Dissertation

Developmental impact of a standardized tube weaning program (EAT: Early Autonomy Training; Graz Model for weaning tube dependency in infancy)

submitted by

Mag. Hannes Beckenbach

for the Academic Degree of

Doctor of Medical Science

(Dr. scient. med.)

at the

Medical University of Graz

Department of General Paediatrics, University Children's Hospital Graz

Under Supervision of

Prof. Dr. Sandra Wallner-Liebmann

Prof. Dr. Peter Jaron Scheer

Dr. med. univ. Priv.-Doz. Christian Fazekas

2011

Declaration

I hereby declare that this thesis is my own original work and that I fully acknowledged by names off all those individuals and organisations that have contributed to the research for this thesis. Due acknowledgement has been made in the text to all other material used. Throughout this thesis and in all related publications I followed the guidelines of “Good Scientific Practice.”

Date,

Acknowledgement

I gratefully thank all persons involved in this work, especially all parents and their children who were actively included in the study and who made this work possible.

Special thanks go to Ronny Scheer for his motivation, confidence, ongoing and enduring patience in the development and performance of my project and above that for his very special and personal support in my scientific interest as well as many other aspects of life. I would also like to thank Marguerite Dunitz-Scheer for opening my doors to Graz in the first place and giving me many opportunities to learn more about life in Graz. My gratitude is also shared with the whole team of the psychosomatic unit of the University Children's Hospital in Graz for all their hours of great discussions on research topics and their spirit of helping and finding a solution for practically all situations.

I also thank Markus Wilken for his interest and ongoing involvement as my scientific work grew and for encouraging me even in times when my endurance could have been better. I thank Vincent Grote for sharing his love for statistics with me. This work might not have come to an end without his great support.

I thank Sandra Wallner-Liebmann for being head of our Doctoral School and leading us in a gentle but firm way to completion and success. Above that I thank the IFW Munich for their support and the space to work on my dissertation.

I also thank my own and future family for accepting me full heartedly to share some leisure time with them which sometimes was interrupted by my need to concentrate and focus on this work in private holidays as well as all times of nights and days.

Lilli Kratky deserves my deepest appreciation and gratitude for standing closely by my side in so many situations, roles and various levels of her energy and personality in the past years and always supported me in the best possible way.

Abbreviations

ANOVA	Analysis of Variance
BMI	Body-Mass-Index
CDI	Child Development Inventory
CP	cereal palsy
d	effect size
EBM	Evidence based medicine
F	F-Value
g	Gramm
GT or G-tube	Gastrostomy Tube
IA	Interaction
ICF	International Classification of Functioning, Disability and Health
KIDS	Inventory of Developmental Skills
kg	kilogram
M	mean value
m	months
n	number
NG	nasogaastric tube
NF	Nissen fundoplication
p	Power
PEG	Percutaneous endoscopic gastrostomy
R	correlation
RA	rapid advancement
SA	slow advancement
SES	socio economic status
SD	standard deviation
SQCP	spastic quadriplegic cerebral palsy
VLBW	very low birth weight
ZTT	Zero to Three

2. Summery

Objective: The use of short-term tube feeding has greatly improved the prognosis of medically fragile children suffering from a wide range of pediatric conditions. Recent systematic reviews have shown heterogeneous and the impact of tube feeding on the general development has never been shown.

Method: The Pediatric Division of the Medical University Graz has developed a highly effective and standardized tube-weaning program. To deliver reliable data based on the outcome of the general development and the areas of social, self-help, motor and communication skills 51 patients were assessed between 2009 and 2010 within a waiting group design with the Kent Inventory of Developmental Skills the Child Development Inventory.

Results: N = 51 exclusively tube fed children (31 male) aged 28,95 (±16,36) months with different underlying medical conditions were measured at three times with an interval of 2 months (T1, T2, T3). T1 to T2 served as a control group, T2 to T3 was defined as the experimental group that was evaluated after treatment had been completed. N = 48 children (94,12%) were completely weaned and had made the transition to exclusive oral feeding. The control group gained 0,92 (±1,04) months of general development within 2 month, the experimental group gained 2,89 (±1,86) months after treatment. The most impressive fact was the change and progress on the motor subscale: The control group lost 0,12 (±7,96) whereas the experimental group gained 3,09 (±2,33) months development. Weight and length was stable or progressed, socioeconomic aspects and underlying medical condition had no effect.

Conclusion: The treatment showed to be highly effective on the development of the formerly exclusively tube fed children of which most of them were sustaining themselves orally at T3. The experimental group made an impressive developmental catch-up and the developmental deficits of the children within the control group could be reduced with even a little catch-up. It is possible that developmental deficits are unintended and neglected side effects of long-term tube feeding in tube dependent children.

3. Zusammenfassung

Ziel: Der temporäre Einsatz von Sondenernährung hat das Überleben und die Prognose von schwerstkranken Kindern verbessert. Übersichtsarbeiten zeigten jedoch heterogene Ergebnisse bezüglich der langfristigen Nutzung enteraler Ernährung. Der Einfluss von Sondenernährung auf die allgemeine Entwicklung wurde bisher noch nie untersucht oder gezeigt.

Methode: Die Medizinische Universität Graz hat ein effektives und standardisiertes Sondenentwöhnungsprogramm entwickelt. Um den Einfluss der Sondenentwöhnung auf die allgemeinen Entwicklung incl. Subskalen zu messen, wurden 51 Patienten zwischen 2009 und 2010 in einem Wartegruppe Design mittels Kent Inventory of Developmental und Child Development Inventory untersucht.

Ergebnisse: N = 51 bisher ausschließlich sondenernährte Kinder (31 männlich) mit dem Durchschnittsalter 28,95 (± 16,36) Monate wurden im Abstand von je 2 Monaten dreimal untersucht (T1, T2, T3). Die Behandlung war bei n = 48 Kinder (94,12%) erfolgreich. Die Teilnehmer der Kontrollgruppe entwickelten sich im Messzeitraum T1 zu T2 um 0,92 (± 1,04) Monate, während die Experimentalgruppe nach der Behandlung eine Entwicklungsbeschleunigung von durchschnittlich 2,89 (± 1,86) Monaten zeigte. Beeindruckend war die Entwicklung der motorischen Fertigkeiten: Die Kontrollgruppe verlor 0,12 (± 7,96), während die experimentalgruppe 3,09 (± 2,33) Monate an Entwicklung gewann. Gewicht und Länge waren stabil, die sozioökonomischen Aspekte und die zugrunde liegenden Erkrankungen zeigten keinen Einfluss auf die Ergebnisse.

Fazit: Die gezielte Behandlung der Sondenabhängigkeit mittels einem effektiven Sondenentwöhnungsprogram wirkt sich sehr positiv auf die allgemeine Entwicklung der betroffenen Kinder aus. Die Experimentalgruppe konnte das gemessene Entwicklungsdefizit aufholen und in positive Entwicklung verändern.

Die vorliegende Studie zeigt somit erstmals, dass der spezielle Aspekt von Entwicklungsdefiziten bei sondendependenten Kindern ein bisher unbekannter und vernachlässigter Nebeneffekt von langfristiger Sondenernährung ist.

4. Comprehensive introduction into the specific field of scientific interest

The following chapter will provide a comprehensive introduction of the presented topic. It starts with information on the fact that nutrition is the biological fundament of growth and development (chapter 4.1.). This very common insight touches various fields of research, ranging widely from biochemical issues and mechanisms of gut absorption to cultural and psychological aspects. Considering the complexity of the chosen topic, my specific interest is aimed at the interaction and interference of nutrition and development between medically fragile children and tube dependence. Any child – independent of its specific medical condition – unable to cover his or her basal metabolic rate naturally and by oral means, will nowadays be helped by tube feeding if the option is available. Tubes are recognized as a useful intervention, as recommended widely and shown in numerous studies (chapter 4.2). Thus, tube feeding in general has become an indispensable and intrinsic part of modern medicine and in particular intensive care medicine. Looking at the wide clinical acceptance of all aspects for tube placement and subsequent tube feeding, a total lack of maintenance programs and exit strategies must be perceived. On a patient's individual level, a distinction is made by professionals between the need and intention for short term versus continuous or even life long enterel feeding. The benefit and advantage of short term enteral feeding for overcoming critical phases in a recovery process is unquestionable but unfortunately also includes a number of risks and side effects as presented in chapter 4.3. Apart from a multitude of research on the nutritional aspects with immediate impact on weight and growth, there is an impressive lack of literature on the topic of standardized evaluation, guidelines and controlled prospective studies in this field. This is highlighted in chapter 4.4. In the specific case of temporary tubes, the necessary and subsequent transition from temporary tube to oral feeding can prove to be difficult for some patients. A specific therapeutic guidance might be necessary in some cases. An overview on successful weaning programs is presented in chapter 4.5.

As much as the interaction between nutrition and growth has been focused on, very little attention has been given to the correlation of tube feeding and development. In particular, the question of general development in the specific population of temporary tube fed infants has hardly been investigated, even more so, the impact of tube weaning and possible differences of development before and after weaning has never ever been looked at before. This is why chapter 4.6 describes the actual topic of research of the presented thesis which focused on a very first descriptive analysis of surprising clinical findings of developmental changes during the process of tube weaning in infancy.

4.1 Nutrition, growth and development

In countries with a high standard of medicine, enteral feeding by tube has become an accepted therapeutic option for any child – independent of the multitude of underlying medical conditions and indications – which is unable to ensure and sustain its growth and developmental requirements exclusively by oral intake.

The wide acceptance of enteral feeding as a therapeutic clinical option can be attributed to the common knowledge that there is no growth and development without sufficient supply of nutrition. Nutrition provides energy for the brain (especially glucose), builds links and compounds (e.g. lipids and amino acids) and provides micronutrients for essential enzymatic and endocrine processes (e.g. iron, zinc, B vitamins and iodine). It is therefore also a source of bio- and psychoactive molecules that exert a multitude of actions, relevant for brain maturation and development (Satter 1990).

Grantham-McGregor (2007) very convincingly pointed out to the devastating and dramatic effects of under- and malnutrition in numerous developing countries.

The results show various influences on the physical, cognitive, motor and social-emotional wellbeing of children suffering from poverty and starvation. Even if the results can’t be applied in industrialized countries some general mechanisms are worthwhile to consider.

A measurement for the long-term nutritional status of a child is its change of weight and length in time. If a child eats too little, its weight will not increase or even diminish and it would not thrive or grow more slowly than expected (i.e. compared with children who eat adequately and can meet their nutritional needs and consequently will thrive). The scientific assumption at present is that if a child is able to meet its nutritional needs, it will be able to express most of its cognitive and creative potential.

In literature this assumption is used widely and recent papers from Martorell et al. (2010) have highlighted this link. The hypothesis presented was that children who received adequate nutrition intrauterine and during the first 24 months (measured by assessing an adequate growth development) would perform superior academically to malnourished children (the data chosen were the highest grade attained, ever failed a grade and age at school entry). Better results in school were associated with superior cognitive functions. The key objective was to assess the relative importance of early thriving as stated by an individual’s weight at birth and weight gain from 0 to 24 months and 24 to 48 months for schooling performance. The presented data were obtained within the framework of a large prospective study using data from 5 locations (Brazil, Guatemala, India, the Philippines, and South Africa) that summed up to a sample of 7945 children. Data showed that weight gain from 0 to 24 months had the strongest correlation with academic performance subsequently followed by the impact of birth weight. Weight gain from 24 to 48 months had a weaker or no relationship to later academic performance. The data showed further that weight gain between 0 to 24 months was even more important for cognitive development in children born small for date. In children born in the lowest percentile of birth weight, 1 SD (standard deviation) increase of weight gain from 0 to 24 months was associated with 0.50 years more of academic performance compared with 0.33 years in those in the upper percentiles. As a result of the study the authors highlight the paramount importance of a sufficient and adequate nutrition especially for children under 24 months and for children with low birth weight in order to reach a higher academic outcome (Martoll et al. 2010).

This finding highlights the importance of catch-up growth and strongly proposes that fast growth in infancy leads to progress in neurological and cognitive development. Additionally Kuklina et al. (2006) showed that small size at birth was significantly associated negatively with child development at 6 and 24 months.

Children’s development was assessed using motor and mental development scores and data relied on n=357 children from rural Guatemala. A higher gain in weight and length in these children during their first 24 months was positively associated with improved child development whereas growth between 24 and 36 months showed no association with the child's motor and mental development.

The results of Martorell et al. (2010) and Kuklina et al. (2006) suggest that effective nutrition in developing countries should start early and before the children are two years old.

A review of Dauncey et al. (1999) summarizes the knowledge about the impact of under nutrition on brain development in industrialized countries. The paper showed that short- and long-term under nutrition can have long lasting effects on behaviour and intellectual performance because many aspects of brain development, like transmitter syntheses and expression of receptor sites are affected. Especially early nutrition effects the development of the hippocampus, a brain structure important for learning, memory and therefore cognitive performance. Similar to the recent results from developing countries (Martorell et al. 2010; Kuklina et al. 2006) Dauncey et al. (1999) showed years before (without distinction between industrialized and developing countries) that children with reduced weight and length showed poorer school performance and therefore a catch-up grow within the first years should be emphasised.

Additionally, the review of Dauncy et al. (1999) highlights another important point regarding possible interference between nutrition and cognitive development: Environmental factors also have a strong effect on the development of cognition and the answer to the question whether nutritional or environmental factors had the heavier impact on the development of cognition was – due to this review – controversial.

Already at this point it becomes clear that the relationship between nutrition, growth and general development cannot be correlated in a linear manner. Never the less, it is paediatric state of the art, that sufficient early nutrition is compulsory for any child to assure adequate brain development.

The focus on "ideal" growth therefore has become a passionately discussed topic in general and in particular in the care of preterm, ill born and malnourished infants (Sullivan 2000, Cooke RJ 2000, 2001) in the last years.

Samara et al. (2010) showed data based on standard questionnaires completed by parents of a sample of n = 223 preterm children (n = 125 males, 56,1%) measured at the age of 6 years, born at (mean) 24,5 weeks (SD $\pm$ 0,7 weeks) in comparison with a matched control group of n = 148 (n = 66 males, 44,6%) of term born classmates. Eating problems were still frequent in the preterm child group at the age of 6 years resulting in a lower BMI as well as oral motor and behavioural problems even when adjusting data for disabilities as gestational age, birth weight and feeding problems at 30 months.
This is a further hint that feeding problems and continued growth failure requires early recognition and intervention.
Franz et al. (2009) presented data of n = 219 (83%) preterm infants in a clinical sample of n = 263 long-term survivors. At mean corrected age of 5,4 years they were tested - amongst other tests - for growth and motor as well as cognitive development. Data showed a significant association between growth starting from birth to discharge and long-term motor development. Weight at birth, early neonatal weight gain and post discharge head circumference were associated with cognitive development.
This study underlines the assumption that birth weight and growth in the first month's leads to more general development and a higher level of functioning. Therefore in order to compensate the negative effects of prematurity in preterm children like growth retardation and medical instability after intensive care catch-up growth had become important. Therefore the guidelines suggested that the earlier a child gains weight, the more stable is its medical condition and the child could be discharged therefore earlier from the intensive care (Braegger et al. 2010).

Children can't develop without nutrition but nutrition alone is not enough to develop. The influence of the closest environment of the family and the wider surrounding like neighbourhood or school also plays an important role too (Maturana et al. 1980). The measurement of how much influence nutrition and how much influence the environment has is a difficult question and will be considered in the discussion of results.
The underlying assumption seems to be, that if a child eats more (and therefore gains weight) its medical condition gets more stable. But if the preterm child

gains weight because its medical condition gets more stable and as a result of that the child can transformed more nutrition into growth or if the supplied nutrition causes the growth, is according to literature ten years back an open research question (Cooke et al. 2001, O´Connor et al. 2001, Latal et al. 2003).
There is a wide field of results of research of children with cereal palsy (CP) that show the difficulty to reach adequate growth by the supply of nutrition alone on the one hand and negative findings of malnutrition on the other hand.
Turck and Michaud (2010) gave an overview on nutrition and growth for children suffering from cereal palsy (CP). 30-40% of CP children are undernourished and 20-30% of patients with CP showed growth failure. The authors noted, that even in absence of malnutrition such a neurological disease might adversely affect linear growth because of endocrinological abnormalities. Thus it may be impossible to reach normal growth by nutrition alone. It also had been shown that malnutrition and growth failure are associated with an increased rate of infections, more days staying in health care, fewer days of social participation and diminished quality of life (Sullivan 2009). It is known that children with CP who have a lower cognitive development also have a higher mortality (Marchand 2006).
It is evident, that growth of most of the inner organs and growth of the body size are in linear correlation with the body weight for children with or without underlying medical conditions. As a consequent of that Pohlandt et al. (2001) requested an optimal nutritional supply for severely ill children. Gestational age or the severity of the illness in a child may be, more focus should be laid on the development of its weight (Ross et al. 2002). Therefore in general a monitored nutrition is recommended for children who are at risk for under nutrition (Cooke et al., 1999).

A Feeding tube is the best way to administer, monitor and control the intake of nutrition. The next chapter therefore will discuss the widely accepted change in institutional feeding routines by using of feeding tubes with a focus on their benefits presented in literature. Risks and side effects of tube feeding will be discussed in chapter 4.3.

4.2 Nutrition and tube feeding as successful intervention

As showed in the pervious chapter, the awareness on optimizing growth by adequate nutrition has increased and led to consideration, acceptance and integration of feeding tubes as standard clinical intervention technique for administering enteral nutrition.

Feeding tubes are especially used in primary intensive care, neonatology and child surgery because monitored nutrition can be best realized by administering after placement of a feeding tube. It is the current state of the art that additional nutritional support by tube should be given in all cases when an infant or child cannot meet its individual nutritional requirements and/or shows inadequate growth or weight losses (Braegger et al. 2010).

An additional and more or loess compulsory indication for tube feeding is the total or nearly total inability to swallow, repeated need of pulmonary inhalation, severe malnutrition, gastric compression and administration of medications otherwise impossible (Sullivan 2009). Percutaneous endoscopic gastrostomy (PEG) is recommended for children with disabilities who will require long-term or even permanent tube feeding (>2–3months) to improve weight and growth and the quality of life of patients and their caregivers (Turck et al. 2010). A PEG is superior to a nasogaastric tube in regard to nutritional efficacy, acceptability and reduces the rate of gastro-oesophageal reflux and aspiration resulting in recurrent pneumonias (Braegger et al. 2010).

The inability to reach the nutritional needs of a child and/or as a consequent a failure to thrive shows a wide range of underlying causes. Miller (2009) presents an overview regarding causes and assessment of paediatric feeding and swallowing problems for these main pathologies: prematurity, spinal muscular atrophy type II, CHARGE syndrome, congenital heart defects, dysphagia, eosinophilic oesophagitis, laryngomalacia, autism, cerebral palsy (CP), Pierre Robin sequence and laryngopharyngeal sensations.

As discussed in chapter 4.1 the main positive effects of tube feeding on weight and growth, is that it is assumed that this intervention ensures good brain development and cerebral maturation (Senez et al. 1996, Byars et al. 2003). Even as shown in chapter 4.3 there is a strong proof that tube feeding can solve the problem of under nutrition for children who can not reach their nutritional needs orally:

Sullivan et al. (2005) showed in a longitudinal, prospective, multicentre cohort study outcome measure of tube feeding via gastrostomy (GT) in children with CP. N = 57 (29 males, 28 females; median age 4y 4mo, range 5mo to 17y 3mo) were assessed before gastrostomy placement and 6 and 12 months afterwards. At baseline half of the children were more than 3 SD below the weight according to their age and sex compared with normal's. The median weight z scores increased over the study time from -3 before tube placement to -2.2 at 6 months and -1.6 at 12 months. Most parents reported a significant improvement of their child's health and a significant reduction in time spent for feeding after tube placement. Serious complications were rare and there was no evidence of an increase in respiratory complications.
The participants of this study showed little weight before insertion of a tube so a treatment was needed. Through the placement of a GT the weight gained within 12 months. Parents seemed to be satisfied, the time needed to feed the child was reduced and there were rare complications.
The data of Kong et al. (2005) showed the similar picture of little weight before treatment. N=62 children with CP who were tube fed were compared with n=48 children also with CP but orally fed. The children with a tube had normal mean weight-for-height z scores whereas the orally fed children (n = 48) showed significant lower weight-for-height z scores compared with normal developed children (n= 119).
These results also highlight that children with CP without an intervention showed very little weight. If the assumption is right that nutrition is needed for good development, it has to be considered that they may not develop all of their developmental capacities.

The question is which intervention gives the most benefit and has the least risks?
Data from the Oxford Feeding Study by Sullivan et al. (2000) based on n = 776 children suffering from cerebral palsy (CP) showed that gastrostomy tube feeding was not associated with a higher morbidity (vomiting, chest infection, etc.) and the caregivers did not report observations of higher nutritional stress (like for example: dumping syndrome) following gastrostomy tube feeding.

Wilson et al. (2010) found similar results about concern of parents before tube placement in his data of n = 64 children. N = 19 were measured retrospectively and n = 45 prospectively. The data show that the concerns of the parents before GT placement became true in 25% and expectations were met in 93%. The feeding time was decreased following the GT placement and satisfaction was reported in 23.6%, being pleased in 16.4% or being very pleased in 60.0%. Wilson et al. (2010) concludes that despite pre-placement concerns most caregivers reported being pleased with the GT following placement and concerns that occurred were of minor medical significance.

In just looking at this finding, benefits of tube feeding for mentally retarded children seems to be clear in the aspects of weight gain and not fulfilling caregivers concerns before tube placement. But the use of feeding tubes is changing because of risks and side effects recently presented and discussed in the following chapter. Recently beside the aim of reaching the child's nutritional needs, the benefits of tube feeding for the patient should not only be a gain in z score height-for-age or bone mineral content but also an improvement of his or her quality of life and that of caregivers (Turck et al. 2010).

In a prospective cohort study Sullivan et al. (2004) already measured the impact of gastrostomy tube feeding on the quality of life of n = 56 (29 males, mean age 4y 4mo, range 5mo to 17y 3mo) carers of children with cerebral palsy (CP) 6 and 12 months after a gastrostomy tube was insert. After 6 months a substantial rise in mental health, role limitations due to emotional problems, physical functioning, social functioning and energy/vitality were observed. At 12 months significant improvements in social functioning, mental health energy/vitality (mean increase >9.8 points, $p<0.03$) an in general perception (mean increase 6.35 points, $p=0.045$) compared to the baseline results. Above that carers reported a significant reduction in feeding times an easier drug administration and reduced concerns about the child's nutritional status.

The study demonstrated a significant improvement in the quality of life of the carer and potentially also of children after tube placement for children with CP. Above that a progress in mental health, social functioning and general perception is shown. Again it's the result highlight that need of nutritional support for children with CP and the progress they can do if the have enough nutrition supplied. It seems in the sample of Sullivan et al. (2004) with the mean age 4 years but a range up to 17years, that development is possible after successful intervention. In the presented studies the placement of a feeding tube is the used intervention to make nutrition usable and therefore the progress possible but there are also data presented that show potential and obvious risks as well as side effects that will be discussed in the following chapter.

4.3 Risks of tube feeding

Apart from the actual or intended benefit on growth, quality of life and medical stability as shown in the previous chapter 4.2 in the literature risks, potential dangers and side effects are described and discussed in the this chapter.

There is strong evidence of a higher mortality of tube fed children: Disabled children (n = 4921) fed via tube showed in a retrospective analysis of a comprehensive state wide data set a higher rate of mortality of tube fed children compared to children with the same grad of disability and oral nutrition (Strauss et al. 1997). The relative risk of mortality associated with tube feeding was in the sample even 2:1. The tube-fed children show a significant higher mortality rate although both groups had the same level of disability. Especially the children with less severe disabilities show a double mortality rate compared to handicapped children fed orally. The authors hypothesize that the increased mortality is associated with an increase in pulmonary disease secondary to overly vigorous nutritional maintenance and subsequent to aspiration after tube placement (Strauss et al. 1997).

Heyman et al. (2004) calculated the mean annual total value of the home care for a tube fed child by the primary caregiver. The presented data of n = 101 show that parents of tube feed children spend 484,5 min/d (± 54,46, n = 51) versus 197,8 min/d (± 30,6, n = 50) (P <.0001) for home care of the parents of orally eating children. The results show, that parents of tube fed children spend between 8 and 10 hours each day for preparation, tube feeding and aftercare, time they couldn’t used to play, learn or foster the child’s development. The translation of this additional time into money was with $ 37,323 three times higher than the time caregiver needed for a child with comparable disabilities without tube feeding ($ 15,004).

Hawdon et al. (2000) shows in his data of n = 35 children born premature that with 6 months the children tube feed children showed more than twice that much excessive vomiting, gagging and nausea than normal feeders. Berezin et al. (1986) showed high rates of gastroesophageal reflux (GER) secondary to gastrostomy tube placement. And Sleight et al. (2004) showed in their review high rates of secondary complications such as dislocation, perforation, infection, dumping syndrome after tube placement. Manikam et al. (2000) reported of massive problem of resistance to reintroduction of oral feeds after even short- but more over long-term tube feeding. The majority of preterm, neurological impaired children and those after post-operative periods take up oral feeding without any problems if the tube feeding does not last longer then 2-3 weeks. Nonnutrive sucking can progress if done while tube feeding. Neonates and infants who have never been orally fed from birth or if the tube feeding lasts for a longer period (from 6 weeks to over 1 year) the reintroduction of oral feeding can be very difficult for the child and the caregivers Gottrand et al. (2010).

It seems that there is even a raising population of children were reintroduction of oral feeding is not happening or not successfully and the children get tube dependent (Trabi 2010, Dunitz-Scheer et al. 2009). Tube dependency is defined as the remaining of the tube for nutrition after successful healing of the underlying disease, which is often accepted as an unintended side effect of the treatment (Trabi et al. 2010).

Blackman et al. (1985) first described the problem of returning to oral feeding after gastrostomy if the medical condition is stabilized. The authors focus strictly to acceptable and non-acceptable candidates. In presented study only n = 10 from n = 17 were accepted to tube weaning. N = 5 manage successfully as out and n = 4 as inpatients. One child with dysphagia aspirated and could not be weaned.

In the aftercare phase of temporary tube placement, when the transition to oral feeds is suggested and recommended, resistance to introduction oral feeds

and tube dependency are the main indications for specific measures of tube weaning, but unfortunately most medical centres neither provide effective maintenance programs nor predictable exit strategies.
Another problem is the general assumption that tube feeding as intervention guaranties a positive impact on growth and weight in all cases which have received the intervention of tube placement and subsequent tube feeding. The analysis of weight and growth of tube dependent children referred for tube weaning shows that the greater part was clearly undernourished for reasons of prevailing and outweighing of negative symptoms in comparison to positive effects (Trabi 2010). Although some negative and traumatizing effects of tube dependency on caregivers have been described since years and recently (Blackmann 1987, Teti 1991, Rudolph 2002, Wilson 2010) they seem to have little effect on clinical considerations and practice.
Troubling side effects, as reported by desperate parents Pederson et al. (2004), tend to be taken for granted as being unavoidable and needing to be tolerated for the overall sake of having the tube (Craig 2004).
Above that there is strong evidence about tube feeding and the development of posttraumatic eating behaviour disorder since years and recently (Chatoor et al. 2001, Arts-Rodas et al. 1998, Benoit et al. 2000, Mason et al. 2005, Jotzo et al. 2005).
If a child is tube fed, the child and caregivers miss mealtimes and socialization experiences (Thorne et al. 1997). Veness et al. (2008) showed the data of n = 20 children with cerebral palsy the importance of mealtime interaction for the children and their mothers as a kind of social training.

Above that parents report of sleep disruption, deprivation, restricted mobility and restricted ability to leave home, child care problems, negative attitudes of others towards tube feeding and difficulties finding a place to eat (Brotherton et al. 2007).
Sullivan et al. (2006) showed in a study with n = 40 children (n = 27 males, media age 8y 6 m (range1y 4mo - 18y 11mo) that overfeeding a child with CP via a GT is possible. The sample existed of a group feed via gastrostomy (n = 22) and a comparable group of orally fed children (n = 18) with CP. The reduced energy needs, including resting energy, total energy expenditure and

physical activity level of children with CP make especially the enteral fed children at risk for overfeeding with the known of adiposities.

The data of Ong et al. (2009) showed that faster weight gain in early infancy between 0 to 2 months and also 2 to 9 months by n = 2715 healthy girls from a prospective UK birth cohort study were associated with increased body fat mass relative to lean mass at age 10 years and also with earlier age at menarche.

As Birch et al. showed as early as 1991 that children do regulate their energy intake very precisely and self regulated. But if enteral feeding is meeting all the energy requirements of infants or children, they will not experience hunger.

Wright et al. (2006) showed prospective on the data of n = 923 children with 13 months that the inherent characteristics appetite of the child is an important risk factor for weight faltering and failure to thrive. Maternal promotion of feeding may also have an adverse influence.

A common problem of exclusively tube feeding are micronutrient deficiencies (like calcium, iron, zinc, selenium and vitamins C, D, and E) (Turk et al. 2010). Recently Schmitt (2010) showed that the organolepetic properties of food like taste, smell and texture might modulate cognition and mood directly.

Additionally, apart from negative physical, psychological, developmental and social effects, the increasing time consumption for caregivers through prolonged tube feeding and associated economic factors unfortunately are completely neglected in the discussions and considerations on tube feeding (Heyman 2004).

"*The data could be telling us that tube feeding itself is dangerous and should be avoided"* (Sulkes, 1991, p. 420) *or "Sucking and feeding are important early neurodevelopmental milestones; when not reached, their impact on further development of feeding skills may be significant" (Rommel 2003, p. 75)* represent some of the very few critical reflections of these points.

Reviewing the connection of tube feeding, nutrition and development (in contradiction to growth) some trends can be found: "*Results of investigations on under nutrition during early childhood suggest that "undernourished children generally had poorer fine and gross motor function, and levels of school achievement and cognitive function*" (Grantham-McGregor et al. 2001, p. 4).

The role of muscular activity for the development of age appropriate crawling, standing up and walking has also been showed to be linked to good nutrition (Rudolph et al 2002).

4.4 The lack of standardized evaluation of tube feeding practises

By comparing chapter 4.3 and 4.4 we see that the results of most studies are inconclusive. There is no clear evidence and picture about the benefits and risks of tube feeding. Judging by interviews with many medical professionals about their general thoughts on the regime of feeding tubes as standard intervention there seem to be some medical institutions who generally are more "in favour" of tubes and early tube placement versus others who try very deliberately and consciously to keep the rate of tube fed patients to a minimum.
For example Vernon-Roberts et al. (2010) examined 14 children (median age 2 years) with severe spastic quadriplegic cerebral palsy (SQCP) and feeding difficulties for whom a clinical decision had been made to insert a gastrostomy feeding tube. Within the study they were fed a low-energy, micronutrient-complete, high-fibre feed. After 6 months there was a significant increase in weight and no significant increase in fat mass index. The children with SQCP who were fed low-energy continued to grow even with energy intakes below 75% of the estimated average requirements.

But straight after the publication of Vernon-Roberts et al. (2010) Somerville and O'Loughlin (2010) wrote a comment with their point of view: They strongly recommend that the interpretation of their findings of Vernon-Roberts et al. (2010) should be done with great care before clinicians alter their practice. The sample age was very young (mean 2 years) and the group of children with severe neurological impairments is very inhomogeneous. Furthermore the assessment of nutritional status is very complicated with controversy discussions. It's commented that a „one size fits all“ approach is inappropriate. Children should be instead regularly monitored in a multidisciplinary setting with focus on general health and quality of life for both child and caregiver can be made.
The papers of Vernon-Roberts et al. (2010) and the comment of Somerville and

O’Loughlin (2010) show exemplarily that there is no “one size fits all” standardized concept of how much nutrition an infant should become but a lack of standardized evaluation.

Sullivan et al. (2000) explored as n = 776 children with CP and found no higher mortality but Strauss et al. (1997) showed a higher mortality of n =4921 tube fed children with disabilities. Wilson et al. (2010) showed that despite pre-placement concerns of caregivers did not occurred after tube placement but Veness et al. (2008) showed exact the difference.

The lack of normative data combined with the complex interaction of nutrition and non-nutrition factors contributing to growth in this population presents real difficulties in management. Although various indications and descriptions of enteral feeding have been reported and published for individual groups of medical diagnosis and clinical situations (Cooke 2001, Ciotti 2002, Sleigh G, Brocklehurst, 2004, Stevenson 2005) there is an impressive overall lack of standardized evaluation, guidelines, controlled prospective studies and research in the field.

A recent systematic review (Sleight et al. 2004) to determine benefits and risks for tube feeding compared with oral feeding failed to identify any randomized controlled trials that met the inclusion criteria. It’s shown that there is still continued uncertainty about the effect of gastrostomy. Moreover there are serious issues raised about potential increased risk of death, the necessity for further surgical procedures and some life threatening complications. Above that the authors highlight evidence that gastrostomy feeding had negative impact for families. The authors argued that the effectiveness of gastrostomy feeding should be demonstrated; out of their systematic review it not possible to draw a firm conclusion that tube feeding gives an overall harm or benefit. The authors strongly recommend well-conducted randomised controlled trials of sufficient size to address some of these important outcomes.

Samson-Fang et al. (2003) critically appraised in another review the effects of gastrostomy feeding in children with CP, even if his review is based on only 10 published studies with relatively small sample and without a control.

The results from reviewing Sleight et al. (2004) and the big studies of Sullivan et al. (2000-2008) show clearly that both studies have very good scientific practise and excellent methods but are controversy and show that there is a

lack of standardized evaluation.
It is astonishing but evident, that even in the well-researched field of short-term enteral feeding of very low birth weight (VLBW) infants controversy exists about the way of tube feeding. Rapid advancement has been associated with increased necrotic enterocolitis but delaying enteral feeding unfavourable effects on nutrition, growth and neurodevelopment (Härtel et al. 2009). Therefore Härtel et al. (2009) compared the short-term outcome of n = 1430 VLBW infants recruited from 13 tertiary neonatal intensive care units in Germany. The units were divide into n = 7 centres with rapid advancement (RA) and n = 7 centres with slow advancement (SA). The mean duration of full enteral feed in all centres was 12,5 days. The VLBW from the SA (n = 713) had a significant higher rate of sepsis (20,4% vs 14,0%) compared with the VLBW infant's born in centres with RA (n = 717) but the authors conclude that to conclusively answer the question whether RA or Sa is preferred, more research is needed (Härtel et al. 2009).
So even the question on the detail of fast or slow tube feeding is at present not fully answered. Bombell et al. (2009) present in a huge systematic review the same unclear results.
Coitti et al. (2002) concludes after showing his data of n = 37 children with cardiac diseases before and after placement of a gastrostomy tube that supplementation using a gastrostomy allows the safe delivery of the caloric intake needed to support malnourished children with cardiac disease. But Trabi et al. (2006) showes that n = 20 patients with congenital heart diseases that could be weaned successfully from the tube. The body weight at admission was even increased after the treatment.

Hofner et al. (2000) presented data on children with severe congenital heart disease who got a PEG. Even the results relies only on n=15 the data is presented here, because it's the only found study were tube fed children maid the transition to oral feeding without additional help. N = 8 children were followed 6 months after PEG insertion and they increased their age-matched body weight more than one standard deviation but tube feeding was needed long-term. N = 2 patients of these group increased more than 0,5 standard deviation. In n = 7 children the tube was removed after 2,5 to 42 months

because enteral support was no longer necessary. Beside initial reservations of the parent, the authors conclude that PEG is a safe and reliable technique to support nutrition.As said above this is the only found study that shows data of tube feed children were the transition back to orally feeding seems to be easy.
These findings again highlight the lack of standardized interventions because other studies describe the problem of transition from enteral to oral nutrition (Dunitz-Scheer et al. 2009) as very severe. The picture drawn from literature seems not to be homogenous but further research needed.
Also the psychosocial aspects of gastrostomy are under-reserarched. Some parents oppose to gastrostomy (Davis et al. 1992, Tawfik et al. 1997, Sleight et al. 2004), others data report more caregiver satisfaction after tube placement (Sullivan et al. 2006, Thorne et al. 1997, Rempel et al. 1988). Above that, the recommendation of placement of a gastrostomy can present ethical dilemmas even for the clinicians and parents (Reilly et al. 2000, Craig 2004).
There is a lack of normative data on the one side and a very complex interaction of nutrition and nonnutrition factors contributing growth and development on the other side what causes in present real difficulties in management (Morag et al. 2010)
What also needs to be considered is the fact that tube feeding could have different effects whether it is used as a temporary intervention or a long-term intervention without a defined end.
The effects of long-term tube feeding are unclear at present (Dunitz-Scheer et al. 2009). Nevertheless, with the argument that tube feeding fosters weight, growth, good brain development and cerebral maturation (Senez et al. 1996, Byars et al. 2003) probably thousands of infants and children are kept on temporary tubes without any methods of evaluation the efficacy of the intervention per se or differentiating positive from aversive influences.
We have to acknowledge that in presence we known little about the general outcome of tube feeding in infancy (Trabi et al. 2010). This situation has not chanced since the review of Sleigh et al. (2004). Further research is still needed.
Davis et al. (2009) comments that tube feeding is an excellent short-term solution as shown by the literature. Above that there are children, were tube feeding as a life-long intervention is needed. But delaying the transition from

tube to orally feeding by children who could be weaned from tube but it's not done, the literature shows many potential harmful side effect that needs to be considered first in the medical intervention and secondary further research is needed to get a clear picture (Davis et al. 2009).

If Strauss et al. (1997), Sleigh (2004), Davis et al. (2009), Dunitz-Scheer et al. (2009), and Trabi et al. (2010) are right and tube feeding clearly show harmful side effects, the results of excellent studies of Sullivan et al. (2000, 2004, 2005, 2009), Kong et al. (2005) and Turck (2010) warn about the negative aspects of malnutrition measurable as negative influence of weight, length and cognitive development. If successful tube weaning would be possible for at least some children without negative outcome on weight, length and development, the inhomogeneous picture of showed data could get closer. The literature would then recommend than tube feeding was an imported short-term solution for children who need it because of underlying medical conditions. As a long-term solution tube feeding should just be indicated if successful tube weaning is not possible or the condition of a child is too frail and weak or because of strong disabilities or aspiration. A need of standardized guidelines seems evident.
The literature presents several tube weaning programs and some case reports discussed in the next chapter.

4.5 Tube weaning programs and case reports presented in the literature

The following passage presents an overview of existing programs with the aim of tube weaning. Facilitated results are presented and discussed.
The here presented data all focus on tube weaning for children with temporary tubes who would not need a tube any more from a medical point of view, but don't start to eat orally without a special treatment. There are other reasons for tubes and tube weaning presented in literature that focus on special topics. Davis et al. (2010a) gives a brief overview.
Although the present literature shows the overall agreement that a multidisciplinary approach is necessary for tube weaning (Wright et al. 2010, Puntis 2008) only few treatments with data of long-term outcomes have been formally described, most of them are based on behavioural models.

A slow weaning program of the University of Glasgow (Wright et al. 2010) is described in a retrospective study with the aim to assess the impact of food reduction on growth. N = 41 children with the aim to withdrawal form nasogastric or gastrostomy feeding which had all been enterally fed for 6 months or more. Their age median was 4.0 years (± 0,7 – 15), n = 27 (66%) were male. The weaning program focused on a slow reduction of food and intensive support for the parents to deal with the possible and happened loss of weight. The follow up after median 1,7 years (± 0,4 – 5,4) n = 32 (78%) were weaned from tube. N = 7 (17%) were still enterally fed and n = 2 (5%) were reliant on oral supplement drinks. N = 37 (90%) stopped tube feeding at some point but n = 3 children re-started.

The reduction of feeds caused a relative and temporary weight loss but there was no evidence that this was associated with a reduction of growth development. After start of treatment age and gender was not a significant predictor but nearly two third of all referrals were boys. Parental anxiety is described as the main factor of delayed food cessation. Enteral feeding provided life saving support in early life for most of the children and weight gain had been of critical importance when the children were ill so much focus was needed for the parents to handle their anxiety so that they don’t leave the treatment.

The study lacks a control group and is retrospectively but presents good follow-up date 1,7 years after treatment and a clear overview over underlying medical conditions. The sample size is with n= 41 compared to other studies high.

The Medical University of Graz (Dunitz-Scheer et al. 2009, Trabi et al. 2010) has since 20 years specialized on the specific and complex topic of interactions between nutritional, physical and psychological variables of long term tube feeding in infancy and early childhood. The special intervention that the Graz team developed, enabling families and infants and children to make the transition from exclusive long term tube feeding without any oral skills before the weaning attempt to sufficient oral intake within 2-3 weeks.

Their recent paper (Trabi et al. 2010) shows a sample of n = 221 exclusively tube fed patients with median age 793,5 days (± 134 – 2,79), n = 118 (53,4%) were male. After treatment n = 203 (91,8%) patients were completely weaned and on exclusive oral intake. In 50% of the patients the tube feeding was stopped completely within 8 days (± 0 – 39). The mean time of the inpatient treatment was 21,6 days (± 2 – 52). The study showed that the chance of successful weaning is higher if the tube is removed earlier in the treatment program. A higher BMI and an increased severity of disease decreased the change for weaning. The data suggest an inverse correlation between gestational age and chance of successful weaning. Preterm born children could be weaned more easily.

The study is retrospective and lacks a control group but has a huge sample size with n = 211, the highest ever presented in literature and the second highest success rate.

Trabi et al. (2006) show above that data from the same weaning program of children with congenital heart diseases. In comparison to patients with other underlying medical conditions the cardiological ill patients showed a significant better chance to get of the tube as the others. An increased body weight at admission increased above that the chance for weaning.

Davis et al. (2009b) shows data from the University of Kansas Medical Centre of n = 9 exclusively tube fed medical fragile toddlers with the mean age 27,3 months (± 15,5). The 14-week outpatient protocol is based on the assumption, that medically fragile toddlers have experienced gastrointestinal pain so the protocol approaches the transition from tube to oral feeding from a pain management perspective using tricyclic antidepressent and/or gabapentin in the combination with hunger provocation. After the treatment all patients (n = 9) received 100% of their energy intake orally. Eight of the 9 were able to maintain weight and never require additional tube Feeding, one child needed 50% of the energy requirements via tube.

The study is of a retrospective design, has a very small sample and no control group but a high success rate. Above that, the use of drugs for tube weaning seems more than questionable (see Marinschek, in prep.)

The Academic Medical Centre Amsterdam (Kindermann et al. 2008) presented a multidisciplinary hunger provocation paradigm in stages program to wean children off tube feeding. N = 10 infant age 9 – 21 months, 7 girls, were exclusively tube fed for 7 – 19 months. They stayed in for mean 17,4 days (± 9 - 33). All but one child started to eat orally within one week. The mean weight loss was 9,2% (± 7,3 – 15,6%) of there weight at admission. The follow up after

3 and 6 months showed that 8 of 10 children were weaned of the tube and gaining weight. Two children resumed with current infections partial tube feeding during follow-up.
The multidisciplinary in hospital program includes: Step 1: 50% of normal allowance is given via tube. Step 2: Oral feeding is offered and completed with 50% with tube feeding after wards. Step 3: Supplementary tube feeding is given by night. Step 4: tube feeding only by sensible weight loss and step 5: When the child has started eating the parent took over the feeding. Unfortunately, the study lacks a control group, is retrospective but supplies follow up at 3 and 6 months. The sample size is small.

Clawson et al. (2007) showed data of n = 9 children with spastic diplegic cerebral palsy at the Children's Hospital Richmond. The intensive day paediatric feeding program is based on oral motor training, behavioural interventions and parental education. There it is mentioned that the children who were tube fed at admission were able to decrease the amount of tube supplementation due to their improved oral intake. They show a improvement in mealtime skills, improved timeliness of swallowing without gagging, expelling or holding food in the mouth. Above they tolerate longer meal sessions and consumed a greater quantity of food resulting in greater caloric consumption

Wilken et al. (2006) presents a German home-based tube weaning program. His data show n = 28 tube fed children with the mean age 29,6 months (range 6m -7m 7y). 50% of the sample was less than 24 months. N = 22 had a chronically deficits in development and the mean duration of intensive care had been 7-10 days. After treatment N = 27 (96,4%) children could be successfully weaned from the tube but at the follow up 3 months after treatment two children needed again to be tube fed (89,5% success rate at the follow up). The study does not show a prospective design and a control group and the sample is quite small. Still this study shows the less time for successful tube weaning with still one of the highest success rates of the presented tube weaning programs.
At the Cincinnati Children's Hospital Medical Center Byars et al. (2003) presented long term data about their multi component feeding program in a prospectively designed treatment study. N = 9 children (4 girl; mean age 3,1 ±

1,2 years) with Nissen fundoplication (NF) and G-tube placement were evaluated before treatment, after treatment and at follow up. The children and their mothers were admitted for treatment for mean 11,4 ± 1,7 days. At discharge n = 4 (44%) children were completely weaned and the sample received in mean of 63.4% ± 18.3% their nutritional needs. At follow up (mean 3,1 ± 0,5 months after discharge) n = 6 (67%) children were completely weaned and the whole sample received 100% of their calculated nutritional need (88% orally, 12% by G-tube). Stability in weight was observed. The treatment protocol emphasized appetite manipulation, time-limited parent training and mainly behavioural treatment with the operant learning principles of positive and negative reinforcement, shaping, discrimination, fading and escape extinction. The study lacks a prospective design and a control group but has a follow up. The sample size is small.

At the Hospital for Sick Children and University of Toronto, Canada Benoit et al. (2000) measured whether the outcome of a behaviour therapy or a nutritional therapy was more effective by children with resistance to oral feeding. N = 64 children (age 4-36 months) which became tube feeding for al least 1 month attended 7 consecutive weeks a weekly clinic with 1-2 dieticians plus 4 follow-up visits. N = 32 joint the behavioural group and n = 15 (47%) were weaned after treatment successful whether none of the nutritional group could be weaned. It could be shown that behaviour therapy with the operant learning principles is more effective in eliminating the need for tube feeding than nutritional counselling alone. This study is the only one with a control group design, is prospective and shows a good sample size.

Senez et al. (1996) presented data of n = 19 children at the Hospital des Enfants Marseille France, were re-establishing of oral feeding was difficult or impossible. The procedure was based on the afferentation or re-afferentation of the oropharyngeal cavity by sensory stimulation and re-establishing of the biological clock by feeding at regular hours. N = 18 children could be successful weaned in mean 53,6 days (± 11-330), in one child the procedure failed. Furthermore it’s described, that it was easier to re-activate an already established function than to activate a function that never was active. This fact was regardless of the amount of brain damage of the children. The study also lacks a prospective design and a control group. The sample size is not bad and this study shows the highest success rate.

Blackmann et al. (1987) presented data of n = 11 patients who were tube fed in a 2- to 3-week inpatient feeding program with the aim to introduce to oral feeding. N = 10 maid the transition successfully with a minimal disruption of family life and parental anxiety, as described. A published earlier from Backmann et al. (1985) the proper selection of oral feeding candidates takes a main part, beside of the preparation of the patient prior to hospital admission an a consistent approach to overcome the child's resistance to oral eating. The treatment is mainly based on behavioural treatments using flooding procedures (Blackmann et al. 1987). The data need to handle with care because follow-up data is missing, the retrospective design, no control group a lot emphasis on the selection of right candidates. But this study shows the first data about tube weaning programs.

In summery there are n = 10 studies presented between 1987 and 2011 with n = 411 participants includes. The main success rate is 78,47% what shows that tube weaning is effective. Weight losses were in sum marginal. The programs were based on slow or fast food reduction, parent training, based on self-regulation, drugs, multidisciplinary, hunger provocation, behavioural trainings (operant learning principles), sensory integration and based on chronological clocks. There are in- and outpatient and home-based weaning programs.

Beside the shown studies there are some interesting case reports presented:

Trabi et al. (2010) reports the weaning from a 5-year-old girl with Marshall-Smith syndrome. Because of respiratory problems and a high risk of aspiration she got a PEG but after stabilization of the respiratory situation, she was able to eat from a medical point of view. After careful medical analysis she was integrated into the specialized tube-weaning program and successful weaned after 3 weeks and gain weight by exclusive self-regulated oral intake. Her motor development gained after two months significant.

McKirdy et al. (2008) presented a school-based intervention were therapeutic feeding goals were individualized integrated into the education program for two 5-year-old children. The program based on behavioural strategies went over 2 years and both children had transitioned form tube to orals feeding ant the end of the program. Addressing feeding difficulties in schools seems a novel idea but the effectiveness of such programs need further research.

Burmucic et al. (2006) presents two children who were weaned successfully from long-term tube feeding after liver transplant because of Alagille syndrome. One child needed 7 days the other 13 days for successful weaning using a standardized highly specialized treatment protocol. A gain of bodyweight was established.

Luiselli et al. (2000) weaned a 3-year-old child with multiple medical disorders and chronic food refusal with behavioural procedures like reinforcement and demand fading. After one year the child was consuming a variety of foods and gained weight.

Gutenberg et al. (2000) presented a successful treatment of a 3-year-old medical fragile girl who refused all presented drinks and food. The treatment focused at the same time on food acceptance through social praise and access to preferred toy play and on the food refusal and disruptive behaviours through ignoring.

Dunbar et al. (1991) presents a single-subject study with 3 children who did not meet their nutritional needs orally. The occupational therapy treatment based on behavioural management methods and presentation of developmentally appropriate play activities. The data show an increase of the oral intake in 2 of the 3 children.

Unfortunately, no prospective randomized controls studies exist on this topic at present but are strongly recommended (Sleigh et al 2004).

The use of program technique like force feeding (Luiselli et al. 2000) has been criticized years ago and recently. Skuse already 1993 clearly believed that no child is able to increase her or his oral intake of food by force-feeding. He states that it seems very problematically that this tactic is often used in the advice of child health workers including paediatricians.

The use of strong medications for tube weaning (Davis et al. 2010, 2009) has also been criticized by Marinschek et al. (in prep). Comparable data of children with the same medical condition who could be weaned without the use of strong medications even more successfully will be shown soon.

Above that operant learning principles like negative reinforcement, shaping, discrimination, fading and escape extinction are very questionable from an ethical point of view, even if they show success and are wide spread.

As far as shown with the above overview, nutrition is of paramount importance for the development of children. If a child can't reach its nutritional needs orally, feeding via tube is indicated. We further saw that the literature about tube feeding is discussed on a data base controversy. Tube feeding as a short-term solution seems to be effective, long-term tube feeding seems to have multiple risks and transition to orally feeding should be done if possible.

A shown in this chapter tube feeding is possible in specialized treatments with good overall success rates and marginal negative affections of weight and length. But unfortunately, there are just too few tube weaning programs published in literature jet.

The open question in now how and in which intensity long-term tube weaning has possible unintended side effects on the infants and children?

4.6 Does tube weaning effect development?

As we could see, tube weaning is basically possible and can be effective (Wright et al. 2010, Trabi et al. 2010) and it can effect the short term weight development but not the development of length (Wright et al. 2010). Follow up data show that the possible loss of weight development does not last for long (Kindermann et al. 2008, Byars et al. 2003, Benoit et al. 2000). As we have seen from the literature from development countries, a lack of nutrition does lead to stunting and further more a lack of cognitive and general development (Martorell et al. 2010, Grantham-McGregor 2007). We have to consider and make sure that while weaning a child off the tube, no under nutrition may occur that could harm the child. This can be controlled by monitoring the weight before, during and after tube weaning and secondly by monitoring the length at and after the treatment and at follow up.

Astonishingly enough, there is no existing data jet on the effect of tube weaning on the general development and on the development of subscales like motor, self-help, communication, cognitive and social development. These could be a third focus to make sure that children are not harmed while they get weaned off the tube. There is no data jet even if this could be a conclusion that tube weaning could effect the general development or some subscales of a child's development.

The interesting point is that at the very successful tube-weaning program at the Medical University Graz (Trabi et al. 2010) in the transition of exclusive tube to sufficient oral feeding, there is the clinical impression within the largest documented study sample of tube dependent children (n>1280, data not published jet), that some children show – apart from the intended and desired learning effects in oral feeding skills – some unexpected and amazing chances in their general developmental while and after the treatment. During the weaning phase the child is submitted to a fast reduction (within one week) of tube feeds with the aim of inducing hunger. As could be expected that less nutritional intake would lead to less energy with adverse effects on performance and development, the clinical impression is different and the question was postulated, whether there were – in addition to the well known nutritional impact - some unknown and neglected side effects of tube feeding which might only become evident after tube weaning.
No data can be found in reviewing the literature about the influence of tube feeding or tube weaning on the general development of the diverse group of per se often preterm born and medically fragile young patients.
Therefore, the aim of the presented study is prospectively to investigate possible effects of long term tube feeding and of the weaning process itself on the general development and the sub areas of social skills (social), self help competences (self help), motor development (motor) and communication.

5. Methods

5.1 Study objective

The treatment program, defined as the “Graz Model” for tube dependent infants enables medically fragile children to be weaned off long term tube feeding. The transition from exclusive tube feeding to eat and drink by self regulation of the child may induce developmental changes on various levels beyond the necessary increase in oral skills.

It is hypothesized that this process improves the general development and decreases developmental deficits in general and in the sub areas social skills, self help, motor skills and communication. Beside that, we hypothesized that infants and children who are long time enterally fed (% of lifetime) suffer generally from a worse developmental deficit that will improve slowly. Furthermore we hypothesized that after tube weaning reduces unintended side effects; secondly infant’s growth should be improved thus stabilizing or even gain.

5.1.1 Treatment description

The treatment tube weaning according to the “Graz Model” was developed since 1989 to treat formerly very ill and/or premature children. It was publicised various times (Dunitz-Scheer et al. 2011, 2010, 2009, 2001). For a clearer understanding of the treatment a brief case report follows (Trabi et al. 2010):

„Chin Lin

Chin Lin was referred to our program at the age of 3 years for tube weaning dependent on NGT feeding. Chin Lin was adopted by her American parents from China at the age of 13 months. She had been cared for in an orphanage in China after being abandoned and left to be found. Since Chin Lin — unlike the other little girls in the orphanage — was reported to show food avoidance and refusal of nearly all feeding attempts, she was severely malnourished when arriving in the United States, and she immediately received an NGT and fortunately recovered quite promptly. At 2 years of age, catch-up growth was sufficient and so weaning her from NGT was discussed as a necessary goal. It

seemed clear to everyone that there were no medical reasons preventing the Chin Lin from learning to eat, but it just did not seem to work.
After 1 1/2 years of unsuccessful trials and feeding programs in and around Philadelphia, the little girl was referred to our program. Intervention this time was organized in a different way: avoiding all kinds of force-feeding and focusing the interventions to self-awareness, autonomy, and self motivated motor skills involved in touching and handling food.
After a brief assessment one morning in which the child met the therapeutic team, the tube volume was immediately reduced by 40% on Day 1, 60% on Day 2, and discontinued entirely at the end of the first week (Day 6). Daily therapeutic sessions (presented later) encouraged Chin Lin to touch and play with food, to feed her dolls, her parents, and her therapists, gradually resulting in great fun and obvious increase of autonomy and self-assurance in many areas of development. Food was repeatedly around the child at nearly all times. Two daily tub baths in warm water with no soap and swimming in the hospital pool encouraged tactile experiences involving water. The tube was removed at the end of the first week. Oral intake gradually increased over the following fortnight. After 3 weeks, the child could be discharged and returned home. Therapeutic work with the parents included psychological topics such as attachment issues, fantasies about the period of time when the child had survived in a clearly deprived world, and the couple's relationship itself.
This case describes the weaning process in an unusually "healthy" child having suffered "only" from failure to thrive by food refusal. The case also shows that tube feeding served as a highly rewarding and successful intervention for nearly 1 year. Thereafter, negative side effects had become greater than the benefits. In contrast to this case, most infants referred to our centre have much more complicated medical histories, most of them being survivors of modern neonatal high-tech medicine.

This weaning program is a multidisciplinary method excluding any kind of force feeding. The method has been presented and published previously (Dunitz-Scheer et al 2001, Trabi, et al. 2006). The principle of the program is the establishment of self-regulated oral intake. The increase of oral intake is based on the allowance of hunger due to rapid reduction of food intake by tube.

Additionally, parents are counselled not to pressure children to eat and are coached to recognize and read their child's hunger cues. The main intervention, therefore, is the promotion of hunger by reduction of tube feeding within 1 to 3 days in a supervised setting, including an intensive, noninvasive monitoring of the child's medical condition and full support of the child's capacity for autonomous food exploration and self-regulation of intake.

The presented treatment approach is not behavioural. Neither appetite manipulation nor reinforcement strategies are used. The principles of the program were derived from non-directive play therapy with toddlers and adapted specifically for this population. Since all patients had a history of medical intensive care and/or experiences with repeated exposure to force feeding, all of them showed signs of post-traumatic feeding disorders.

There is no formal structure or routine placed a round meals. The only repetitive event is the daily eating therapy session, defined as playpicnic. This central therapeutic item consists of

A 1-hr group picnic (seven times weekly at noon to 1 p .m.) of 3 to 6 infants and small children in the presence of at least one of their parents, who are told only to interfere on strict demand for help by their child. Food is presented at the picnic as a finger-food buffet in the middle of the room. All food is located on the floor, using plastic dishes. Touching and playing with it is the main goal. Licking, smelling, touching, biting, or drinking is not reinforced specifically.

Members of the therapeutic weaning team are often present, but in a very unstructured and unpredictable fashion. The team and the parents are told to eat — if they want to. They often are fed by the children. Parents are strictly told not to feed their child. All other contact with food happens in a more or less unstructured manner regulated solely by cues from the children and the readiness of the staff and family to react appropriately. The child can see, smell, and touch food at nearly all times of the day, but is never told to eat. Every contact with food happens only if the child wants to.

All patients are treated according to the standardized treatment protocol with four to six individual- and group-treatment sessions per day as shown in Figure 1.

The team supports the parents to review their feeding activities and feeding *attempts, and helps them to learn to accept self-regulated behaviour of the child within an environment offering food on demand. Speech therapy, occupational therapy, nutritional guidance, psychological counselling and physical therapy are performed according to the individual needs of the child. In addition, parents are encouraged to discuss their anxieties and any emotional distress with all members of the team.*

One of the greatest challenges is to convince the clinical staff to make organizational changes.

(…) Learning to eat can happen only in a clinical environment with a high level of knowledge and expertise about normal eating, feeding development, failure to thrive, starvation, malnutrition and other medical, developmental or psychological conditions associated with food refusal. The core team offers three medical rounds per day and is available day and night. In some cases a psychiatrist is needed to support the parents (Dunitz et al. 1996). All other members of the medical team are highly trained in the concept of the weaning program.

The responsibilities of the team members are as follows:

1. The paediatric team is responsible for coordinating diagnostic and therapeutic items and monitoring the child's medical condition. All paediatricians have additional training in developmental psychology and child psychotherapy. Three paediatricians have specific training in methods of play therapy and attachment theory in infancy. Additional paediatric diagnostic procedure is permitted only in cases of misdiagnosis or emergency.

2. The nursing team is responsible for observing the children and any interventions to reduce parental stress. In the course of the last decade the nursing team has been trained to perceive the physical and mental health condition of the children and the parents. The team also prepares finger-food trays and appropriate dishes for the daily play picnic and makes food available all day.

3. Eating therapy: The specific invention of the Graz model is the daily play picnic group session. Based on psychoanalytically oriented play therapy it encourages any kind of self motivated actions the infants will present individually and in the group. Any aversive reactions of the children are tried to *be prevented. interference, wiping, cleaning up, force feeding and any kind of harassing, intrusive or constant offering of food is prohibited.*

Active distraction such as the offering of attractive toys or an reinforcements is also not permitted.

4. Video-analysis is performed to assess and identify intrusive behaviour and other specifically maladjusted patterns of child-parent interaction. One parent is usually present at the play picnic, the other one can observe the session through a one-way-mirror. Comments of the parents are identified and positively reframed. This technique reflects video-therapy as described by Reck et al. 2004.

5. Patient deficits in functional emotional development are detected by the developmental psychologist during play sessions using puppets and other creative instruments.

6. Interaction-focused guidance is applied in a task-oriented, unstructured, non directive and undemanding way by all members of the team.

7. Psychoanalytic oriented psychotherapy with the parents is needed to work on traumatic events in the child and parent's history, offered only if parents ask for additional support. Marital distress is perceived in many cases; often the acknowledgement of prolonged trauma due to the severe illness of the child encourages the parents to assist their child through the weaning and to postpone any required couple-therapy until after the child's treatment.

8. Speech Language Pathologists (SLP): Non-traumatic stimulation of the oro-facial area is directed to correct earlier traumatic oral experiences. SLP also offers differentiated diagnosis of dysphagia and other pathologies of swallowing function. The risk of aspiration must be minimized and sometimes requires additional diagnostic procedures.

9. Individual occupational therapy sessions are used to promote tactile mastery, coordination, cognition and sensory integration through stimulation of the vestibular system. All tactile stimulation is done by offering "biological" textures since most tube-fed children are often oversensitive toward tactile stimulation of materials other than plastics.

10. Physiotherapy deals with motor tone and non-constructive feeding patterns. The frequency varies from 3-6 times weekly, and the sessions may include the parents.

Parents are encouraged to foster independence. It is common for parents to be overanxious and excessively protective of tube-fed children. Behavioural issues of this kind are frequent topics in the motor-oriented sessions.

11. Nutritional counselling advises the parents in the transition to normal age-appropriate nutrition or special diets if needed. Parents accustomed to tube feeding their child face the challenge of needing to learn about normal food and the specific tastes of their child within a short time-span.

12. Early intervention is helpful for integrating the new situation into everyday life. Organizing an effective team for aftercare is necessary.

Figure 1: The weekly Time schedule of the tube weaning program according to the „Graz Model“

Time	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
8 – 9	Ward round (daily)						
9 – 10	PhT	OT	SLP	PhT	SLP	Free for family activities	
10–11		PhT		Staff-meeting			
11–12	SLP		OT		PhT		
12 – 1	Play picnic (daily)						
1 – 2	Psy	Baby swimming	Baby swimming	PTDev	Nutr		
2 – 3	Ward round (daily)						
3 – 4	Nutr	PTP			OT		
evening	Family time						

5.2 Study design

The study was designed to investigate prospective the outcome of the tube weaning treatment “Graz Model” in respect to developmental age, growth, length and reduced unintended side-effects of long term tube feeding. For the design of this monocentric, quasi-experimental longitudinal study (cohort study) a single armed within-subject design with switching replications was chosen (Möller et al. 2003). Thus the study uses the waiting cue design, taking everybody in who applied for the sake of tube weaning in Graz. Due to the study design the participants were measured at three approximately equidistant measurement times (T1 to T3) as shown in Table 1:

Table 1: Measurement times

Measurement times	
T1:	2 months before the start of treatment and baseline measurement
T2:	Start of treatment: Admission in the tube weaning program according to the “Graz Model”
T3:	2 months after the start of treatment

At T1 the baseline measurement (as shown in 6.1 participants) two months before start of treatment was done. Between T1 and T2 no specific intervention focused on tube weaning was performed beside the normal medical care the child received on behalf of its specific underlying medical condition. T2 was defined as the start of the tube weaning program according to the “Graz Model.” T3 was defined at 2 months after the start of treatment.

The focused change from T1 to T2 was compared with the developmental change from T2 to T3 and functioned as control (T1 to T2) and experimental (T2 to T3) group.

The waiting group design is the best kind of proving the success by using the group in itself as a control. The prospective design allows assessing the patient and his parents before, during and after treatment. By that it is possible to evaluate effects of treatment in itself. A classical control group design would not serve as good as this design, because there are no patients affected by similar problems (total enteral feeding) who do not undertake treatment of whatever kind while the incidence group is treated. Secondly the pre-, post design makes sure that the scientifically researched subjects are in the same stable condition, medically spoken and the bias, like age, gender and kind of underlying disease cannot arise. The waiting group design was specially used in prospective psychotherapy research and proved to be able to detect therapy effects.

5.3 Outcome measure

The biometric data were measured and documented by the paediatric staff with our routinely documentation system ArchiMed (Dorda et al. 1999). The numbers of feeding problems occur before, between or after the feeding situation (unintended side effects of tube feeding) were measured with the Anamnestic Questionnaire TEFF (Wilken & Jotzo, 2007) filled in by the parents. If was measured how often per month, week or day vomiting, uncommon eating habits (like takes food only when playing, watching TV or be distracted another way), gagging, force feeding, food refusal and chocking.

The developmental age was measured from birth to 15 months with the Kent Inventory of Developmental Skills (KIDS) (Reuter et al. 2000) and from the developmental age 15 months onwards using the Child Development Inventory (CDI) (Ireton et al, 1977; Ireton 2004) applying the German translation made by Rauh et al. (1991).

5.3.1 KIDS

The Kent Inventory of Development Skills (KIDS) is a precise behavioural assessment instrument that yields reliable and valid measures of developmental status and progress in the developmentally young. Completed by the parents of the child being evaluated, the KIDS is appropriate for use with all infants healthy or at risk. It’s designed for children under 6 years of age who can have developmental disabilities and are developmentally under 15 months of age.

The KIDS has been used to assess the development status of healthy infants in a well-baby clinic, premature infants, infants with craniofacial anomalies, young children with developmental disabilities, infants of teenage mothers and others. The age-norms have been developed and published in the U.S., the Netherlands, Spain, Hungary, Germany and the Czech Republic. Through its use in various contexts and countries the KIDS has shown psychometrically robust and important clinical a research purposes.
The Inconsistency (INC) Scale was designed to identify logical developmental inconsistencies in a caregivers report. A high INC score could indicate that the caregiver was careless or misunderstood the KIDS items or directions. The INC consists of a 53 pairs of items that were selected because the items in each pair were logical and developmental dependent on one another (e.g. Item 15: "Will play with toys alone for 15 minutes" depends on Item 138 "Plays alone with toys"). An INC score higher than 4 is a rare occurrence and needs to be checked.
The KIDS should be completed by an informant who is responsible for a significant portion of the child's daily care, like a parent, a teacher, a nurse, a baby-sitter or a childcare worker. Caregivers who have a sixth-grade evaluation will be able to complete the KIDS within about 30 minutes.

5.3.1.1 Subscales of the KIDS

To maximize reliability and prescriptive utility, the KIDS was constructed with 252 items that describe observable behaviours that are characteristic for an infants in the first 15 months of life. These items cover a brad range of behaviour divided into five Domains on the basis of their content. The developmental age based on the full scale development score can be used for the determination of the overall development status.

5.3.1.1.1 Cognitive Domain

Items in the Cognitive Domain describe various intelligent behaviour like: sensomotoric coordination, development of object permanence, responses and attitude to environmental changes, imitation, intention and meaning as well as reaction and simple responses to visual, audio and social experience (Reuter et al. 2000).

5.3.1.1.2 Motor Domain

The Motor Domain items describe the child's ability from being held in arms of an adult, to rolling, crawling and standing up to the attainment of independent upright mobility. Paralleling this gross motor development is the fine motor development that begins by a crude reflexes grasp, proceeds through the attainment of pincer grasp and culminates in two-hand manipulation of toys and tools (Reuter et al. 2000).

5.3.1.1.3 Communication Domain

The Communication Domain describes the development of pre-language skills beginning with vocalization repertoires and both verbal and nonverbal expression of feeling, responses to simple communications from other people, the recognition of names and imitation of sounds. By the end of their first year children understand the concept of words as sounds that convey meaning and they can be said to use language (Reuter et al. 2000).

5.3.1.1.4 Self-Help Domain

The Self-Help Domain encompasses the early stages of learning to care for one self. In the first year, most of this development centres on eating behaviours. Therefore many items in this domain describe the developmental steps children take to go from nursing form the breast or bottle to being able to deed themselves and drink from a cup. In addition, this domain contains items that describe the beginning of rudimentary dressing and grooming behaviours that can be encouraged by caregivers (Reuter et al. 2000).

5.3.1.1.5 Social Domain

Items in the Social Domain assess a child's emerging abilities to engage in reciprocal social interactions with familiar adults, teachers and other children. Included in this domain are the early development of expressive skills, the ability to maintain pleasant social interchanges for longer periods, the development of skills for dyadic interactions and the ability to acceptable express negative feelings and resistance towards others. Children begin their social development by attending and reacting to the actions and expressions of other persons. At the end of the first year they are able to sustain useful social exchanges with strange and familiar adults and children (Reuter et al. 2000).

5.3.1.2 Standardization of the KIDS

The sample that provides the normative foundation of the KIDS consisted of n = 706 children between the age 0.3 months and 15.8 months. All Infants of the normative group were born full-term and without any significant medical complications and they had not suffered any serious illnesses since birth. Beside this group, two groups of children with disabilities (age 0 – 36 months, n= 313 and age 36 - 72 months, n = 300) were combined with the normative group and delivered the calculation of the raw scores in correlation of the developmental scores to get reliable and valid measures of the developmental status (Reuter et al. 2000).

The scale consistence was measured with the inter correlation of the developmental and raw scores from the sub and the full scale. Each subscale had with the other subscales and with the full scale a high coefficient from .88 to .98. To assess the retest reliability there was a second assessment of the children between 13 – 139 days after with a correlation from .91 to .94. 20 parents of assessed children both mothers and fathers filled out the questionnaire. The calculated measures of the scales show a correlation from .85 to .95. For the concurrent validity the Bayley Scales were used. N = 38 children of different age show a mean correlation of the full and subscales around .90 (Müller 1993).

Prochazkova et al. (1997) show in a longitudinal study data of n = 36 health full-term infants assessed monthly between 1 and 14 months with the Kent Infant Development Scale. A full licensed and trained psychologist assessed the same children at 3, 6, 9 and 12 months with the Bayley Scales. The assessment of the Kent Infant Development Scale correlated significant with the Bayley Scales assessment at 6 months (Rho = .43, p = .0088), at 9 months (Rho = .66, p = .0001) and at the 12 months (Rho = .62, p = .001). The authors conclude that the Kent Infant Development Scale delivers reliable data of infant development within the first 14 months. The items of the individual domains are highly internal consistent.

5.3.2 CDI

The Child Development Inventory (CDI) is a research based parent questionnaire with wide acceptance nationally and internationally. Versions exist in Spanish, German, Russian, French, Polish, Chinese, Japanese, Korea, Portuguese and Arabic. The CDI has been researches in Canada, Chile, Portugal, Russia and Germany. The CDI for the assessment of children from 15 months to six years of age and for older children who are judged to be functioning in the one to six years range. It contains 270 statements that describe the developmental skills of young children that are observable by parents in every day situations. Scoring is done by counting the number of Yes responses for each of the scales using a single scoring template. The scores are recorded in the profile sheet that pictures the child’s development in comparison to norms for children age.

The inventory format may be inappropriate for parents of some racial and cultural groups and for parents with less than high school education. The validity of DCI results depends on the parent’s ability to read and understand the Inventory instructions and items (Ireton 2005).

5.3.2.1 Subscales of the CDI

The 270 development items are grouped to from scales including: Social, Self Help, Gross Motor, Fine Motor, Expressive Language, Language

Comprehension, Letter, Numbers and General Development. These scales measure the areas of development and learning that are identified in the child development literature, various psychological tests and early childhood/special education eligibility guidelines.

5.3.2.1.1 Social Domain

The Social Domain includes interaction with parents, children and other adults from individual interceptions to group participation. The child's maturity is reflected in the scales results and by the presence or absence of behavioural problems (Ireton 2005).

5.3.2.1.2 Self Help Domain

The Social Domain includes eating, dressing, bathing, toileting, independence and responsibility. The development of these skills is based partly on the child's drive towards self sufficiency, expressed in the words "I want to do it myself" (Ireton 2005).

5.3.2.1.3 Gross and Fine Motor Domain

The Gross Motor Domain includes walking, running, climbing, jumping, riding, balance and coordination. The Fine Motor Domain includes eye-hand coordination from picking up objects to scribbling and drawing. Both Domains describe the child's development of physical skills. They include large muscle and whole body coordination and the development of more finely tuned eye-hand coordination (Ireton 2005).

5.3.2.1.4 Expressive Language and Language Comprehension Domain

The Expressive Language Domain includes expressive communication from simple gestures, vocal and verbal behaviour to complex language expressions. The Language Comprehension Domain includes Language understanding from simple comprehension to understanding of concepts (Ireton 2005).

5.3.2.1.5 Letters Domain and Numbers Domain

The Letters Domain includes knowledge of letters and words, including printing and early reading. The Numbers Domain includes knowledge of quantity and numbers from simple counting to solving simple arithmetic problems (Ireton 2005).

5.3.2.1.6 General Development Domain

The General Development Domain is a summary scale that provides an overall index of development. It includes 10 of the most age discriminating item from each of the development scales (Ireton 2005).

5.3.2.2 Standardization of the CDI

The age norm and the validity are based upon a sample for 568 children of a community sample, N = 303 five-year from different Kindergartens, N = 248 less than four-years old, N = 248 three-years old, N = 198 two years old and N = 227 one-years old. The developmental scales correlate closely with age (r= .84).

Reliability of the developmental scales, correlation among the CDI scales and correlation of the General Development Scale with the individual development scales at the selected ages is given (Ireton 2005).

The inventory was tested using the Bayley Scales (n = 568) as a comparison and showed validity and reliability (Rauh & Berry 1991).

5.3.3 Combination of KIDS and CDI

To cover the whole age range of the treatment's patients, we combined the KIDS and the CDI sub-scale: gross motor and fine motor of the CDI by adding the means of the developmental age to a new combined subscale motor. The same procedure combined the scales expressive language and comprehension of language of the CDI to the new scale communication. The new subscales motor and communication are comparable to the scales of the KIDS respectively in respect of the sub scales content.

Because of the young developmental age of the sample, the results of the Letters and Numbers domains were not used. The subscale cognitive development was just measured for the children measured with the KIDS because it does not exist in the CDI.

The KIDS includes 252 items, the CDI consists of 270 items. Each item describes a child's behaviour. The parents are asked to report, whether the child can or cannot perform a defined behaviour. The results are presented on a profile – comparing to a norm population, which was used to standardize the tests – of each child's development.

Both developmental inventories rely on parent's reports, what has been shown to be a good clinical assessment. Besides the international population (see 6.1 Participants) of our sample made this way of assessment the best one. The KIDS and CDI avoids the bias of artificial test environments (Reuter et al. 2000).

Both inventories take about 30 minutes time and they are absolutely non-invasive for the child and independent of the child's emotional willingness to cooperate. The KIDS and the CDI were sent digital and independent of place and time. The results were transformed first into Excel and secondly into SPSS databases. The date T1, T2 and T3 were measured when the whole inventory and questionnaire was returned fully filled in per Email or T2 per Hand.

5.3.3.1 Dependent variables

The study was based on the following dependent variables: developmental age (CDI, KIDS), developmental deficit (developmental age minus chronological age), weight and length (kg and cm assessed from the medical staff) and the socio economic aspects (Hollingshead Four Factor Index).

The Hollingshead Four Factor Index of social status was designed and testes by the Yale University. It counts the school degree, vocational qualification, the

kind of employment and the earning per month to a Index between 0 to 22. The Hollingshead Four Factor Index is widely used for scientific reasons to detect bias through socio economic aspects (Hollingshead 1975).
To realize comparability, we combined the raw scores of the Hollingshead in three comparable groups.

5.3.3.2 Independent variables

The independent variable were: baseline vs. treatment, weaned or not weaned (paediatric protocol), severity of diseases (International Classification of Functioning, Disability and Health), group of main pathology (paediatric protocol) and chronological age of study population.

Weaned or not weaned were defined for children with NGT tube by the final and constant removal of the tube. For children with PGT tube weaning was as total cessation of the tube feeding.

The severity of diseases was assessed according to the International Classification of Functioning, Disability and Health (ICF; Simeonsson et al. 2003, World Health Organization, 2001). The offered six scores in ICF were done by paediatricians, neurological specialists and the parents. Out of statistical considerations we grouped 1-3 as none to moderate and 4-7 as over average to extreme.
The paediatric staff did the classification of the group of main pathologies.

5.4 Participants

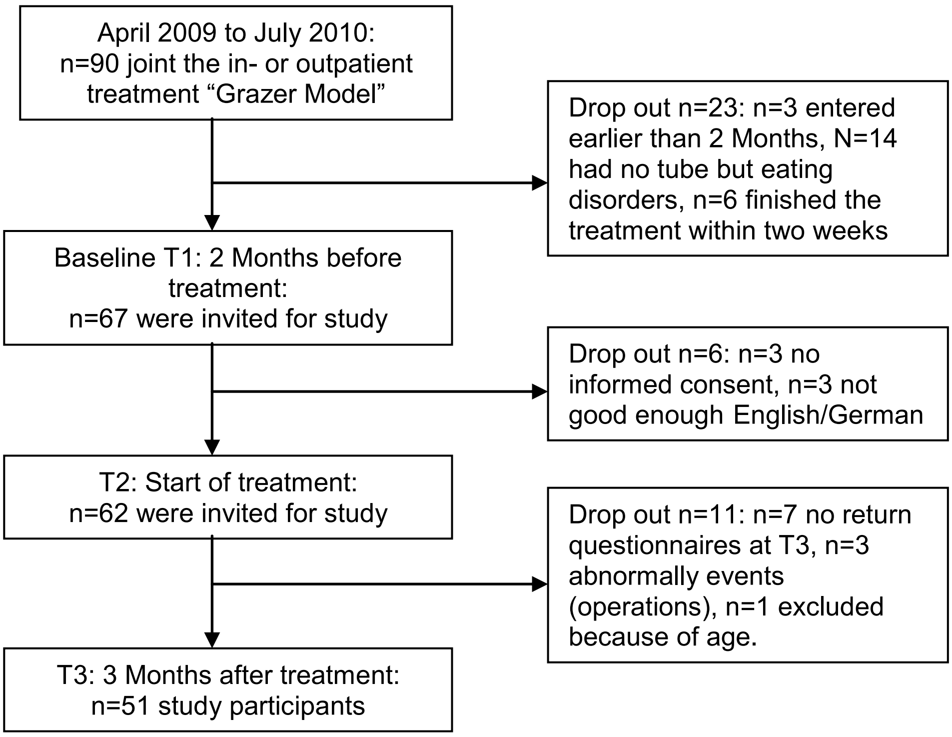
All children who took part in the study were transferred to the treatment as “not weanable.” The analysis of their data has been collected per protocol.

Children were eligible for the study if they met the following inclusion criteria: Tube feeding had been commenced as medical intervention for reasons of not meeting an adequate oral nutritional intake, age between 0-6 years, enrolled in the waiting list for the in- or outpatient tube weaning according to the “Graz

Model" at least 2 months before treatment, join the whole 3 week standardized program and return the last questionnaire 90 days after start of treatment, spoke well English or German (no need for a interpreter) and signed a written informed consent. Exclusion criteria were: danger of aspiration, abnormally events like operations or participation in another tubes weaning program or special program to foster the development within study time.

Patient's collection was from February 2009 – September 2010: n = 90 patients joint the treatment and n = 67 satisfied the inclusion criteria at baseline and were invited to join the study. Twelve of these 67 patients had to be excluded in the course of the study: 3 refused to give informed consent, 7 didn't return the questionnaire at T3, in three language skills turned out to be too weak, three had abnormally events (operations) and one child was excluded because it was older than 6 years. So 51 children could be assessed within the study and were examined from February 2009 – September 2010.

Table 2: Flow diagram with drop out



The Ethical Commission of the Medical University Graz granted ethical approval for the study protocol and written informed consent was given by all patents/caregivers before their child became part of the study.

5.5 Statistical Analysis

The statistical analysis was performed with depended t-tests and (multivariate) analyse of variance for measuring repetitions. The levels of measurement of the used metrics are mostly of metric quality. The statistical mathematic requirements for the use of parametric methods are mostly given. If not and non-parametric calculations are used, this is always denoted. Statistical significance was defined as $p>0.05$ tested in both sides. Significance $p>0.05$ are signed as $p=.05^{*}$ (significant), $p>0.1$ as $p=.01^{**}$ (high significant), $p>0.001$ as $p=.0001^{***}$ (most significant). There is no α- adjustment. Only patients with completed data set are part of the statistical analysis. No missing data had been replaced.

The formal sample size calculation by the chosen study design and 51 patients shows adequate statistical power: For a medium-level effect of $d=.5$ with a retest reliability of .60 21 patients at two measurement times would be necessary.

6. Results

6.1 Participants

N=51 participants joined the whole study and showed the following characteristics at baseline (see Table 3): 61% were male weighing (mean) 10,6kg (± 2,8; range 6,5-17,5), length of 83,1cm (± 11,2; range 64-124). 100% were exclusively tube fed. Age at admission was 28,9 months (± 16,4; range 6-125) the developmental age was 13,1 months (± 8,3; range 1-42). The duration of tube feeding was 22,61 months (± 14,88; range: 3 - 62) which is 65,56% (± 25,32; range: 12,13 - 98,64) of their lifetime. 41% of the patients had a NG Tube, 30% a PEG and 27% a PGT or a Gastro button. The severity of disease (ICF) of 51% of the patients was none to moderate and 49% over average to extreme.

The predominant pathology were in 13% genetic syndromes, 11% complicated prematurity, 7% malformation or disease of the gut, 6% congenital malformations of the heart, each 4% neurological diseases and pulmonary problems, 3% congenital metabolic diseases and 3% were healthy with no somatic diagnosis.

The international group of participants came of 66,6% from European countries, 19,6% from Australia or New Zealand, 7,8% from South Africa, 3,9% from USA and Canada and 1,9% from India.

The numbers of feeding problems occur before, between or after the feeding situation (unintended side effects of tube feeding) were at T1 234,22 (±182,99; range: 182,75 – 285,68), at T2 230,61 (± 181,06; range: 179,68 – 281,53) and at T3 86,69 (±97,28; range 59,33 – 114,05).

The socioeconomic status (Hollingshead Four Factor Index) was in 14 slightly about average (average = index 12) for industrialized western countries.

Table 3: Baseline characteristics at T1 of the N=51 study participants:

	N	*%*
Nr. of patients included	51	100
Male	31	60,8
Female	20	39,2
Type of tube		
NGT	21	41,2
PEG	16	31,4
Button	14	27,5

	M	*range*	*SD*
Age at baseline (months)	28,94	5-67	16,365
Developmental age at baseline (months)	13,07	1-35,5	8,27
Weight at baseline (kg)	10,56	5-16,5	2,81
Length at baseline (cm)	83,09	59-110	11,24
Duration of tube feeding before weaning (months)	23,68	3-62	15,99
Duration of tube feeding (%of lifetime)	65,56	12,1-98,6	25,32

Serverness of disease[1]	*N*	*%*
None – moderate	26	51
Over average – extreme	25	49

[1] International Classification of Functioning, Disability and Health, WHO; Part 1a, 1b and 2. Group 1-3 are combined to “none to moderate”, group 4-7 as “over average to extreme.

Group of main pathology	*N*	*%*
Genetic syndromes	13	25,5
Complicated prematurity	11	21,5
Malformation or disease of the gut	7	13,7
Congenital malformation of the heart	6	11,8
Neurological disease	4	7,8
Pulmonary problems	4	7,8
Congenital metabolic disease	3	5,9
Healthy, no diagnosis on Axis 3 of ZTT	3	5,9

Socioeconomic status (Hollingshead Four Factor Index)

M	*range*	*SD*
13,78	7-19	3,02

Countries of origin	*N*	*%*
Europe	34	66,6
Australia and New Zealand	10	19,6
South Africa	4	7,8
USA and Canada	2	3,9
India	1	1,9

Note. NGT: nasogastric tube; PEG percutaneous endoscopic gastrostomy; ZZT: Zero to Three

The time between T1 and T2 was 57 (±5,3) days; time between T2 and T3 was 81 (±11,5) because of irregular return of some of the last questionnaires. This needs to be considered when looking at the following data.
The developmental age of N = 23 patients were less or 15 months, so there were tested with the KIDS, N = 28 were tested with the CDI.
The Inconsistency Scale (INC) score was in mean 1,8 (± 1,5) points and all parents who filled out the developmental inventories had at least a sixth-grad education and were fully capable of understanding to read and understand the

inventory instructions and items. There were no absence or missing responses within the inventories.

6.2 Changes of Developmental Age

6.2.1 General Development

The measured values of the general development at the three measurement times was at T1 13,07 (±8,27; range 1,00-35,50), at T2 13,99 (±8,47; range 1,00-35,75) and at T3 16,88 (±9,48; range 2,20-39,00) as seen in table 4.

Table 4: Changes of Developmental Age (Subscale General)			
	Mean	Standard Deviation	N
T1 Developmental Age	13,07	8,27	51
T2 Developmental Age	13,00	8,47	51
T2 Developmental Age	16,88	9,48	51

All changes have a high power of inner subject (F=103,70), are highly significant (p=.000***) and show a strong effect (Eta^2=.657) as shown in Figure 1 and 2.

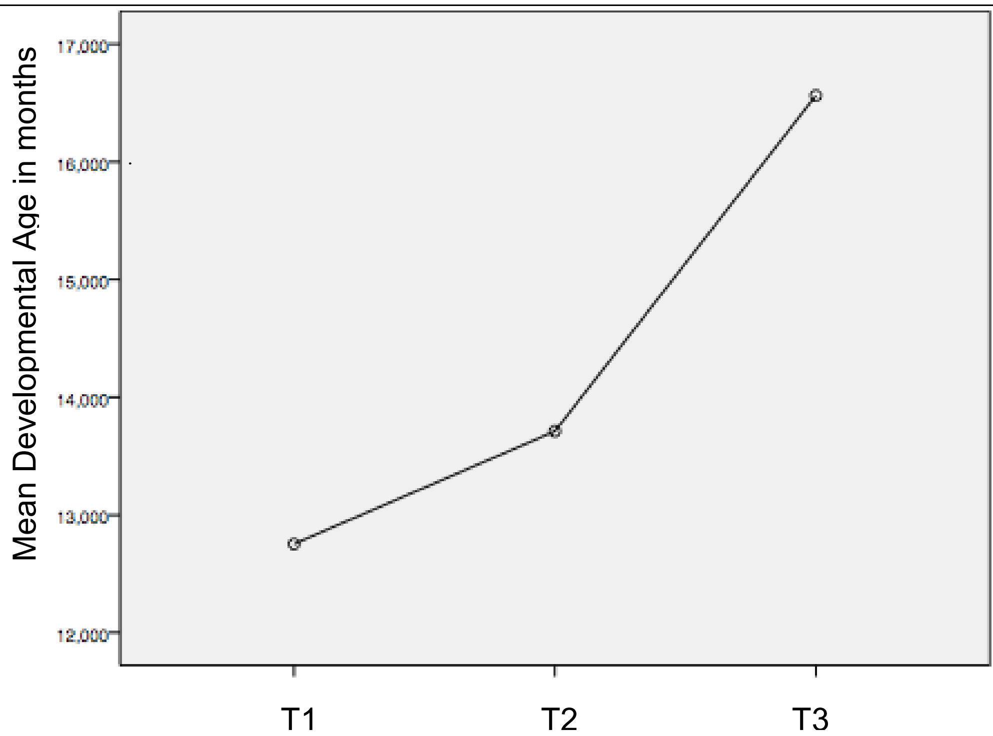


Figure 1: Changes of Developmental Age

The mean developmental age was at T1 13,07 (±8,27), T2 13,99 (±8,47) and T3 16,88 (±9,48). The power of inner supject was F=103,703 (Greenhouse-Geisser), the result are most significant p=.000*** and show a strong effect (part. Eta^2: .675); Post-Hoc_{LSD} (all p<.000).

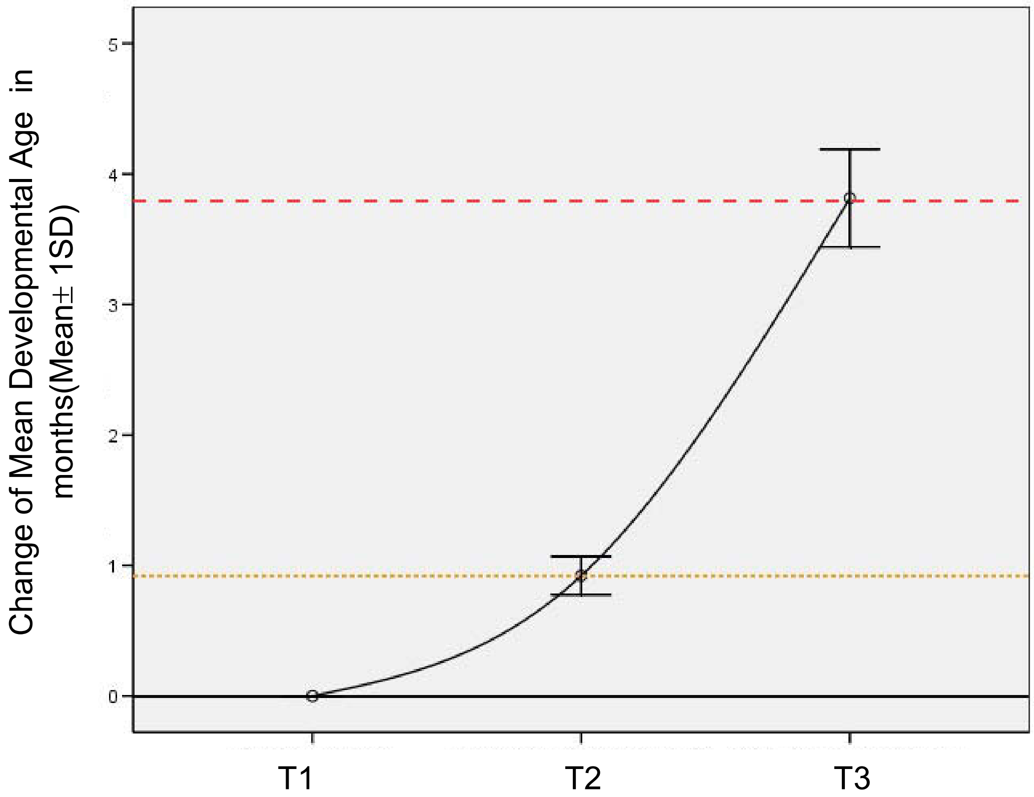


Figure 2: Changes of Developmental Age over time course

Changes of developmental age over the time course. Re-test Reliability: T1 vs T2 r=.992; T2 vs T3 r=.985. Innersubjekteffekte: F=103.798 (Greenhouse-Geisser); p=.000*** (part. Eta^2: .675); Post-Hoc (all p<.000). The figure shows an most significant effect. The dashed lines underline the results at T1, T2 and T3.

The control group (T1 – T2) gained in nearly two months (T1 to T2, mean 57 days) 0,92 months (±1,04) development. The experimental group (T2 – T3) gained in roughly the same period of time (T2 to T3, mean 81 days) 2,89 months (±1,86) development.

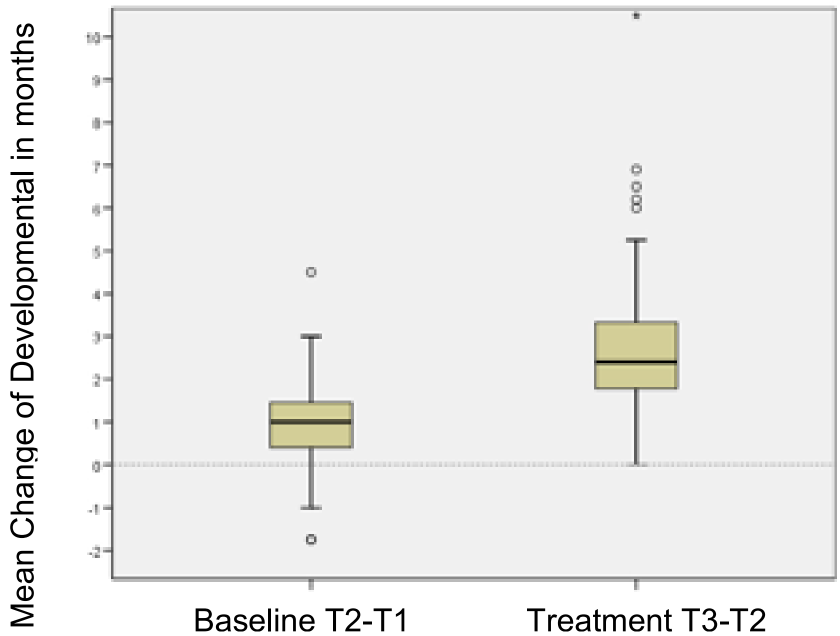


Figure 3: Changes of the development between T1-T2 and T2-T3 (Subscale General)

The changes of development between T1 and T2 are shown. Power within subject: F=103.199 (Greenhouse-Geisser); p=.000*** (part. Eta^2: .674); Post-Hoc (all p<.000). The changes are most significant with a strong effect. Multivariate Tests are most significant as well: F=61.856 (Pillai-Spur); p=.000***. The dashed line shows no development.

In summery the data showed that the experimental group gained a big amount of general development and the change compared to the control group is significant and has a strong effect.

Comparable but more precisely results are presented by looking at the change of development of the subscales in the next passage.

6.2.2 Subscale Social

The subscale social changed from T1 12,57 months (±7,78; range 10,38-14,75) to T2 13,64 months (±7,59; range 11,51-15,77) to T3 17,07 months (±9,19; range 14,49-19,66). The developmental growth of the control group was 1,07 month (±2,05; range 0,50-1,65). The growth of the experimental group after treatment was 3,43 months (±3,14; range 2,55-4,32).

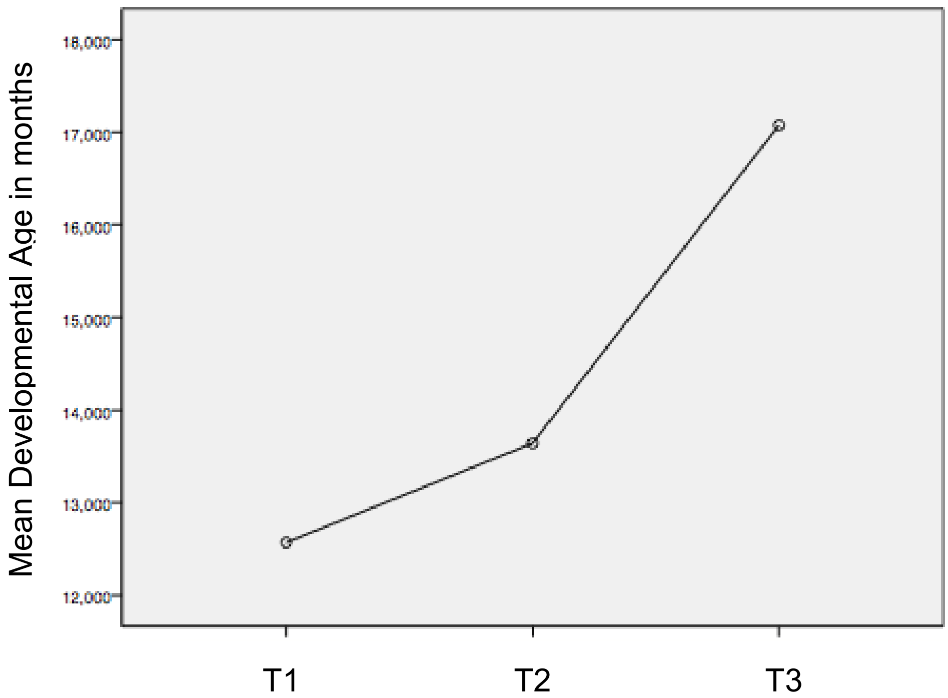


Figure 4: Developmental changes of the subscale Social

The significant change between the three measurement points is shown. F=71,41, p=.000***, Eta2=.76. The Eta2 shows that there is strong effect.

The post-hoc test (LSD) of the subscale social shows a significant change between the control [T1 vs T2 MD=1,05 (p=.000***) and experimental group (T2 vs T3 MD=2,46 (p=.000***)].

6.2.3 Subscale Self help

The subscale self help changed from T1 9,71 months (±7,45) to T2 10,73 months (±7,86) to T3 14,34 months (±9,68). The developmental growth of the control group was 1,01 month (±1,42; range 0,61-1,41). The growth of the experimental group after treatment was 3,61 months (±3,24; range 2,70-4,53).

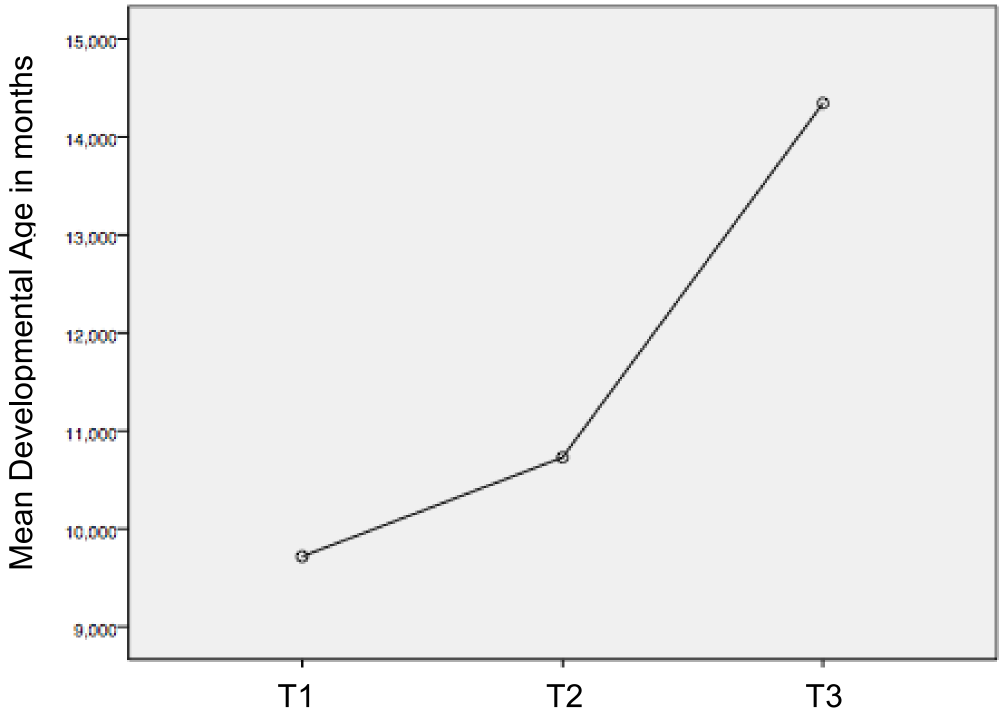


Figure 5: Developmental changes of the subscale Self help

The significant change between the three measurement points is shown. Inner subject was F=71,06, correlation p=.000*** and the Eta^2=.76 shows a strong effect.

The post-hoc test (LSD) for the subscale self-help shows a significant change between the control [T1 vs T2 MD=1,01 (p=.000***) and experimental group (T2 vs T3 MD=3.61 (p=.000***)].

6.2.4 Subscale Motor

The subscale motor changed from T1 12,87 months (±7,77; range 10,69-15,06) to T2 13,81 months (±8,17; range 11,51-16,11) to T3 16,90 months (±9,79; range 14,15-19,65). The developmental growth of the control group was 0,93 month (±2,77; range 0,15-1,71). The growth of the experimental group after treatment was 3,09 months (±2,33; range 2,43-3,75).

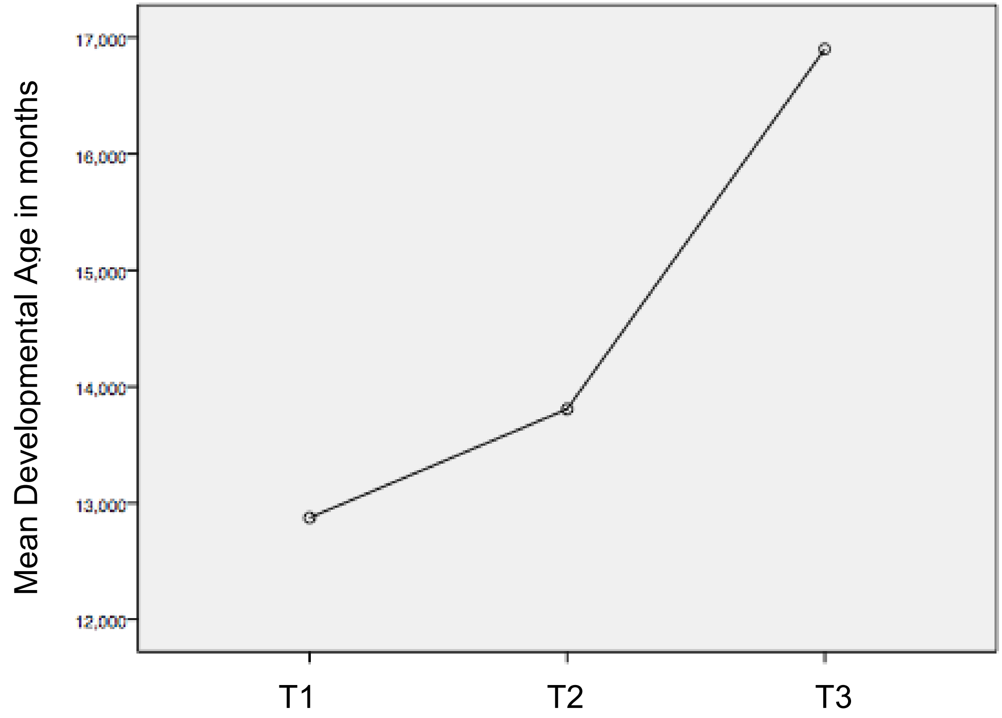


Figure 6: Developmental changes of the subscale Motor

The significant change between the three measurement points is shown. The inner subject was F=83,34, the correlation p=.000*** and a strong Eta^2=.80.

The post-hoc test (LSD) for the subscale motor shows a significant change between the control [T1 vs T2 MD=0.94 (p=.020*) and experimental group (T2 vs T3 MD=3.09 (p=.020*)].

6.2.5 Subscale Communication

The subscale communication changed from T1 12,89 months (±8,09; range 10,61-15,17) to T2 13,61 months (±8,20; range 11,30-15,91) to T3 17,17 months (±9,21; range 14,58-19,76). The developmental growth of the control group was 0,72 (±2,16; range 0,11-1,32). The growth of the experimental group after treatment was 3,56 months (±2,16; range 2,95-4,17).

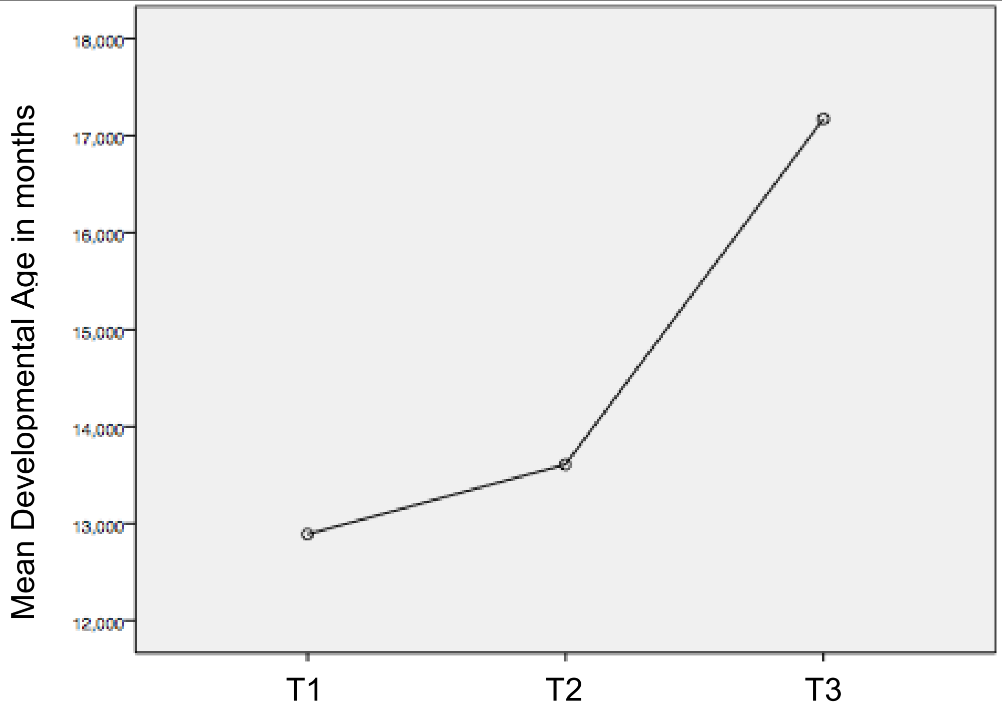


Figure 7: Developmental changes of the subscale Communication

The significant change between the three measurement points is shown. The inner subject was F=83,34, the correlation p=.000*** and the Eta^2=.80, what is a strong effect.

The post-hoc test (LSD) for the subscale communication shows a significant change between the control [T1 vs T2 MD=0.72 (p=.021) and experimental group (T2 vs T3 MD=3.56 (p=.000***)].

6.2.6 Summery of the developmental changes of the subscales

When the different subscales (dependent variables (DV): differences from T2 vs T1 and T3 vs T2) of developmental age were tested simultaneously with a dependent ANOVA, the time effect stayed significantly with $F_{multivariat}=17,24$; $p=.000$ $Eta^2= .595$.

With a univariate testing the subscale self-help showed the best developmental change ($Eta^2=.439$) followed from the development in the communication ($Eta^2=.430$), social ($Eta^2=.318$) and motor ($Eta^2=.282$).

Table 5: Summery of developmental changes of the subscales

Subscale	F	p	Eta^2	MD T1-T2	CI	MD T2-T3	CI
Social	23,35	.000***	.318	1,07	0,50–1,65	3,43	2,5–4,31
Self-help	39,09	.000***	.439	1,01	0,61-1,41	3,61	2,70-4,52
Motor	19,67	.000***	.282	0,93	0,15-1,71	3,10	2,44-3,75
Communication	37,11	.000***	.430	0,72	0,11- 1,32	3,56	2,95-4,17

6.3 Changes of the Developmental Deficit (Diffage)

As shown in Table 3: Baseline characteristics the study participants had a mean chronological age of 28,95 months (±16,36) and a developmental age of 13,07 months (±8,27) at baseline.

At T1 the participants showed therefore a developmental deficit (Diffage) of -16,01 months (±13,37), at T2 it was - 17,80 months (±13,29) and at T3 it was - 17,63 months (±12,35) with significant changes shown in Figure 6.

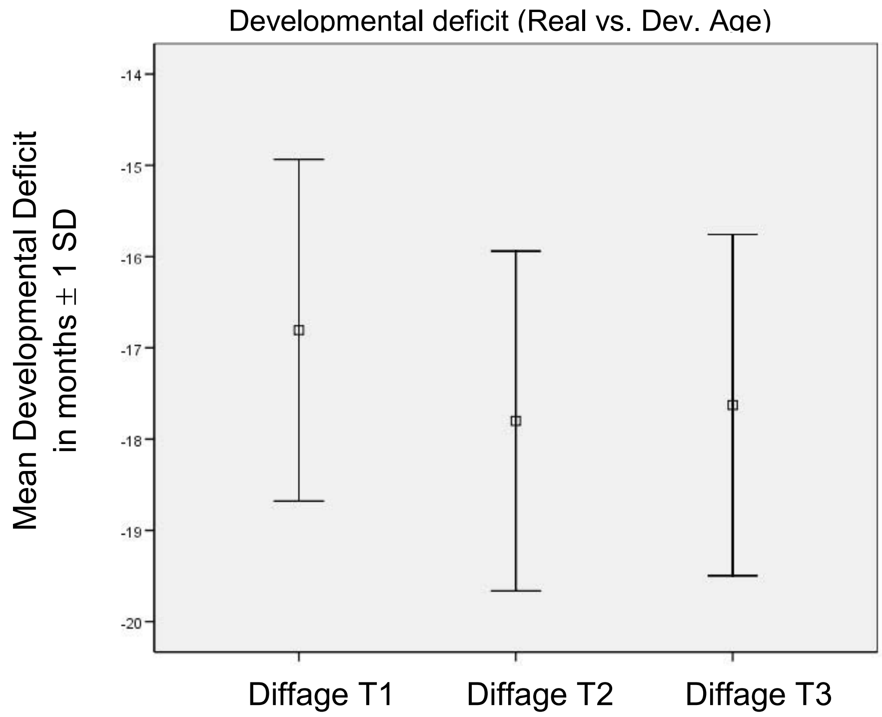


Figure 8: Changes of the developmental deficit

At T1 the participants showed a developmental deficit of -16,01 months (±13,37), at T2 it was - 17,80 months (±13,29) and at T3 it was - 17,63 months (±12,35). The Greenhouse-Geisser shows an F=7.63, the changes are high significant (o=.001**) and an effect with Eta2=.132. The effects between the groups are most significant: The Post-Hoc (LSD) of the control group (T1-T2) p=.000*** and experimental group (T2-T3) p=.496.

The control group (T1 – T2; mean 57 days) developed 0,92 months (±1,04) and with that their developmental deficit up to 0,99 months (±1,04). The experimental group (T2 – T3; mean 81 days) with treatment developed 2,89 months (±1,86) and reduced their developmental deficit for 0,17 months (±1,81) within the measurement times. These findings are most significant as shown in Figure 9:

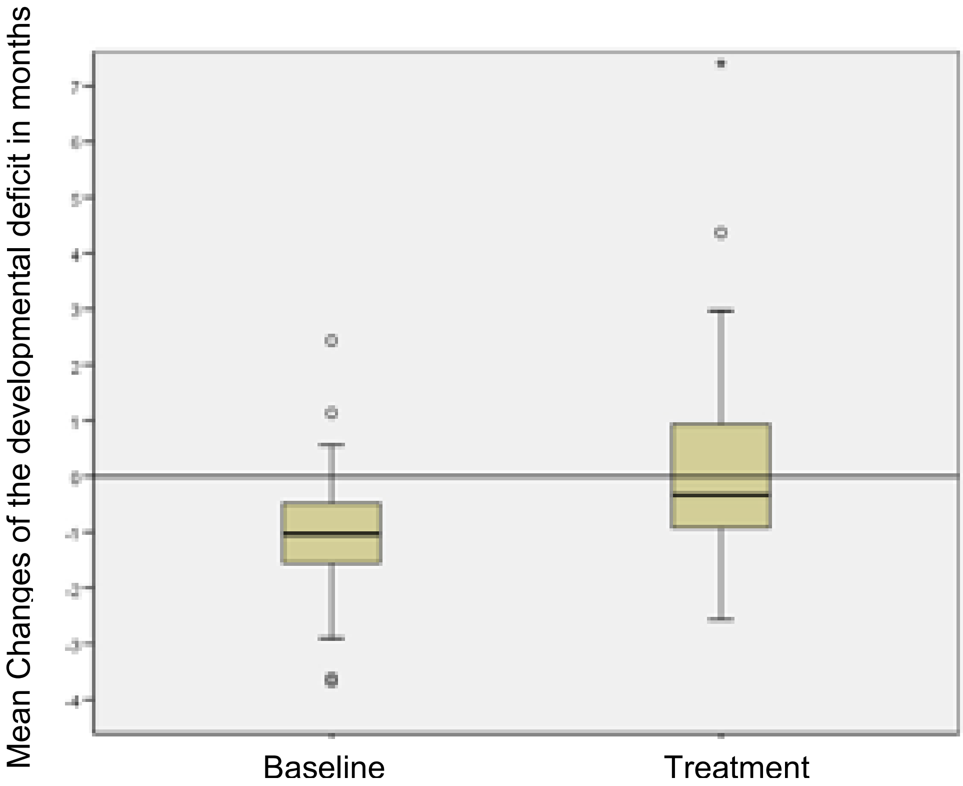


Figure 9: Mean Changes of the developmental deficit

The developmental deficit of the control group (T1–T2) grows by 0,99 months (±1,04). The experimental group (T2–T3) reduced their developmental deficit by 0,17 months (±1,81). The multivariate testing show F=48,58, most significant results (p=.000***) and a good effect with Eta2=.665.

In sum, the control group increased their developmental deficit whereas the experimental group could increased the development so fast, that the developmental deficit was overcome and the participants even gained a little general development.

6.4 Cognitive Development for a Subpopulation n=23

For the participants tested with the KIDS Inventory (n=23, developmental age >15 months) the cognitive development was tested additionally to the other subscales.

The measurement were at T1: 5,6 (±2,85; range 4,37-6,83), at T2: 6,57 (±3,13; range 5,22-7,93) and at T3: 8,93 (±3,59; range 7,41-10,44) months as shown in figure 10.

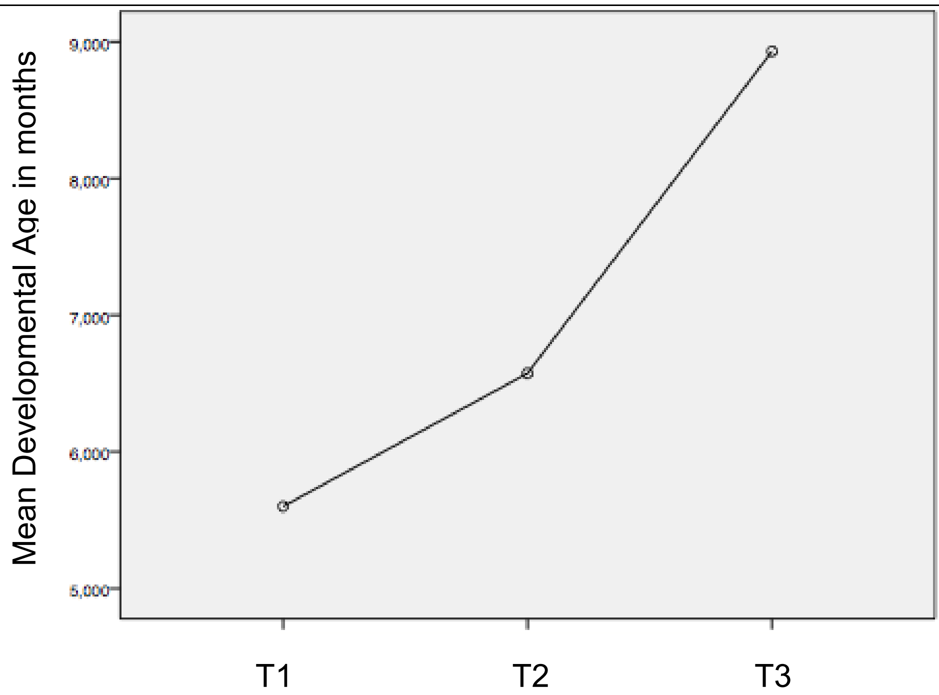


Figure 10: Cognitive Development for a Subpopulation n=23

The developmental changes T1: 5,6 (±2,85; range 4,37-6,83), T2: 6,57 (±3,13; range 5,22-7,93) and T3: 8,93 (±3,59; range 7,41-10,44) months. The F_{mulit} (T1 - T3) = 23,65, p=.000***, Eta2=.948.

The developmental change between control and experimental group was 2,36 months. These effects were most significant as seen in Table 5.

Table 5: Summery of developmental changes of the subscales							
Subscale	F	p	Eta^2	MD T1-T2	CI	MD T2-T3	CI
Social	71,41	.000***	.764	1,05	0,71-1,40	2,46	1,75–3,16
Self-help	71,96	.000***	.764	0,64	0,43-0,86	2,68	1,97-3,38
Motor	83,34	.000***	.791	0,85	0,61-1,07	1,59	1,18-2,00
Communication	94,64	.000***	.811	0,75	0,37- 1,12	2,84	2,19-3,49
Cognitive	12,09	.000***	.355	0,97	0,65-1,29	3,14	0,91-5,36

In summary we see that the cognitive development of the subgroup of n=23 children developed comparable to the other subscales. The cognitive development of the experimental group was more strong but also more heterogeneous.

6.5 Development of Weight, Length and BMI

In the following passage will be the description of the development of the weight (in kg), length (in cm) and Body-Mass-Index (BMI) of the participants between the measurement times.

6.5.1 Weight

The weight of the participants was at T1 10,55 kg (±2,81; range 6,5-17,5), at T2 10,81 kg (±2,99; range 6,6-18,0) and at T3 10,98 kg (±3,05; range 6,5-21,3). The change of weight of the control group (T1 – T2) was in mean 0,26 kg and the weight changes from the experimental group (T2 – T3) in mean 0,17 kg. As seen in Figure 11 the effects are significant.

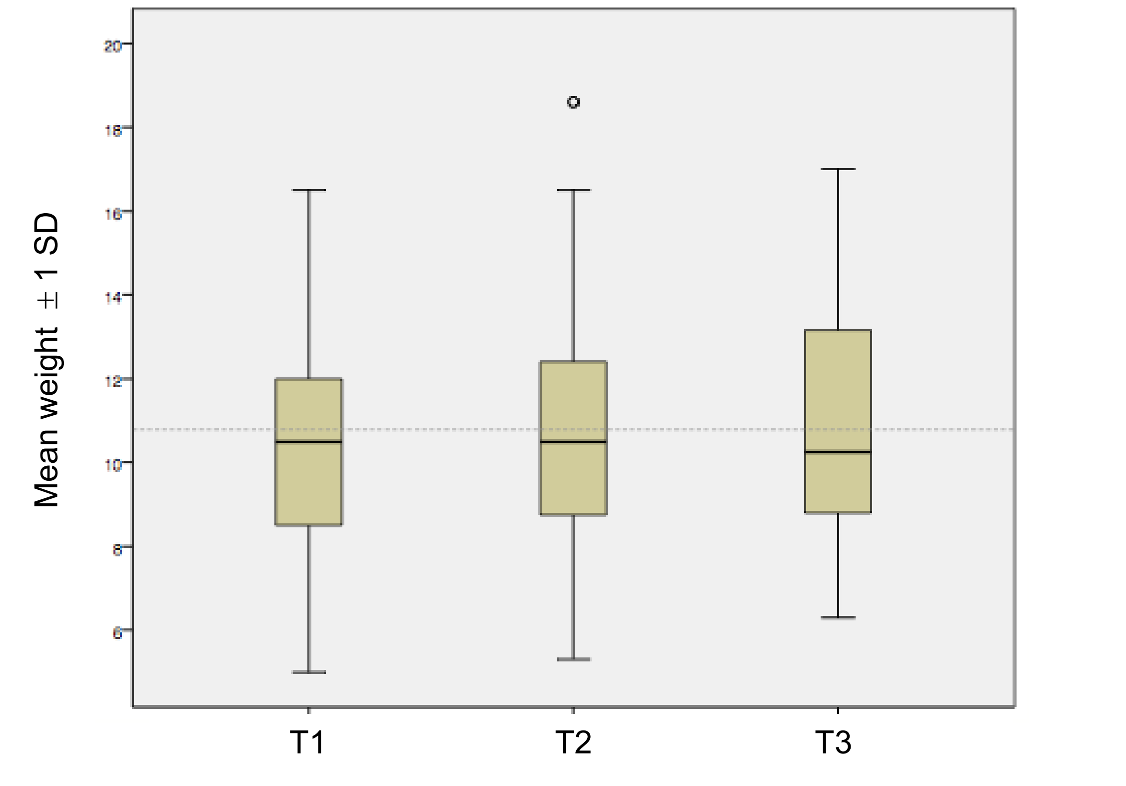


Figure 11: Development of weight

The mean weight ± SD: T1 10,55 (±2,81) kg, T2 10,81 (±2,99) and T3 10,98 (±3,05). The dashed line is the overall mean weight of the three measurement points with 10,78kg. The quantity testes was F=5.48, the result are significant (p=.012*) and the effect was Eta^2=.099

6.5.2 Length

The length of the participants was at T1 83,09 (±11,24; range 59-124) cm, at T2 84,19 (±11,24; range 59-126) cm and at T3 86,78 (±10,37; range 63-130) cm. The change of weight of the control group (T1 – T2) was 1,10 cm and the weight change from the experimental group (T2 – T3) was 2,59 cm. As seen in Figure 12 the effects are significant.

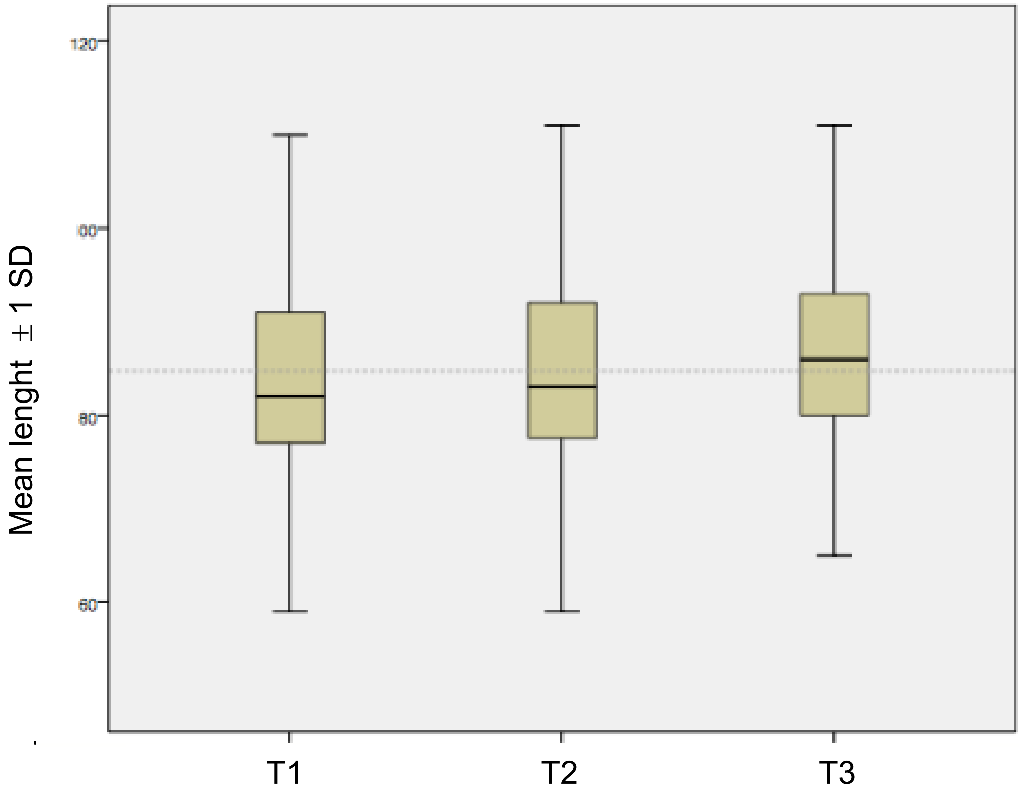


Figure 12: Development of length

The y-axis shows the mean length ± SD: T1 83,09 (±11,24) cm, T2 84,19 (±11,24) and T3 86,78 (±10,37). The x-axis shows the three measurement times. The dashed line is the overall mean length of the three measurement points with 84,69kg. The quantity testes was F=55,9, the result most significant (p=.000***) and the effect was Eta^2=.528

6.5.3 BMI

The BMI of the participants was at T1 15,10 (±1,63), at T2 15,04 (±1,59) and at T3 14,32 (±1,56). The change of the BMI of the control group (T1 – T2) was with -0,06 stable compared to the change of the experimental group (T2 – T3) with -0,72. As seen in Figure 13 the effects are significant.

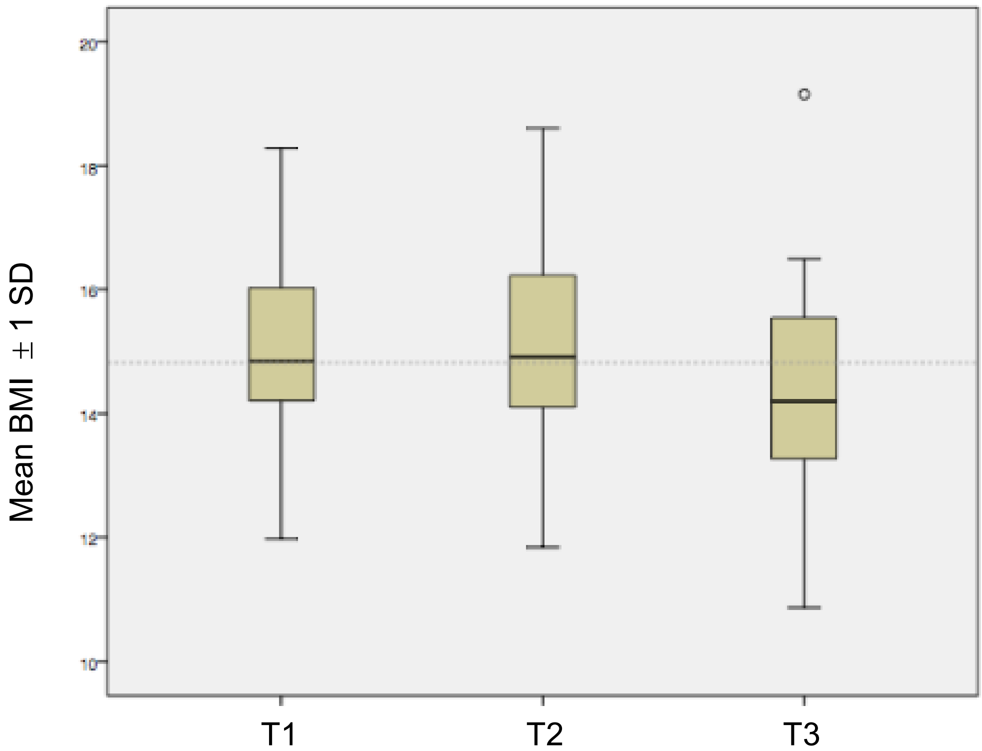


Figure 13: Development of the BMI

The y-axis shows the mean BMI ± SD: T1 15,10 (±1,63), T2 15,04 (±1,59) and T3 14,32 (±1,56). The x-axis shows the three measurement times. The dashed line is the overall mean with 14,82. The quantity testes was F=8,7, the result high significant (p=.003**) and the effect was Eta^2=.146

6.5.4 Comparison of Experimental versus Treatment group of weight, length and BMI

The post-hoc test (LSD) showed a high significant change of weight of the control group (T1 vs T2: MD=0.26; p=.002**) but not of the experimental group (T2 vs T3 MD=0.12; p=.26).

The post-hoc test (LSD) of the length development showed most significant change between control (MD=1.10; 0=.000***) and experimental group (MD= 2,60; p=000***).

The post hoc test (LSD) showed no significant change of the BMI development of the control group (MD=0.55; p=558) but high significant change of the experimental group (MD=0.72; p=003**).

In summery the weight development of the control group showed a slightly progress, whereas the weight of the experimental group stayed stable. Both children of the control and the experimental group gained weight and the BMI of the control group did not changed where as the BMI of the experimental group decreased.

6.6 Socio economic aspects

6.6.1 Distribution of the participants within the Hollingshead Four Factor Index

In order to get reliable results, the participants N = 51 were divided into three groups at Baseline dependent on each value of the Hollingshead Four Factor. N = 22 (43,14%) with a factor index of 12 or less points and were calculated as group 1. N = 20 (39,22%) with an index between 13 to16 points and were calculated as group 2. N = 9 (17,65%) had an index of 17 or more points and were calculated as group 3.

The means of the developmental age of all three different Hollingshead groups stayed stable over the three times of measurement as you can see in Table 6.

Table 6: Means of the developmental age of the different Hollingshead groups

	Hoolingshead Index (0-22) (divided into areas)	M	SD	N
T1 Developmental age	< = 12	14,38	8,94	22
	13 – 16	12,53	7,49	20
	17 +	10,99	8,57	9
	total	12,07	8,27	51
T2 Developmental age	< = 12	15,11	8,92	22
	13 – 16	13,63	7,76	20
	17 +	12,03	9,32	9
	total	13,09	8,46	51
T3 Developmental age	< = 12	17,75	9,37	22
	13 – 16	16,46	9,00	20
	17 +	15,69	11,54	9
	total	16,87	9,46	51

There was no main effect (p>.69/.43) and no interactions (p>.48/.32) by the absolute values of the developmental age as well as by the different values between control and experimental groups.

But there are some tendencies, showed in the Appendix.

6.7 Tube time and its influence to development

As shown in chapter 6.1 the overall mean duration of tube feeding of the sample was 22,61 months (± 14,88; range: 3 - 62) which is 65,56% (± 25,32; range: 12,13 - 98,64) of their lifetime.

Duration of tube feeding showed an expected correlation with the age of the children (r=.77) whereas the duration of tube feeding in percent of lifetime had no correlation with age (r=.07).

When the duration of tubefeeding in % of the patients lifetime was catigorized in three sub populations (< 50 (n = 14), 50 – 75 (n = 11), <75 (n = 26)) no effect on developmental age was detected (GLM for repeated measurement: Interaction (IA) p=.576; main effect tubefeeding in % of lifetime category p=.876. Pearson correlation showed no correspondance between tubetime % of lifetime versus difference in develomental age over the time course (r=.04 developmental from T2 to T3 versus tube percentage of lifetime).

In summery the data showed that a longer tube time itself or a higher procentage of lifetime were a child was tubefeed maid no difference on the general development of the children.

6.8 Success rate and its influence on development

The treatment tube weaning according to the “Graz Model” with the aim to learning to eat and drink by self regulated motivation of the child itself was defined as successful by n=48 (94,12%). N=3 (5,88%) could not be weaned after treatment.

No significant difference (chronological age, socio economic status, weight, length or BMI) between the successfully weaned children and not weaned children were found. There was also no significant difference between the developmental age, the change of developmental age or the developmental deficit. It has to be considered that the group of not weaned children has just n=3 participants.

A percise case describtion about the n=3 not weaned children is presented in the appendix.

6.9 Serverity of the underlying medical condition and its influence to development

As shown in Table 3 n=26 (51%) were in the group “none – moderate” severity and n=25 (49%) were in the group “over average – extreme” severity of the underlying medical condition.

There was no significant difference between the two groups in the development and in the BMI in the control and experimental group.

6.10 Influence of chronological age on development

As shown in Table 10 the control group (T1 – T2; mean 57 days) in mean developed 0,92 (±1,04) months. The experimental group (T2 – T3; mean 81 days) with developed 2,89 (±1,86) months.

Through matching the whole sample into three groups (youngest, middle, older) with each n=17 participants, we looked on the effect of the chronological age on general development within the control and experimental group.

Group 1 (youngest) (n=17) had a chronological age less than 19,10 months, group 2 (middle) a chronological age 19,11 – 36,57 months and group 3 (older) a chronological age 36,58 or higher.

In the control group the gain of developmental age of group 1 was 0,73 (± 0,51) months, group 2 showed 0,98 (± 0,99) and group 3 had 1,05 (± 1,45) months.

The experimental group showed group 1 a change of developmental age of 2,00 (± 0,57) months, group 2 3,22 (± 1,86) and group 3 3,46 (± 2,39) months.

Table 7: The influence of the chronological age on development

	T1 real age in months (divided into areas)	M	SD	N
Contr_dev	< = 19,10	,72	,50	17
	19,11 – 36,57	,98	,98	17
	36,58 +	1,05	1,45	17
	total	,92	1,03	51
Treat_dev	< = 19,10	2,00	,56	17
	19,11 – 36,57	3,22	1,86	17
	36,58 +	3,46	2,39	17
	total	2,88	1,86	51

As shown in table 7 there was a significant main effect, that the participants of group 2 and 3 had a higher developmental change than the children from group 1.

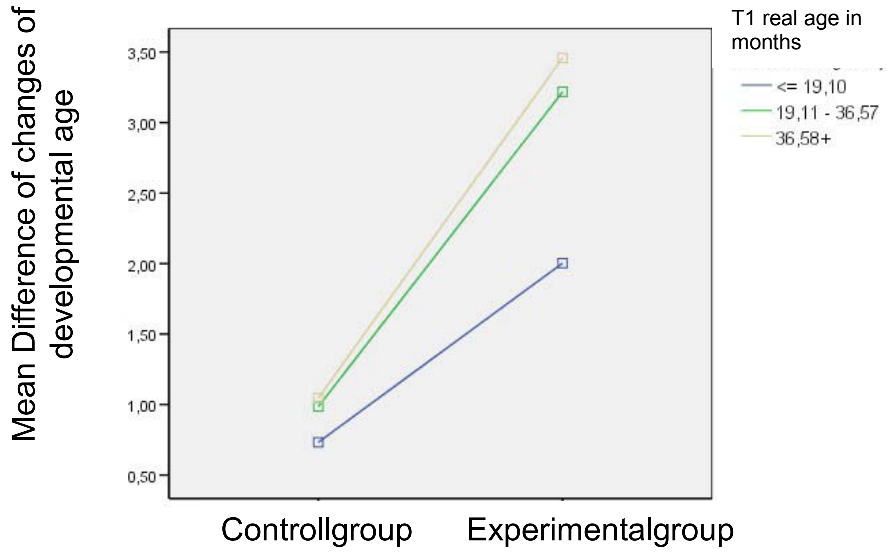


Figure 14: Changes of the developmental age according to the chronological age (chronological age measured at T1)

The group > 19 months shows a slower increase in developmental age as the older children. It's a significant slightly effect (F=3,66, p=.033*, Eta2=.132).

As shown in Figure 15, all changes of development of the CDI showed significant better results than the developmental changes of the KIDS. Therefore there was a significant interaction and main effect between the measurement with the CDI or KIDS which will be considered carefully in the discussion.

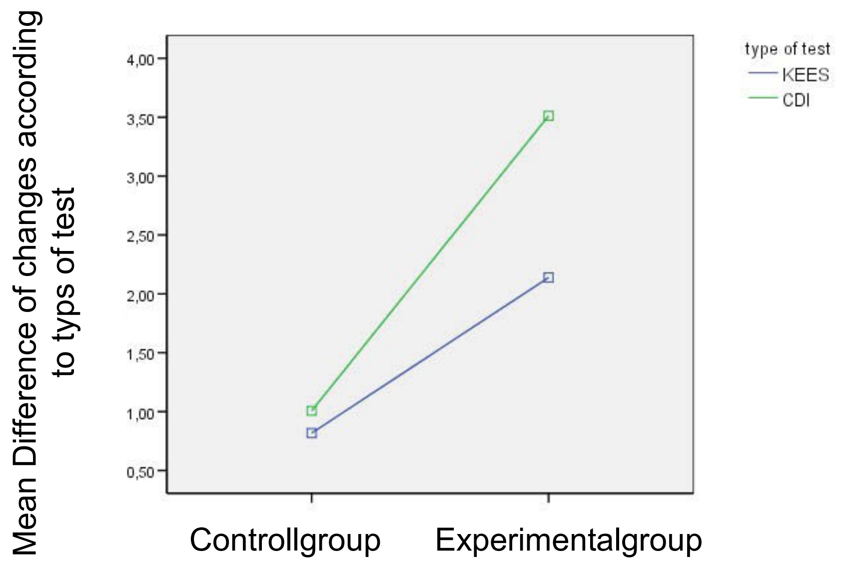


Figure 15: Developmental results of the CDI and KIDS

The Figure shows the different values of developmental changes between the control and experimental group. The difference between T2 - T1 versus T3 – T2 is F=114,43, p=.000***, Eta2=.700. The interaction between time and type of test is F=10,95, p=.002**, Eta2=.183. The single main effect type of test F=4,633, p=.036*, Eta2=.086.

6.11 Changes of unintended side of effects of long-term tube feeding

The number of the unintended side effects due to tube feeding (as listed in 5.3 outcome measure) were measured per month at T1 234,22 (±182,99; range: 182,75 – 285,68) times, at T2 230,61 (± 181,06; range: 179,68 – 281,53) times and at T3 86,69 (±97,28; range 59,33 – 114,05) times as shown in Table 8.

Table 8: Number of unintended side effects

	M	SD	N
per month	234,22	182,99	51
per month	230,61	181,05	51
per month	86,69	97,28	51

As shown on Figure 16 the decrees of unintended side effects are significant.

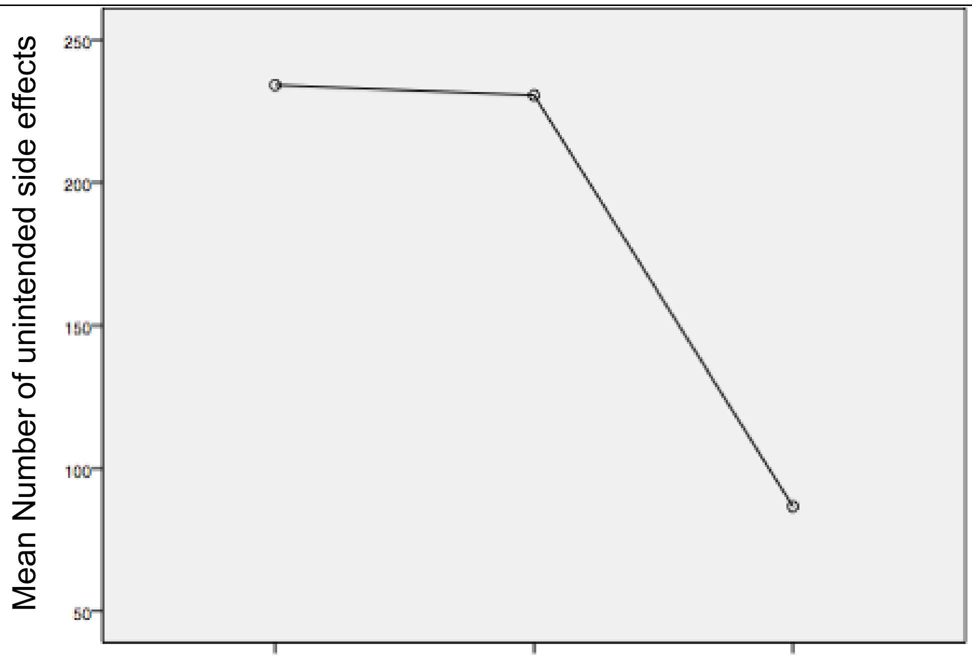


Figure 16: Number of unintended side effects

The y-axis shows the number unintended side effects, the x-axis the three measurement times. The difference between T1 and T2 are not significant p=.65 (LSD), the differences between T2 and T3 (p=.000***) are most significant.

The multivariate test of the observed six unintended side effects of tube feeding (vomiting, uncommon eating habits, gagging, force feeding, food refusal and chocking) showed significant differences between the time points ($F=2,70$, $p=.009^{**}$, Eta2=.454).

The control group showed significant more unintended side effects of tube feeding than the experimental group.

7. Discussion

The effects of N = 51 patients joining the tube weaning program "Graz model" on their general development and on the subscales social development, self-help, motor and communication had been measured. In the year 2000 Sleight et al. (2000) indicated in a Cochrane review the need for more research on enteral feeding to proof evidence for the efficacy and safety of this increasingly used technique (see chapter 4.2). Sullivan et al. (2006) showed recently that enteral feeding improves health and overall weight gain. But Strauss et al. (1997) observed some years before a higher mortality rates among less severely disabled children who were tube fed. Benefits and risks of tube feeding are under discussion. This study focused on an aspect that has not been focused until now: the developmental impact of enteral feed, and oral rehabilitation (tube-weaning) on children.

For the presented prospective study a single armed within-subject design with switching replications was chosen (Möller et al. 2003). This design takes profit of the possibility to compare the effects of the treatment of the intern control group (T1-T2) with the experimental group (T2-T3). The control and the experimental group are comparable and no unintended side effects can arouse because of group heterogeneity. As shown in chapter 5.2 none of the N=51 participants received within the first part of the study intervention focused on tube weaning beside the normal medical care the child received on behalf of its specific underlying medical condition.

Möller et al. (2003) discusses the so called: waiting group design of an intervention study assuming that the design with switching replications may hinder patients with lower socio economic status and/or a lower assertiveness to get into treatment (Möller et al. 2003). We made sure that a first come first served arrangement was strictly observed thus omitting any influence of either of these conditions. There was no stepping forward or backward.

Use of a blind or double blind method was impossible as it is always in psychotherapy studies. As psychotherapy is delivered directly the requisites of pharmacological studies can not be obtained. Comparison of the tube weaning program "Graz model" which is the focus of research with a standardized treatment protocol from elsewhere was impossible because - as shown in

chapter 4.5 - there is no defined standardized tube weaning in any EBM classes.
The design of switching replications was found appropriate as the assumption was that the impact of the defined intervention could be measured easily when using the same group. The statistical methodology makes the waiting list design easier as dependent groups can be calculated thus enhancing the statistic effect and allowing to generalize results. De Jager et al. (2010) assumed that not only randomized studies are able to picture the variety of influence factors on nutrition and its effect on the brain. They suggested a battery of systematic reviews, meta-analyses, epidemiological studies and animal studies. Our study adds a puzzle stone focusing on development in children being enteral fed and transit to oral eating. Funnily enough we started from the clinical observation that – even when food is reduced in the first time – development takes a step forward.
Never the less the presented results need to be handled with care because the statistical power of the switching replication design is reduced compared to randomized controlled studies (Möller et al. 2003). The single armed within subject design with switching replications belongs to the category of pre-/post comparisons. When statistical power is less mighty than in randomized controlled studies, they are commonly used in outcome measurement and regularly in medical science especially to obtain a low cost and relatively fast overview regarding research questions.
Craig et al. (2006) made a pre-post comparison of medical, surgical and health outcomes of gastrostomy fed children before and after treatment. They used a waiting group design applying a waiting period of three month while the children waited for surgery as controls. In this study it could be shown that – although major unintended side effects arouse due to the operation – the intervention in itself achieved the necessary aims, making it possible to have a catch-up growth in the affects disabled children. Thus we feel enforced to apply the study design to our similar research question.
Sleigh et al. 2004 showed that even when reviewing the literature systematic studies are still rare. He advocated systematic studies showing that the so-called "gold standard" namely a prospective, randomized study even reducing its research focus solely on the direct effect of enteral feeding is nearly

impossible. This is even more true when assessing complex health conditions including developmental profiles and the impact of transition from enteral feeding to oral food intake. Therefore the use of a pre-post design as used in Craig et al. 2006 Seems a further step for the development of science. Arts-Rodas et al. (1998) used a similar pre-/post design to identify and propose a program to manage feeding problems in infancy and early childhood. As presented in chapter 4.2 most of the existing tube weaning programs used similar designs for outcome measurement. Therefore our research design is orientated in so far according to published studies.

It must be mentioned that a certain bias can arouse when seeing that the time between T1 - T2 and T2 - T3 (as seen in chapter 6.1.) is not completely the same. Whereas the first period was 57 (SD: ±5,3) days the second period was 81 (SD: ±11,5) days because of parent driven return of some questionnaires. The fact that experimental group had 24 days more time to develop is a possible bias. The effect might be of minor importance because children develop very little in 24 days normally but it needs to be considered. In order to obtain a maximum of patients included and to prevent drop-outs (see table 2) needed some extra time. It was necessary to undergo this challenge considering Schmitt et al. (2010) who pointed out that designing and executing nutritional trials include specific methodological gaps and pitfalls.

As seen in figure 1 the changes of the mean developmental showed a highly significant effect. These findings are surprising as food intake during intervention was less measurable and sometimes less at all. It might be assumed that these results support our hypotheses that tube weaning enhances development.

Additionally the results presented in figure 2 show the changes of developmental age over time and show that the experimental group after treatment developed nearly two times quicker than the controls. We assume that the measured developmental changes are due to treatment knowing that sometimes children develop faster, sometimes slower. (Simeonsson et al. 2003) These changing rates of development were taken into account in the construction of the tools we applied. (Reuter et al. 2000, Ireton 2005). So it is more than feasible that measured development progress was due to the intervention.

As seen in table 5 developmental changes in the subscale self-help was most clear followed by communication, social and motor development. The ranking of the results of these subscales fits into our assumptions we had beforehand. We made sure that – as far as possible – parents were not influenced in any way in filling out the questionnaires. Further on we describe these results according to their ranking in the impact the treatment had on them.

Self-help (figure 5) includes skills and abilities in order to eat as well as bathing, toileting, independences and responsibility. The development of these skills is based on the child's drive towards self sufficiency expressed in the words "I want to do it myself." As seen in the treatment description (chapter 5.1.1) independence and self-regulation is a major aim of the evaluated treatment (Trabi et al. 2010a). The data show that the major aim of the treatment was achieved loading on the appointed subscale and supported statistically.

Communication (figure 7) loaded as the second affected subscale. A central part of the social interaction is "eating". Thus it may be that the treatment affected communication strongly. The process of eating includes a lot of verbal (asking, requiring, refusing) and nonverbal (showing mimical expressions) expressions and understanding of the signals of others. As many children of the sample suffered from underlying medical conditions as shown in the baseline description presented in table 3 and therefore received intensive medical treatment in the past parents tended to treat their children over protectively. As part of the treatment overprotection should be reduced as shown in Dunitz-Scheer et al. 2010. If protection is reduced it is necessary for the children to communicate with their parents and the staff on their own. Data support that this happened during the observed treatment which might show that treatment reached its aims.

Social development (figure 4) loaded as third in the ranking of the developmental subscales. The child's ability to engage in reciprocal social interactions with parents and staff is part of the treatment goals. Some children showed abnormal eating behaviours and habits at the start of the treatment but could change this during treatment (Dunitz-Scheer et al. 2011). Social development includes the child's ability to deal with negative emotions and feelings. When weaned from enteral feeding eating has to be learned and it is necessary to cope with frustrating experiences (e.g. swallowing, chocking etc.). This produces negative emotions because the learning requires coping with frustration in order to learn a functional way of eating. Therefore the developmental change in the field of social development seems to be linked to communication and it seems understandable that this change occurs as well. This is feasible due to clinical observations which sowed that the treated children became more interested in social contact.

Motor development (figure 6) improved as well. Learning to eat includes the will and competence to move towards the food especially, because this treatment focuses also on self-regulation (Dunitz-Scheer et al. 2010). Grasping of food and bringing food from the hands to the mouth, then chewing and swallowing are complex physical abilities that seem to have improved during treatment. Data support the clinical impression that learning to eat has an unintended but favourable side-effect for these children.

Few studies exist - due to our knowledge - that show prognostic data referring to the above named subscales for development and are able to give insight into future development in certain areas. Cognitive development with focus on brain functions like attention and memory finds more attention in research. De Jager et al. (2010) and Schmitt (2010) both showed data referring to the possibility to detect mental retardations by measuring development early. In our cognitive development (figure 10) could be measured only in 23 members of the study sample because of used tests. CDI does not cover the subscale cognition (Reuter et al. 2000). The subpopulation of n = 23 were all within the first year of life that makes measuring possible and they achieved results comparable to the other subscales (table 5). The cognitive subscale includes sensomotoric coordination and the development of object representation. These skills are necessary for self-regulated eating as well as adequate responses to visual, audio and social experiences (Reuter et al. 2000). These skills are trained within the treatment program and their progress makes sense according to the data set that supports their development.

As shown in chapter 4 the specific interest of the presented study is aimed at the impact of nutrition on development in medically fragile children that are tube

depended. Because of the common knowledge that there is no growth and development without sufficient supply of nutrition tube feeding in general has become an indispensable and intrinsic part of modern medicine and in particular intensive care medicine (Satter 1990). Martorell et al. (2010) highlight the devastating effect of under nutrition on long-term school outcome. Therefore tube weaning and its possible harmful consequences of under nutrition is discussed (Braegger et al. 2010). The consequence of tube weaning could be that children might not be able to reach their complete capacities especially in brain functioning.
To evaluate this meaningful discussion we compare them with our data. In our sample the under nutrition occurred as well in the enterally fed children as in those eating orally and surprisingly tube weaning had a positive effect on development in the time span we observed. Our data support the assumption that development is enhanced by oral eating, be it that tasting, smelling and swallowing in itself has the potential to speed up development, be it that the additional therapeutic attention resulted in a developmental up rise. A short-term with less nutrition may even promote development. This seems to be uncharted scientific territory.

The highlighted question weather in our sample oral eating enhances development could be shown. Never the less the long lasting effects of under nutrition could not be studies, because the children sustained themselves orally and had only short periods of weight loss. As we did not report the daily caloric intake we can not deliver data on the amount of food, thus – by measuring the daily weight – the effect shows to our understanding clearly that under nutrition did none occur while observing the sample. Data of weight at admission, demission and at the end of the observation period are at hand and show no substantial weight loss.

But some very interesting furtherer aspects can be highlighted out of the presented data: Both the control- and the experimental group showed a clearly reduced developmental age compared to the chronological age at baseline as shown in table 3 at the start of the study. The developmental deficit of the control group gained already in the measurement time of nearly two months

about one month. Therefore it seems like the population of tube fed children built up in one month two weeks developmental deficit. This effect is dramatic and stringent if we compare the chronological age of the whole sample (table 3) that is about 30 months and the chronological age of the whole sample (table 3) that is about 15 months. By looking at the underlying medical conditions (table 3) it is obvious that the children of the sample had developmental delays (Scheer et al. 2003). But the fact that the developmental age is about half of the chronological age is important in the sample characteristics and makes further medical treatment and care with an especially focus on developmental improvement necessary.
If we compare the developmental change of the experimental group (figure 9) we see that they didn’t encounter an even stronger developmental deficit. Instead they caught up in respect of their developmental deficit. The sample under treatment gained additional development although they had a deteriorating effect in their waiting time. When treated this effect turned around and they started gaining. This effect is strong and may be one of the most important results of the presented data. The treatment withhold the further deterioration and turned it around. Whether this is a long lasting effect can not be answered in this data set.

As shown in figure 11 the weight of our patients were stable during measurement time. This is a promising finding as well. The children gained length as shown in figure 12. That led to a slightly but significant reduction of the BMI as shown on figure 13. The stability of the weight and the gain of length seem promising to us, but both weight and length should be observed long-term in further studies to make sure that aversive effects do not occur later. Other tube weaning treatments described in literature in shown chapter 4.5 show similar results. The weight seems to be stable in all treatments during treatment and the following weeks. Some long-term data are also described. Especially Wright et al. (2010) looks closely over 1,7 years into weight and length and did not find any negative effects. Kindermann et al. (2008) measured weight and length of their sample after 3 and 6 months and showed that 8 of 10 children who were weaned of the tube gained weight subsequently. So weaning children off the tube is possible without negative side effects on weight and length and we found no data that showed a dramatic decrease of weight, length or BMI in literature.

The presented sample included slightly more boys that girls (60 vs. 40%) which is comparable to similar treatment programs (Wright et al. 2010, Benoit et al. 2000, chapter 4.5). There was no gender effect in any terms data. This is the same in published data (see chapter 4.5).
There was also no impact of the socioeconomic situation on development. Individual and family socioeconomic data had no effect on outcome weather in our study or in literature. Wilken et al. (2006) applied similar SES measures and had also no measurable effect on development and tube weaning.
Additionally the time span that children of our sample were tube fed had no effect on the success rate of the tube weaning program or the improvement of development either. There were also no statistical relevant differences when comparing the underlying medical conditions or the severity of diseases.
Detailed sample information is of some interest and rare in literature. One cannot compare our data set with other studies because they do not display these kinds of data. Wilken et al. (2006) highlighted the problem that many treatment protocols for oral eating do not describe their sample adequately, especially the underlying medical conditions. This leads to problems when comparing. There are two already mentioned studies looking at children with cardiac diseases. Coitti et al. (2002) concludes that tube feeding should be implemented, whereas Trabi et al. (2006) showed that children with congenital heart diseases could be weaned successfully without substantial weight loss.
So – as in our data shown – if development is not affected by the underlying medical condition or the severity of diseases the question arises what factors influence the development before and after tube weaning?

As shown in chapter 4.5 the tube weaning according to the “Graz Model” was very effective in the past. Our observation confirmed this effect. 94,12% of the sample was weaned off the tube successfully. Interestingly the children who couldn’t be weaned of the tube (n=3) did profit from the program in the same developmental way as the weaned children (chapter 6.8). Because in our study the numbers of not weaned children were very small this effect cannot be explained. It might be that the children benefited from the treatment also when they did not reach enteral feeding. Therefore it could be possible, that joining the treatment improves development independently of eating behaviour. It could be possible, that this study therefore measured the effect of treatment itself and not the impact of the way of eating. Further studies using bigger samples may answer this question because more dropouts can be expected. It may very well be that the success rate of the observed therapy protocol hinders the achievement of answers in that respect. In the Appendix there are brief case studies presented. Even one of the no-responder to our treatment is described.

As shown in table 7 we splitted the whole sample - according to their age - in three groups of same size in order to obtain statistically generated information about the effect of the chronological age. As shown in figure 14 the group of the youngest did less profit in a developmental way than the two other groups. It has been shown that the younger children can be weaned easier than the older ones. It might be that the younger children had a shorter time-span of suffering, although the duration of enteral feeding had – as shown above – no side-effect in respect of the weanability. As tube weaning is more successful around the first year of life (personal correspondence Marguerite Dunitz-Scheer 26.10.2011) the developmental impact is not so striking. Additionally Trabi et al. (2010) could show that the chance for successful tube weaning was increased if the tube was removed as soon as possible when in the treatment program. Rommel et al. (2003) discussed in their data of n=700 children whether there is a critical or a sensitive period around the first year of life for acquisition of oral feeding skills. They mentioned that if the critical period is missed learning the skills to eat could become more difficult or even impossible. These findings contradict our findings and might be wrong. It might be that the construction of our measurement tools contribute to the observation as is discussed later. It might also be that enteral feeding affects children in their first year of life less, than later on. Thus development might be less stained and by that improves less than in the other two groups (table 7).

A methodological bias should be carefully considered because - as shown in figure 15 - the children of the experimental group who were tested with the

KIDS showed significantly lower developmental improvement than the children tested with the CDI. This might attribute to the applied test and not to the sample itself. Nevertheless the questions in the applied tool does not disclose any reason why this should be the case, so it is more feasible that the sample itself bears this difference.

Although the result that younger children (defined as chronological age) showed less increase in their cognitive-developmental age could be a bias of the used test inventory (KIDS versus CDI) it is – as discussed above – not conclusive. It may be that that the used scales do not match perfectly. It could also be that the CDI is more conservative (namely in respect to cognitive behaviour observed by parents) or the period that was catched by the test finds the child in an age where development is slower than in the next period of a child's life. This assumption was ruled out by the authors of the test (Reuter et al. 2000, Ireton 2004). The author's of the inventories looked very closely in the question of the chronological age and adjusted the scales accordingly.

When discussing the second possibility, that the tests are different in their construction we find, that by single comparison of the 270 items of the CDI and the 252 items of the KIDS there are no hints that the CDI is more conservative although a difference was shown. Whereas the KIDS items ask questions about development within the first year of life (e.g.: Item 16 "Shakes rattle placed in hand," item 105 "Smiles at mirror image" or item 123 "Turns from back to side") the CDI assesses development between 18 month and six years (e.g.: item 1 "Helps a little with household tasks," item 65 "Stays dry all night" or item 232 "Understands what "before" and "after" means; uses these words correctly"). Out of the data and test descriptions and the literature we cannot find any why one of the discussed biases should be in place at the moment.

One finding of our data set should be still discussed: The frequency of unintended side effects like vomiting, uncommon eating habits, gagging, force feeding, food refusal and chocking related to tube feeding between T1 and T2 (= control group). As shown in figure 16 the control group had more than 230 unintended side effects within one month that is a little above than 7 unintended side effects per day statistically. The experimental group between T2 and T3 (= intervention group) showed about 85 per week that is less than 3 per day as a mean. We found no literature which that measured the frequency of unintended side effects of tube feeding. 230 per month seems to be an impressing frequency of problems and the reduction of these to less than 3 per day seems to be a great relief as well as for children as for parents. Tube weaning by itself may so contributor to the joy of life, the quality of daily life and chores and thus enhance development by reducing adverse experiences during everyday life.

Our presented study has strengths. For the first time a study focused on the effect on general development of tube weaning which includes in the case of the Graz model an interdisciplinary approach and multimodal therapies. Besides that it looked into relevant subscales of development. The effect of tube weaning in Graz on the child’s development are strong and significant. Before generalising one might consider that our study maybe measured an effect that occurs although it is not the intention of those who planed and delivered the treatment. We found that participating in the tube weaning program according to the “Graz model” is very effective in weaning children off the tube and that the children involved perform developmentally better afterwards which has been found for the first time.

But it may be that the jump in developmental maybe occurs as a favourable but unintended side effect of tube weaning, although the reduction of problems with feeding during enteral feeding may contribute a lot. That is why – from a research point of view – it could be that the assumption of that the treatment is responsible for the developmental jump may be questioned. It may be that it occurs due to the massive interventions as it seems to happen also in those three children that were not successfully weaned. This could be attributed to the fact that the children received within the three weeks about 55 hours of therapy as shown on figure 1. The data of this study clearly shows that these therapies have an impressive positive effect on the development of the children as shown on chapter 6.2. Beside that nearly all children manage the transition form tube to oral feeding (see chapter 6.8). Further studies should look closely at the factors that hinder weaning.

In Dauncy et al. (1999) the authors highlighted the interaction between nutrition and it’s effect on cognitive development. They found that environmental factors too may have a strong effect on the development of cognition and the answer to

the question whether nutritional or environmental factors were mainly responsible for the development of cognition is uncertain.
As Dauncy et al. (1999) described they could neither say whether the nutritional change had the main impact on the development of the children or environmental factor are of big importance. Neither can we conclude weather the nutritional factors are more responsible for developmental jumps than others. We have to consider a combination of nutritional (enteral vs. oral eating) and environmental (therapies, therapist, different environment, etc.) factors.
Our findings are in close relation with Walker et al. (2005). They measured the effect of psychosocial stimulation and/or nutritional supplementation on Jamaican children that were growth stunted on cognition and education and on IQ scores. The data showed that stimulation had a bigger effect than nutritional supplementation. That result wasn't expected, one thought that nutrition would have a superior effect. It could be that in our study a similar effect in respect to the amount of therapies might be the more effective intervention than the tube weaning alone, although we suspect that the possibility to eat, smell, swallow and conquer the world food-wise in itself may introduce additional learning for the children, whereas "normal" eating may enhance joy and reduce anxiety in parents.

Our study is one off the very rare prospective studies in the field of tube weaning. The number of cases is higher than in similar studies (see also chapter 4.5.)
Data in our sample show that the children sustained their weight and progressed in length undergoing tube weaning and progressed in development, as described in chapter 4.1. Reduction of nutrition was not followed to a halt in cognitive development opposing conclusions drawn from results stemming from developing countries (Grantham-McGregor 2007). Therefore we conclude that our sample kept up their cognitive level within the observation. It would be additional informative to follow up some years until school data would be available. This could possibly proof that tube weaning imposes no negative effect on cognition. We found that it has a positive effect on cognition and general development and the other subscales mentioned at least in the weeks at and after tube weaning.

Despite of the very promising results and their discussion, there are other facts that need to be considered before generalising this data.

In order to draw data for all children with different ages it was necessary to use two test inventories, the KIDS and the CDI as told above. All children of developmental age 15 month less were tested using KIDS that is applicable from 0 – 15 months.

In order to get on overview over the whole sample we used in the statistical calculations the developmental age of all children. When including the subscales of both developmental tests we put them together and calculated accordingly. A special focus was laid on the subscale “cognitive development” as described in chapter 5.3.3. We were conscious that we interfered slightly in the construction and validities of the test inventories. In order to diminish the impact of our scientific intervention into the applied test we used the scores calculated for each developmental age and not the raw scores. As presented in the mentioned chapter there might be a bias because the CDI seems to be slightly more conservative than the KIDS. This possible bias should be considered as having possibly an impact on the possibility of generalization of our data. We did not mix single items of both test inventories but we used calculated results and compared them. Thus we tried to minimize the possible effect on which we reflected in the discussion of data. On the other hand this procedure made it possible to cover the whole age spectrum of the treatment sample.

Another possible shortcoming with less influence on the data needs to be mentioned: Data rely on parent’s reports. That is that each a parent answered the 270 or 252 questions about their child’s performing and behaviour. To question critically that procedure a possible bias could be in that, that parent’s perception is biased by wished of the well-being of their child and love and therefore lead to a unclear picture of the developmental status of their child: It might be that a trained specialist using a developmental test like Bayley Scales (Bayley 2006) would find different results. The authors of the used developmental inventories that rely on parent reports were conscious of this possible bias and compared their results in a statistical robust manner with developmental assessments finding their test appropiate. Reuter et al. (2000) points out that there are reasons to be concerned and think carefully about relying developmental test on caregiver's report. However it is important to consider that the information provided by caregivers is highly structured by items and response choices. Although the reliability and accuracy of caregiver's reports have been debated, the psychometric integrity of caregivers observations as reported using the KIDS and the CDI has been consistently demonstrated through empirical research (Reuter et al. 2000).

The use of inventories relying on parent's reports is common. Beside the presented test for reliability (Reuter et al. 2000, Ireton et al. 2005) other evaluations have been done. For example Doig et al. (1999) enrolled primary caregiver of n = 63 toddlers and preschooler at a routine neonatal high-risk follow-up in a study using the CDI. N = 43 successfully completed CDIs were included. The CDI quotient General Development was compared with the Clinical Adaptive Test/Clinical Linguistic and Auditory Milestone Scale (CAT/CLAMS) and the Bayley Scales of Infant Development, 2nd Edition (BSID-II). Data showed sufficient correlations between the CDI, the CAT/CLAMS (r= .87, P< .001) and the BSID-II (r= .86, P< .001). No correlations between CDI results, parent education and income were found and the results show the high sensitivity (80% to 100%) and specificity (94% to 96%) of CDI. The authors conclude that the CDI is a useful and cost-effective screening tool for measuring development in high-risk infants.

Literature shows that many data rely on parent's reports. Santosh et al. (2009) uses parent reports for the diagnosis of autistic spectrum disorders and present data of n = 879 children and young people. Wilson et al. (2009) present a parent report study in the area of medically assessed speech-language pathology. Dobbelsteyn et al. (2008) show data of prevalence, risk factors and prognosis of feeding difficulties relying on parent's reports.

Johnson et al. (2008) uses the Parent Report of Children's Abilities (PARCA) in a previous revised and again validated version (PARCA-R) assessing formerly very-low birth weight (VLBW) infants at two years corrected age. This recent evaluation used the Mental Development Index (MDI) of the Bayley Scales of Infants Development, second edition (DSID-II). The PARCA-R was filled out by parents and the MDI was completed by trained and licensed specialists.

Correlations between PARCA-R Parent Report Composite (PRC) scores and MDI scores (r=.77, 95 confidence interval, CI 0.69-0.82, p>0.01) showed impressive validity of the tool. Therefore Johnson et al. (2008) describe tests relying on parent's reports as an inexpensive alternative to standard testing.
Sullivan et al. (2006) used parental perception as one measurement tool in order to measure whether the health of tube fed children with cerebral palsy was improved or reduced.

The developmental and outcome measurements relying on caregiver reports are based on many observations of behaviour across a wide range of conditions. The structured developmental inventories provide advantages that surpass sometimes professional evaluation and observations because a caregiver's report provides an insight into children's behaviour that is not limited by the child's state during a 1- or 2-hour professional examination (Rauh et al. 1991).
Another advantage of relying on the caregivers report is that direct involvement of a professional assessor can impact children different (Reuter et al. 2000). This was also considered when appointing the measurement tools for our study. Participants are children that are in medical treated for tube weaning and have a history of a verity of traumatic procedures undergone which were applied by clinical staff (Jotzo et al. 2005). Thus testing in the realm of a clinical setting could very well influence obtained results. Ireton (2005) mentioned that concerned parents welcomed the opportunity to be involved in the assessment of their children. Parents became partners in the assessment process rather than passive observers.
Nevertheless we consider that the development and application of the KIDS and the CDI are already some time ago even if recently new publications came out (Reuter et al. 2000, Ireton et al. 2005). Both test inventories used to be very popular in the end of the 20^{th} century but the use of them seems to have diminished. We do not understand the reasons for that due to literature. It seems that the standard tests of development like the Bayley Scales (Bayley 2006) did establish more on the scientific market. This should not play a negative role. Main basis for the decision for the KIDS and the CDI were the

validity and the option the send this developmental test digital to the parents that can use them independently from place and time.
The fact that all parents signed the informed consent and were therefore informed about the aim and the methods of the study make the threat of social desirability possible, although we got no hint that this has been happening because the study was done independently from the treatment staff. N = 3 parents did not sign the informed consent and were handled as dropouts. This number is much less than in other studies.
The fact needs to be mentioned that some parents judge their children stricter than strangers. As the measurement of the children relies on answers in a questionnaire, namely the KIDS and the CDI they need to be handle with care. It is as well possible that a very strict parent judges it's child much less developed than it actual is. We could avoid this of bias because of the sample size of n=51. Within the group of so many parents the parents with the strict evaluation and the parents with a very optimistic evaluation offsets each other and in the an normal distribution is to be expected (Ireton 2005). Above that we asked parents that it should be always the same parent to fill out the questionnaire in order to achieve stable results.

To sum up the weaknesses of the presented study need to be carefully considered:
1. the design with switching replication,
2. that the developmental test inventory relied on parents reports and the KIDS and the CDI were – in their representative calculated scores – calculated together.
Concluding – apart from these shortcomings – we could show that tube weaning treatment according to the "Graz Model" is very effective in weaning children off the tube and that all children did improve their development compared to the development of the control group. The experimental group could even reverse their developmental deficit into positive development over the time.
So we can generalize that taking part in the treatment according to the "Graz Model" does not negatively effect the general or cognitive development on a short-term but instead leads to a developmental jump. Most children learn to eat

orally. In our sample development rose after learning to eat orally. Weight and length were stable over the time.
In the end the economic aspect of the program needs to be mentioned. As Trabi et al. (2010) already mentioned the costs for the tube weaning according to the “Graz Model” costs $ 864 (US) per day. The mean costs for the three weeks inpatient treatment are $18.000 (US). As Heymann et al. (2004) showed the yearly costs for enteral feeding are $ 37.232 (US). Beside the possibility to gain development and the reduction of unintended side effects the costs for the treatment are already after approx. 1.5 years covered. Even if a progress of development is outstanding the treatment is cost effective.
Above that Heymann et al. (2004) calculated that children on enteral feeding needed more than twice as much doctoral visits as children without a tube. Taking this into account regarding the influence of environmental factors (Walker et al. 2005) it is possible that some of the developmental improvement stems from the additional time parents could spend with their children. This also needs to be considered because tube feeding is often done in cycles like every 4 hours at day and at night (Breagger et al. 2010). Because some children are tube fed since years and some since birth, the fact that parents can sleep for more than 4 hours regularly could have a positive effect on the parent-child relationship as well and may account additionally as positive environmental factor (Largo et al. 1996).
Black (2008) supports this hypotheses in a Lancet commentary were he highlights that besides nutrition the emotional quality is similar important for the upbringing. Therefore it may be that the parent-child interaction is improved after tube weaning. As shown in chapter 5.1.1 the parent-child interaction is a focus of treatment so that the progress in parent-child relationship could have a positive effect on the child’s general development and the subscales. Above that Craig et al. (2003) pointed out that gastrostomy surgery might be considered as a low-tech operation by the medical staff. Our data show on the contrary that the parents had a lot of emotional concerns towards all aspects of tube feeding. A reduction of parental concerns could also smooth the parent-child interaction and lead to a better general development.

Whereas our presented study does not fulfil the criteria of a randomized controlled study with long-term follow up that were particularly demanded by Sleight et al. (2000) after a Cochrane review) in order to proof evidence for the efficacy and safety of enteral feeding the presented study shows prospectively the effect tube weaning has on the affected children. Data show say that tube feeding harms development but we could show a developmental progress occurred by taking part in our tube weaning program and nearly all children got rid of the tube. This is promising especially when considering the observed higher mortality rate by Strauss et al. (1997) due to enteral feeding we showed that joining the tube weaning program did enhance development and reduced unintended side effects.

When discussing the hypotheses at the beginning of our work we assumed that tube feeding could withhold developmental potential. The hypothesis raised from clinical impression. Originally Senez et al. (1996) suggested that a lack of oral feeding in infancy could lead to a deficit in cortical development because motor and sensory pathways between the oropharynx and the cortex are not established.

That hypothesis cannot be answered now. This is due to the success of the program: it had been only three children that were not weaned. Further studies could clarify this point.

The most impressing result of the study is that a huge developmental deficit seems to be correlated with tube feeding. Taking part in the tube weaning program according to the “Graz Model” did not even reduce but turned the developmental deficit into positive development within weeks. If the developmental deficit, which was turned into positive development and add to that the correlation higher mortality rate found by Strauss et al. ((1997) it was 2.1 higher that children without a tube)) we have to acknowledge that development delay might be an additional risk of tube feeding. Therefore the long-term use of feeding tubes should be evaluated continually and when the placement of a tube is planed the tube weaning should be a part of the planning. Tube weaning should take place as soon as possible as Mason et al. (2005) pointed preferably within the first year when eating is still bound to inborn reflex’. Otherwise the risk of a developmental delay may occur.

Further studies should explicitly monitor the caloric intake of children before, while and after tube weaning in order to answer the assumption if less caloric intake leads to developmental delay already in short time. It would be necessary to follow up these children at age one and three and even better at two another times in school in order to achieve long-term developmental data.

8. References

Arts-Rodas, D. & Benoit, D. Feeding problems in infancy and early childhood: identification and management. Journal Paediatr Child Health 1998; 3:21-27

Bayley N. Bayley Scales of Infant and Toddler Development (3rd ed.) 2006. Administration Manual. San Antonio: Psychological Corporation

Benoit D, Wang EE, Zlotkin SH. Discontinuation of enterostomy tube feeding by behavioral treatment in early childhood: a randomized controlled trial. J Pediatr 2000; 137: 498 – 503

Berezin S, Schwarz SM, Newman LJ, Halata M. Gastroesophageal reflux secondary to gastrostomy tube placement. Am J Dis Child. 1986; 140:699 –701

Bombell S, McGuire W. Early trophic feeding for very low birth weight infants. Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD000504.

Birch LL, Johnson SL, Andresen G, Peters JC, Schulte MC. The variability of young children’s energy intake. New England Journal of Medicine 1991; 324: 232 – 5

Blackman JA, Nelson CL. Rapid introduction of oral feedings to tube-fed patients. J Dev Behav Pediatr 1987; 8: 63 – 7

Blackman JA, Nelson CL. Reinstituting oral feedings in children fed by gastrostomy tube. Clinical Pediatrics 1985; 24: 434–438

Brotherton AM, Abbott J, Aggett PJ. The impact of percutaneous endoscopie gastrostomy feeding: the parental perspective. Child Care Health Dev 2007; 33: 539-546

Burmucic K, Trabi T, Deutschmann A, Scheer PJ, Dunitz-Scheer M. Tube weaning according to the Graz model in two children with Alagille syndrome.

Pediatric transplantation 2006; 10 (8), 934-7

Byars KC, Burklow KA, Ferguson K, et al. A multicomponent behavioral program for oral aversion in children dependent on gastrostomy feedings. J Pediatr Gastroenterol Nutr 2003; 37: 473 – 80

Chatoor I, Ganiban J, Harrison J, Hirsch R. Observation of feeding in the diagnosis of posttraumatic feeding disorder of infancy. J Am Acad Child Adolesc Psychiatry 2001; 40: 595-602

Ciotti G, Holzer R. Pozzi M, Dalzell M. Nutritional support via percutaneous endoscopic gastrostomy in children with cardiac disease experiencing difficulties with feeding. Cardiology in the young 2002; 12 (6): 537-41

Cooke, R. J. & Embleton, N. D. (2000). Feeding issues in preterm infants. Archives of Diseases in Childhood, Fetal Neonatal Edition 2000; 83: F215-F218

Cooke, R. J., Embleton, N. D., Griffin, I. J., Wells, J. C. & McCormick, K. P. (2001). Feeding preterm infants after hospital discharge: Growth and development at 18 months of age. Pediatric Research 2001; 49: 719-722

Cooke RJ, McCormick K, Griffin IJ, Embleton N, Faulkner K, Wells JC. Rawlings DC. Feeding preterm infants after hospital discharge: Effect of on body composition. Pediatric Research 1999, 46: 461-464

Craig GM, Carr LJ, Cass H, Hastings RP, Lawson M, Reilly S, Ryan M, Townsend J, Spitz L. Medical, surgical and health outcomes of gastrostomy feeding. Dev Med Child Neurol 2006; 48: 353 – 60

Craig GM. (2004) Mother knows best: gastrostomy feeding in disabled children – professional and parental discourses. (Thesis). University of London

Dauncey MJ, Bicknell RJ. Nutrition and neurodevelopment: mechanisms of developmental dysfunction and disease in later life. Nutrition research reviews

1999; 12 (2): 231-53

Daveluy W, Guimber D, Uhlen S, Lescut D, Michaud L, Turck D, Gottrand F. Dramatic changes in home-based enteral nutrition practices in children during an 11-year period. Journal of pediatric gastroenterology and nutrition 2006; 43 (2): 240-4

Davis AM, Bruce A, Cocjin J, Mousa H, Hyman P. Empirically supported treatments for feeding difficulties in young children. Current gastroenterology reports 2010; 12 (3): 189-94

Davis AM, Bruce A, Cocjin J, Mousa H, Hyman P. Moving from tube to oral feeding in medically fragile nonverbal toddlers. Journal of pediatric gastroenterology and nutrition 2009; 49 (2): 233-6

De Jager AC, Kovatcheva A. Summary and discussion: Methodologies to assess long-term effects of nutrition on brain function. Nutrition Reviews 2010; 68 Suppl 1: S53-8

Dobbelsteyn C, Peacocke SD, Blake K, Crist W, Rashid M. Feeding difficulties in children with CHARGE syndrome: prevalence, risk factors, and prognosis. Dysphagia 2008; 23 (2): 127-35

Doig KB, Macias MM, Saylor CF, Carver JR, Ingram PE. The Child Development Inventory: A developmental outcome measure for follow-up of the high-risk infant. The Journal of pediatrics 1999; 135 (3): 358-62

Dorda W, Wrba Th, Duftschmid H, Sachs P, Gall W, Rehnelt Ch, Boldt G, Premauer W. ArchiMed: A Medical Information and Retrievel System, Method of Information in Medicine 1999; 38: 16-24

Drewett, R., Wolke, D., Asefa, M., Kaba, M. & Tessema, F. Malnutrition and mental development: Is there a sensitive period? A nested case-control study. Journal of Child Psychology & Psychiatry 2001; 42: 181-187

Dunbar SB, Jarvis AH, Breyer M. The transition from non oral to oral feeding in children. Am J Occupat Ther 1991; 45: 402–8

Dunitz-Scheer M, Marinschek S, Beckenbach H, Kratky E, Hauer A, Scheer PJ. Tube Dependence A Reactive Eating Behavior Disorder. ICAN: Infant, Child, & Adolescent Nutrition 2011; 3: 209-215

Dunitz-Scheer M, Huber-Zyringer A, Kaimbacher P, Beckenbach H, Kratky E, Hauer A, Scheer PJ. Sondenentwöhnung Pädiatrie 2010; 4+5: 1-7

Dunitz-Scheer M, Levine A, Roth Y, Kratky E, Beckenbach H, Braegger C, Hauer A, Wilken M, Wittenberg J, Trabi T, Scheer, PJ. Prevention and Treatment of Tube Dependency in Infancy and Early Childhood. ICAN: Infant, Child, & Adolescent Nutrition 2009; 1: 73–82

Dunitz-Scheer M, Wilken M, Lamm B, Scheitenberger B, Stadler B, Schein A, Scheer PJ. Sondenentwöhnung in der frühen Kindheit. Monatsschrift Kinderheilkunde 2001; 149: 1348-1359

Franz AR, Pohlandt F, Bode H, Mihatsch WA, Sander S, Kron M, Steinmacher J. Intrauterine, Early Neonatal, and Postdischarge Growth and Neurodevelopmental Outcome at 5.4 Years in Extremely Preterm Infants After Intensive Neonatal Nutritional Support. Pediatrics 2009; 123 (1): e101-e109

Gardner, S. L. & Hagedorn, M. I. Physiological sequeal of prematurity: the nurse practionerãs role. Part V: Feeding Difficulties and growth failure. Journal of Pedatric Health Care 1991; 5: 122-134.

Gottrand F, Sullivan PB. Gastrostomy tube feeding: when to start, what to feed and how to stop. European journal of clinical nutrition 2010; 64 Suppl 1: S17-21

Gutenberg S, Hammer D. Shaping oral feeding in a gastronomy tube-dependent child in a natrual setting. Behav Modif 2000, 24: 395-410

Grantham-McGregor, S., Cheung, Y.B., Cueto, S., Glewwe, P., Richter, L., Strupp, B. & The International Child Development Steering Group. Developmental potential in the first 5 years for children indeveloping countries. Lancet 2007; 369: 60–70

Grantham-McGregor S, Ani C. A review of studies on the effect of iron deficiency on cognitive development in children. The Journal of nutrition 2001; 131 (2S-2): 649S-666S

Härtel C, Hasse B, Browning-Carmo K, Gebauer C, Kattner E, Kribs A, Serger H, Teig N, von der Wense A, Wieg C, Herting E, Göpel W. Does the enteral feeding advancement affect short-term outcomes in very low birth weight infants?. Journal of pediatric gastroenterology and nutrition 2009; 48 (4): 464-70

Hawdon JM, Beauregard N, Slattery J, Kennedy G. Identification of neoates at risk of developing feeding problems in infancy. Dev Med Child Neurol. 2000; 42(2): 235-9

Heyman MB, Harmatz P, Acree M, Wilson L, Moskowitz JT, Ferrando S, et al: Economic and psychologic costs for maternal caregivers of gastrostomy-dependent children. J Pediatr 2004; 145: 511–516

Hofner G, Behrens R, Koch A, Singer H, Hofbeck. Enteral nutritional support by percutaneous endoscopic gastrostomy in children with congenital heart disease. Pediatric cardiology 2000; 21 (4): 341-6

Ireton H, Thwing E, Currier SK. Minnesota Child Development Inventroy: Identification od Children with Developmental Disorders. Journal of Pediatric Psychology 1977; 2 (1): 18-22

Ireton H. Child Development Inventory Manual. Child Development Review 2005. Minnesota

Johnson S, Wolke D, Marlow N. Preterm Infant Parenting Study Group. Developmental assessment of preterm infants at 2 years: validity of parent reports. Developmental medicine and child neurology 2008; 50 (1); 58-62

Jotzo M, Poets C. Helping parents cope with the trauma of premature birth: an evaluation of a trauma-preventive psychological intervention. Pediatrics 2005; 115 (4): 915-9

Kindermann A, Kneepkens CM, Stok A, et al. Discontinuation of tube feeding in young children by hunger provocation. J Pediatr Gastroenterol Nutr 2008; 47: 87 – 91

Kong CK, Wong HSS. Weight-for-height values and limb anthropometric composition of tube-fed children with quadriplegic cerebral palsy. Pediatrics 2005; 116 (6): e839-45

Kuklina EV, Ramakrishnan U, Stein AD, Barnhart HH, Martorell R. Early childhood growth and development in rural Guatemala. Early human development 2006; 82 (7): 425-33

Largo RH, Molinari L, Siebenthal K, von Wolfsberger U. Does a profound change in toilet-training affect development of bowel and bladder control? Developmental Medicine and Child Neurology 1996; 38: 106-116

Latal B, von Siebenthal K, Kovari H, Bucher HU, Largo RH. Postnatal Growth in VLBW Infants: Significant Association with Neurodevelopmental Outcome. Journal of Pediatrics 2003; 143: 163-170

Levy Y Levy A, Zangen T, Kornfeld L, Dalas I, Samuel E, Boaz M, Bevis NB, Dunitz M, Levine A. Diagnostic Clues for Identification of Non-Organic vs Organic Causes of Food Refusal and Poor Feeding. Journal of pediatric gastroenterology and nutrition 2008; 47: 1-8

Luiselli KJ. Cueing, demand fading and positiv reinforcement to establish self-feeding and oral consumption in a child with chronic food refusal. Behav Modif 2000; 24: 348-358

Manikam R, Perman AJ. Pediatric feeding disorders. Journal of clinical gastroenterology 2000; 30 (1): 34-46

Martorell R, Horta BL, Adair LS, Stein AD, Richter L, Fall CHD, Bhargave SK, Biswas SKD, Perez L, Barros FC, Victora CG, Consortium on Health Orientated Research in Transitional Societies Group. Weight Gain in the First Two Years of Life Is an Important Predictor of Schooling Outcomes in Pooled Analyses from Five Birth Cohorts from Low- and Middle-Income Countries. Journal of Nutrition 2010; 140 (2): 348-354

Marchand V, Motil KJ and the NASPGHAN Committee on Nutrition. Nutrition support for neurologically impaired children: a clinical report of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr 2006; 43: 123–35

Mason SJ, Harris G, Blissett J. Tube feeding in infancy: implications for development of normal eating and drinking skills. Dysphagia 2005; 20: 46–61.

Maturana H, Varela F. Autopoiesis and Cognition: The Realization of the Living 1980; Boston: D. Reidel

McGrath SJ, Splaingard ML, Alba HM, Kaufman BH, Glicklick M. Survival and functional outcome of children with severe CP following gastrostomy. Arch Phys Med Rehabil 1992; 72: 133–137

McKirdy LS, Sheppard JJ, Osborne ML, Payne P. Transition from tube to oral feeding in the school setting. Lang Speech Hear Serv Sch 2008; 39: 249-260

Miller CK. Updates on pediatric feeding and swallowing problems. Current Opinion in Otolaryngology & Head and Neck Surgery 2009; 7 (3): 194-9

Morag A, Sullivan P. Growth in cerebral palsy. Nutrition in clinical practice: official publication of the American Society for Parenteral and Enteral Nutrition 2010; 25 (4): 357-61

Möller HJ, Laux G, Kapfhammer HP. Psychiatrie und Psychotherapie 2003; Springer, Berlin

Müller B. Die Erfassung des Entwicklungsstandes in der frühen Kindheit durch Elternurteil 1993, unpublished Dilpomarbeit of the Institut for Psychology of the Freien University Berlin

Norton B, Homer-Ward M, Donnely MT, Long RG, Homes GKT. A randomised prospective comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding after acute dysphagic stroke. BMJ (Clinical research ed) 1996; 312 (7022): 13-6

O'Connor DL, Hall R, Adamkin D, Auestad N, Castillo M, Connor WE, Connor SL, Fitzgerald K, Groh-Wargo S, Eugenie-Hartmann E, Jacobs J, Janowsky J, Lucas A, Margeson D, Mena P, Neuringer M, Nesin M, Singer, L, Stephenson T, Szabo J, Zemon V and on behalf of the Ross Preterm Lipid Study. Growth and Development in Preterm Infants Fed Long-Chain Polyunsaturated Fatty Acids: A Prospective, Randomized Controlled Trial. Pediatrics 2001; 108: 359-371

Ong KK, Emmett P, Northstone K, Golding J, Rogers I, Ness AR, Wells JC, Dunger DB. Infancy weight gain predicts childhood body fat and age at menarche in girls. The Journal of clinical endocrinology and metabolism 2009; 94 (5): 1527-32

Pederson SD, Parsons HG, Dewey D. Stress levels experienced by the parents of enterally fed children. Child Care Health Dev 2004; 30: 507-513

Pohlandt, F. & Mihatsch, W. A. Wichtige Aspekte der enteralen Ernährung von sehr kleinen Frühgeborenen. Monatsschrift Kinderheilkunde 2001; 149: 38-45

Puntis JW. Specialist feeding clinics. Arch Dis Child 2008; 93:1 64–7

Prasse J, Kikano G. An overview of pediatric dysphagia. ClinPediatr 2009; 48: 247–251

Prochazkova E, Brichacek V, Dittrichova J, Sobotkova D, Vondracek J. Parent’s concerns regarding infant development: Kent Infant Development Scale (KIDS). Studia Psychologica 1997; 39 (4): 263-265

Rauh H, Berry P. Differentielle Entwicklungsveräuft bei Kleinkindern mit Down-Syndrom. In: Teichmann H, Meyer-Probst B, Roether D (Ed) (1991). Risikobewältigung in der lebenslangen psychischen Entwicklung. Berlin: Spring Verlag

Reck C, Weiss R, Fuchs T, Downing G, Mundt C. Psychotherapy for postpartum depression with a focus on mother–child interaction. Nervenarzt 2004; 75: 1068–1073

Reilly S, Carr L, Wisbeach A. 2000 Assessing feeding in children with neurological problems 2000. In: Southall AM, Schwartz AL, editors. Feeding Problems in Children: A Guide for Health

Rempel GR, Colwell SO, Nelson RP. Growth in children with CP fed via gastrostomy. Pediatrics 1988; 82: 857–862

Reuter J, Gruber C. Kent Inventory of Developmental Skills. Western Psychological Services 2000. Los Angeles

Rommel N, DeMeyer AM, Feenstra L, Veereman-Wauters G. The complexity of feeding problems in 700 infants and young children presenting to a tertiary care institution. Journal of pediatric gastroenterology and nutrition 2003; 37 (1): 75-84

Ross ES, Browne JV. Developmental progression of feeding skills: an approach to supporting feeding in preterm infants. Seminars in Neonatology 200; 7: 469-475

Rudolph CD, Link DT. Feeding disorders in infants and children. Pediatric Gastroenterology and Nutrion 2002; 49(1): 97-112

Santosh PJ, Mandy WPL, Puura K, Kaartinen M, Warrington R, SKuse DH. The construction and validation of a short form of the developmental, diagnostic and dimensional interview. European child & adolescent psychiatry 2009; 18 (8): 521-4

Samara M, Johnson M, Lamberts K, Marlow N, Wolke D. Eating problems at age 6 years in a whole population sample of extremely preterm children. Developmental medicine and child neurology 2010; 52 (2): e16-22

Samson-Fang L, Butler C, O'Donnell M. Effects of gastrostomy feeding in children with cerebral palsy: An AACPDM evidence report. Dev Med Child Neurol. 2003; 45(6):415-26.

Satter, E. The feeding relationship: Problems and interventions. Journal of Pediatrics 1990; 117: 187-189

Scheer P, Dunitz-Scheer M, Schein A, Wilken M. DC0-3: in pediatric liaison work with eating behavioral disorder. *Infant Mental Health J* 2003; 24: 428-436

Schmitt JAJ. Nutrition and cognition: meeting the challenge to obtain credible and evidence-based facts. Nutrition Reviews 2010; 68: S2-S5

Senez C, Guys JM, Mancini J, Paz Pardes A, Lena G, Chous M. Weaning children from tube to oral feeding. Childs Nerv Syst 1996; 12: 590–4

Simeonsson RJ, Leonardi M, Lollar D, Bjorck-Akesson E, Hollenweger J, Martinuzzi A. Applying the International Classification of Functioning, Disability and Health (ICF) to measure childhood disability. Disability and Rehabilitation 2003; 25: 602–610

Skuse D. Identification and management of problem eaters. Archives of disease in childhood 1993; pp. 1-5

Sleigh G, Brocklehurst P. Gastrostomy feeding in cerebral palsy: a systematic review. Archives of Diseases in Childhood 2004; 89: 534-539

Sleigh GS, Sullivan PB, Thomas AG. Gastrostomy feeding versus oral feeding alone for children with CP. Cochrane Database Syst Rev 2000; 3

Somerville H, O'Loughlin E. Gastrostomy feeding in cerebral palsy: enough and no more. Developmental medicine and child neurology 2010; 52 (12): 1076

Strauss D, Kastner T, Ashwal S, White J. Tubefeeding and Mortality in Children With Servere Disabilities and Mental Retardation. Pediatrics 1997; 99: 358-362

Sulkes SB. Life expectancy of profoundly handicapped people. The New England journal of medicine 1991; 324 (6): 420

Sullivan PB (ed). Feeding and Nutrition in Children With Neurodevelopmental Disability. London, UK: Mac Keith Press; 2009: 196

Sullivan PB, Alder N, Bachlet AM, et al. Gastrostomy feeding in cerebral palsy: too much of a good thing? Dev Med Child Neurol 2006; 48: 877 – 82

Sullivan PB, Juszczak E, Bachlet AM, Lambert B, Vernon-Roberts A, Grant HW, Eltumi M, McLean L, Alder N, Thomas AG. Gastrostomy tube feeding in children with cerebral palsy: a prospective, longitudinal study. Dev Med Child Neurol 2005; 47: 77–85

Sullivan PB, Juszczak E, Bachlet AM, Thomas AG, Lambert B, Vernon-Roberts A, Grant HW, Eltumi M, Alder N, Jenkinson C. Impact of gastrostomy tube feeding on the quality of life of carers of children with cerebral palsy. Dev Med

Child Neurol 2004; 46: 796–800

Sullivan PB, Lambert B, Ford-Adams M, Griffiths P, Johnson A. The prevalence and severity of feeding and nutritional problems in children with neurological impairment: the Oxford Feeding Study. Dev Med Child Neurol 2000; 42: 674–680.

Tawfik R, Dickson A, Clarke M, Thomas AG. Caregivers' perceptions following gastrostomy in severely disabled children with feeding problems. Dev Med Child Neurol 1997; 39: 746–751

Teti DM, Gelfand DM. Behavioral competence among mothers of infants in the first year: the meditational role of maternal self-efficacy. Child Dev1991; 62: 918–929

Thorne SE, Radford MJ, McCormick J. The multiple meanings of long-term gastrostomy in children with severe disability. J Pediatr Nurs 1997; 12: 89–99

Thorne SE, Radford MJ, Amstrong EA. Long-term gastrostomy in children: caregiver coping. Gastroenterol Nurs 1997; 20: 46-53

Threats T. Use of the ICF in dysphagia management. Semin Speech Lang 2007; 28: 323–333

Turck D, Michaud L. Growth in Children With Neurological Impairments. Journal of pediatric gastroenterology and nutrition 2010; 51 (Suppl 3): S143-S144

Trabi T, Dunitz-Scheer M, Kratky E, Beckenbach H, Scheer PJ. Inpatient tube weaning in children with long-term feeding tube dependency: A retrospective analysis. Infant Mental Health Journal 2010a; 31 (6): 664-681

Trabi T, Beckenbach H, Ring S, Dunitz-Scheer M, Scheer PJ. A Grain of Normality. ICAN: Infant, Child & Adolescent Nutrition 2010b; 2: 112-116

Trabi T, Dunitz-Scheer M, Scheer PJ. Weaning in Children with Congenital Heart Diseases from Nutritional Tube Is Easier than in Other Children. Cardiology 2006; 106 (3): 167-167

Veness C, Reilly S. Mealtime interaction patterns between young children with cerebral palsy and their mothers: characteristics and relationship to feeding impairment. Child: care, health and development 2008; 34 (6): 815-24

Vernon-Roberts A, Wells J, Grant H, Adler N,Vadamalayan B, Eltumi M, Sullivan P. Gastrostomy feeding in cerebral palsy: enough and no more. Developmental medicine and child neurology 2010; 52 (12): 1099-105

Weinreb, L., Wehler, C., Perloff, J., Scott, R., Hosmer, D., Sagor, L. & Gundersen, C. Hunger: The impact on children´s health and mental health. *Pediatrics* 2002; 110: 41-49

Wiggins RC, Fuller G & Enna SJ Undernutrition and the development of brain neurotransmitter systems. Life Sciences 1984; 35: 2085 - 2094

Wilken, M. & Jotzo, M. Homebased tube weaning: Therapy for children with special needs [german]. Die Kinderkrankenschwester 2007; 26: 102-108

Wilken M. Kann es auch ohne gehen? Praxis und Evaluation der ambulaten Sondenentwöhnung. Ernährung auf eine besondere Art – Behandlungskonzepte bei gestörter Nahrungsaufnahme (2006). SPS Verlagsgesellschaft mbH, Heilbronn, Gernamy

Wilson M, Gosche J, Bishop P, Lui H, Moore T, Nowicki MJ. Critical analysis of caregiver perceptions regarding gastrostomy tube placement. Pediatrics International 2010; 52 (1): 20-25

Wilson EM, Hustad KC. Early Feeding Abilities in Children with Cerebral Palsy: A Parental Report Study. Journal of medical speech-language pathology 2009; vol. March: nihpa57357

Wolke D, Schmid G, Schreier A, Meyer R. Crying and feeding problems in infancy and cognitive outcome in preschool children born at risk: a prospective population study. Journal of developmental and behavioral pediatrics: JDBP 2009; 30 (3): 226-38

Wright CM, Cameron K, Tsiaka M, Parkinson KN. Is baby-led weaning feasible? When do babies first reach out for and eat finger foods? Maternal & child nutrition 2011; 7 (1): 27-33

Wright CM, Smith KH, Morrison J. Withdrawing feeds from children on long term enteral feeding: factors associated with success and failure. Archives of disease in childhood 2010; pp. 1-8

Wright CM, Parkinson KN, Drewett RF. How does maternal and child feeding behavior relate to weight gain and failure to thrive? Data from a prospective birth cohort. Pediatrics 2006; 117 (4); 1262-9

World Health Organization (2002). Report of the expert consultation on the optimal duration of exclusive breast-feeding. Department of Nutrition for Health and Development and of Child and Adolescent Health and Development, World Health Organization: Geneva

World Health Organization (2001). International Classification of Functioning, Disability and Health (ICF). Geneva, Switzerland

Zeisel SH (1986) Dietary infuences on neurotransmission. Advances in Pediatrics 33, 23 ± 47