergeneeskunde - Brugge	1.4
2014	LOK/GLEM UZ Gent	0.2
2014	Annual meeting BAPA Brussels	1.0
2014	Joint congress of the Belgian Pain Society (BPS), Belgian Headache Society (BHS) and the Belgian Neurological Society (BNS), Brussels	1.0
2014	2nd International Paediatric Psychology Conference, Amsterdam, Netherlands (poster)	0.4
2014	Postgraduate ZNA J. Palfijn	0.5
2014	Refereeravond Kinderanesthesie, Erasmus MC	1.0
2015	Congres Vereniging van Vlaamse Operatieverpleegkundigen VVOV), Blankenberge	1.0
2015	Ochtendonderwijs dienst anesthesiologie, UZ Leuven	0.3
2015	Eerste Antwerpse Pediatrisch Pijnsymposium – Antwerpen	1.0
2016	Joint Refresher Course: BAPA & SKA – Leuven	1.4
2016	The XXIX Marius Plouzhnikov International Conference of Young Otorhinolaryngologists, Saint Petersburg, Russia	1.0
2016	Postgraduate department of Anesthesia, UZ Leuven	1.0
2017	Annual Congress BAPA, Namur	1.0
2017	Annual congress Belgian Pain society, Brussels	1.0

2017	2de Antwerpse pijn symposium (Hasselt – Antwerpen)	1.0
2018	AEPC Psychosocial conference, Leicester, England (oral presentation)	0.4
2018	Sectie Kinderanesthesie (SKA) – Summer Congress	1.0
2018	European Society for Paediatric Anaesthesiology (Brussels)	1.4

Research meetings		ECTS
2013	Research meeting department of Child and Adolescent Psychiatry	0.5
2014	Research meeting department of Child and Adolescent Psychiatry	0.5
2014	Department Anesthesiology Erasmus MC Rotterdam	0.5
2016	Research meeting Pediatric Psychology	0.2

Attended International Conferences		ECTS
2011	European Society for paediatric Anaesthesiology, Mallorca, Spain	1.0
2012	European Society for paediatric Anaesthesiology, Stresa, Italy	1.0
2013	European Society for paediatric Anaesthesiology, Genève, Switzerland	1.0
2014	European Society for paediatric Anaesthesiology, Prague Czech Republic	1.0
2014	Second International Paediatric Psychology Conference in Europe Amsterdam	0.3
2016	Euroanesthesia, Londen, UK	1.0
2018	Bi-annual conference the Association of the European Pediatric Cardiologists (AEPC) LEICESTER, U.K.	1.0
2018	Euroanesthesia, Kopenhagen, Denmark	1.0
2018	European Society for paediatric Anaesthesiology, Brussels Belgium	1.0

National Conferences		ECTS
2010 – present	All the annual meetings and refresher courses (17) of the Belgian society for Paediatric anesthesiology (BAPA)	3.6

Teaching		ECTS
2006-2018	Trainees Anesthesia & Reanimation (17): supervising scientific work	6.0

2010-2014	Co-supervision Bachelor degree theses Department of Applied Psychology, Thomas More University College Antwerp (5)	2.0
2015	Co-supervision Bachelor after Bachelor (BANABA), Thomas More University College Antwerp (campus Lier)(2)	0.5
2014	Co-supervision of Master theses, Faculty of medicine University of Antwerp	1.0
2016	Master theses, Faculty of Product Development University of Antwerp	1.0
2004 – present	Medical and Nursing Aspects concerning & Pediatric Neonatal anesthesia	0.1 / year
2011 – present	Medical-Technical Care - Anesthesia, Fundamental Principles (8 hrs.)	0.3 / year
2008 – present	Emergency Care and Reanimation in Children (5 hrs.) 0.2/year	
2007 – 2014	Pain in children, general terminology and physiology course (2hrs.) 0.1/year	
2006 – present	Neonatal Anesthesia (SARB website)	0.1

ECTS = European Credit Transfer and Accumulation System total = 68

OTHER

Meeting abstracts, presented at international scientific conferences and symposia, published or not published in proceedings or journals

1. Virtual reality exposure as psychological preparation for elective pediatric day care surgery: a randomized controlled trial
   Robin Eijlers, Jeroen S. Legerstee, Bram Dierckx, Lonneke M. Staals, Johan Berghmans, Marc P. van der Schroeff, René M.H. Wijnen, Elisabeth M.W.J. Utens.
   EPPC congres September 2018
2. Parental non-adherence to postoperative prescribed pain management for their child is not associated with higher pain scores
   Anna Vanstraelen, Elisabeth Utens, Marten Poley, Frank Weber, Björn Stessel, Johan Berghmans.
   Euroanaesthesia - Copenhagen, Denmark, June 2018
3. Postoperative pain scores at home after adenotonsillectomy in children between 6 and 12 of age are associated with pre-existing emotional/behavioral problems
   Pieter Jan Snaterse-Broekhuijse, Elisabeth Utens, Marten Poley, Thierry Pirotte, Frank Weber, Johan Berghmans.
   Euroanaesthesia – Copenhagen, Denmark, June 2018
4. Postoperative observational FLACC scores by nurses do not reliably reflect children's and parental Colored Analogue Scale ratings of children's pain
   Phillippe Leire, Elisabeth Utens, Marten Poley, Thierry Pirotte, Frank Weber, Johan Berghmans.
   Euroanaesthesia – Copenhagen, Denmark, June 2018
5. Does the Child Behaviour Checklist predict levels of preoperative anxiety at anesthetic induction and postoperative emergence delirium? A prospective cohort study
   Berghmans J, Poley M, Weber F, Van de Velde M, Adriaenssens P, Klein J, Himpe D, Utens E. Bi-annual conference of the Association of the European Pediatric Cardiologists (AEPC), 7 – 9 March, 2018, LEICESTER, U.K.
6. Pulsed radiofrequency as additional treatment for frozen shoulder
   Budts E, Berghmans J, Goossens S, Himpe D, Opsomer F.
   Residents meeting BSAR at UCL (Louvain la neuve), June 2017
7. Acetate-versus lactate-based balanced colloid used as priming solutions for cardiopulmonary bypass: an experimental pilot study
   Cauwenberghs H, De Backer A, Neel H, Deblier I, Berghmans J, Himpe D.
   29th Annual Congress of the European Society of Intensive Care, Milan, Italy, November 2016
8. What is the agreement between nurses and parents as to pain scores for toddlers?

Beeckman S, Poley M, Himpe D, Utens E, Berghmans J
Congress of the European Society for Paediatric Anaesthesiology (ESPA), Belgrade, Serbia, September 2016

9. The Additional Structured Behavior Observation, a new tool to assess emergence delirium in children after surgery
Timur Issaev, Elisabeth Utens, Frank Weber, Francis Veyckemans, Dirk Himpe, Johan Berghmans
Euroanaesthesia - London, UK, 2016.
10. Postoperative observational pain measure by nurses does not reliably reflect parental Visual Analogue Scale ratings of children's pain
Sofie Denkens, Elisabeth Utens, Frank Weber, Francis Veyckemans, Dirk Himpe, Johan Berghmans
Euroanaesthesia - London, UK, 2016.
11. The influence of preoperative emotional and behavioral problems of children on postoperative emergence delirium after dental care' Liesbeth Geelen, Elisabeth Utens, Frank Weber, Francis Veyckemans, Dirk Himpe, Johan Berghmans
Euroanaesthesia - London, UK, 2016.
12. Does the child behavior checklist predict levels of preoperative anxiety at anesthetic induction and postoperative emergence delirium? A prospective cohort study'
Berghmans J, Poley M, Weber F, Van de Velde M, Adriaenssens P, Klein J, Himpe D, Utens.
2nd International Paediatric Psychology Conference, September 2014, Amsterdam, Netherlands
13. Preoperative emotional/behavioral functioning of a child is associated with higher postoperative pain at home after adenotonsillectomy
Poels S, Berghmans J, Poley, Veyckemans, Weber F, Van de Velde M, Schmelzer B, Himpe D, Utens E.
Presented during - best free paper competition at the annual congress of the European Society for Paediatric Anaesthesiology (ESPA), September 2014, Prague, Czech Republic
14. Changes in the sensory profile of children following anesthesia
Berghmans J, Poley M, Rietman A, Weber F, Schipper S, Simmers M, Himpe D, Utens E.
Annual congress of the European Society for Paediatric Anaesthesiology (ESPA), Prague, Czech Republic, September 2014
15. Informatiestromen tussen verpleegkundigen en ouders i.v.m. postoperatieve pijn bij kinderen. Fraiponts H, Raes M, Lynen V, Berghmans J, De Beul C, De Dooy J, Roete A, Van Den Heuvel M, Geboers A, Van Gorp I, Allegaert K. Belgische Vereniging Kindergeneeskunde, March 2014, Bruges, Belgium
16. A two-year retrospective quality control for bleeding after adenotonsillectomy

Styranka A, Berghmans J, Roofthooft E, Poley M, Klein J, Himpe D.
Presented at the annual congress of the European Society for Paediatric Anaesthesiology (ESPA), September 2012, Stresa, Italy

17. The validation of a Visual Analogue Scale for parents as an assessment tool for their child's anxiety at induction of anesthesia
de Chaffoy de Coursel C, Berghmans J, Utens L, Weber F, Van de Velde M, Himpe D.
Presented at the annual congress of the European Society of Anesthesiology (ESA), June 2012, Paris, France

18. The Child Behaviour Checklist as an assessment tool in predicting perioperative maladaptive behaviour
Valckenborgh M, Berghmans J, Weber F, Hilgert T, Roofthooft E, Deboutte D, Himpe, D.
Presented and awarded with first price - Best Free Paper competition - annual congress of the European Society for Paediatric Anaesthesiology (ESPA), September 2011, Palma de Mallorca, Spain

19. Bleeding after adenotonsillectomy: a one-year retrospective anesthesia chart review and analysis
Van de Calseijde S, Berghmans J, Van De Plas G, Roofthooft E, Schmelzer A, Klein J, Himpe D.
Congress of the European Society for Paediatric Anaesthesiology (ESPA), September 2011, Palma de Mallorca, Spain

20. Could audiovisual aid prior to induction of a child decrease state anxiety of the accompanying Dutch-speaking parent?
Van Akoleyen C, Berghmans J, Weber F, Veereman G, Adriaenssens P, Himpe D.
Best Free Paper competition at the annual congress of the European Society for Paediatric Anaesthesiology (ESPA) in Berlin, Germany, September 2010

21. Audiovisual aid moderates the existing relationship between parents' and children's anxiety just prior to anesthesia
Peperstraete H, Berghmans J, De Vel, Vermeylen K, Vandermeersch E, Himpe D.
European Congress of Paediatric Anesthesia and Founding Congress of the European Society for Paediatric Anaesthesiology (ESPA), Warsaw, Poland, September 2009

22. Comparison of dP/dt estimates measured by Picco and transesophageal echocardiography during off-pump cardiac surgery
Velghe D, Berghmans J, De Worm E, Vandermeersch E, Himpe D.
Annual meeting of the European Association of Cardiothoracic Anaesthesiologists (EACTA), June 2008, Antalya, Turkey

23. Penile Block with levobupivacaine 0,25 % or ropivacaine 0,25 % produced similar analgesic effects in children after circumcision

Bryon B, Berghmans J, Van der Auwera D, Van Wesemael G, Duchateau J, Vandermeersch E, Himpe D. Congress of the European Society of Anaesthesiologists (ESA), June 2006, Madrid, Spain

24. Left ventricular response to remifentanil: a transesophageal echocardiographic study
Berghmans J, Darmon PL, Watremez C, Coriat P.
Annual congress of the European Society of Anaesthesiologists (ESA) annual congress, May 1999, Amsterdam, The Netherlands

Journal Reviewer

1. Acta Anaesthesiologica Belgica (IF 0.84)
2. Journal of Child Health care (IF 1.28)
3. Journal of Medical Internet Research (IF 5.2)
4. International Journal of Nursing Studies (IF 4.2)
5. Pediatric Anesthesia (IF 2.25)
6. Pediatric Research (IF 2.8)

Additional Research related to the PhD

1. The influence of preoperative emotional and behavioral functioning of children between 6 and 12 on postoperative pain after adenotonsillectomy in day care [a prospective observational cohort study]
Dutch Trial Register number: NTR3956 acronym CBCL-A/AT-POK 6-12 Principal investigator J. Berghmans – in collaboration with the Department of Child and Adolescent Psychiatry/Psychology, Erasmus MC - Sophia Children's Hospital, Rotterdam, The Netherlands

2. The influence of preoperative emotional and behavioural functioning of children between 1.5 and 12 on postoperative emergence delirium (ED) after dental surgery in day care Trial Register number: ISRCTN06510793
Principal investigator J. Berghmans – in collaboration with the Department of Child and Adolescent Psychiatry/Psychology, Erasmus MC - Sophia Children's Hospital, Rotterdam, The Netherlands

Multicenter Observational Trails

1. **Anesthesia Practice in Children Observational Trail (APRICOT – study ESA) - October 2014**
   Principal Local Investigator – Queen Paola Children's Hospital
2. **Neonate Children Study of Anesthesia Practise in Europe (NECTARINE – study ESA) – September 2016**
   Principal Local Investigator – Queen Paola Children's Hospital
3. **Peri-interventional Outcome Study in the Elderly (POSE): European, multicentre, prospective observational cohort study. POSE (NCT0312734) 2018**
   Principal Local Investigator – ZNA Middelheim

LIST OF PUBLICATIONS

Berghmans J, Weber F, van Akoleyen C, Utens E, Adriaenssens P, Klein J, Himpe D: Audio-visual aid viewing immediately before pediatric induction moderates the accompanying parents' anxiety. Pediatr Anesth 2012; 22: 386-92

Berghmans J, Poley M, Weber F, Van De Velde M, Adriaenssens P, Klein J, Himpe D, Utens E: Does the Child Behavior Checklist predict levels of preoperative anxiety at anesthetic induction and postoperative emergence delirium? A prospective cohort study. Minerva Anestesiol 2015; 81: 145-56

Berghmans JM, Poley MJ, van der Ende J, Weber F, Van de Velde M, Adriaenssens P, Himpe D, Verhulst FC, Utens E: A Visual Analog Scale to assess anxiety in children during anesthesia induction (VAS-I): Results supporting its validity in a sample of day care surgery patients. Pediatr Anesth 2017; 27: 955-961

Berghmans JM, Poley MJ, van der Ende J, Rietman A, Glazemakers I, Himpe D, Verhulst FC, Utens E: Changes in sensory processing after anesthesia in toddlers. Minerva Anestesiol 2018; 84: 919-928

Berghmans JM, Poley MJ, van der Ende J, Veyckemans F, Poels S, Weber F, Schmelzer B, Himpe D, Verhulst FC, Utens E: Association between children's emotional/behavioral problems before adenotonsillectomy and postoperative pain scores at home. Pediatr Anesth 2018; 28: 803-81

PUBLICATIONS NOT RELATED TO THE PhD

Carvalho H. Verdonck M. **Berghmans J.** Poelaert J: Development and validation of an android-based application for anaesthesia neuromuscular monitoring. J Clin Monit Comput (2018). https://doi.org/10.1007/s10877-018-0224-2

Eijlers R, Legerstee JS, Dierckx B, Staals LM, **Berghmans J**, van der Schroeff MP, Wijnen RM, Utens EM: Development of a Virtual Reality Exposure Tool as Psychological Preparation for Elective Pediatric Day Care Surgery: Methodological Approach for a Randomized Controlled Trial. JMIR Res Protoc 2017; 6: e174

Habre W, Disma N, Virag K, Becke K, Hansen TG, Johr M, Leva B, Morton NS, Vermeulen PM, Zielinska M, Boda K, Veyckemans F: Incidence of severe critical events in paediatric

anaesthesia (APRICOT): a prospective multicentre observational study in 261 hospitals in Europe. Lancet Respir Med 2017; 5: 412-425

Najafi N, Veyckemans F**, Berghmans J**, De Groote F, De Ville A, Huys J, Lauweryns J, Loveniers B, Pirotte T, Roofthooft E, Veeckman L, Verhaeghen T, Vermeulen PM, Vermeylen K: Belgian Association for Paediatric A: Belgian recommendations on perioperative maintenance fluid management of surgical pediatric population. Acta Anaesthesiol Belg 2012; 63: 101-9.

Engelen S, Himpe D, Borms S, **Berghmans J**, Van Cauwelaert P, Dalton JE, Sessler DI: An evaluation of underbody forced-air and resistive heating during hypothermic, on-pump cardiac surgery. Anaesthesia 2011; 66: 104-10.

Vermeylen K, **Berghmans J**, Van de Velde M, De Leeuw T, Himpe D: Ultrasound as guidance for a combined bilateral supraclavicular and caudal block, in order to reduce the total anaesthetic dose in a two year old child after a pneumococcal sepsis *Acta Anaesthesiol Belg*. 2011;62(3):151-5.

Allegaert K. on behalf of the Scientific Committee of the Paediatric Acute Pain Group, Belgian Pediatric Society. Sucrose 24 or glucose 30% for procedural analgesia in neonates: a statement following the Lancet paper perceived (in) effectiveness *Journal du Pédiatre Belge* 2011; vol. 13 – Nr. 1-2 /61.

Barvais L; SARB board members. Non-anesthesiologist administration of propofol?
Acta Anaesthesiol Belg. 2010;61(4):181-2.

Engelen S, **Berghmans J**, Borms S, Suy-Verburg M, Himpe D: Resistive heating during off-pump coronary bypass surgery. Acta Anaesthesiol Belg 2007; 58: 27-31.

Non Peer-Reviewed

Twintig jaar later … anesthesie bij kinderen / Twenty years later… anesthesia in children: Veyckemans F, **Berghmans J**. *Percentiel* 2015.

Preparation of children and parents for anesthesia, both psychologically and medically: **Berghmans J**, Peperstraete H, Cooreman H, Himpe D. *Percentiel* 2007; vol. 13 nr 1: 7-11.