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Poliklinik für Kieferorthopädie

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# Quantitative analysis of subharmonic and noise phenomena in vocalizations of young infants:

# Comparing infants with and without orofacial clefts

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# List of abbreviations

| | |
|---|---|
| ALR | Amplitude-to-Length Ratio |
| APGAR | Activity/ Pulse/ Grimace/ Appearance/ Respiration |
| APQ | Amplitude perturbation Quotient |
| ATRI | Amplitude Tremor Intensity Index |
| BERA | Brainstem Evoked Responce Audiometry |
| Bp | Biphonation |
| CDAP© | Cry Data Analysis Program |
| CLP | Clefts of the Lip and Palate |
| CSL | Computer Speech Laboratory |
| CNS | Central Nervous System |
| CPDD | Centre for Pre-speech Development/Developmental Disorders |
| CPO | Cleft Palate Only |
| Cps | Cries per second |
| $FH^-$ | Negative Family History |
| $FH^+$ | Positive Family History |
| $F_0$ | Fundamental frequency |
| FFT | Fast Fourier Transformation |
| GLaD-Study | German Language Acquisition and Development Study |
| HA | Hyaluronic Acid |
| HD | Harmonic Doubling |
| HGG | High-Speed Glottography |
| IQR | Interquartile Range |
| LAHSHAL | Lip-Alveolar-Hard palate-Soft palate-Hard palate-Alveolar-Lip |
| MA | Multiple Arc |
| MCI | Melody Complexity Index |
| MFR | Maximum Flow Rate |
| MPT | Maximum Phonation Time |
| MDVP | Multi Dimensional Voice Program |
| Ms / s | Milliseconds / Seconds |
| NB | Noise Band |
| NCC | Not Classified Class |

| | |
|---|---|
| NI | Noise Index |
| OAE | Otoacoustic Emission |
| OPM | Other Phonation Manners |
| PPQ | Pitch Perturbation Quotient |
| PQ | Phonation Quotient |
| PTA | Pure Tone Audiometry |
| SA | Single Arc |
| SH | Subharmonics |
| SI | Segmentation Index |
| SL | Signal Length |
| SPSDD | Specific Pre-Speech Development Disorder |
| UVFI | Unilateral Vocal Fold Immobility |

# 1 Introduction

Crying is the first tool of communication and human infants use it to express their needs and feelings from birth (cf. Várallyay et al., 2004). In young infants, crying is mainly based on the laryngeal activity during which the vocal folds vibrate. This presumes a well-functioning respiratory, laryngeal and supralaryngeal muscle network as well as its neuro-physiological co-ordination through the central nervous systems (CNS), (Newman, 2007).

In the last 50 years much research has been done on different aspects of the infant cry such as anatomical, physiological, psychological and phonetic features (Zeskind et al., 1996; LaGasse et al., 2004; Manfredi et al., 2008; Verduzco-Mendoza et al., 2009). Generally it is believed that the phonation of newly born infants may predict malfunctioning in neuro-muscular activities (Michelsson et al., 1975; Titze, 1994; J. Hirschberg, 1996; Wermke et al., 2002). Research into infant crying began systematically in the 1960's and was carried out mainly in Helsinki, Finland (Wasz-Höckert et al., 1962). Such analyses were based on spectrographic analysis from cry signals recorded from healthy or sick infants. Spectrograms are visual representations of the frequencies of sound signals over time. Therefore, instationary spectral analysis of infant cries may be a useful tool for many medical applications, e.g., to determine the degree of respiratory activity, by measuring the maximum phonation time (MPT) or to identify the degree of undisturbed/disturbed laryngeal activity, by doing acoustic analysis (measuring $F_0$, intensity, fluctuation of pitch and amplitude and noise).

These and other properties can provide a detailed analysis of vocal fold vibration (function) as well as the CNS activity underlying cry production (Titze 1993).

The anatomy of the laryngeal structures in newborns and young infants differs from those in adults (e.g. Vestergaard et al., 2009). The vocal folds in adults are about 10-15 mm long and 3-5 mm thick, while those of infants are much smaller. The infant vocal folds consist of an immature monolayer and mature to a three layer tissue with age (see chapter 1.1.2). As such, the composition of ground substances like hyaluronic acid (HA) and fibrous components in vocal folds of newborns and young infants differs from those of adults, and this plays

a role in the vocal biomechanics (Chan, Gray and Titze; 2001, Schweinfurth and Thibeault; 2008). The maturation of the vocal folds is accompanied with changes in the cellular constitution from birth (Hirano et al., 2001; Boseley & Hartnick, 2006), also explained in chapter 1.1.2.

A key parameter is the amplitude-to-length ratio (ALR) of the vocal folds in newborns or young infants compared to adults. In newborns, this ratio is "extremely large, resulting in strong nonlinearities in the restoring forces" (Titze, Baken and Herzel, 1993; p. 175).

Due to this constellation, the enormous subglottal pressure during crying evokes irregular vibrations and instabilities of the infant's vocal folds (Wermke; 2002). The irregular vibration is visible on spectrograms as phonatory noise bands or subharmonics. This phenomenon is caused by nonlinearities in the vocal fold mechanics (Titze, Baken & Herzel, 1993; Mende et al., 1990b). They are assumed to be manifestations of nonlinear dynamics (noise bands, voice breaks, and creaky voice) as described for infant cries in the literature by Titze (1993). In a former paper (Mende et al. 1990a); those phenomena were interpreted as bifurcations and low-dimensional chaos for the first time.

Complex bifurcations and chaos have been found in cries of healthy infants as well as in sick infants (Lind, 1965; Mende et al., 1990b). Therefore, such phenomena like subharmonics and "noise" are not necessarily a sign for pathological conditions. These characteristics are also present in the sounds from chimpanzees. Indeed, this non-linear behaviour of the vocal folds is a common phenomenon in mammals including nonprimates (Mende et al., 1990a; Riede et al., 1997; Tembrock, 1998; Wilden et al., 1998; Tokuda et al., 2002; Riede et al., 2004).

As the healthy infants get older the occurrence of such irregularities are expected to reduce significantly (Mende et al., 1990a).

With methods of high-speed glottography (HGG) such vibration irregularities were quantitatively described (Eysholdt et al., 2003). Applying HGG to selected clinical cases, two types of irregularities were measured: there was a frequency difference either between left and right vocal folds (horizontal asymmetry) or on one side between the ventral and dorsal third (vertical asymmetry). This

assumption is supported by recent findings, see e. g. (Mende et al., 1990; Hsiao et al., 1994; Buder et al, 2006).

In cases of infants with cleft palates, the open connections seem to cause those phenomena to occur more frequently and more severely than in healthy infants (Hauschildt, 2006). Due to the nasal impedance and the resulting increase in subglottal pressure, the relative small vocal folds tissues are forced to function at their physical limits. The open connection between oral and nasal cavity causes air to escape and much more subglottal pressure is generated to produce loud cry sounds. This results in such infants producing more "noise" and subharmonics in their cries than observed in healthy infants. However, the neuro-physiological laryngeal control may be positively influenced through a pre-orthodontic treatment using a palate plate, see chapter 2.1.

Hauschildt (2006) and Steck-Walter (2007) systematically analysed cries from orofacial cleft infants. They stated that the occurrence of those non-linear phenomena differed in proportion to pre-orthodontic treatment (wearing a palate plate), see chapter 1.1.4. However, their results are based on subjective evaluations only but quantitative normative data of the frequency in occurrence of those non-linear phenomena according to age are not yet available. Hence, in deciding whether the observed high degree of subharmonics and noise segments in infants with orofacial clefts is typical or just normal is still an open question not yet answered by existing studies.

Therefore, the present thesis aims at investigating these phenomena using systematic analysis from two groups of infants. For this study 30 infants (10 with orofacial clefts and 20 without orofacial clefts) were recruited, see chapter 2.1. We investigated whether a decrease in the frequency of occurrence of such non-linear phenomena could be expected with pre-orthodontic treatment and maturation compared to healthy infant’s. The aim of the study is summarized in chapter 1.2 and the hypotheses are formulated in chapter 1.2.1.

## 1.1 Respiratory, laryngeal structures and their regulation

Figure 1 shows the respiratory tract and basic components of the airway system: the lungs, bronchi, trachea (windpipe), larynx, pharynx, oral and nasal cavities as well as the esophagus located directly behind the trachea.

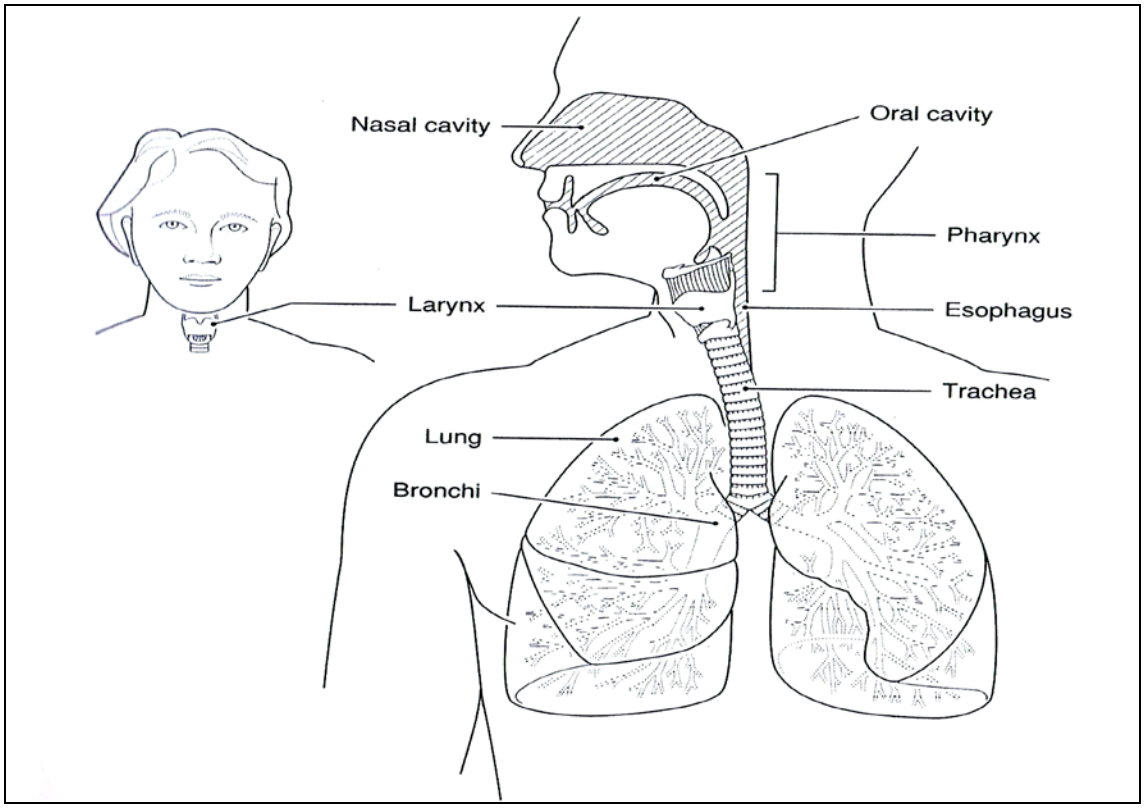



Figure 1: Basic components of the airway system in the head, neck and chest

(Taken from Titze, 1993; p. 2)

The airflow from the lungs is the driving force for sound production and the vocal folds play a crucial role in producing glottal sounds. The glottal sound is resonated on its way through the vocal tract and becomes finally radiated through the mouth and nose (see Figure 2). The voice production system (phonation) is regulated by complex processes including nerve control of the muscular activities. These muscles may as well be used for other functions like breathing, swallowing, and crying. Intrinsic laryngeal muscles open the vocal folds (posterior cricoarytenoid) or close them (interarytenoid, thyroarytenoid and lateral cricoarytenoid), while the cricothyroid elongate the vocal folds (see Figure 4).

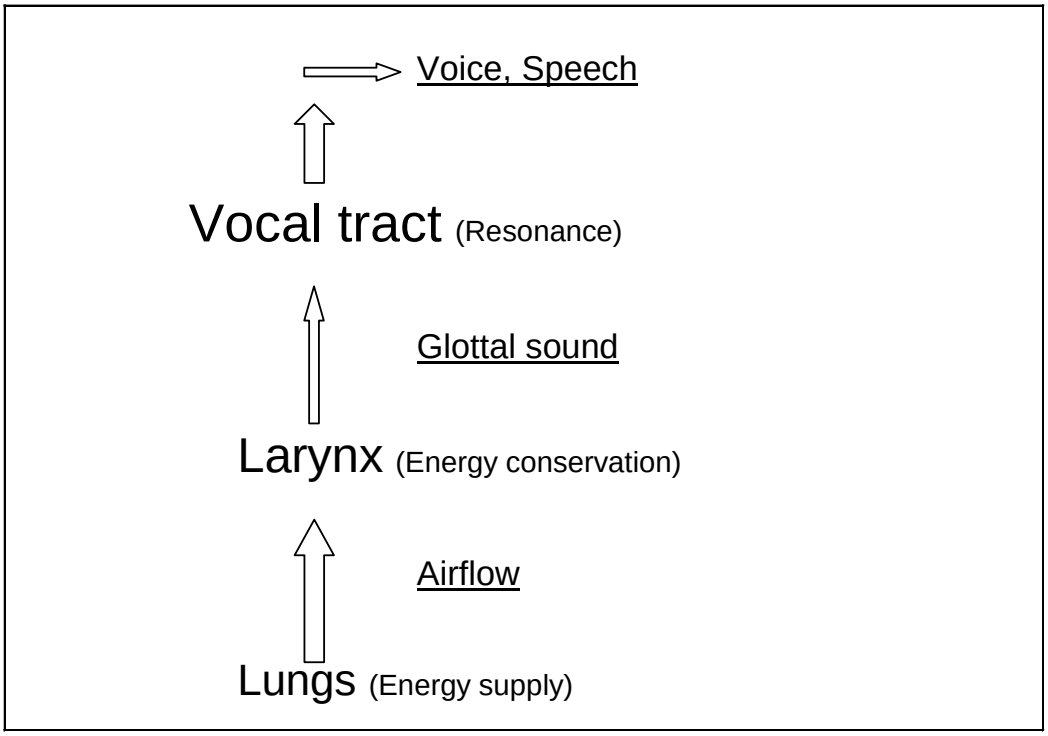



Figure 2: Showing how voice production occurs
(Taken from Yumoto, 2004; Fig. 1, p. 167)

The larynx is made up of 4 cartilages which are connected with the hyoid bone through ligaments, membranes, intrinsic and extrinsic laryngeal muscles (see Figure 3). This framework is completed through nerves, blood vessels and skin (for detailed explanations see Netter, [1989], Table 71-74).

The air space between the vocal folds is called the glottis. The point of attachment of the vocal ligaments is called the vocal process, and that of the vocal muscles the muscular process. Varying the positions of these processes may cause an abduction (moving apart) or adduction (bringing together) of the vocal folds. The extrinsic laryngeal muscles which are subdivided into the infra-hyoid and supra-hyoid groups connect the larynx to surrounding structures.

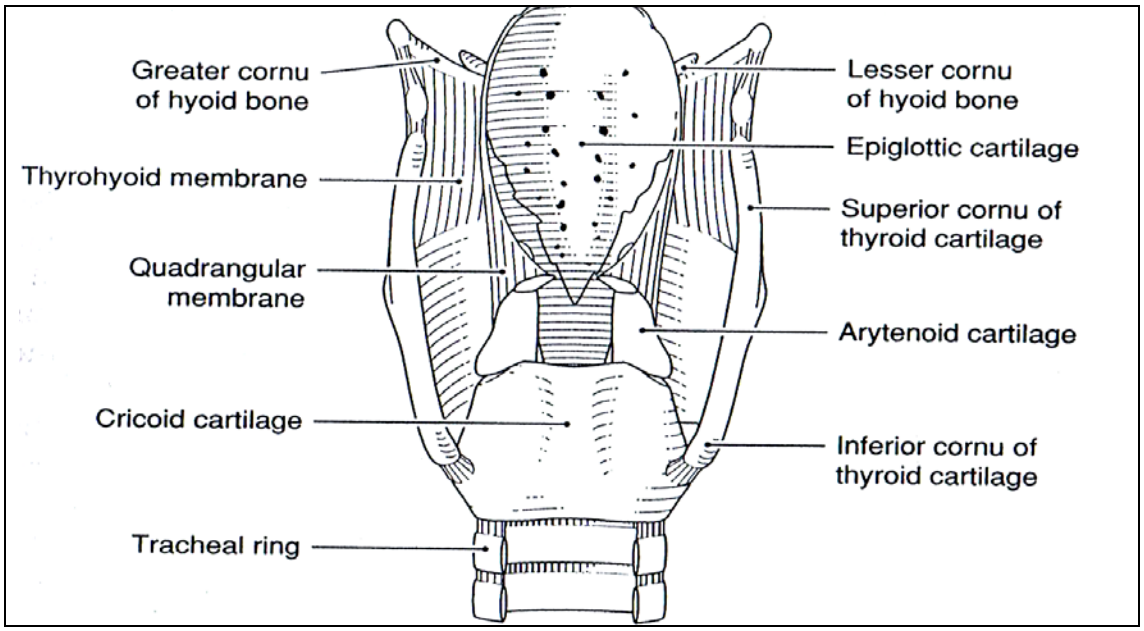



Figure 3: Framework of the Larynx from a posterior view

(Taken from Titze, 1993; p. 5)

Intrinsic laryngeal muscles interconnect the cartilages of the larynx, and Figure 4 illustrates how these muscles function in abducting or adducting the vocal folds. During expiration the airflow from the lungs causes an increase in subglottal pressure and opens the vocal folds. When they open, air passes between the folds and reduces the pressure between them (Bernoulli's Principle[1]) causing a return to the midline for closure. This passive vibration continues as long as there is a transglottal pressure difference; that is a higher subglottal than the supraglottal pressure causing air flow across the folds to induce vibration.

The extrinsic laryngeal muscles change the position of the larynx in the neck by rising (using the thyrohyoid) or lowering (using the sternothyroid) the thyroid cartilage.

[1] Bernoulli's Principle states that as the speed (velocity) of a moving fluid increases, the pressure within the fluid decreases. Fluids include liquids and gases; air is a mixture of gases and therefore a fluid.

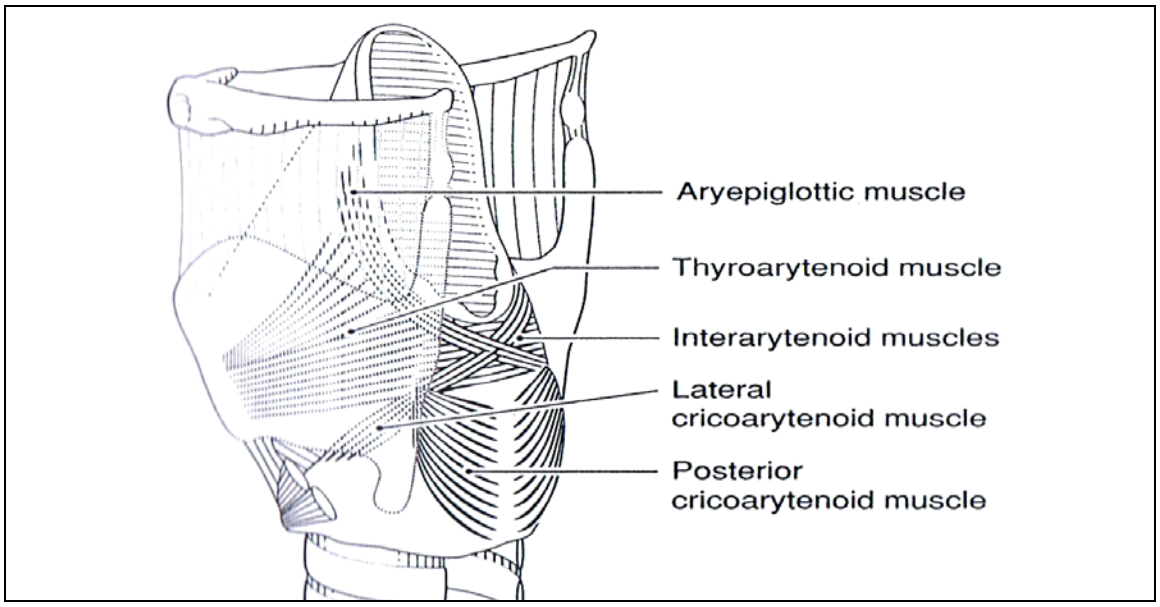



Figure 4: Posterior-lateral view of the intrinsic laryngeal muscles
(Taken from Titze, 1993; p. 5)

Most functions involving the larynx require both intrinsic and extrinsic muscle control. Honda et al. (1999) could show that raising or lowering the fundamental frequency of vocal fold vibrations depends on the interaction of the cricothyroid and the sternothyroid. Titze et al. (1989) described how these two opposing muscles may be used synergistically throughout the pitch range to alter the frequency of vocal folds vibration by changing their length and tension.
The vagus nerve innervates all larynx muscles with Nn laryngei recurrentes (Nn. laryngeus inf.) except the cricothyroid muscle (R. externus of the Nn. laryngeus sup.).

### 1.1.1 Comparing anatomical constellations in young infants and adults

The infant's vocal tract is more like that of a lower primate than that of an adult human (Sloan, 1967; Wind, 1970; Liebermann et al., 1971; Fletcher, 1973; Bosma, 1975; Laitman and Crelin, 1976; DuBrul, 1977; Sasaki et al., 1977).
Infants compared to adults have shorter vocal tracts with a relatively shorter pharyngeal cavity. The mandible is still underdeveloped, resulting in an anterior tongue mass with a short and broad oral cavity. A gradually sloping bend of the oropharyngeal channel and a higher positioned larynx are also anatomic differences. The epiglottises of newborn babies as well as that of a gorilla are

situated about C1 (first cervical vertebrae) with the bottom part of the cricoid cartilage at C4 (fourth cervical vertebrae). We find the epiglottis of adults around C3 (third cervical vertebrae) whereas their bottom part of the cricoid cartilage ranges till C6 (sixth cervical vertebrae).

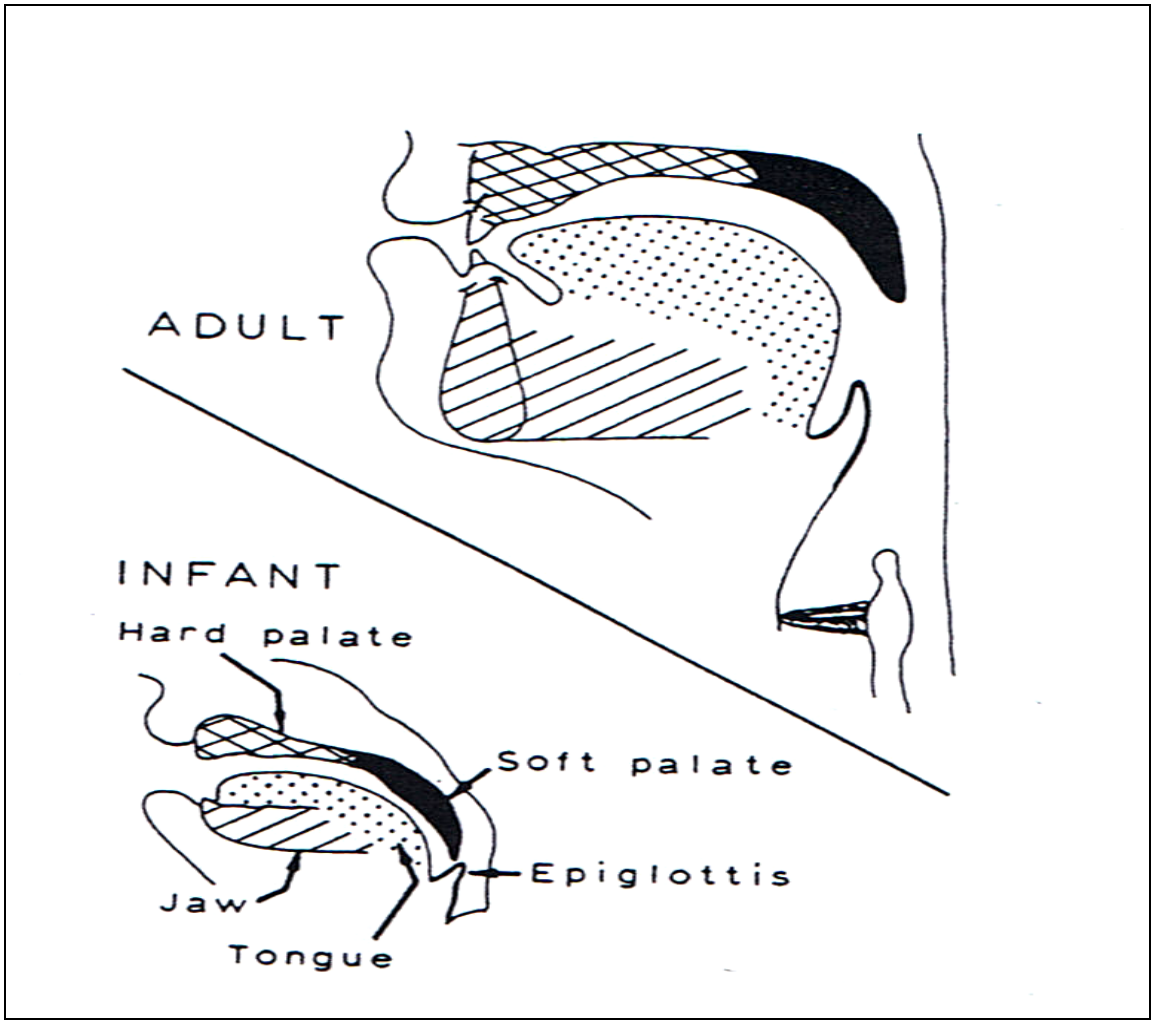



Figure 5: Infant`s vocal tract compared to an adult vocal tract
(Taken from Kent & Murray, 1982; p. 402)

Figure 5 shows an infant and adult vocal tract; the velum and epiglottis are separate between 4-6 months (Sasaki et al., 1977). These anatomic differences may have consequences on sound production. Infants are obligate nasal breathers and nasal vocalizers.

In children at the age of 4-6 months the larynx descends, resulting in a 90 degree bend in the oropharyngeal channel, similar to that in adults. Infants begin to produce what Oller (1978) described as fully resonant nuclei. They

start to emit non nasal vowel sounds and he called this period the expansion stage of phonetic development.
The larynx of a child differs from the adult larynx with respect to size, position, consistency and shape (Hudgins et al., 1997).

### 1.1.2 Maturation and functioning of the larynx

As already mentioned in chapter 1.1.1, certain anatomical and histological structural differences exist between the infant and adult larynges.
The cell density of the lamina propria in neonatal vocal folds plays an important role (hypercelullar monolayer) and it decreases by the 27$^{th}$ week of gestation (Rosenberg el al., 2009). However Hirano & Sato (1995, 1997) found that newborns did not really have a true lamina propria but instead cellular regions called "maculae flavae". They are located at the anterior and posterior ends of the membranous vocal fold parts with unique histological structures. Their composition of fibroblast, ground substances, elastic and collagenous fibers also play an essential role in the biomechanics and functioning of the infant larynx. It is suggested that they are also responsible for the synthesis of fibrous components of the vocal folds (Hirano et al., 2001).
Confirming Hirano`s observation, Hartnick et al., (2005) defined each layer through changes in its cellular concentration. Although differentiations are proposed much earlier (Rosenberg et al., 2009), the first differentiations into a bilaminar structure of distinct cellular concentration were observed at 2 months of age (Hartnick, Rehbar, Prasad; 2005): The superficial layer is less densely populated than the deeper layer. Between the ages of 11 months and 5 years, a three layered structure is noticed with different cellular concentration. The superficial layer is still hypocellular following an intermediate more hypercellular layer and a deeper hypercellular layer just above the vocalis muscle. Although in all specimens a three layered vocal fold structure based on cellular population densities was noted to exist by 7 years of age (the middle layer contains elastin and collagen fibers while the deeper layer is now hypocellular), this is still not comparable to the adult tissue. A complete maturation of the vocal folds is not achieved till 13 years of age. At this age, the layers can be

defined through their differential fiber compositions (elastin and collagen fibers) rather than their cellular population. By age 17 years and in older specimens the lamina propria of the vocal folds takes the adult three layer pattern, with a hypocellular superficial layer followed by a middle layer dominated with elastin fibers and a deeper layer of collagen fibers.
In the already mentioned studies (Hartnick et al., 2005; Rosenberg et al., 2009) only those changes in cellular concentrations which occur while vocal folds mature are described.

Detailed results have been presented on the changes in the morphology of the human larynx during the first 5 years (Eckel et al., 1999) as well as the anatomy of the glottis and subglottis in the infant larynx (Eckel et al., 2000). The subglottic airway increases considerably in size during the first 2 years of life (from 13- 28 $mm^2$ in mean) while further growth follows a linear mode. The relative proportion of the mucosal lining of the subglottic airway occupies approximately 50% of the subglottic cartilaginous cross-section during the first 2 years of life, while decreasing to 30-40% between the ages of three and five. The authors concluded that some of the adaptation of the human larynx as opposed to other vertebrates is not fully developed at birth, but undergoes postnatal maturation, demonstrated through the relative proportions of the cartilaginous and membranous parts of the vocal folds. In newborn infants the posterior 'respiratory' (cartilaginous) glottis accounts for some 60-75% of the total length of the vocal folds (glottic length). Its relative proportion decreases throughout the first years of life (the anterior ligamentous part of the glottis outsize’s its posterior cartilaginous portion), thus finally attaining the proportions of the adult larynx. Eckel (2000) detected no sexual dimorphism in the series of examined infant larynges.

### 1.1.3 Irregularities in vocal sound production (Dysphonia)

Pathologic cries are caused by cerebral dysfunctions with neurological disorders or may be due to peripheral disorders (cleft palates, and laryngeal diseases). This is described in more details on Tab. 1.

## CNS Disorders

Most of the experts who performed cry analysis on healthy and sick infants maintain the view that early vocalizations give impressions on the CNS regulation as well as the development and functioning of the vocal tract (Michelsson et al., 1977a and 1977b; Raes et al., 1982; Michelsson et al., 1983; Wasc-Höckert et al., 1985; Lester et al., 1985; Wermke, 1987).

Sirviö and Michelsson (1976) also concluded that cry characteristics of infants with pathological features involving the central nervous system (CNS) deviate in their pattern from normal cries. In these children, cries with noise concentrations and instable fundamental frequencies were common as well as abnormal types of melody. Other observed features were very high maximum and minimum pitches, biphonation and tone glides. Since these abnormal patterns are not present or at least rarely seen in healthy cries or in cries from infants with peripheral disorders, they might have an expressive role in neurological involvement (Michelsson & co-workers between 1971 and 1983).

Tab. 1: Examples of important spectrographic features of sounds in sick children or by malformation of vocal tract structures (Hirschberg, 1985)

| **CNS Disorders** | | **Peripheral Disorders** | |
|---|---|---|---|
| **Neurological** | **Spectrograph featuring** | **Disease** | **Spectrograph featuring** |
| Central Asphyxia | Noise concentrations | Hypothyroidism | Alternate melody types |
| Bacterial Meningitis | Instable fundamental frequencies | Cleft palates | Biphonation and glides |
| **Cerebral** | **Spectrograph featuring** | **Laryngeal** | **Spectrograph featuring** |
| Hyperbilirubinemia | Phonation breaks (furcations) and glides | Acute laryngitis | Noise concentrations |
| Marasmus | High maximum and high minimum pitches | Papilloma laryngitis | Incomplete formants and structures appear washed |
| Morbus Down | Noise components | Larynx atresis and stenosis | Whistling phonations with inspiratory stridor |
| Cri-duchat Syndrom | Abnormal melody types | Recurrent nerv paresis | Stridor phonations often with high pitches |

## Peripheral Disorders

Pathological cry patterns of peripheral origin are mostly caused by dysfunction of the larynx. Most of these peripheral disorders are often accompanied by a

stridor (pharyngeal, laryngeal, tracheal and bronchial stridor). For detailed explanations, see Hirschberg and Szende (1985).

### 1.1.4 State of research

Fabia Franco (1984) analysed the different manners of phonation in infant cries on the basis of a communicative aspect. Three different categories (discomfort cries, protest cries and call cries) showed dysphonations, hyperphonations and voiceless cries on their spectrographic analysis. Truby and Lind (1965) already suggested dysphonations and hyperphonations to be a result of extremely effortful performance and therefore egressive phonations.

Four infants aging 4 to 10 months were observed longitudinally and the percentage occurrence of these other phonation manners (OPM) in the three categories differed as well as their average durations. In three infants a dominance of vocalizations with dysphonation during discomfort and protest cries could be registered and in one of them there were more hyperphonations. The average durations of voiceless vocalizations were shorter (approx. 400 ms) and those with hyperphonations were considerably longer (approx ≥ 1000 ms). Despite dysphonation being the most variable cry pattern in all 4 infants, the cries were always shorter than those with hyperphonation but longer than those with voiceless phonation (Fabia Franco, 1984).

In order to gain more information on the spectrographic features that infants with larynx dysfunctions produce, Michelsson and her research group published in 1982 the results of spectrographic analysis they conducted between 1973 and 1981. Raes et al. (1982) reported on pain cries from 30 children with infectious and congenital larynx disorders after comparing them with a control material consisting of 120 pain cries from healthy babies aging 0-7 months. Making the data useful for further spectrographic analysis, these studies also considered other cry parameters based on descriptions by Bosma et al., 1965; Wasz-Höckert et al., 1968; Sirviö and Michelsson (1976), Michelsson et al., 1977 and from Thodén & Koivisto (1980). From the 21 cry parameters thus distinguished, inspiratory stridor appeared in 77% of the cries from infants with laryngeal disorders and was absent in cries from healthy babies. Supported by

reports Hirschberg made in 1966, 1972 and in 1980, respiratory stridor is a phenomenon mainly found in laryngeal diseases, it can however also be a symptom of supralaryngeal or tracheal pathologies involving a vocal tract stricture.

Significant increases in the occurrence of cry attributes like high maximum pitch indicate neurological disturbances, while high minimum pitch, abnormal melody types, biphonation and glides on the other hand are indicators of CNS pathologies. Although some of these 6 characteristics may be present in infants with peripheral diseases, they are believed to have a neuropathognomic value.

Although features like tonal pit occurred in 22% of cries produced by infants with cleft palates (CLP), they were absent in cries from healthy babies and do not seem to be present in those who had neurological disorders. These features cannot be seen as having diagnostic value in cleft palate cases alone because they were also present in the cries of two infants with laryngomalacia in another control group. Hirschberg (1980) concluded that some features like noise concentrations, instable fundamental frequencies, vibrato (occurrence varying in different materials from 0% to 54% in healthy babies) and double harmonic breaks need further investigation and are not pathognomic for any specific disease.

Further studies carried out by Michelsson and co-workers in 1999 focused their interest on the fundamental frequencies in cries of healthy and sick infants. Attributing that newborn are capable of producing two types of cries, a pain and a non pain cry (mostly when hungry), their mean fundamental frequency varied between 400 and 600 cps. In another study (Michelsson et al., 2002), a mean fundamental frequency of 1836 pain cries in 172 infants was 496 cps. In most cries of healthy infants shifts and glides were rare and the melody contour was falling or falling-rising. In sick children abnormal cry characteristics appeared for a longer period of time the more severely ill they were. The fundamental frequency increased in premature born infants, for example, and the more immature they were, the higher the pitch.

More research was carried out by Hirschberg (1999) based on dysphonia in infants. He concluded that the dysphonic voice may be characterised by a

sudden change in melody or pitch of the fundamental (glide, shift, break, bitonality) and by turbulent noises (developed as a consequence of incorrect glottis closure).

In newly born infants, dysphonic voice may be caused by an immature larynx innervation due to perinatal CNS lesion. This disintegration in balance between the CNS and glottal closure gradually improves and may disappear spontaneously (Hirschberg, 1999).

Other researchers analysed the cries of 4 infants with unilateral cleft, lip and palate (UCLP) during the first 9 months of life (Wermke et al; 2002a). Although the number of children with UCLP in this study was limited, three cry parameters were analysed. We know that the results of fundamental frequencies ($F_0$) and other parameters (etc. PPQ) reflecting a regular vocal fold oscillation could be used in characterising laryngeal development processes and control mechanism (Titze, 1994; Larson 1998). In young infants the upper vocal fold is immature and therefore these parameters are suitable for describing sound characteristics (Titze, 1994; Larson, 1998). Decreasing values in fundamental frequency were recorded, and this backed up results of previous studies analysing pre-speech vocalisations of infants with clefts of lips and palates (CLP) [Michelsson et al., 1975; Mühler, 1996]. These authors concluded that these parameters, especially $F_0$ and the PPQ of pre-speech sounds (in spontaneous cries), are significant during the first 9 months of life of patients with orofacial clefts.

Many therapy concepts for infants with orofacial clefts implement a palate plate from birth (see page18). Some advantages are for example harmonising the jaw segments to one another and holding the tongue away from the fissure as well as reducing the effects of an open mouth to nose passage. Hauschildt et al. (2006) analysed voice signals of infants born with cleft malformations during the first six months of life, both with and without a palate plate in place. Infants with orofacial clefts compared to a control group exhibited a clear development delay in certain aspects in time organisation of their phonation (Steck-Walter, 2007). In Hauschildt's analysis, there was a significant appearance of more noise components when the infants did not wear the palate plate, as well as the

dependence of these noise components on the degree of their malformations. A noise index was created and clinically tested in order to quantitatively analyse the lengths of these noise components in a cry series. In cries uttered by infants wearing the plate, a significant decrease in the mean fundamental frequency was registered. This dependence of $F_0$ on the use of a palate plate was particularly significant at the age of 5 months. Moreover, a sensitive period of pre-speech development was noticed when the infants were 3 months old. These findings support the postulated positive influence of palate plates on pre-speech development and support also other known advantages from an orthodontic perspective. [McNeil, 1956; Fish, 1972; Hotz & Gnoinski, 1976 and 1979; Hotz et al., 1978; Weil, 1987; Opitz et al., 1992; Stellzig et al., 1999; Zeipert et al., 2000].

Apart from infants born with orofacial clefts, some research has been done on the pre-speech utterances of those infants with a family history of speech acquisition disorders ($FH^+$). Denner (2007) analysed 11.652 cry signals from 21 $FH^+$ infants (11 female and 10 male) born between January 2001 and September 2002. The utterances from the $FH^+$ infants were compared to a control group (19 age appropriates, 10 female and 9 male) and all with a negative family history for speech acquisition disorders ($FH^-$), during the first four months of life. The determination of structure categories in the infant's utterances was done on the basis of defined melody types (Wermke 2002, 2004). Comparing the groups $FH^+$ and $FH^-$ during the first four months of life, she found some differences in the occurrence of certain structural characteristics in their utterances. There was a tendency of a difference in the distribution level of some structure characteristics in the female and male infants.

Blohm (2007) also compared pre-speech utterances from $FH^+$ infants (2 female and 1 male) to those of age-appropriate $FH^-$ infants (2 female) born between November 2002 and May 2003. She analysed 1533 babbling utterances from these infants between the $16^{th}$ and $52^{nd}$ week of life. The relative percentage occurrence of chosen acoustic features in the babbling utterances showed subharmonics (4.2% and 9.2%) and corresponding total noise elements (4%

and 6.3%) in the $FH^-$ group. For the $FH^+$ group the ratio of subharmonics to noisy elements was 4.6%, 3.3% and 5.3% to 1.8%, 0% and 0% respectively.

## 1.2 Aim and Hypothesis

Infants born with orofacial clefts are at a high risk of showing difficulties in phonatory development; (cf. /e.g. Russel and Grunwell, 1993; Morris and Ozanne, 2003; Steck-Walter, 2007). These difficulties were postulated to be related to irregular patterns of vocal fold vibration (see chapters 1.1.4 and 2.2). However, a systematic objective analysis of the occurrence of such irregular patterns is still pending.

The present study aims to quantitatively analyse subharmonics and noise phenomena in vocalizations of both infants born with orofacial clefts (group A) and those born without orofacial clefts (group B) during the first 4 months of life, i.e. from crying to the stage of early babbling. Additionally, the potential influence of innate factors on early vocal development was investigated by also considering the family history of language impairments. Our control group B consisted therefore of infants with a negative family history for language disorders (group B1 or $FH^-$) and those with a positive family history (group B2 or $FH^+$). In chapter 2.1, this subdivision of group B infants is also explained.

This study tested the following hypotheses:

### 1.2.1 Hypotheses

1. The noise index (NI) of utterances from cleft infants over a period of 4 months differs from the noise index (NI) of utterances from non-cleft infants, because of the effect of a vocal tract malformation.

2. The specific physiological conditions of the cleft group A and the non-cleft group B2 (positive family history for a specific language disorder), give rise to the following hypothesis Whilst a continuous decrease of subharmonics (SH) and chaotic episodes (NB), and therefore reduced values of NI is expected in the control group B1, such a decreasing

course in the value of NI is not expected for the other two groups (A and B2).

3. Due to electroglottic research, it is expected that the age dependent decrease of the NI in the control group B1 will mainly be based on a decrease of SH.

4. It is expected that the mean duration of single cries does not affect the noise index (NI) in all three groups, proving that the NI should be an indicator of vocal control and not of the respiratory capacity.

# 2 Materials and Methods

## 2.1 Subjects

In this thesis, cry signals were analysed coming from 10 infants (5 females and 5 males) in group A and from 20 infants (10 females and 10 males) in group B. The infants in group A were born with orofacial clefts of different types as shown in Tab. 2 and they were undergoing treatment in the Department of Orthodontics at the University of Wuerzburg, directed by Prof. Dr. A. Stellzig-Eisenhauer. In cleft patients, there is an open passage between the nasal and oral cavity and these infants are not capable of building up the pressure needed during breast feeding, since the air escapes into the nasal cavity. Many therapy concepts use a palatal obturator (palate plate) to simulate the natural oronasal conditions found in healthy newborn.

The palate plate prevents nasal regurgitation during breast feeding and has a positive influence on the growth of the separated segments by preventing the tongue pushing them apart. It is proven that the plate reduces the cleft palate width and improves the alveolus bow form (Keiichi et al., 2005). These positive effects of such palate plates (Carlstedt K. et al., 2003) enable more favourite conditions for later surgery, since the fissure between the minor and major separated segments become smaller (Hotz & Gnoinski, 1976; Stellzig et al., 1999). Hence, in such cases the natural oronasal condition is more or less substituted with pre-orthodontic treatment using a palatal plate. Thus, pre-linguistic sound production in orofacial cleft infants can be positively influenced (Hauschildt, 2006; Steck-Walter, 2007).

Six of the infants from group A had pre-orthodontic therapy with a palate plate. Four infants suffered from a minor form of orofacial cleft and two of these did not have pre-orthodontic treatment with a palate plate (see Tab. 2). For our analysis we therefore only had cry signals taken from two subjects without a palate plate (the infants LA and EA).

Tab. 2: Orofacial cleft infants in Group A and their malformations

| Symbol | Sex | Code | Malformations |
|---|---|---|---|
| LU | Female | LAHSH | Unilateral cleft lip and palate (UCLP) |
| SH | Female | hSHAL | Unilateral cleft lip and palate (UCLP) |
| LA* | Female | hSh | Isolated cleft palate (CPO) |
| EA* | Female | hSh | Isolated cleft palate (CPO) |
| TA | Female | hSh | Isolated cleft palate (CPO) |
| AN | Male | hSHAL | Unilateral cleft lip and palate (UCLP) |
| TO | Male | HSHAL | Unilateral cleft lip and palate (UCLP) |
| DL | Male | LAHSh | Unilateral cleft lip and palate (UCLP) |
| DN | Male | hSHAL | Unilateral cleft lip and palate (UCLP) |
| SE | Male | hSh | Isolated cleft palate (CPO) |

* Infants without pre-orthodontic treatment with a palate plate

LAHSHAL code defined by Koch, Grzonka and Gundlach (2003). Incomplete clefts are represented with lower case letters and complete clefts with upper case letters. L-Lip, A-Alveolus, H-Hard palate and S-Soft palate on the left and right sides of the face.

All 10 infants in this group A had a non-symdromic orofacial cleft and were all healthy, without severe hearing impairments. Documentation of the hearing capabilities in orofacial cleft infants is very important. In these infants there is often insufficient air ventilation in the middle ear, thus increasing the risk of a middle ear inflammation and a secretory otitis media (Quante et al., 1971; Goudy et al., 2006). Some researchers could prove that the resulting temporary hearing impairments influenced the speech and speech developments in these infants (Hubbard et al., 1985; Jocelyn et al., 1996; Shriberg et al., 2003). Existing data for group A on their paedaudiologic examinations during the first six months of life are summarized on Tab. 3.

Infants from group B were participants of the German Language Development Study (GLaD) established at the children's hospital Lindenhof, Charité in Berlin-Germany. This study (www.Glad-study.de) aimed at identifying early risk markers for later specific language development disorders. These disorders are assumed to be based on genetic factors which is the reason why in the Glad-study the family history of dyslexia, late onset of speaking and specific language impairments was documented. Infants having a positive family history of these

behaviours were classified as $FH^+$, while infants without a background of these disorders classified as $FH^-$. [2]

Tab. 3: Hearing capabilities of group A infants during the first six months

| Category | Hearing ability | BERA | Free field or PTA[3] |
|---|---|---|---|
| 0 | Proper | 0 – 40 dB | 0 – 60 dB |
| 1 | Mild hearing impairment | 40 – 60 dB | 60 – 80 dB |
| 2 | Moderate hearing impairment | 60 – 70 dB | 80 – 100 dB |

| Infants | Category of hearing ability | Type of examination |
|---|---|---|
| LU | 1 | BERA |
| SH | 1 | BERA |
| LA | 1 | BERA |
| EA | 1 | BERA |
| TA | 1 | Freefield |
| AN | 0 | BERA |
| TO | 2 | BERA |
| DL | 1 | Freefield |
| DN | 1 | Freefield |
| SE | 2 | Freefield |

Provided by: Klinik und Poliklinik für Hals-, Nasen- und Ohrenkrankheiten, plastische und ästhetische Operationen, Würzburg (Priv.-Doz. Dr. med. Christiane Völter)

Despite the presence of the family history, all infants developed normal language performance up to the age of $2^{1/2}$ years. As part of the GLaD-study (Pädaudiologische Basisdiagnostik)[4] an examination of the hearing capabilities of the infants in group B was done at 1, 2, 4, 6, 8, 12 and 18 months of age. The complete hearing capability was accessed from the results of an Otoacoustic emission (OAE) and also through a brainstem evoked response audiometry

[2] Data on the hearing capability of the infants (Sprachproduktion und Sprachverständnis) were made and friendly provided by PD Dr. Zvi Penner and Prof. Dr. Petra Schulz at the Charité Berlin, directed by Prof. Dr. Manfred Gross.
[3] PTA (Pure tone audiometry) is a key hearing test in determining the degree, type and configuration of hearing loss in an infant.
[4] (Pädaudiologische Basisdiagnostik) Data on the hearing capability of the infants were made and friendly provided by Prof. Dr. Manfred Gross and Dr. Carsten Nubel, Clinic for Audiology and Phonation, CBF Berlin-Germany.

(BERA).[5] Therefore only children without any medical disabilities were considered and further analysed in this study.

We subdivided group B into group B1 ($FH^-$) and group B2 ($FH^+$), each group consisting of 5 females and 5 males. The subjects in group B1 all had a negative family history, while the subjects in group B2 all had a positive family history.

The idea of including $FH^+$ infants in our control group was based on former findings which proved that pre-speech sounds of these infants often exhibit irregularities in the fundamental frequency ($F_0$), phonatory noise and subharmonics (Blohm, 2007). Another reason to include this group are findings that demonstrate very similar acoustic properties in cries from $FH^+$ / orofacial cleft infants (Wermke et al., 2010).

All 30 children from groups A and B had to fulfil certain selection criteria in order to be included in the present study (see Tab. 4). We only considered infants term born without any pre, - peri- and postnatal disorders, and who had no other diseases except the orofacial malformation in group A. All infants therefore had no development retardations and undertook regular medical and developmental check-ups. The child named DN is an exception, he was a pre-term twin born at a gestational age of 34 completed weeks, who developed normally and was included in order to ensure having at least 10 infants in group A.

Tab. 4: Selection criteria for children recruited in the analysis

| **Selection criteria** |
|---|
| - at least 5 prophylactic medical examinations during pregnancy |
| - a regular course of pregnancy |
| - no signs of Hyperglycaemia or Hypoglycaemia |
| - no signs of placenta insufficiency or intrauterine growth retardations |
| - APGAR 5' ≥ 8 and 10' |
| - apart from orofacial clefts in group A, no other diagnosed diseases |
| - no diagnosed neurological disturbances |
| - parents approval of child's participation in the studies |

[5] BERA (Brainstem evoked response audiometry) is an electro-physiological test procedure which studies the electrical potential generated at the various levels of the auditory system starting from the cochlea to the cortex. It is used for screening deafness in newborns and determines if and to what extent damage has occurred to the inner ear (sensor) or to the auditory nerve (neural).

### 2.1.1 Cry Data Summary

All analyzed cry signals (7.969 cries) were taken from the sound archive of the Center for Pre-Speech Development and Developmental Disorders (CPDD), Department of Orthodontics at the University Hospital in Wuerzburg, Germany.

Tab. 5: Summary of Patient's ages, gender, appointments and cry signals

| Children | Sex | Appointments | Age in weeks | | | | | | | | | | | | | | | Cry Signals |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | |
| | | | Age in days | | | | | | | | | | | | | | | |
| | | | 0-7 | 8-14 | 15-21 | 22-28 | 29-35 | 36-42 | 43-49 | 50-56 | 57-63 | 64-70 | 71-77 | 78-84 | 85-91 | 92-98 | 99-105 | |
| LU | F | 6 | 5 | | 21 | | | 41 | | | | | 76 | | 87 | | 99 | 186 |
| SH | F | 6 | 1 | 8/14 | | | 35 | | | | 57 | | | | 90 | | | 271 |
| LA | F | 6 | 2 | | 16 | | 31 | | 43 | | | | 76 | | 91 | | | 223 |
| EA | F | 6 | | | 19 | | | | | 54 | 63 | | 71 | | 89 | | 99 | 117 |
| TA | F | 6 | | | 17 | 27 | | 39 | | 54 | | | 77 | | | 96 | | 90 |
| AN | M | 6 | 2 | 8 | | | | 40 | | | 59 | | 77 | | | 96 | | 227 |
| TO | M | 6 | | 8 | | 22 | | | 43 | | | | 73 | | 88/89 | | | 121 |
| DL | M | 6 | | 13 | | 27 | | 40 | | 51 | | | 72 | | | | 99 | 39 |
| DN | M | 6 | | 10 | | 26 | | 37 | | 52 | | | 74 | | | | 99 | 60 |
| SE | M | 6 | | 10 | | | | | 44 | | 62 | 67 | | 83 | | 98 | | 89 |
| AE | F | 14 | 3 | 10 | 17 | 24 | 32 | 37 | | 52 | 59 | 66 | 73 | 80 | 87 | 94 | 103 | 514 |
| AK | F | 15 | 4 | 10 | 17 | 24 | 31 | 40 | 45 | 52 | 61 | 66 | 73 | 80/83 | | 96 | 101 | 476 |
| AL | M | 13 | 3 | 11 | 18 | 25 | 32 | 39 | 46 | 53 | 60 | 67 | | 81 | 88 | 95 | | 484 |
| BZ | M | 16 | 3 | 13 | 20 | 28 | 34 | 41 | 48 | 55 | 62 | 69 | 76 | 83 | 90 | 97 | 104 | 289 |
| AX | F | 6 | 3 | | 16 | | 29 | | | 51 | | | 74 | | | 93 | | 214 |
| BF | F | 6 | 4 | | 17 | | | 38 | | 52 | | | 72 | | | 93 | | 282 |
| BI | F | 6 | 5 | | 15 | | 29 | | | 56 | | | 71 | | | | 99 | 280 |
| AB | M | 6 | 3 | | 16 | | 32 | | | | 63 | | | | 87 | 95 | | 160 |
| AS | M | 6 | 4 | | 20 | | | 40 | | 56 | | | | 83 | | 98 | | 159 |
| BM | M | 6 | 3 | | 16 | | | 37 | | 51 | | | 77 | | | 92 | | 144 |
| BO | F | 6 | 3 | 9 | | | 31 | | | 52 | | | 73 | | | 94 | | 201 |
| AT | F | 6 | 4 | 12 | | | 33 | | | 54 | | | 75 | | | | 100 | 223 |
| CM | F | 6 | | 12 | 19 | | 32 | | | 56 | | | 74 | | | 95 | | 145 |
| CU | F | 6 | 7 | | 20 | | 32 | | | 56 | | 68 | | | | 95 | | 304 |
| DG | F | 6 | 3 | | 16 | 27 | | | | 50 | | | 71 | | | | 99 | 307 |
| CD | M | 6 | 4 | | 18 | | 30 | | | 55 | | | 75 | | | 96 | | 260 |
| CX | M | 6 | 4 | | 18 | | 32 | | | 53 | | | | 78 | | 98 | | 401 |
| DU | M | 6 | 4 | | 21 | | 35 | | | 56 | | | 77 | | | 98 | | 304 |
| FI | M | 6 | | 13 | | | 33 | | | 54 | | | 74 | | 89 | 97 | | 192 |
| FS | M | 6 | 4 | | 17 | | 30 | | | 53 | | | 73 | | | 95 | | 286 |
| **Total** | | **214** | | | | | | | | | | | | | | | | **7048** |

Allocation of colours: Group A: red, Subgroup B1 ($FH^-$): green, Subgroup B2 ($FH^+$): blue

The cry signals from the infants in both groups were recorded using a transportable (Sony TCD-D100) digital tape recorder and a SONY ECM-950/957 stereo microphone. To achieve high qualities in the recordings very quiet areas in the hospital or at home were chosen. The infants lay on their backs in their parent's presence during the recordings and a distance of about 15 cm was kept between the child's mouth and the microphone. Only spontaneous vocalizations were recorded (when the subjects were hungry, thirsty, cold, wet, bored etc.) and no cries were induced through inflicting pain.

From group B, we analysed cry signals from the first until the 15$^{th}$ week of life. In order to get a hint of the later development with respect to the above analysed phenomena, four infants in this group were analyzed up to the 20$^{th}$ week of life (Tab. 6) because we had their data. With enough analysable data we extended our observation period until the 20$^{th}$ week for these 4 infants in group B1, as our findings may be helpful in interpreting future results. For objective reasons we also tried to analyse cry signals from the infants taken at the same ages in days or weeks, but this was not possible in all cases (Tab. 5/Tab. 6) so, partially data were pooled.

Tab. 6: Analysis of four children from Group B1 till the 20th week

| Children | Sex | Appointments | Age in weeks / Age in days | | | | | Cry signals |
|---|---|---|---|---|---|---|---|---|
| | | | 16 | 17 | 18 | 19 | 20 | |
| AE | F | 5 | 108 | 115 | 122 | 129 | 136 | 256 |
| AK | F | 5 | 110 | 117 | 124 | 130 | 136 | 330 |
| AL | M | 3 | 109 | | 123 | | 137 | 64 |
| BZ | M | 5 | 111 | 118 | 125 | 132 | 139 | 271 |
| Total | | 18 | | | | | | 921 |

### 2.1.2 Data analysis

Spectral analyses of all recorded cries were done with the speech analysis hardware system CSL-4500 (Cry Speech Lab.) from Kay Pentax, a division of pentax Medical Company (Lincoln Park, NJ 07035 – 1488 USA). This is a high flexible audio processing package designed to provide a wide variety of speech analysis operations. As a standard system it is commonly used for analysing speech, phonation and pre-speech sounds in clinical linguistics (Kent, 1991; Boltezar et al., 1997; Campisi et al., 2000). Many infant cry research teams use this system and much experience could be acquired in recent years (Wermke, 2002, 2006). Data analyses comprised several steps which are described in the following paragraphs.

### 2.1.3 Frequency Spectrogram

Spectral analyses were based on Fast Fourier Transformation (FFT) using Hanning windowed segments of 1024 data points. Resulting spectrograms consist of hundreds of subsequent short-time power spectra of overlapping segments of the cry sample. They reflect acoustic properties of cry signals in three parameters; the length of the signals (time) in seconds (s) represented on the X-axis, the frequency components of the signals on the Y-axis (kHz) and its intensity represented by a gray scale (William J. Hardcastle and John Laver; 1997). Instationary spectrograms, especially narrow-band spectrograms (45 Hz) are helpful in analysing pre-speech vocalizations. The narrow-band spectrograms which we used for our analysis were characterised by a high degree of frequency resolution. Spectrograms provide a variety of visual representations of the frequencies of a signal over time, such as harmonics and subharmonics as well as certain noise-like phenomena. Also other changes like sudden frequency jumps (shifts), bifurcations and chaos are well visible in spectrograms. In Figure 6, a typical spectrogram of an infant cry is displayed. For this thesis we made spectrographic analysis of all cry signals from the chosen children and their spectrograms were all produced in the same way.

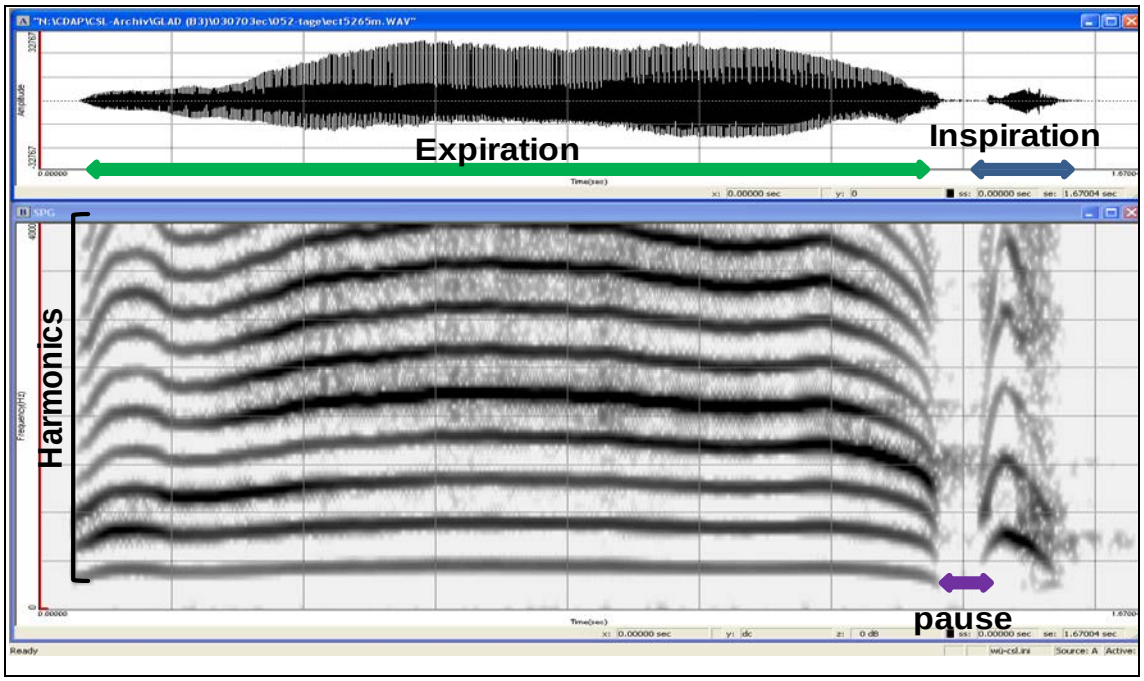



Figure 6: Time waveform and narrowband spectrogram of an infant cry

Wave form on top window (Amplitude vs. Time). Window below displays the typical time narrowband spectrogram of the signal analysed using KAY-CSL. The frequency of the signal represented on Y-axis (till 4 kHz) vs. time (in s) on X-axis.

## 2.2 Analysis of spectral features

As described in chapter 1.1, the sound production of young infants is mainly based on laryngeal activity involving vocal fold vibration (oscillation); often described with the term 'phonation'. When the vocal fold oscillation becomes abnormal, the resulting cries are referred to as 'dysphonic' (Truby and Lind 1965, page 33).

Speech production is a rather complicated process conditioned by nearly periodic oscillations of the vocal cords which excite resonances in the vocal tract. Feedback mechanisms from the central nervous system control phonation and articulation. From a physical point of view certain features of speech production are related to the problem of turbulence which is one of the most difficult areas of human sound production. However, in the last decade much progress has been made in this field which is intimately related to the term 'deterministic chaos'. Mende et al. (1990) were the first to apply methods from nonlinear dynamics, thus providing an organizing framework for vocal vibratory regimes (Buder et al., 2008).

Newborn cries as a specific kind of phonation were analyzed using computer spectrograms and methods from nonlinear dynamics. Observations are made on a variety of bifurcations[6] (e.g. period doubling) and episodes of irregular behaviour (sudden transitions to aperiodicity) in infant cries. Poincaré sections and the analysis of the underlying attractors[7] suggest that these noise-like episodes are low dimensional deterministic chaos (Herzel et al., 1991).

These attractors govern the dynamics for constant external parameters such as vocal fold tension or in case of phonation subglottal pressure. Often these parameters vary slowly and may feature sudden transitions to new attractors. Transition to new attractors is referred to as bifurcations (see chapter 2.2.1).

When applied to the voice, steady state behaviour occurs when the vocal folds are resting. Then with a rise in the subglottal pressure a Hopf bifurcation occurs pushing the steady state attractor into a limit cycle as the vocal folds begin producing normal periodic vocal fold vibrations (see Figure 7).

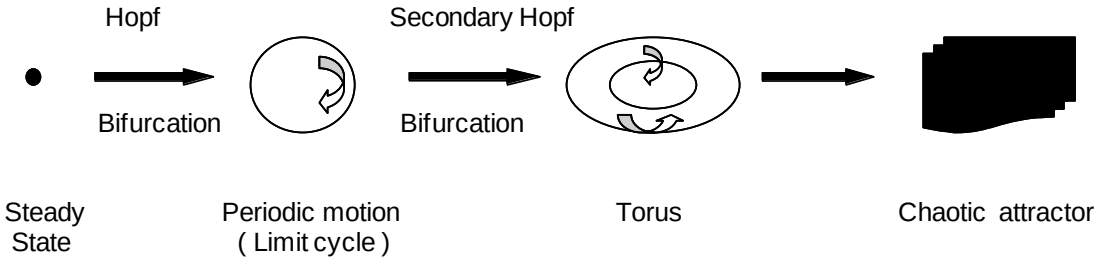



Figure 7: Attractor types and their associated bifurcations

Further studies established the consistency of these phenomena with two-mass models of the vocal folds (Herzel et al., 1991; Titze et al., 1993; Herzel et al., 1994) Figure 8 and Figure 9 show spectrograms of cries containing complex subharmonics, bifurcations and chaos. Buder et al. (2006) defined acoustic criteria for vibratory regimes of vocal cords in relation to the theory of nonlinear dynamics, in order to classify pre-verbal vocal behaviour in infants during the

[6] Bifurcations are transitions to new attractors (from Ruelle, 1981 and Milnor, 1985).

[7] An attractor is a geometrical object in phase space and four types have been identified: 1) Steady state, a behaviour whose variables are constant; 2) Limit cycle, periodic behaviour (repeating itself continuously); 3) Torus, a two-dimensional object in phase space resulting from the superposition of two independent oscillations (producing biphonations); 4) Chaotic attractor, a nonperiodic behaviour never repeating but staying within a limited space.

ages of 3, 6 and 11 months of age. The 'modal regime' containing neither subharmonics nor phonatory noise-bands prevailed at all ages, followed by subharmonics and "pulse regimes" (very closely spaced harmonics). The latter is also typical for noise-like phenomena.

### 2.2.1 Subharmonics (SH)

The focus of the present study was the analysis of bifurcation scenarios (subharmonics) and noise-like phenomena ("chaos").

Subharmonics are also referred to as bifurcations and occur when small changes in the parameter values cause sudden qualitative or topological changes in its dynamic behaviour (Mende et al., 1990; Jiang et al., 2003; Robb, 2003). The most important bifurcations are the period doubling bifurcations[8] and secondary Hopf bifurcations[9] (see also Feigenbaum, 1983). During period doublings a new oscillation cycle prevails and becomes stable with almost double the original period. This means we observe an alternation of large and small amplitudes or periods on the time domain with the appearance of SH of the original fundamental frequency ($F_0$).

Period doubling bifurcations occur often during speech or song and lead to subharmonic oscillations in dynamic systems[10]. Subharmonics may be classified as a folded limit cycle that often appears through transitions from periodic oscillations to an oscillation with alternating amplitudes, or as an addition of a second periodic source, locked at frequency ratio 1:2.

Secondary Hopf bifurcations represent signal modulations with another independent frequency (superposition of two or more oscillations may occur).

We also frequently observed the sudden jump from the original oscillation cycle to another cycle with a different period and amplitude. Such deviations in periodicity as described above are influenced by many factors, including parameter values, changes in muscle tension or subglottal pressure.

[8] Period doubling bifurcations are transitions from a limit cycle to a folded limit cycle.
[9] Secondary Hopf bifurcations are transitions from a limit cycle to a torus.
[10] Dynamic systems are systems within a phase space and at every moment, the behavior of the system may be represented by a single phase space point. After initial transients, systems frequently reach a particular dynamic regime which corresponds to a geometrical object in phase space, termed an attractor.

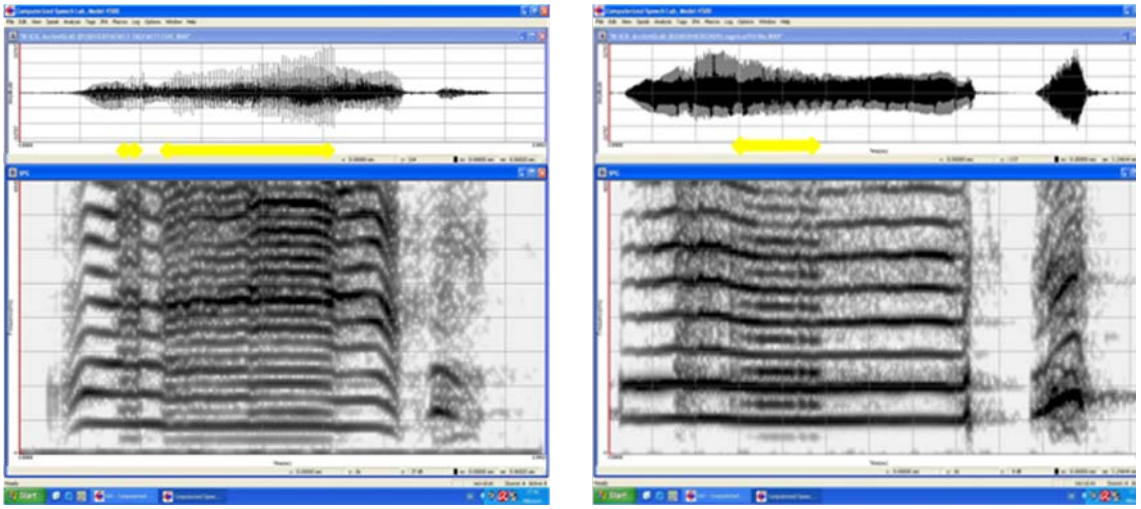


Figure 8: Spectrograms of cries showing subharmonics

Although not frequent the phenomenen featuring two or more independent frequencies is still found in speech. This is also referred to as biphonation and may be produced as a result of (left-right) asymmetrical vocal fold vibrations.
SH are characterized through the abrupt appearance of intervening harmonics, doubling, tripling or even higher integer multiples in relation to the surrounding set in narrowband spectrograms. They sometime fade to noise-like phenomena (chaos) in spectrograms (see chapter 2.2.2)

### 2.2.2 Chaotic segments (Deterministic chaos)

Considering the vocal folds as a desynchronised coupled oscillator generating non-periodic, irregular vibrations called deterministic chaos (May, 1976; Bergé et al., 1984; Glass & Mackey, 1988; Jiang et al., 2006), detailed explanations were also made with methods of non-linear dynamics.
Chaotic vocal folds oscillation is characterised by irregularity with in extreme cases no repeating periods at all. With the appearance of SH, most dynamic systems fulfil all conditions of a chaotic system (Feigenbaum; 1978, 1979 and 1980). These non-linear phenomena are not only noticed in human infants but have also been observed in non-human primates (Gouzoules et al., 1984; Riede et al., 1997; Riede et al., 2004). This therefore suggests that the primate voice production apparatus can easily enter chaotic vibratory patterns referring to episodes of non-random noise.

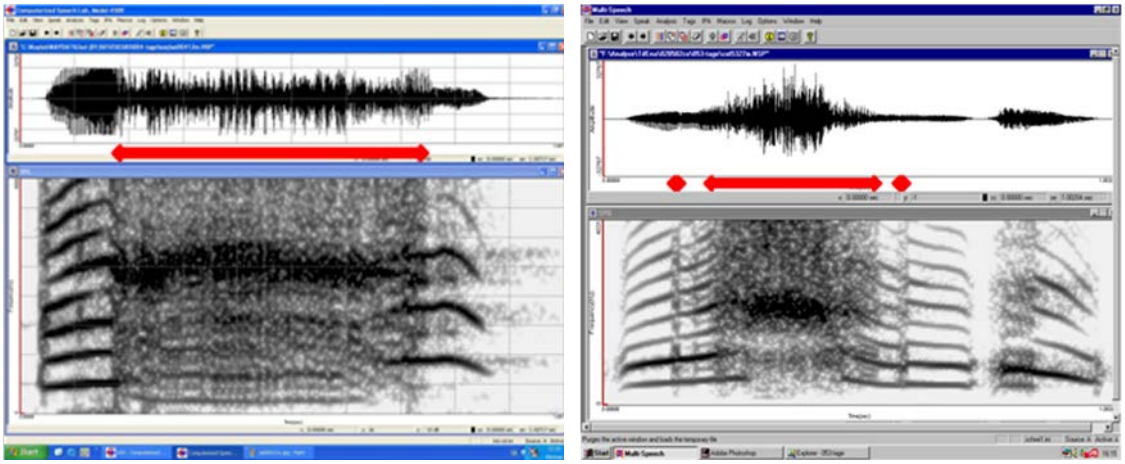
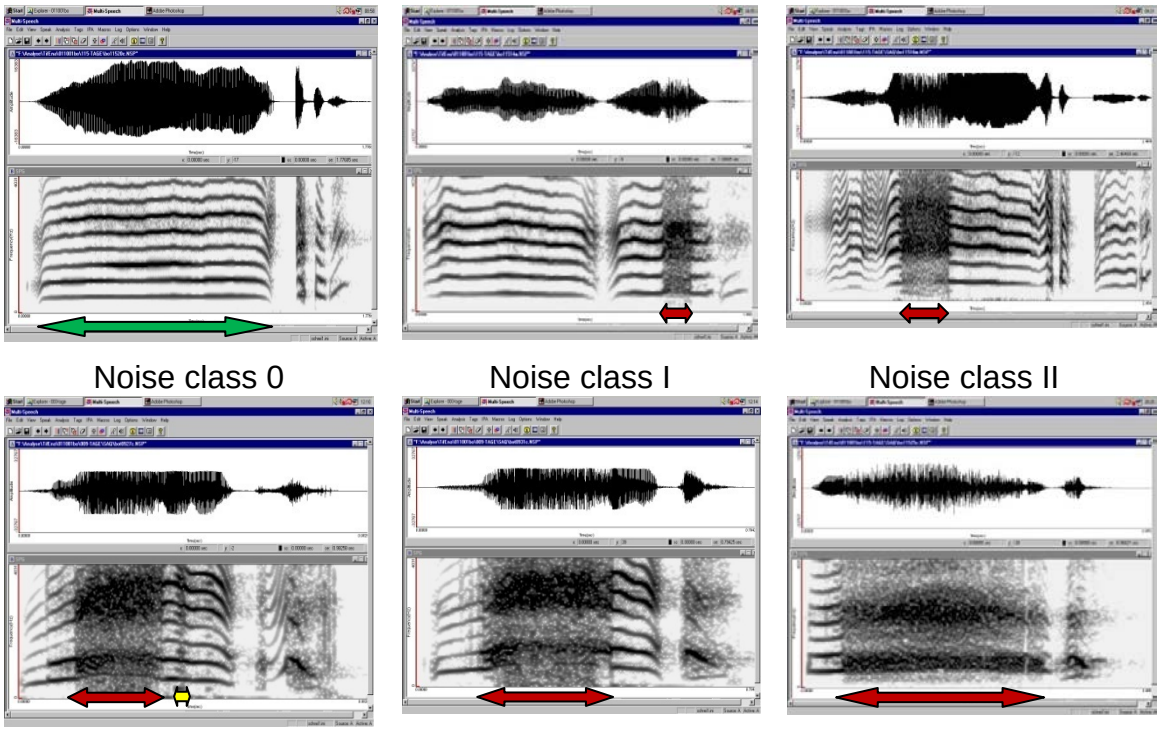


Figure 9: Spectrograms containing chaotic segments

Subharmonics and tori (Biphonations) are often forerunners of proceeding 'chaotic' noise segments which have been analysed with methods of non-linear dynamics and characterized as 'deterministic chaos' (Mende et al.,1990). Chaos is marked by the absence of tonality and the appearance of a non-harmonic spectral structure as shown in Figure 9.

In a preceding study of infants with orofacial clefts, Hauschildt, (2006) analysed such noisy segments. She used a classification system based on the proportions of visual noise-segments in spectrograms as shown in Figure 10 (noise classes' 0-V). In the present study this classification system was also used as explained in chapter 2.3.2.

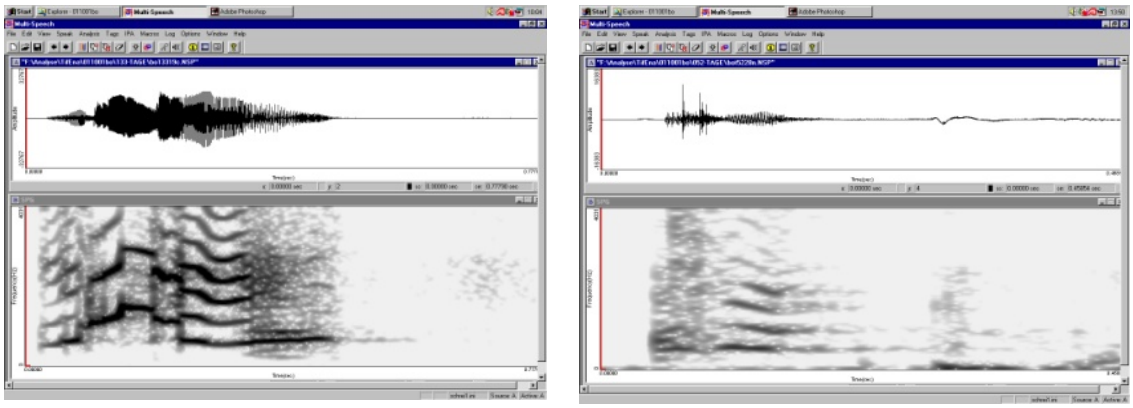
A pre-selection of suitable cry signals reduced the number for further analysis from originally over 8.500 to 7.969 cry signals through exclusion. Using the calculated frequency spectrograms (chapter 2.1.3) pre-analysis was performed in a next analysis step. Not all recorded vocalizations could be unambiguously assigned to the six classes defined by Hauschildt (2006). So a seventh class (Not Classified Class or NCC) was defined for those vocalizations that were either too short (<0.4 s) or which displayed frequency shifts (see examples in Figure 11) and were not considered in our calculations.



Noise class 0 Noise class I Noise class II

Noise class III Noise class IV Noise class V

Figure 10: Cry classification according to Hauschildt (2006)



Not Classified Excluded

Figure 11: Examples of cries removed in our final analysis

## 2.3 Quantitative measurements of subharmonics and chaotic segments

### 2.3.1 Measurement procedure

We used KAY-CSL for analysing the narrowband spectrograms after configuring our wave-files. In Figure 12, subharmonics (SH) marked with yellow borders and noise bands (NB) marked with red borders are the phenomena we examined and analysed in this study. Figure 12 shows a noise band in the interval from point A to point B. When we insert a blue vertical cursor at point A and another at point B, this interval and therefore the duration in seconds can be calculated. Subtracting the value read at point A from that read at point B is the duration (in s) of this noise band. With this method all noisy episodes (SH and NB) in a cry spectrogram can be added together, obtaining a total duration of the noise portion in seconds. A slight error margin is inevitable here, as the cursor is placed manually and thus there is a discrepancy of up to 0.02 seconds.

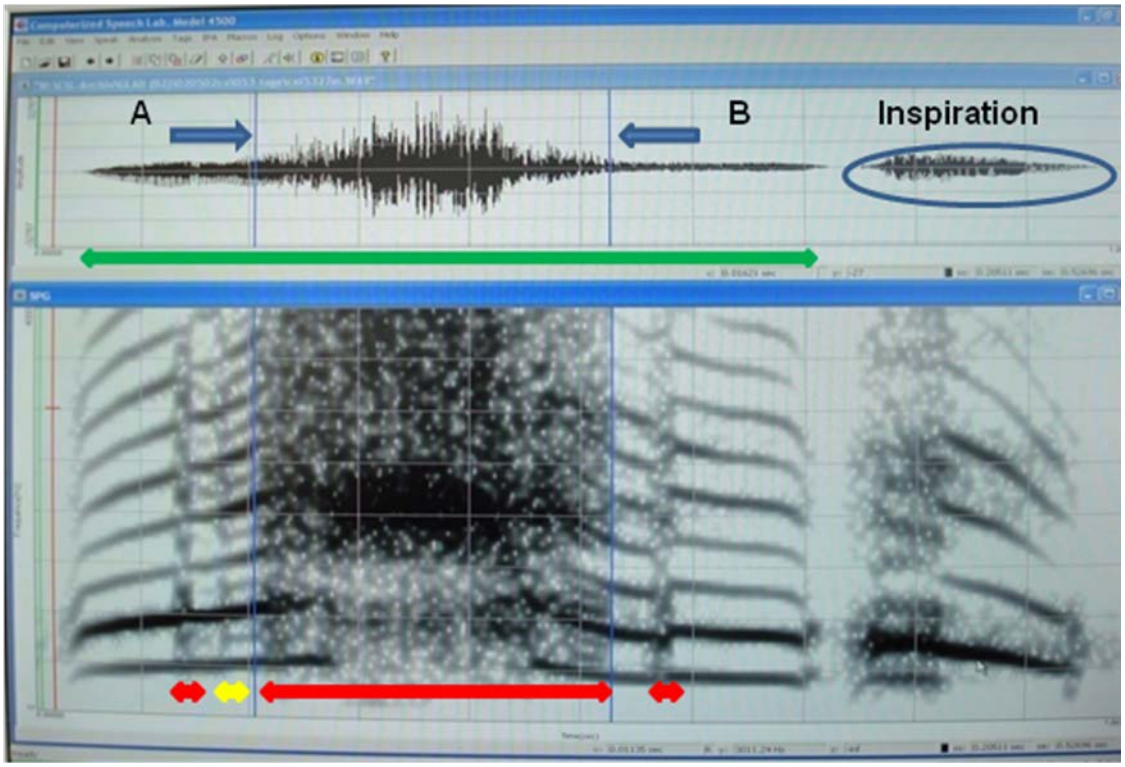



Figure 12: Analysing the spectrograms using KAY-CSL
Range of noise band with red borders
Range of subharmonics with yellow borders
Total duration of the expiratory part of signal with the green borders

### 2.3.2 The noise index (NI)

Hauschildt (2006) defined a noise index (NI) after analysing sound spectrograms from orofacial cleft infants with and without them wearing a palate plate. Her NI characterises the frequency of occurrence of cries containing phonatory noise or subharmonics within a cry sequence (see Tab. 7). The noise index (NI) allows the evaluation of laryngeal function for individual infants. Cry signals can be assigned into various noise classes. Hauschildt`s six classes are characterised by values ranging from 0 (noise-free cry) to 0.875 (cries with > 75% noise structures). Typical examples are shown in Figure 10.

Tab. 7: Description of the noise index developed by Hauschildt (2006)

| **Noise Portion** | | | **Factor for the noise Portion** |
|---|---|---|---|
| Noise class 0 | $rk_0$ | 0% | 0 |
| Noise class I | $rk_1$ | > 0% - 12.5% | 0.0625 |
| Noise class II | $rk_2$ | > 12.5% - 25% | 0.1875 |
| Noise class III | $rk_3$ | > 25% - 50% | 0.375 |
| Noise class IV | $rk_4$ | > 50% - 75% | 0.625 |
| Noise class V | $rk_5$ | > 75% | 0.875 |
| The noise index (NI) was calculated with the formula below: [1] $NI = rk_0 * x_o + rk_1 * x_1 + rk_2 * x_2 + rk_3 * x_3 + rk_4 * x_4 + rk_5 * x_5$ **Cry** | | | |
| $rk_0$ = portion without noise segments | | | $x_0$ = Factor for noise class 0 |
| $rk_1$ = portion with noise class I | | | $x_1$ = Factor for noise class I |
| $rk_2$ = portion with noise class II | | | $x_2$ = Factor for noise class II |
| $rk_3$ = portion with noise class III | | | $x_3$ = Factor for noise class III |
| $rk_4$ = portion with noise class IV | | | $x_4$ = Factor for noise class IV |
| $rk_5$ = portion with noise class V | | | $x_5$ = Factor for noise class V |

Hauschildt analysed cry spectrograms of infants with orofacial clefts by a visual inspection. Each cry was assigned to one of the six classes described in Tab. 7. So, she could determine the percentage of cries belonging to each of the classes 0 – V for certain observation periods. By using fixed factors (x) to describe the noise degree of each class and this percentage (rk), she calculated a NI using the formula [1] given in Tab. 7.

In the present study, this approach was improved by quantitative analysis of noise and subharmonic elements. Both variables x and rk from Hauschildt`s formula for NI were determined by objective measurements. While Hauschildt (2006) analysed the relative frequency of occurrence of cries belonging to the classes 0 – V, I calculated a noise index (NI 1) that is based on the total cry time instead of the number of cries within a cry sequence.

The total duration of all cries from a sequence i.e. signals produced by the infants at each appointment was determined (see chapter 2.1.1 and Tab. 5). It represents the total signal length (SL in s) used as basics for the NI calculations. In Figure 12 for example, the green arrow marks SL.

In a next step, all noise periods (NB) and subharmonic (SH) elements within these cries were determined. After classifying the noise episodes in their various noise classes (0 – V), the total duration (TD) of the daily noise episodes (NB and SH) in each class was calculated.

Doing so, the variable rk was quantitatively determined by summarizing the total durations (TD) of cry signals assigned to a noise class / SL * 100.

[2] rk = (TD / SL) * 100

As a continuing project on objective quantitative analysis of noise and subharmonic segments in infant cries, we modified the noise index of Hauschildt. For the analysis in this study, we did not use this class-specific fixed x factor (Tab. 7) in calculating the noise index (NI). Instead, we calculated individual factors for x which we obtained by using the formula:

[3] x = [(TD SH+NB) / y] / 100

y = total number of cry signals assigned to noise class.

In this manner, the variables $x_0$, $x_1$ or $x_2$ can be calculated for each cry signal assigned to any noise class as in Tab. 7.

With the exception of the infants without a palate plate as pre-orthodontic therapy (see p. 18), all the cry signals from group A infants analysed in this study were taken when they carried a plate. As such, a comparison of the results by calculating the NI 1(with the modified variables) and NI 2 (with

Hauschildt`s variables) from the orofacial cleft infants (in chapter 3.1) is possible.

## 2.4 Statistical analysis

Statistical analyses were done using the SPSS statistics package for Windows XP (version 17.0, SPSS Inc., Chicago, IL) after creating compatible data from the original excel tables. These data were calculated as arithmetical means (averages) on their daily occurrence. In this study, the analysed variables were the noise index (NI 1 and NI 2), duration of cry sequence (SL), amount of subharmonics (SH) and noise bands (NB). We made analysis on monthly and on two-weekly intervals (periods). For the monthly analysis of each variable, we used an arithmetic mean (average value) of this variable during the month. In comparing the results in two-weekly intervals, we calculated the variables also as an arithmetic mean in two-weekly intervals (periods).
The results of NI 2 were used in this study only in making direct comparison with NI 1 from the orofacial cleft infants (see chapter 3.1). For further interpretations of the noise index, only the results from NI 1 were considered.

The outcome of the Shapiro-Wilk test decided on the application of non-parametric tests (non-normal data distribution) or parametric tests (normal data distribution) respectively for investigating the group means.

For applying the ANOVA test we assumed that: our observations are independent, the sample data have a normal distribution and the scores in the different groups pose a homogeneous variance. When $p>.05$, the ANOVA test was applied and, there were no statistical differences between the compared groups. Therefore, it was not necessary to run a Post-hoc comparison between the groups. Post-hoc comparisons between the groups (when $p<.05$) using the Tukey HSD test indicate the presence of significant differences between them.
The displayed box plot diagrams represent a lower quartile (*Q1*, $x_{.25}$), the median (*Med*, $x_{.5}$) and an upper quartile ($Q3$, $x_{.75}$) of the analysed data. The horizontal lines (the "whiskers") extend to at most $1^{1/2}$ times the box width (the interquartile range) from either or both ends of the box. The bottom and top of these boxes always represent the $25^{th}$ and $75^{th}$ percentile respectively (lower

and upper quartiles) and the band near the middle of the box is always the $50^{th}$ percentile (the median). As such these boxes carry 50% of our values with their borders showing a minimum and maximum of them in the interquartile range (IQR = *Q3* - *Q1*). 25% of our values are situated between the 2 whiskers as well as between the bottom and top borders of the boxes.

The gaps between the different parts of the box help to indicate the degree of dispersion and skewness in the data. Any data observation which lies more than $1.5^{x}$IQR (lower than the first quartile) or $1.5^{x}$IQR (higher than the third quartile) is considered an outlier. "Extreme" outliers, or those which lie more than three times the IQR ($3^{x}$IQR) to the left and right of the first and third quartiles respectively, are indicated by the presence of a star."Mild" outliers are marked with circles; they lie between $1.5^{x}$IQR and $3^{x}$IQR.

In order to make comparisons of the box plot diagrams obtained from the statistical analysis, slight modifications were necessary. Filling them with red, green and blue colours, it was easy to tell from which group the box plot came. The cleft infant’s box plots (group A) were filled with red colours, while those from the control groups were filled with green (group B1) and blue colours (group B2), respectively. A marker was set on the vertical axis exactly on the median of our control group B1. Therefore, exact visual differences between the boxes could be seen and comparisons between and within the groups could be made on a monthly and weekly basis (see chapter 3).

# 3 Results

The research for this study consisted of making a spectrographic analysis of over 7.969 cries from 30 infants during their first four months of life from two main points of view, monthly comparisons between/within the groups and a comparison for four children on a weekly basis. For the latter, the analysis of the vocalizations of 4 infants from group B1 was extended until the 20$^{th}$ week and a summary was made in two-weekly intervals.

The following problems regarding the analysis of the cries were encountered:

- There were difficulties in getting all the required recordings from all infants at exactly the same ages (in days or weeks) because of the nature of the samples at our disposal. The recordings could only be made when the infant was brought to the hospital for an appointment or visited at home, and so their ages in days varied.
- The number of data which were suitable for the described analysis varied in the group of infants at the required ages depending on the spontaneous crying of the infants.

In order to draw significant conclusions from the results of the analysis it was decided to group the data on a monthly and on a two-weekly basis, as will be explained in chapters 3.3 - 3.5. As we already mentioned in the statistical analysis, the variables we analysed in this study were arithmetical means or averages acquired either at monthly or at two-weekly intervals.

## 3.1 Comparing NI 1 and NI 2 in group A across 4 months

In this part of this study, we compared the methods of calculations from Hauschildt (2006) for NI 2 and the significance of minimal changes that we had implemented in obtaining NI 1 (from our calculations). We aimed at comparing the results of NI 1 and NI 2 for group A over our entire period of analysis. Applying the Shapiro-Wilk test, we found that the mean values of NI 1 and NI 2 were not normally distributed (see Tab. 8) over the period of 15 weeks, and so we implemented a further non-parametric test. Figure 13 shows box plots of NI 1 and NI 2 over 15 weeks for the orofacial cleft infants (group A).

Tab. 8: Descriptive statistic summary comparing NI 1 and NI 2 in group A

| Group A (N=60) | Shapiro-Wilk test significance (p) | Mean | Std. Dev. | Std. Error | Median | Min | Max |
|---|---|---|---|---|---|---|---|
| | **NI 1 p= .085** | 0.21 | 0.13 | 0.02 | 0.18 | 0.00 | 0.64 |
| | **NI 2 p= .004** | 0.19 | 0.14 | 0.02 | 0.17 | 0.00 | 0.68 |

N is the number of cry appointments

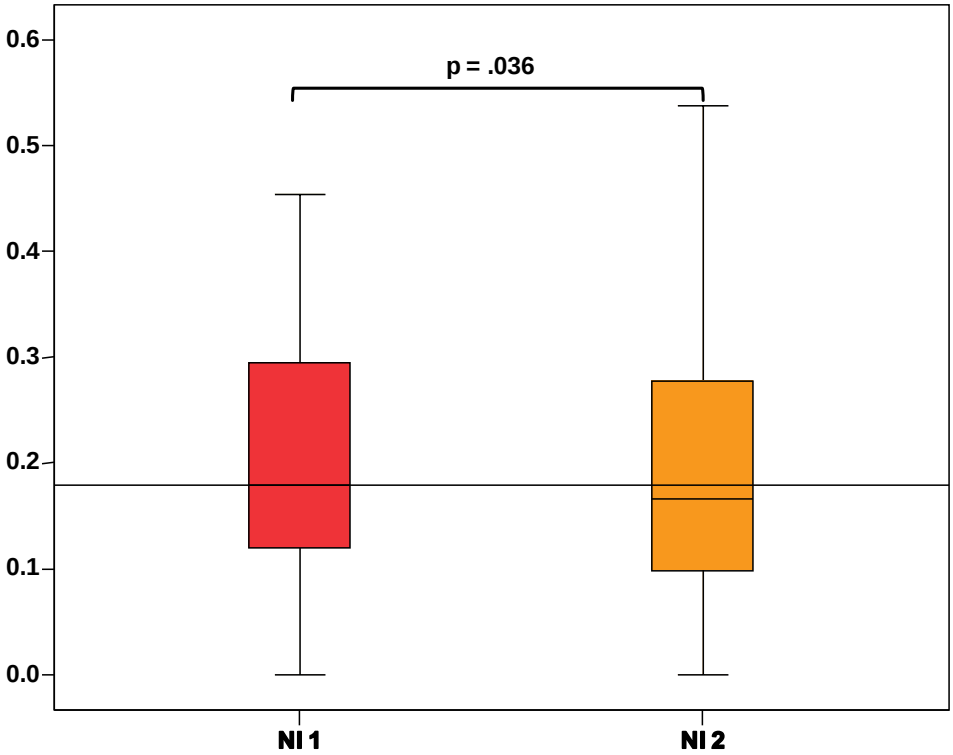



Figure 13: Box plot comparing NI 1 and NI 2 for group A (0 - 4 months)

Using a t-test for the paired samples NI 1 and NI 2 (descriptive statistical analyses are given in Tab. 9), we obtained a significant difference (p= .036) between the samples NI 1/NI 2 in group A across a period of 4 months.

Tab. 9: T-test for paired samples NI 1 and NI 2 in group A

| Pair NI1/NI2 | Mean | Std. Dev. | Std. Error | Correlation | Confidence Interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| | 0.0134 | 0.0484 | 0.0062 | .937 | 0.0089 | 0.0259 |

With the Wilcoxons test we further compared the results for the mean NI 1 and NI 2 from each child during the period of four months. There was a significant difference (p= .028) between NI 1 and NI 2 from the child LA, meanwhile a tendency towards a significant difference (p= .075) between NI 1 and NI 2 could be obtained from the children AN, EA and SE. There existed no significant differences in the results of mean NI 1 compared to NI 2 in the other children.

The results of this comparison between NI 1 and NI 2 were box plotted for each child in group A (shown in Figure 14). Despite obtaining no significant differences by comparing the mean NI 1 to NI 2 in some children as mentioned above, we noticed other differences in their box plots. There was a wider IQR and more data skewness for NI 2 in LU, for example (see Figure 14).

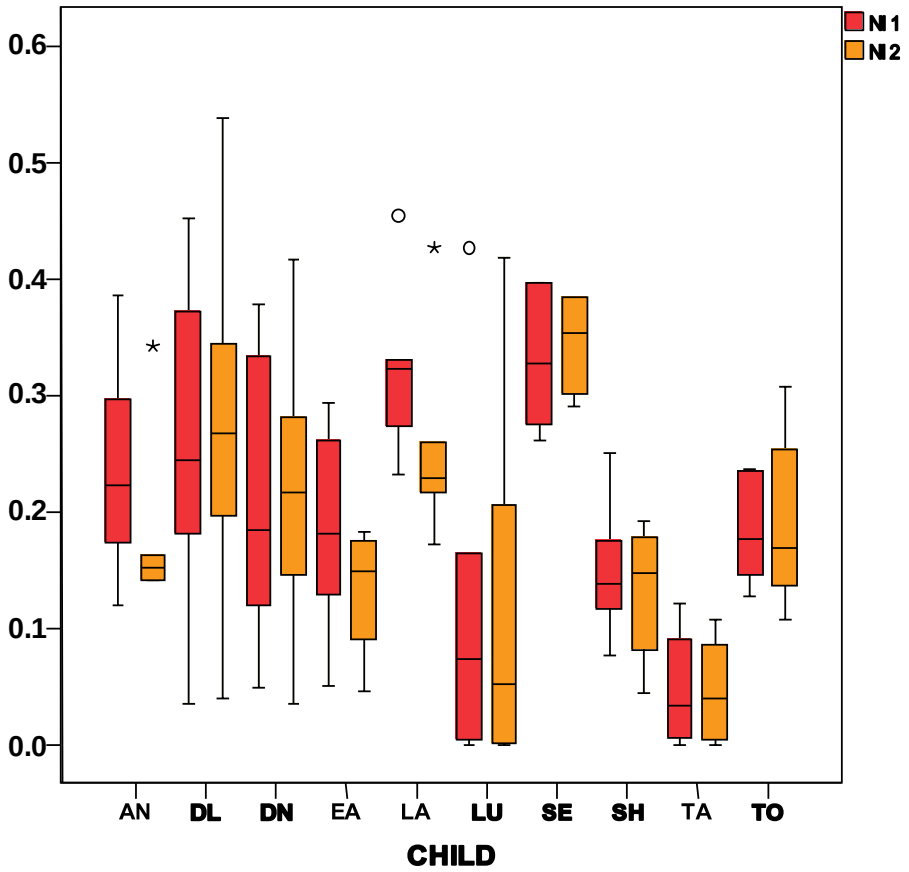



Figure 14: Box plot comparing NI 1 and NI 2 for each child from group A

## 3.2 Analysing noise phenomena and signal length through first 4 months

### 3.2.1 Comparison of mean noise index (NI 1) between all groups

The distribution analysis with the Shapiro-Wilk test for each group at the beginning of this statistical survey (see Tab. 10) decided between using a non-parametric test or a parametric test. Descriptive statistics are summarized in Tab. 10 for the mean value of the NI 1 for each group across a period of 4 months. The mean NI 1 for each group was compared on a monthly basis (chapter 3.3.1) as well as within the groups (chapter 3.4.1)

Analysis of the noise index (NI 1) during the first 4 months in the three groups showed remarkable differences (Tab. 10 and Figure 15).

Tab. 10: Descriptive statistic summary for analysis of NI 1 in all groups

| **Groups (N)** | **Shapiro-Wilk Test significance (p)** | **Median [s]** | **Percentile** | |
|---|---|---|---|---|
| | | | **25% [s]** | **75% [s]** |
| **A (60)** | < .0001 | .184 | .116 | .297 |
| **B1 ($FH^-$) (112)** | < .0001 | .114 | .062 | .222 |
| **B2 ($FH^+$) (60)** | .003 | .181 | .099 | .296 |

N is the number of cry appointments

To examine the hypothesis whether the share of noise-like elements in pre-speech vocalizations differed between the three groups, results of their NI 1 were box-plotted and compared (Figure 15).

Applying the Kruskal-Wallis test for comparisons between the three groups resulted in a statistically significant difference (p = .009). Despite reaching statistical significance, the actual difference in mean values between the groups was quite small. We implemented the Mann-Whitney test on comparing the groups with each other. Group A and group B1 differed significantly from one another (p= .008) as well as group B1 from group B2 (p= .021). Comparing group A and group B2 using the Mann-Whitney test, no significant difference was found between them (p= .625).

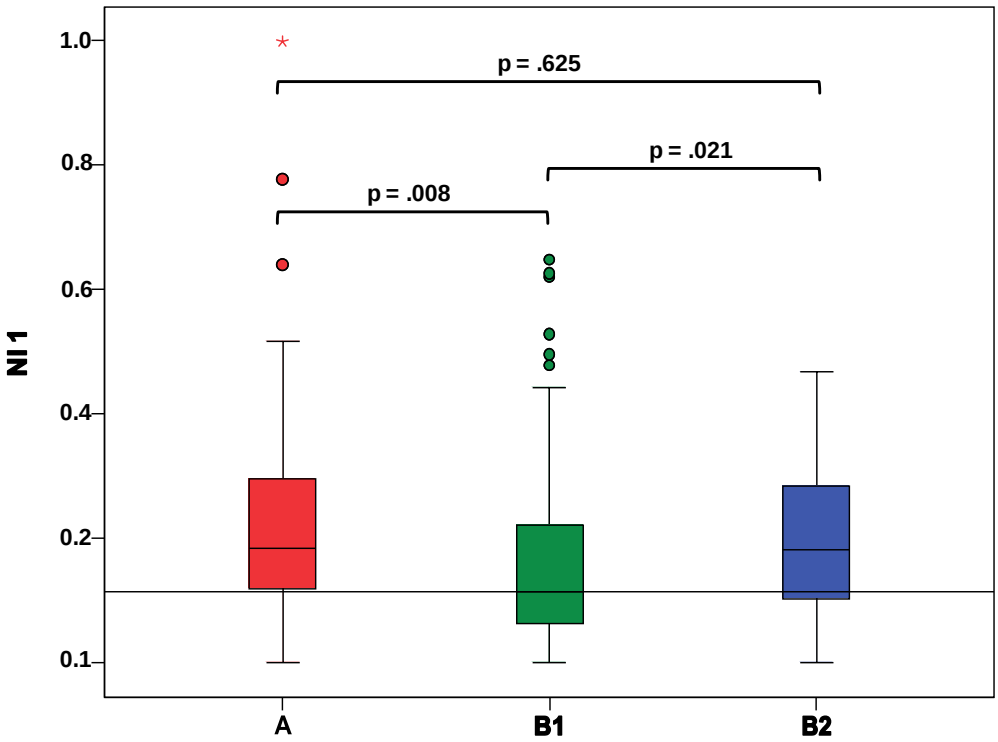



Figure 15: Box plot showing NI 1 in the three groups (0 - 4 months)

### 3.2.2 Comparison of mean signal length (SL) between all groups

Applying the Shapiro-Wilk test for each of the three groups, we began our statistical analysis of mean values of signal length across a period of 4 months. The mean signal lengths were also compared on a monthly basis between the groups (in chapter 3.3.4) and within the groups (in chapter 3.4.4).

Tab. 11: Descriptive statistic summary for analysis of SL in all groups

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| **A (60)** | .001 | 1.192 | .929 | 1.528 |
| **B1 ($FH^-$) (112)** | < .0001 | 1.559 | 1.195 | 1.889 |
| **B2 ($FH^+$) (60)** | < .0001 | 1.243 | .914 | 1.529 |

N is the number of cry appointments

Applying the Kruskal-Wallis-test for comparisons between the three groups resulted in a statistically significant difference (p< .0001).
We implemented the Mann-Whitney test in comparing the groups with each other. Group A and group B1 differed significantly from one another (p< .0001) as well as group B1 from group B2 (p= .001). Meanwhile group A and group B2 compared with each other did not differ significantly for SL (p= .980).

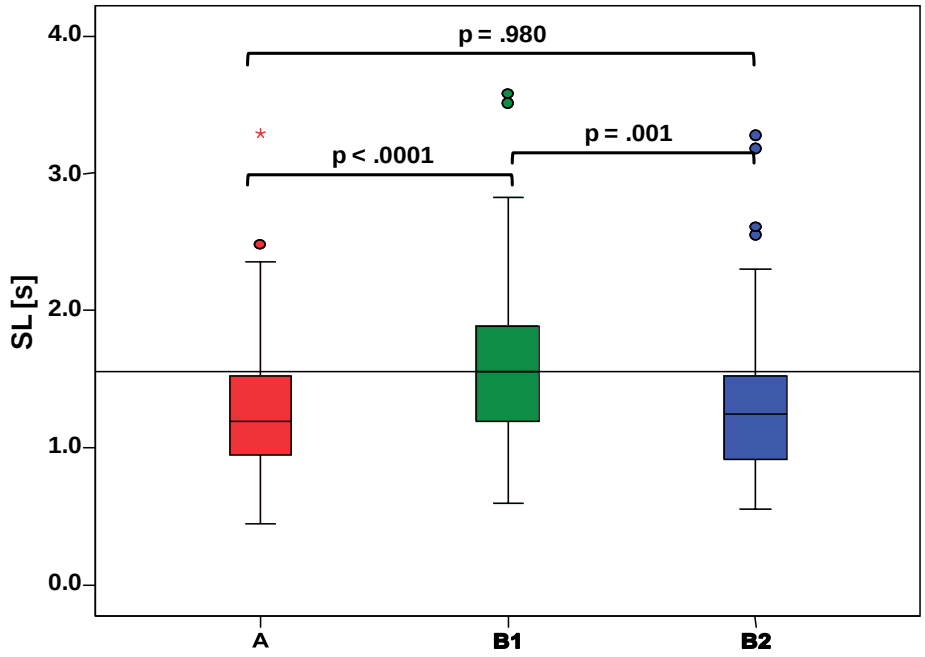



Figure 16: Box plot showing SL in the three groups (0 - 4 months)

Across a period of 4 months (in Figure 16), the box plots from two groups (A and B2) had almost the same interquartile range and median which were different from group B1. In Figure 15, more than 50% of the signals from group A and B2 had a NI above the marker set at the median of group B1. We noticed the reversed phenomenon when considering our marker in Figure 16, set at the median of group B1. The median of the signal length in phonations from group B1 infants lies 50% above the length of the signals from infants in group A and B2 over a period of 4 months. There were no significant differences between group A and B2, meanwhile we noticed that infants in group B1 produced longer signals on average (see Tab. 11).

## 3.3 Monthly analysis of mean values between the groups

### 3.3.1 Analysis of mean noise index (NI 1)

#### 3.3.1.1 First month

Tab. 12: Descriptive statistic summary of NI 1 for the first month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25%[ s] | 75% [s] |
| **A (10)** | .024 | .246 | .125 | .310 |
| **B1 ($FH^-$) (10)** | .476 | .243 | .090 | .386 |
| **B2 ($FH^+$) (10)** | .641 | .192 | .112 | .343 |

N is the number of infants in the group

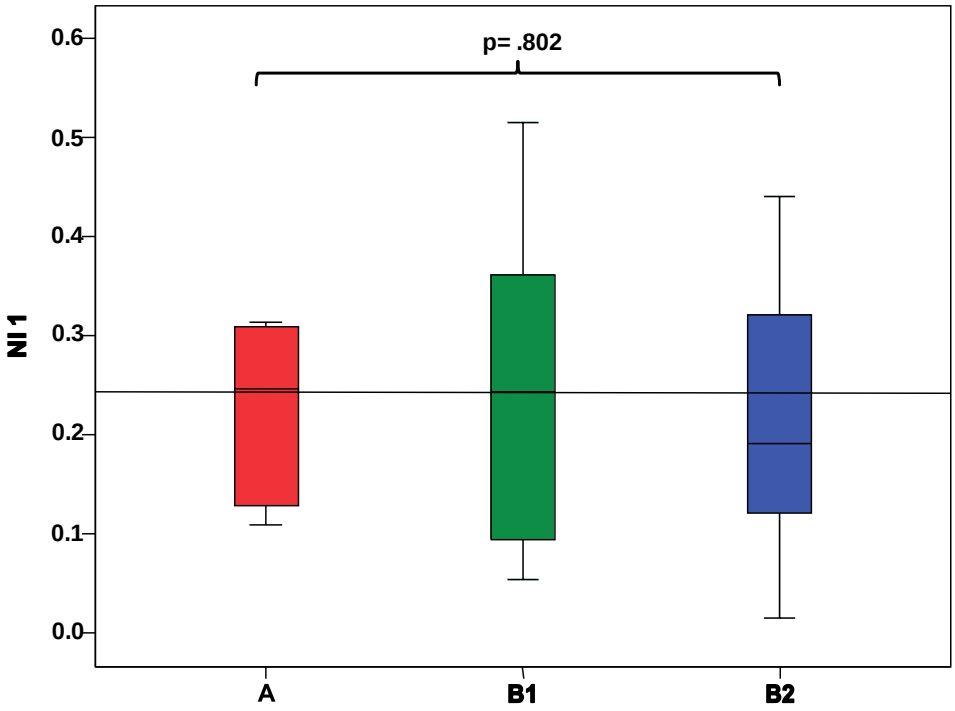



Figure 17: Box plots showing the results of NI 1 during the first month

Applying an overall non-parametric test (Kruskal-Wallis test) for comparisons between the three groups during the first month resulted in a statistically non-significant difference (p= .802). In this case, we needed no paired comparisons

between the groups during the first month. The median value of group B2 was lower than that of the groups A and B1, albeit not significantly lower.

### 3.3.1.2 Second month

Tab. 13: Descriptive statistic summary of NI 1 for the second month

| Groups N=10 infants | Mean | Std. Dev. | Std. Error | Median | Min | Max |
|---|---|---|---|---|---|---|
| **A p= .607** | .222 | .122 | .038 | .201 | .003 | .412 |
| **B1 ($FH^-$) p= .343** | .158 | .094 | .029 | .148 | .049 | .315 |
| **B2 ($FH^+$) p= .376** | .214 | .112 | .035 | .216 | .056 | .354 |

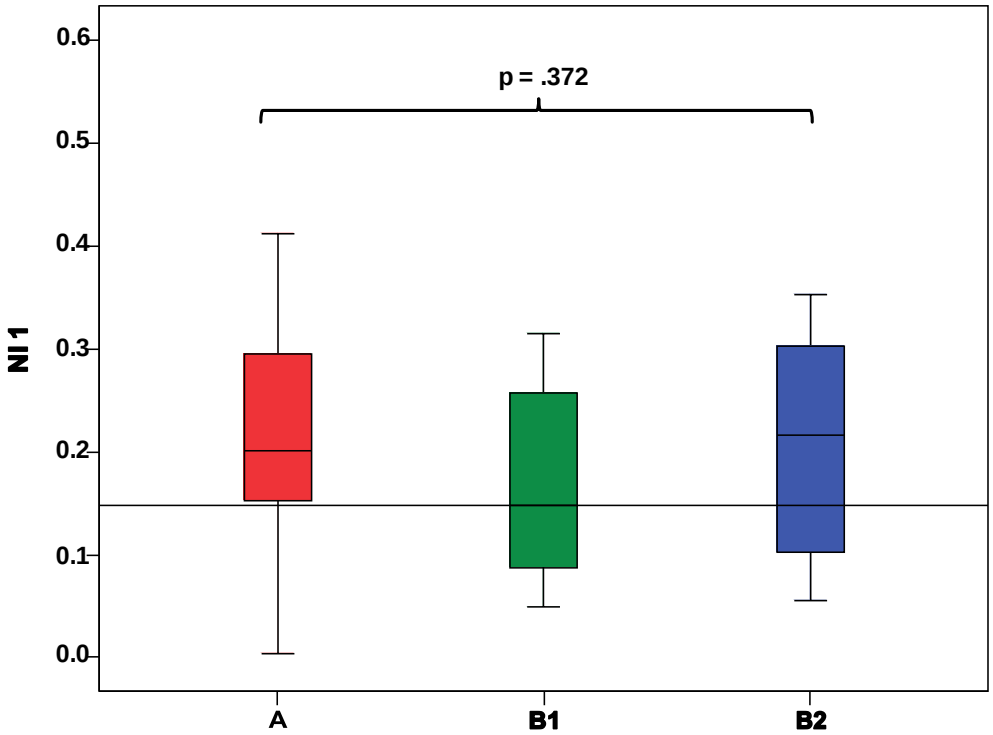



Figure 18: Box plots showing the results of NI 1 during the second month

The test of homogeneity on our variables (Levenes statistics) resulted in a non-significance (p= .838), as such applying a one-way ANOVA, there was no statistically significant difference for the three groups during the second month: F (2, 29) = 1.026, p= .372. The effect size, calculated using eta squared, was

0.267. Non-significance after conducting our overall test (ANOVA) made further comparisons between the groups during the second month unnecessary. However, there was a trend for the median value of NI 1 from group B1 to be lower than that of the two other groups.

### 3.3.1.3 Third month

Tab. 14: Descriptive statistic summary of NI 1 for the third month

| Groups N=10 infants | Mean [s] | Std. Dev. [s] | Std. Error [s] | Median [s] | Min [s] | Max [s] |
|---|---|---|---|---|---|---|
| **A p= .745** | .185 | .138 | .044 | .149 | .000 | .446 |
| **B1 ($FH^-$) p= .222** | .093 | .075 | .024 | .075 | .014 | .248 |
| **B2 ($FH^+$) p= .077** | .150 | .140 | .044 | .095 | .002 | .463 |

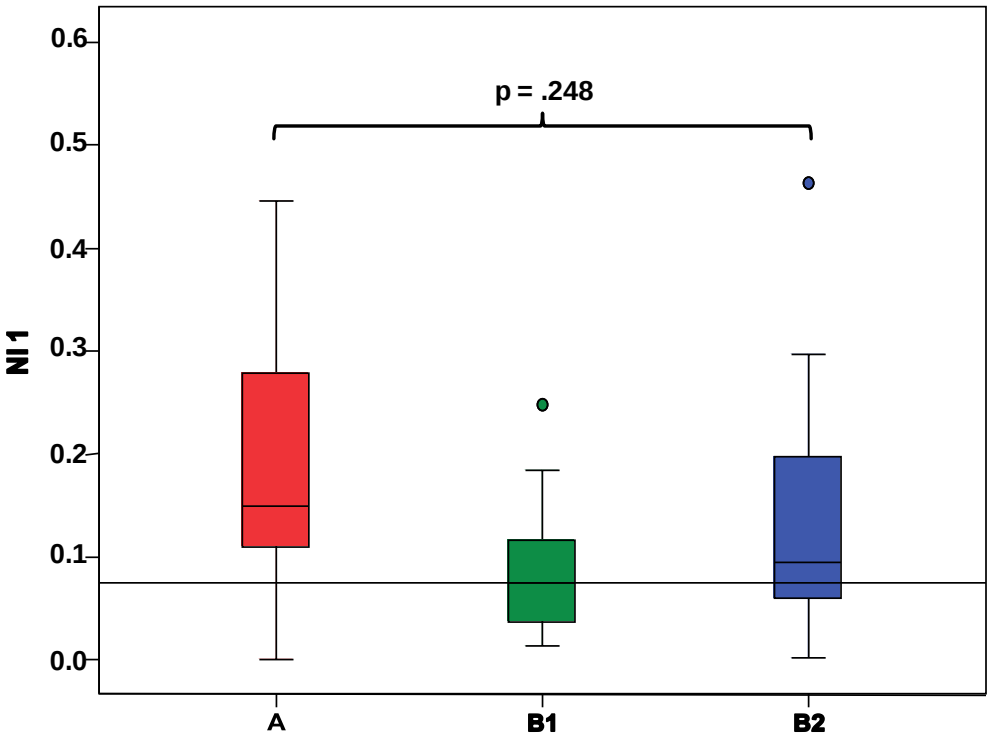



Figure 19: Box plots showing the results of NI 1 during the third month

The test of homogeneity on our variables (Levenes statistics) resulted in a non-significance (p= .197), as such we were able to apply the ANOVA. Applying a

one-way ANOVA, there was no statistically significant difference for the three groups during the third month: F (2, 29) = 1.470, p = .248. The effect size, calculated using eta squared, was 0.315. The median NI 1 value from group A was higher than that of the two other groups. Group B1 exhibited a marked smaller IQR than the two other groups.

#### 3.3.1.4 Fourth month

Tab. 15: Descriptive statistic summary of NI 1 for the fourth month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| **A N=10** | .426 | .237 | .049 | .397 |
| **B1 ($FH^-$) 10)** | .007 | .085 | .065 | .183 |
| **B2 ($FH^+$) (10)** | .167 | .204 | .088 | .288 |

N is the number of infants in the group

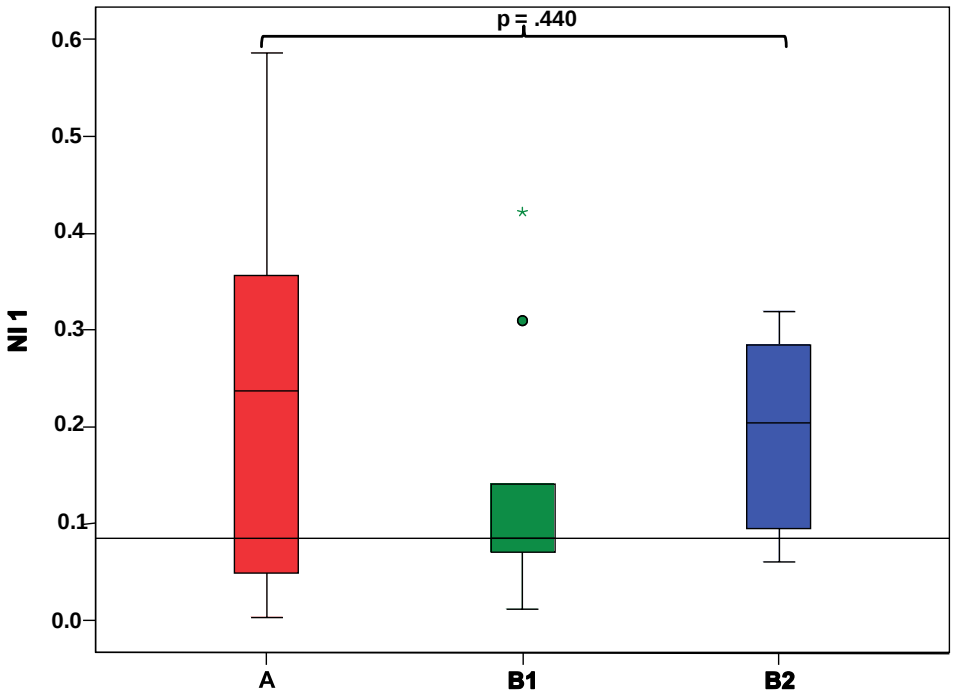



Figure 20: Box plots showing the results of NI 1 during the fourth month

Applying an overall non-parametric test (Kruskal-Wallis test) for comparisons between the three groups during the fourth month resulted in a statistically non-significant difference (p = .440). We therefore needed no paired comparisons between the groups during the fourth month.

Here there was also a higher median NI 1 value from group A than that of the two other groups. In group B1, the IQR was again smaller than that of the other two groups.

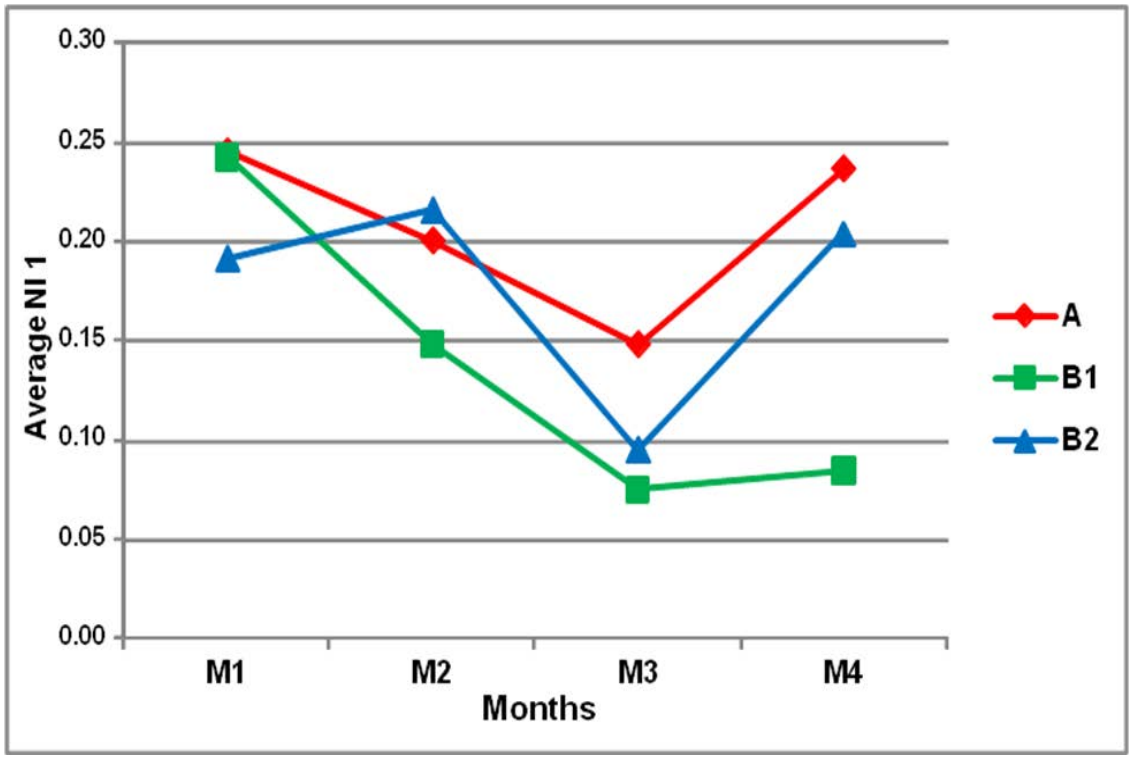



Figure 21: Average NI 1 in the groups from M1 - M4

The average results of the NI 1 from the groups was summarized on a monthly basis (M1 – M4) and we saw differences when displaying them graphically (see Figure 21). The average NI 1 in group B1 always lay below that of the other two groups except during the first month (M1). The curve from the group B2 infants differed from the other two groups from M1 to M2. From M2 to M3, it takes a steep gradient almost reaching the average NI 1 in group B1. However, it accelerates towards values found in group A while getting to M4.

### 3.3.2 Analysis of mean noise band (NB)

#### 3.3.2.1 First month

Tab. 16: Descriptive statistic summary of NB for the first month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| A (10) | .003 | .104 | .068 | .221 |
| B1 ($FH^-$) 10) | .184 | .217 | .065 | .324 |
| B2 ($FH^+$) 10) | .001 | .076 | .056 | .194 |

N is the number of infants in the group

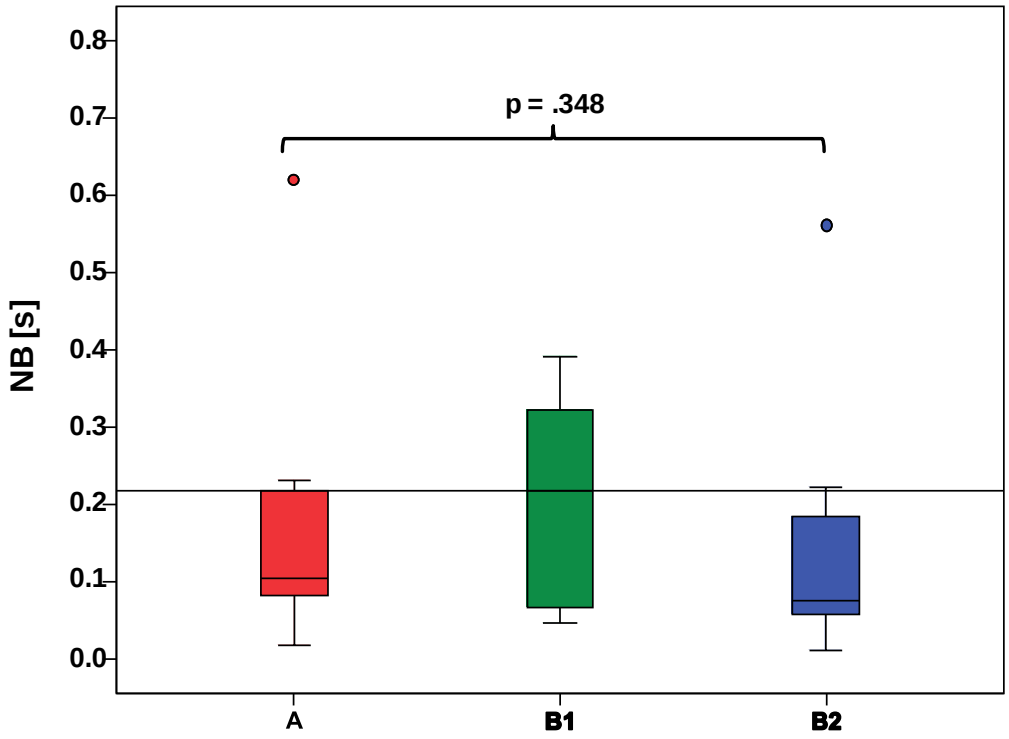



Figure 22: Box plots showing results of NB for the first month

Applying an overall non-parametric test (Kruskal-Wallis test) for comparisons between the three groups during the first month resulted in a statistically non-significant difference (p= .348). We therefore needed no paired comparisons between the groups during the first month.

The median NB value from the group B1 infants was higher than the groups A and B2. In group B1, there was a wider IQR for the mean NB value during the first month while the box plots from group A and B2 were similar in size.

### 3.3.2.2 Second month

Tab. 17: Descriptive statistic summary of NB for the second month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| A (10) | .110 | .079 | .039 | .238 |
| B1 ($FH^-$) (10) | .007 | .136 | .072 | .277 |
| B2 ($FH^+$) (10) | .001 | .139 | .093 | .162 |

N is the number of infants in the group

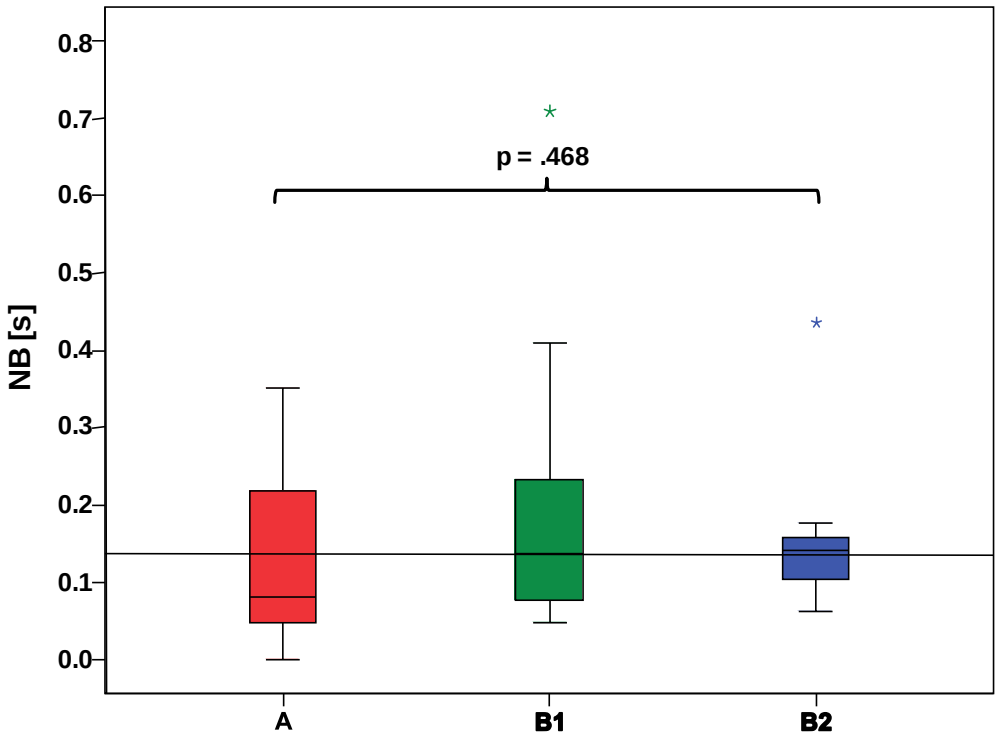



Figure 23: Box plots showing results of NB for the second month

Applying an overall non-parametric test (Kruskal-Wallis test) for comparisons between the three groups during the second month resulted in a statistically non-significant difference (p= .468). We therefore needed no paired comparisons between the groups during the second month.

The median value for NB was similar in the groups B1 and B2, although the IQR in group B2 was smaller.

### 3.3.2.3 Third month

Tab. 18: Descriptive statistic summary of NB for the third month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| **A (10)** | .052 | .115 | .043 | .311 |
| **B1 ($FH^-$) (10)** | .001 | .097 | .028 | .154 |
| **B2 ($FH^+$) (10)** | .002 | .053 | .011 | .255 |

N is the number of infants in the group

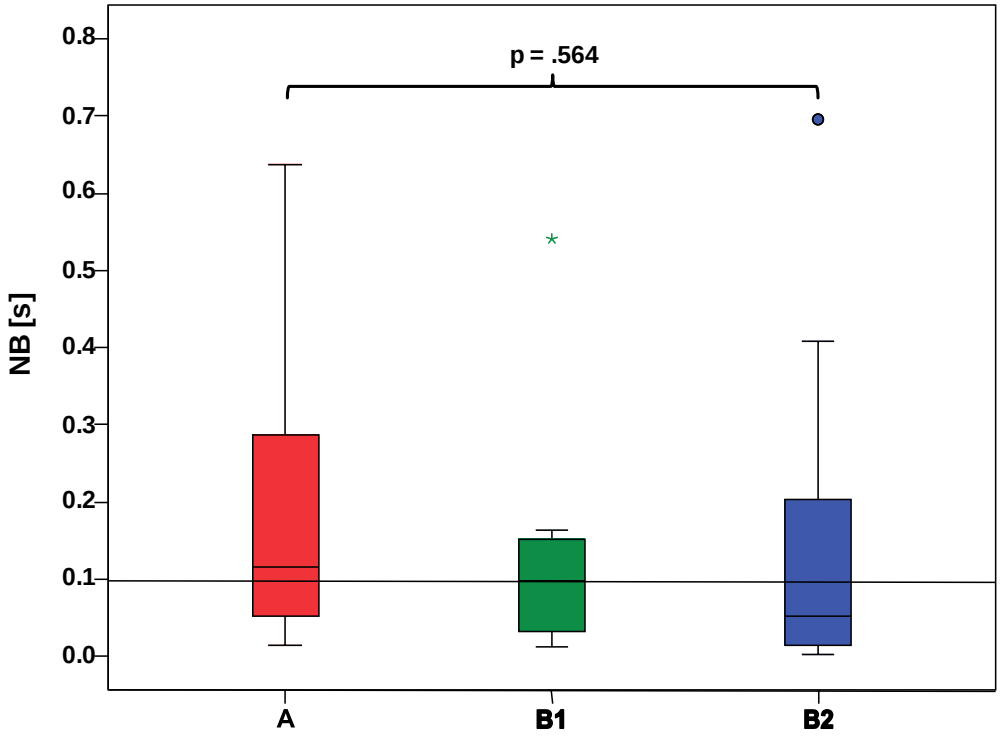



Figure 24: Box plots showing results of NB for the third month

Applying an overall non-parametric test (Kruskal-Wallis test) for comparisons between the three groups during the second month resulted in a statistically non-significant difference (p= .564). We therefore needed no paired comparisons between the groups for this month.

The median value for NB increased for group A as well as the IQR. In group B2, the median value decreased with a wider IQR.

### 3.3.2.4 Fourth month

Tab. 19: Descriptive statistic summary of NB for the fourth month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| **A (10)** | .005 | .061 | .020 | .373 |
| **B1 ($FH^-$) (10)** | < .0001 | .101 | .075 | .202 |
| **B2 ($FH^+$) (10)** | .099 | .139 | .037 | .257 |

N is the number of infants in the group

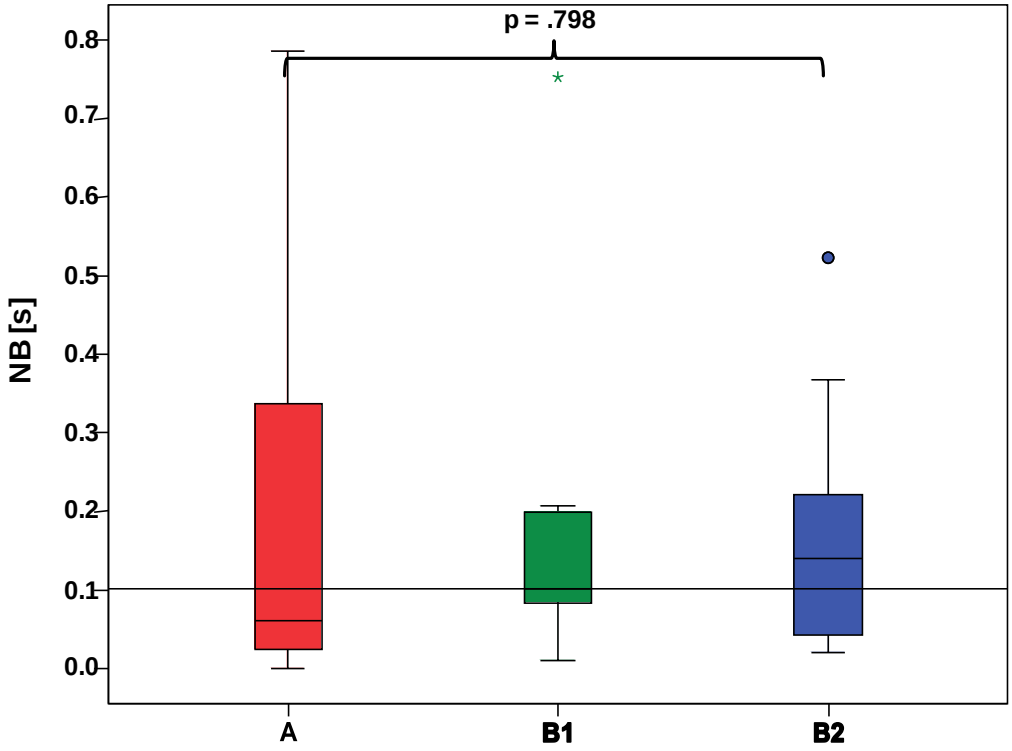



Figure 25: Box plots showing results of NB for the fourth month

Applying an overall non-parametric test (Kruskal-Wallis test) for comparisons between the three groups during the fourth month resulted in a statistically non-significant difference (p= .798). We therefore needed no paired comparisons between the groups for the fourth month.

The median value for NB in group B1 remained almost constant, meanwhile in group A the IQR increased.

### 3.3.3 Analysis of mean subharmonics (SH)

#### 3.3.3.1 First month

Tab. 20: Descriptive statistic summary of SH for the first month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| **A (10)** | .735 | .084 | .049 | .137 |
| **B1 ($FH^-$) (10)** | .218 | .077 | .019 | .203 |
| **B2 ($FH^+$) (10)** | < .0001 | .067 | .041 | .125 |

N is the number of infants in the group

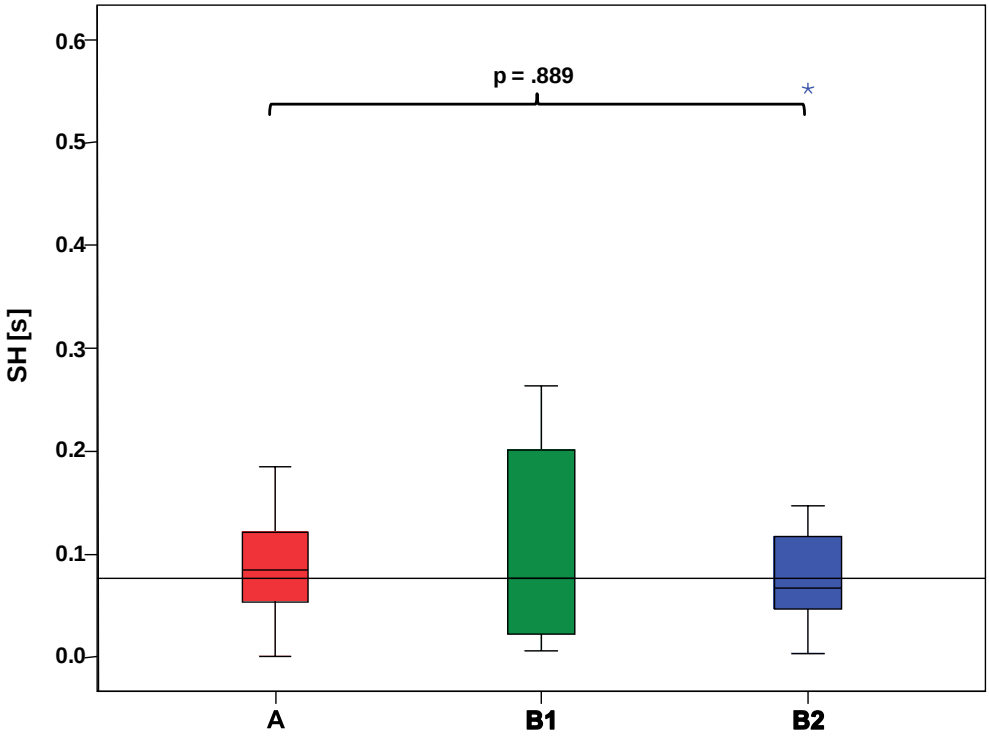



Figure 26: Box plots showing results of SH for the first month

A Kruskal-Wallis test for comparisons between the three groups during the first month resulted in a statistically non-significant difference (p= .889).

Despite there being no statistical differences in the median SH values, the IQR from group B1 was wider than that of the other two groups.

### 3.3.3.2 Second month

Tab. 21: Descriptive statistic summary of SH for the second month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| **A (10)** | .012 | .024 | .008 | .136 |
| **B1 ($FH^-$) (10)** | .072 | .033 | .015 | .103 |
| **B2 ($FH^+$) (10)** | .754 | .047 | .029 | .072 |

N is the number of infants in the group

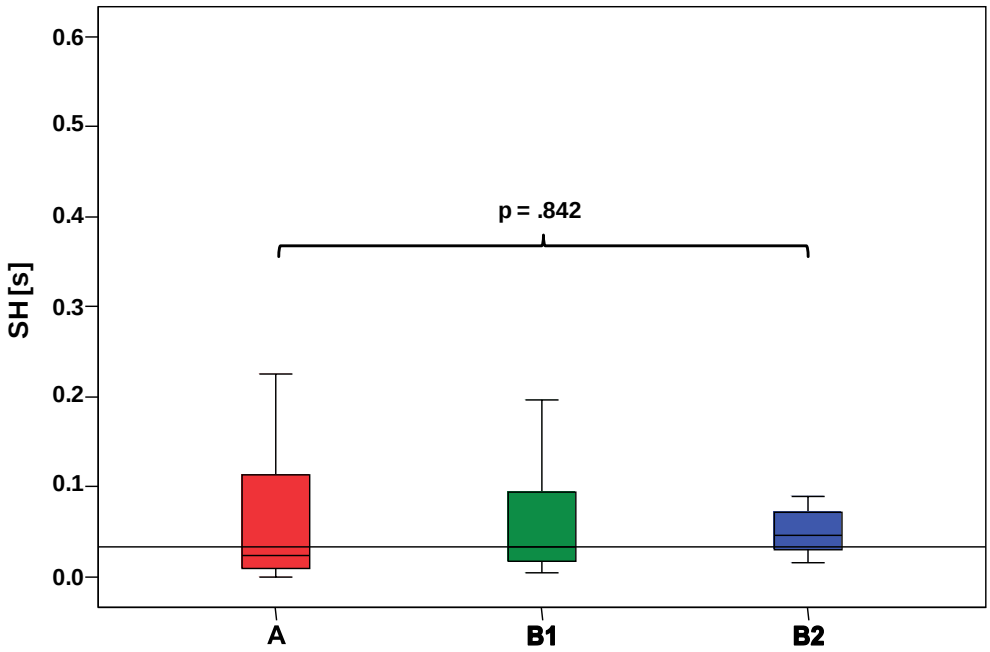



Figure 27: Box plots showing results of SH for the second month

A Kruskal-Wallis test for comparisons between the three groups during the second month resulted in a statistically non-significant difference (p= .842).

The median SH value further decreased for all three groups with decreasing IQR`s for the groups B1 and B2.

### 3.3.3.3 Third month

Tab. 22: Descriptive statistic summary of SH for the third month

| Groups N=10 | Mean [s] | Std. Dev. [s] | Std. Error [s] | Median [s] | Min [s] | Max [s] |
|---|---|---|---|---|---|---|
| **A p= .070** | .043 | .047 | .015 | .033 | .000 | .148 |
| **B1 ($FH^-$) p= .069** | .019 | .015 | .005 | .014 | .005 | .051 |
| **B2 ($FH^+$) p= .677** | .038 | .029 | .009 | .029 | .000 | .095 |

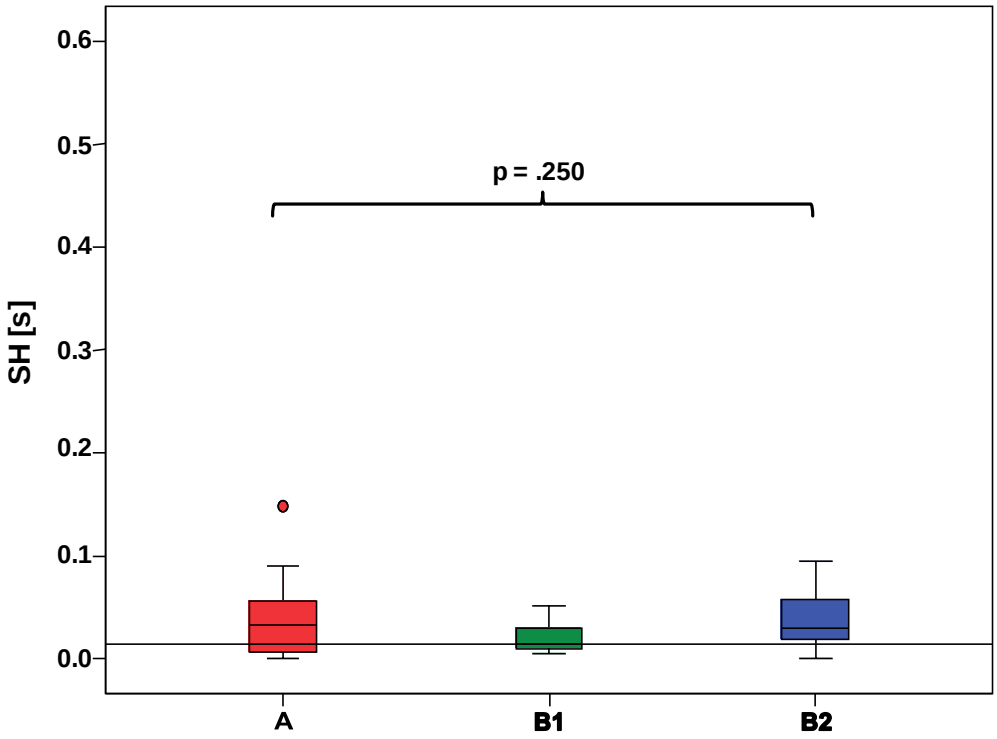



Figure 28: Box plots showing results of SH for the third month

The test of a homogeneity on our variables resulted in a significance (p= .044), as such applying a one-way ANOVA, there was no statistically significant difference in SH between the three groups: F (2, 29) = 1.459, p = .250. The effect size, calculated using eta squared, was 0.302.

The median SH value further decreased for group B1 with significant changes in the IQR`s in groups A and B1.

### 3.3.3.4 Fourth month

Tab. 23: Descriptive statistic summary of SH for the fourth month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| **A (10)** | < .0001 | .048 | .011 | .079 |
| **B1 ($FH^-$) (10)** | < .0001 | .018 | .007 | .035 |
| **B2 ($FH^+$) (10)** | .001 | .037 | .032 | .045 |

N is the number of infants in the group

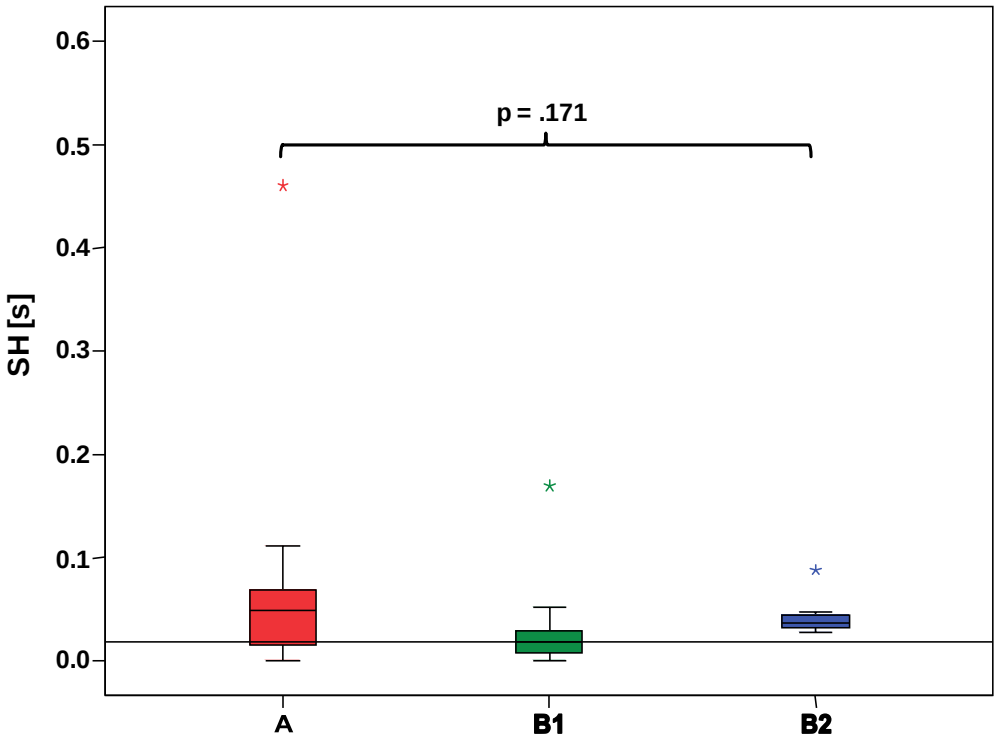



Figure 29: Box plots showing results of SH for the fourth month

A Kruskal-Wallis test for comparisons between the three groups during the fourth month resulted in a statistically non-significant difference (p = .171).

The median SH value was higher for group A, and the IQR in group B2 decreased significantly (Figure 29). Meanwhile, the median SH value in group B1 did not change significantly as well as the IQR.

### 3.3.4 Analysis of mean signal length

#### 3.3.4.1 First month

Tab. 24: Descriptive statistic summary of SL for the first month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| **A (10)** | .925 | 1.275 | .948 | 1.420 |
| **B1 ($FH^-$) (10)** | .279 | 1.385 | 1.002 | 1.588 |
| **B2 ($FH^+$) (10)** | .005 | 1.063 | .806 | 1.280 |

N is the number of infants in the group

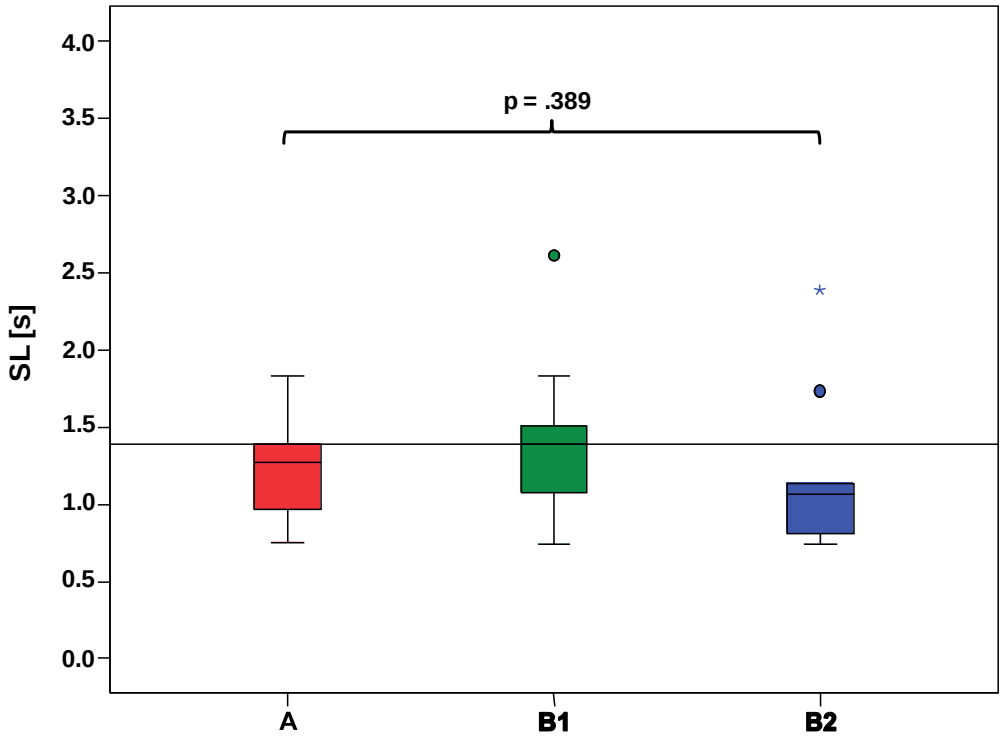



Figure 30: Box plots showing results of SL for the first month

A Kruskal-Wallis test for comparisons between the three groups during the first month resulted in a statistically non-significant difference (p= .389).

The median value of SL from group B1 was higher than the other two groups while the IQR`s in groups A and B1 were similar. In group B2, there was a marked decrease in the IQR.

### 3.3.4.2 Second month

Tab. 25: Descriptive statistic summary of SL for the second month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| **A (10)** | .337 | .976 | .830 | 1.284 |
| **B1 ($FH^-$) (10)** | .549 | 1.737 | 1.301 | 2.183 |
| **B2 ($FH^+$) (10)** | .033 | 1.182 | .951 | 1.683 |

N is the number of infants in the group

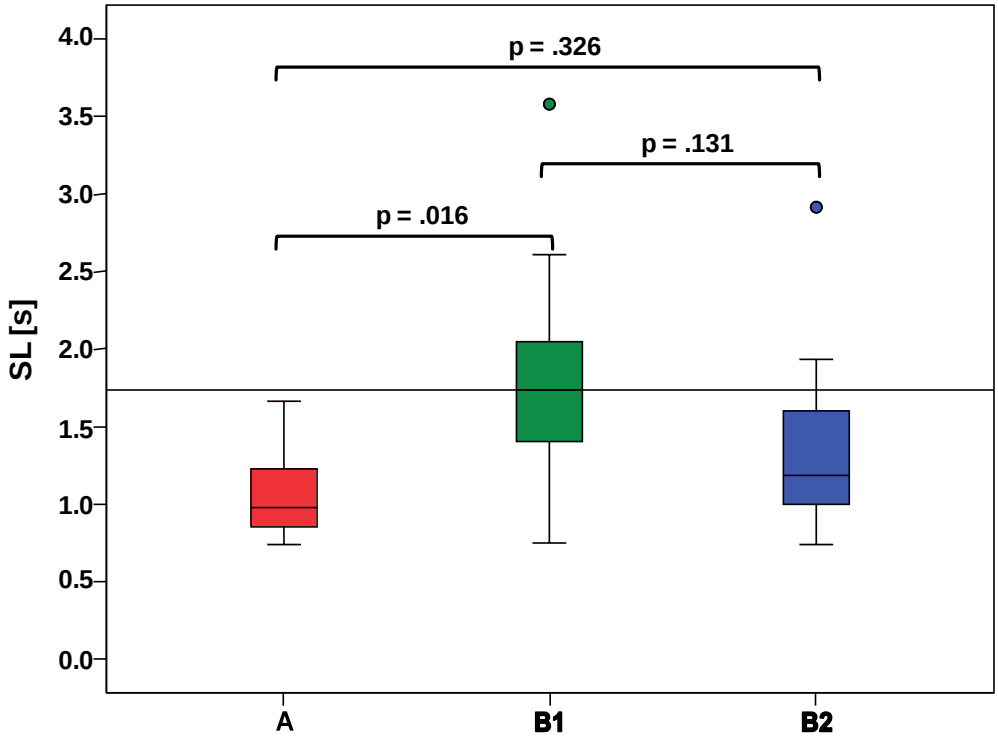



Figure 31: Box plots showing results of SL for the second month

Applying an overall non-parametric test (Kruskal-Wallis test) for comparisons between the three groups during the second month resulted in a statistically significant difference (p= .046). In this case, we needed paired comparisons between the groups during this month.

We implemented the Mann-Whitney test in comparing the groups with each other. Group A and group B1 differed significantly from one another (p= .016).

Meanwhile comparing group A and group B2 using the Mann-Whitney test, no significant difference was found between them (p= .326). There was also no significant difference between group B1 and group B2 (p= .131).
The median SL value increased in groups B1 and B2, meanwhile there was a decrease in the median SL value in group A.

### 3.3.4.3 Third month

Tab. 26: Descriptive statistic summary of SL for the third month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| A (10) | .195 | 1.332 | .916 | 1.672 |
| B1 ($FH^-$) (10) | .787 | 1.565 | 1.171 | 1.842 |
| B2 ($FH^+$) (10) | .008 | 1.456 | .926 | 1.640 |

N is the number of infants in the group

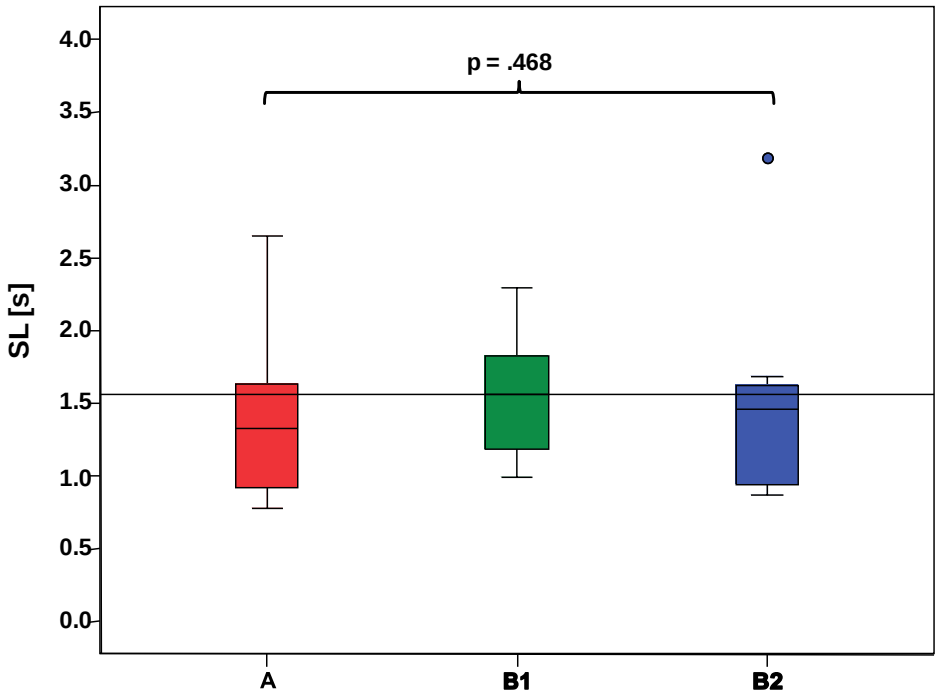



Figure 32: Box plots showing results of SL for the third month

A Kruskal-Wallis test for comparisons between the three groups during the third month resulted in a statistically non-significant difference (p= .468).

### 3.3.4.4 Fourth month

Tab. 27: Descriptive statistic summary of SL for the fourth month

| Groups (N) | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|
| | | | 25% [s] | 75% [s] |
| **A (10)** | .255 | 1.393 | .898 | 1.672 |
| **B1 ($FH^-$) (10)** | .326 | 1.533 | 1.415 | 1.848 |
| **B2 ($FH^+$) (10)** | .010 | 1.322 | 1.091 | 1.401 |

N is the number of infants in the group

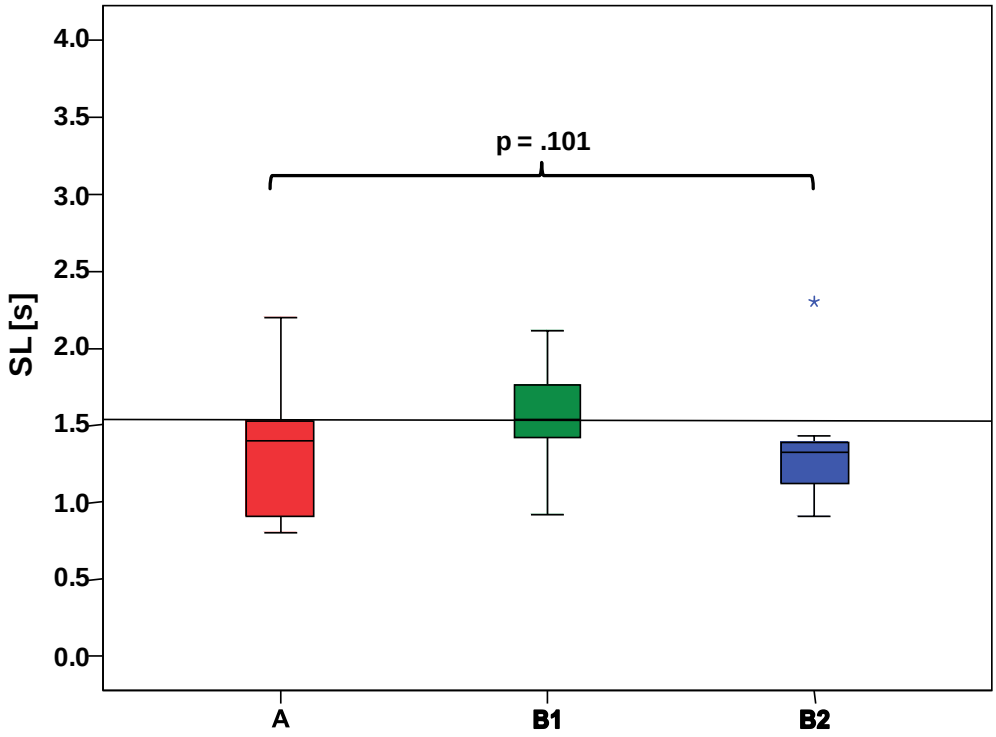



Figure 33: Box plots showing results of SL for the fourth month

A Kruskal-Wallis test for comparisons between the three groups during the fourth month resulted in a statistically non-significant difference (p= .101).

The infants from group B1 maintained a stable and higher median SL than the other two groups. There was also a marked decrease in the IQR in the B2 group during the fourth month (comparing Figure 31 - Figure 33).

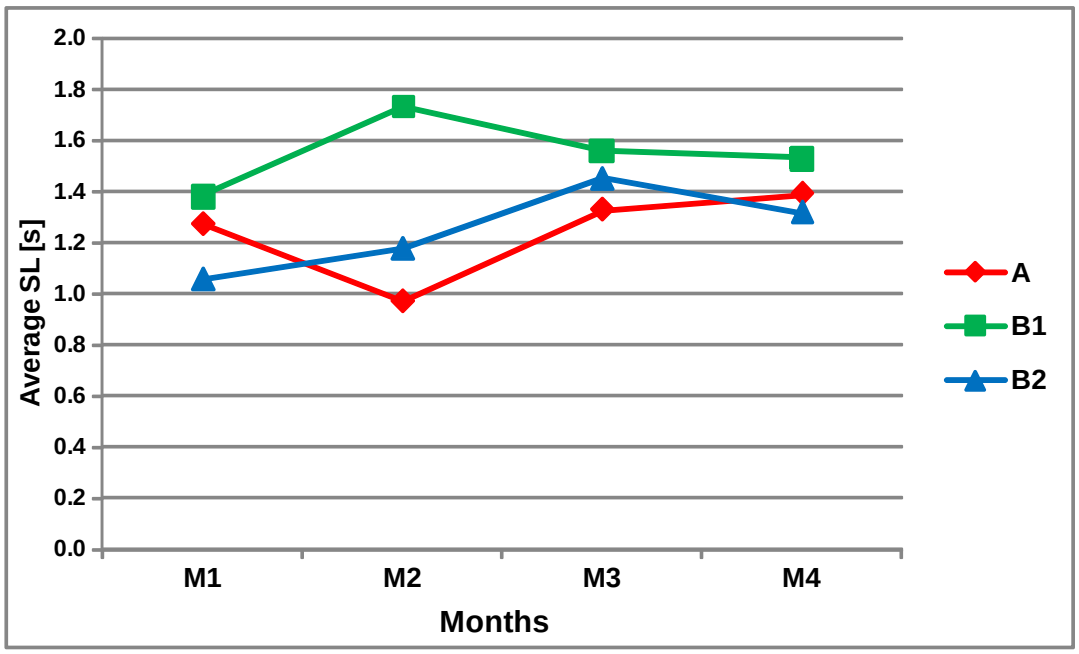



Figure 34: Average SL in the groups from MI - M4

In a graphical summary of the average SL from the three groups in a period of four months (M1 - M4), the infants in group B1 always produced higher values than the other two groups. While the average SL from group B1 and B2 increased from M1 - M2, it decreased in group A. While the average SL values in group A and B2 increased from M2 - M3, the value decreased in group B1 but was still above that of the other two groups (see Figure 34)

## 3.4 Monthly analysis of mean values within the groups

### 3.4.1 Analysis of mean noise index (N1 1)

Distribution Analysis: The distribution analysis (Shapiro-Wilk test) for each group was the condition ruling which statistical test we applied. In group A and B1 there was a statistical significant difference, but no significant difference was found in group B2.

#### 3.4.1.1 Group A

Tab. 28: Descriptive statistic summary for mean monthly NI 1

| | Months | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|---|
| | | | | 25% [s] | 75% [s] |
| Infants N=10 | M1 | .024 | .246 | .125 | .310 |
| | M2 | .607 | .201 | .151 | .321 |
| | M3 | .745 | .149 | .086 | .288 |
| | M4 | .426 | .237 | .049 | .397 |

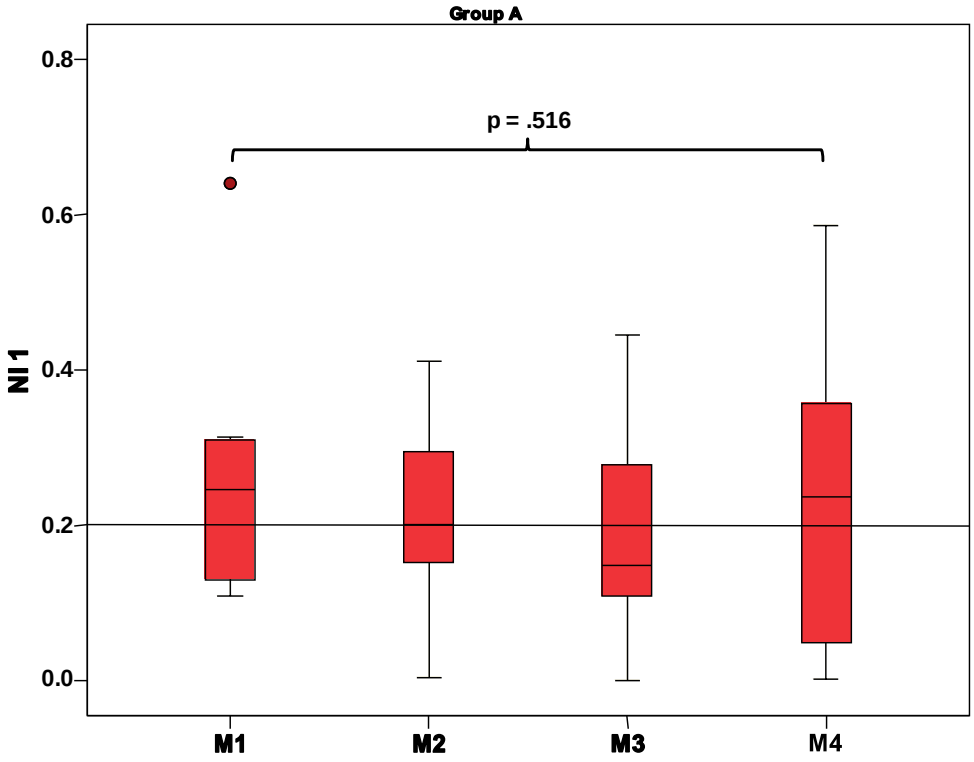



Figure 35: Box plot showing monthly results of NI 1 in group A

The mean monthly values of NI in group A were not significant to one another with p= .516, as our analysis with the Friedmann's test showed.

### 3.4.1.2 Group B1

Tab. 29: Descriptive statistic summary for mean monthly NI 1

| | Months | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|---|
| | | | | 25% [s] | 75% [s] |
| Infants N=10 | M1 | .476 | .243 | .090 | .386 |
| | M2 | .343 | .148 | .078 | .257 |
| | M3 | .222 | .075 | .032 | .134 |
| | M4 | .007 | .085 | .064 | .183 |

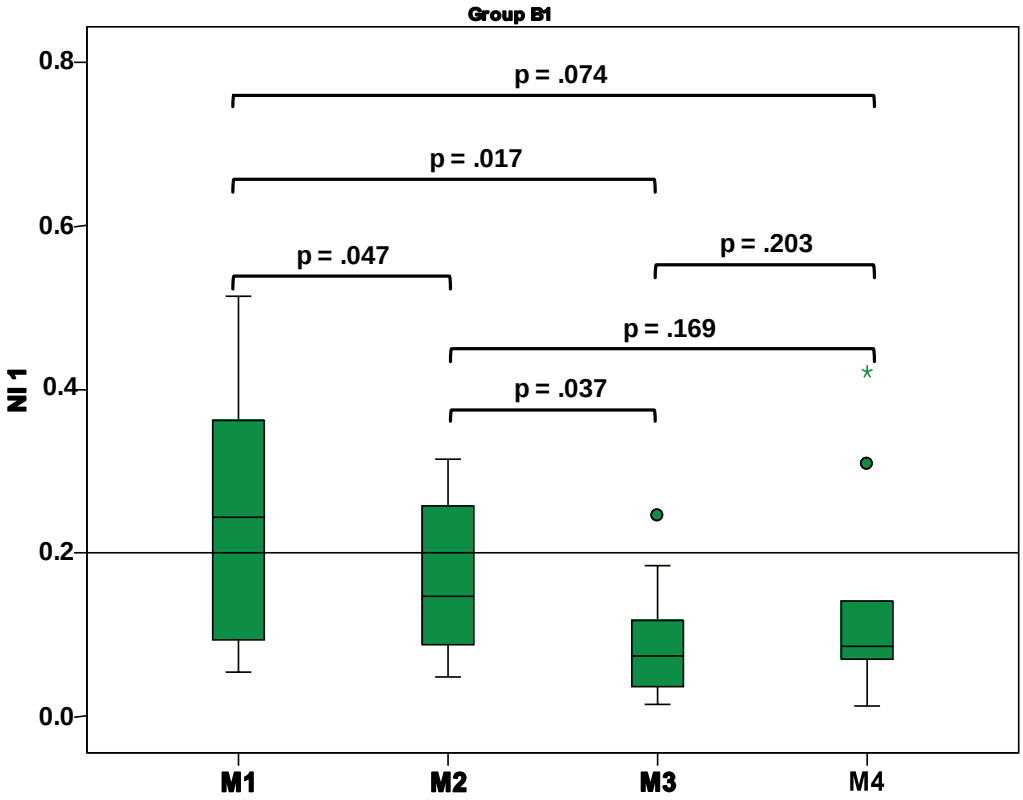



Figure 36: Box plot showing monthly results of NI 1 in group B1

A non-parametric test (Friedmann's test or paired test) compared the mean monthly NI values, resulting to a significance of p= .008.
Testing their mean monthly NI values using the Wilcoxon test (tests independent valuables within groups) we obtained significant and non significant differences as summarized in Tab. 30.

Tab. 30: Wilcoxon's test comparing paired samples

| **Mean SH pairs** | **M1-M2** | **M1-M3** | **M1-M4** | **M2-M3** | **M2-M4** | **M3-M4** |
|---|---|---|---|---|---|---|
| **Sig. (p)** | .047 | .017 | .074 | .037 | .169 | .203 |

### 3.4.1.3 Group B2

Tab. 31: Descriptive statistic summary for mean monthly NI 1

| | **Months p** | **Mean [s]** | **Std. Dev. [s]** | **Std. Error [s]** | **Median [s]** | **Min [s]** | **Max [s]** |
|---|---|---|---|---|---|---|---|
| **Infants N=10** | **M1 p= .641** | .216 | .136 | .043 | .192 | .016 | .440 |
| | **M2 p= .376** | .214 | .112 | .035 | .216 | .056 | .354 |
| | **M3 p= .077** | .150 | .140 | .044 | .095 | .002 | .463 |
| | **M4 p= .167** | .189 | .101 | .032 | .204 | .061 | .319 |

Applying a one-way ANOVA for repeated samples, there was no statistically significant difference obtained (p= .449). The effect size, eta squared was .092.

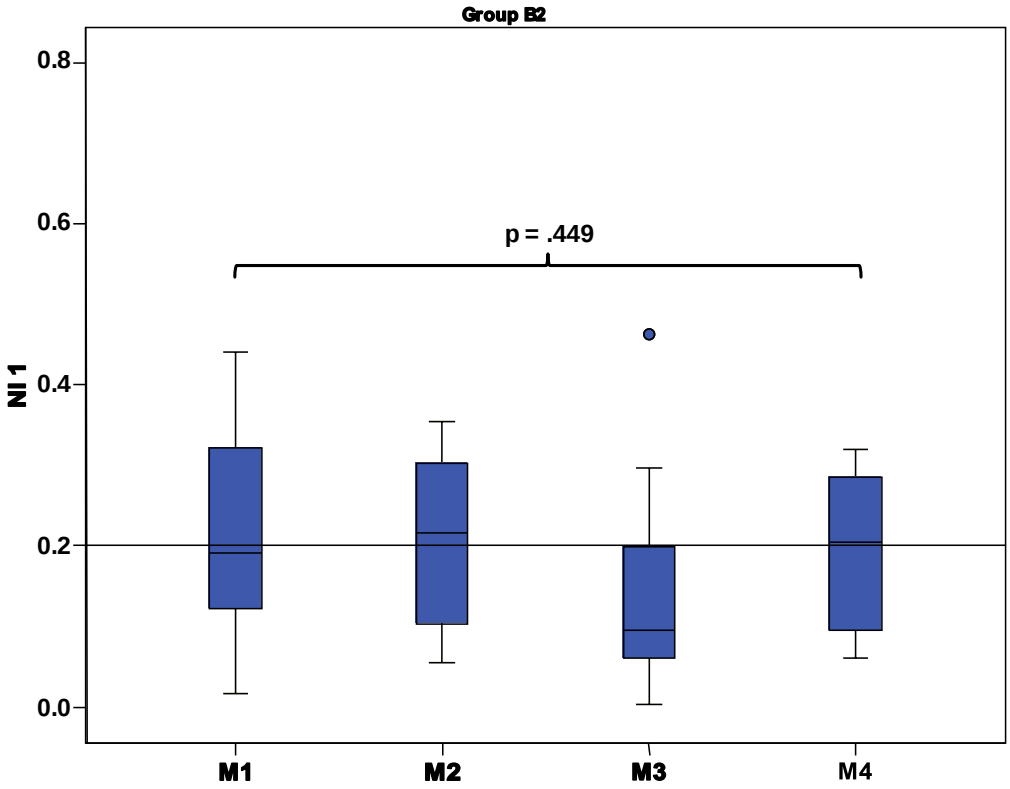



Figure 37: Box plot showing monthly results of NI 1 in group B2

### 3.4.2 Analysis of mean noise band (NB)

Distribution Analysis: The distribution analysis (Shapiro-Wilk test) for each group was the condition ruling which statistical test we applied. In group A, B1 and B2 there was a statistical significant difference.

#### 3.4.2.1 Group A

Tab. 32: Descriptive statistic summary for mean monthly NB

| | Months | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|---|
| | | | | 25% [s] | 75% [s] |
| Infants N=10 | M1 | .003 | .104 | .068 | .221 |
| | M2 | .110 | .079 | .039 | .238 |
| | M3 | .052 | .115 | .043 | .311 |
| | M4 | .005 | .061 | .020 | .373 |

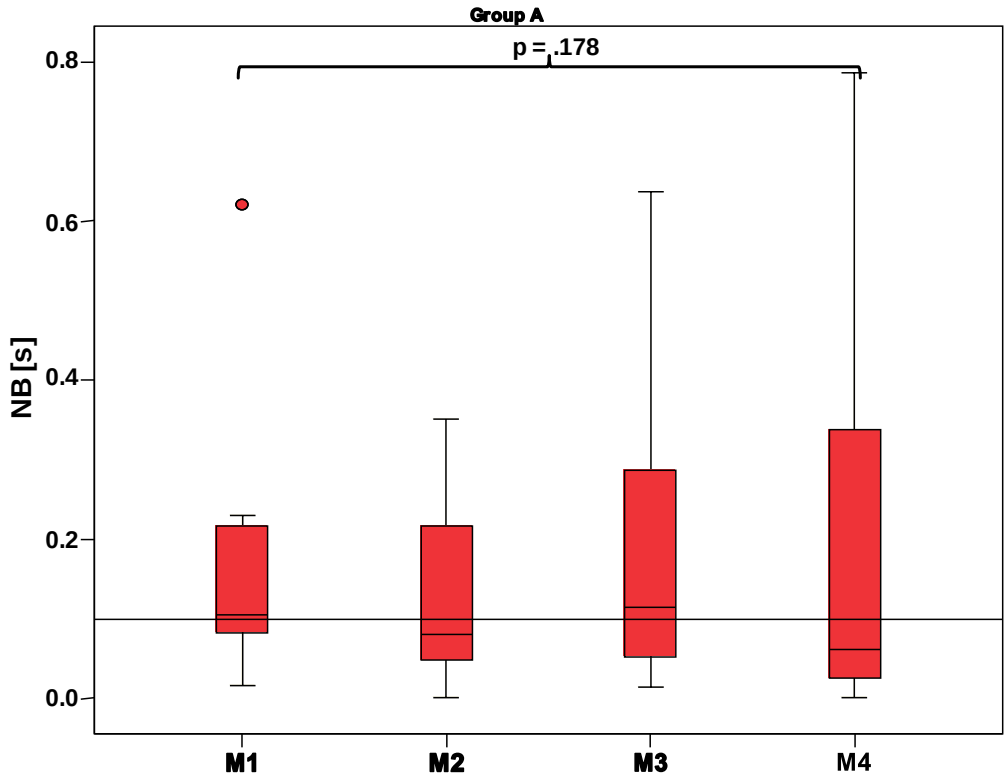



Figure 38: Box plot showing monthly results of NB in group A

A non-parametric test (Friedmann's test or paired test) compared the mean monthly NB values, resulting in a non-significance of p= .178.

### 3.4.2.2 Group B1

Tab. 33: Descriptive statistic summary for mean monthly NB

| | Months | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|---|
| | | | | 25% [s] | 75% [s] |
| Infants N=10 | M1 | .184 | .217 | .065 | .324 |
| | M2 | .007 | .136 | .072 | .277 |
| | M3 | .001 | .097 | .028 | .154 |
| | M4 | < .0001 | .101 | .075 | .202 |

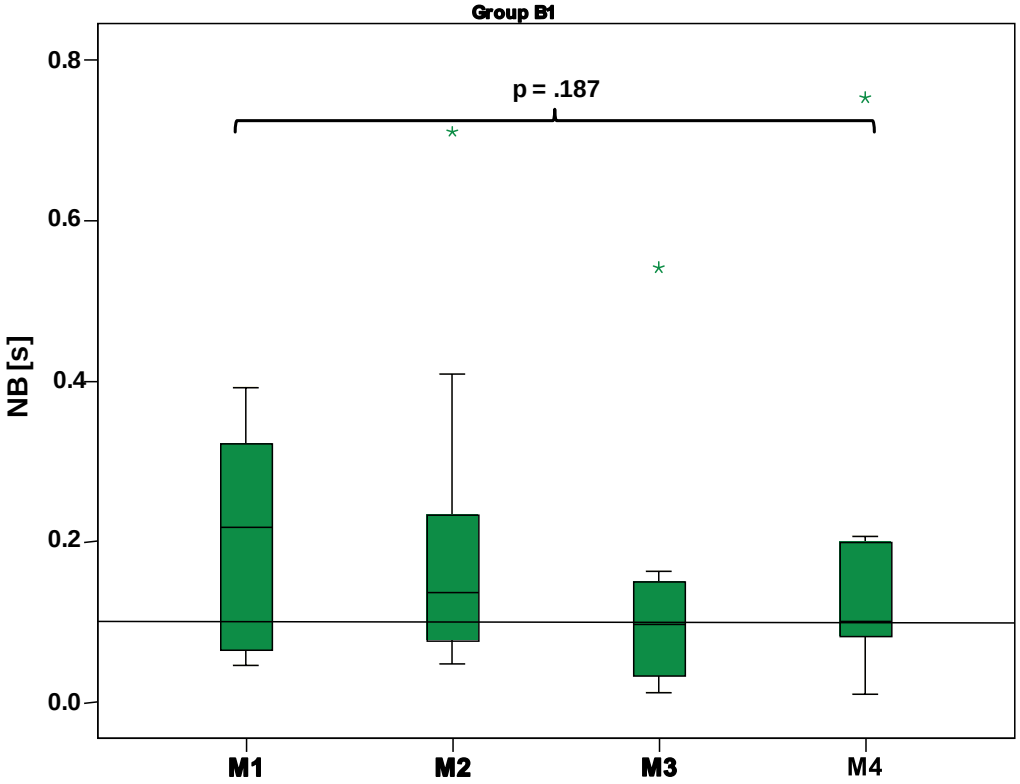



Figure 39: Box plot showing monthly results of NB in group B1

Testing their mean monthly NB values using the Friedmann's test, we obtained non-significant differences (p= .187) within the months M1-M4 as a whole.

### 3.4.2.3 Group B2

Tab. 34: Descriptive statistic summary for mean monthly NB

| | Months | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|---|
| | | | | 25% [s] | 75% [s] |
| Infants N=10 | M1 | .001 | .076 | .055 | .194 |
| | M2 | .001 | .139 | .093 | .162 |
| | M3 | .002 | .053 | .011 | .255 |
| | M4 | .099 | .139 | .037 | .257 |

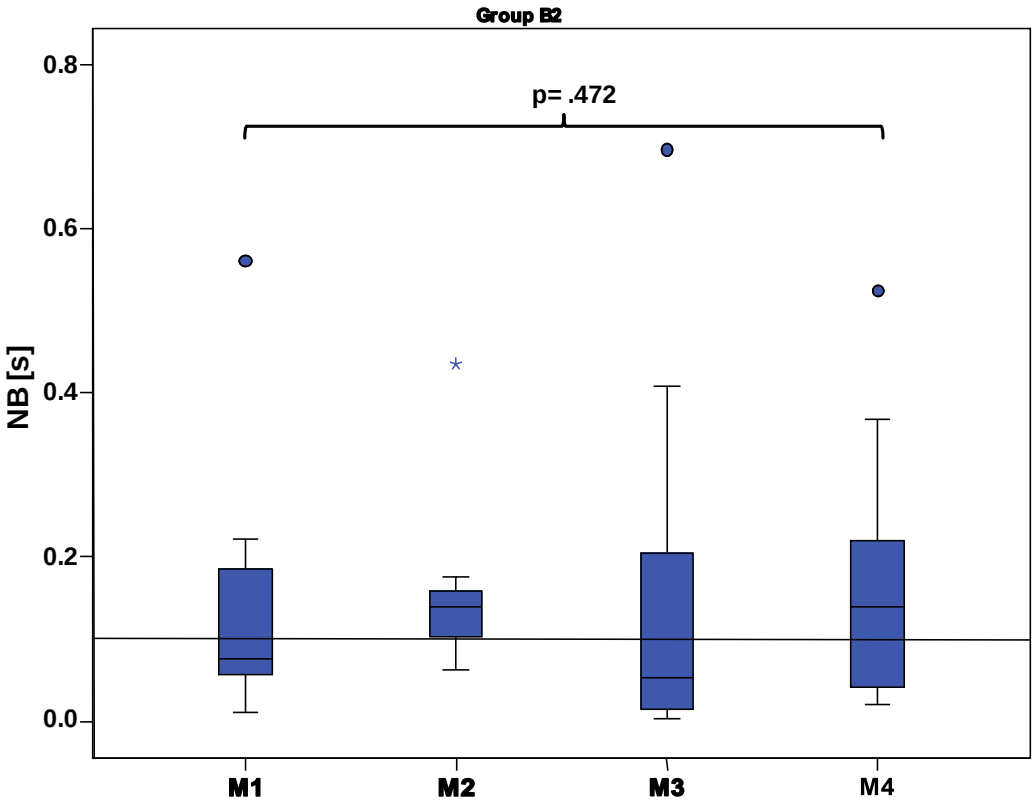



Figure 40: Box plot showing monthly results of NB in group B2

Using the Friedmann's test our mean monthly values for NB were compared to each other, with the result of a non significance within M1 and M4 (p= .472).

### 3.4.3 Analysis of mean subharmonics (SH)

Distribution Analysis: The distribution analysis (Shapiro-Wilk test) for each group was the condition ruling which statistical test we applied. In group A, B1 and B2 there was a statistically significant difference.

#### 3.4.3.1 Group A

Tab. 35: Descriptive statistic summary for mean monthly SH

| | Months | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|---|
| | | | | 25% [s] | 75% [s] |
| Infants N=10 | M1 | .735 | .084 | .049 | .137 |
| | M2 | .012 | .024 | .008 | .136 |
| | M3 | .070 | .033 | .004 | .064 |
| | M4 | < .0001 | .048 | .011 | .079 |

Using the Friedmann's test our mean monthly values for SH were compared to each other with the result of a significance within M1 and M4 (p= .042).
Therefore applying the Wilcoxon test in comparing the mean monthly SH results, we obtained no significant differences (see Tab. 36).

Tab. 36: Wilcoxon's test comparing paired samples

| Mean SH pairs | M1-M2 | M1-M3 | M1-M4 | M2-M3 | M2-M4 | M3-M4 |
|---|---|---|---|---|---|---|
| **Sig. (p)** | .333 | .139 | .110 | .445 | .799 | .074 |

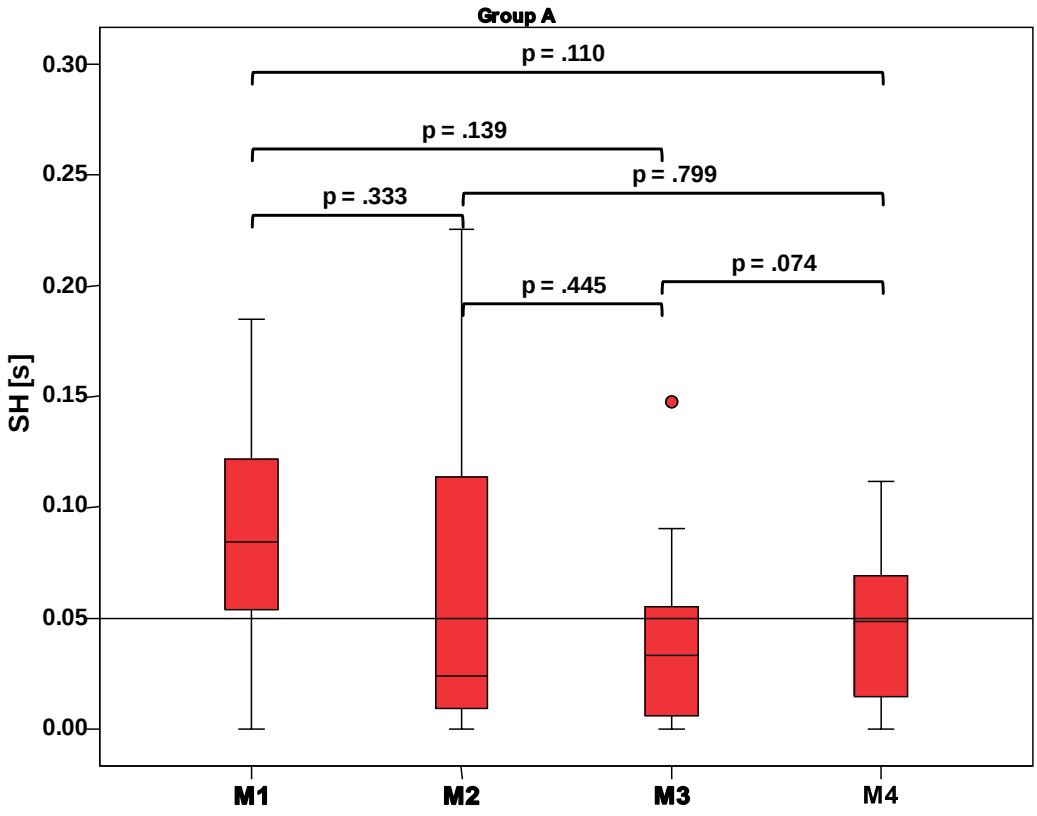



Figure 41: Box plot showing monthly results of SH in group A

### 3.4.3.2 Group B1

Tab. 37: Descriptive statistic summary for mean monthly SH

| | Months | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|---|
| | | | | 25% [s] | 75% [s] |
| Infants N=10 | M1 | .218 | .077 | .019 | .203 |
| | M2 | .072 | .033 | .015 | .103 |
| | M3 | .069 | .014 | .008 | .029 |
| | M4 | < .0001 | .018 | .007 | .035 |

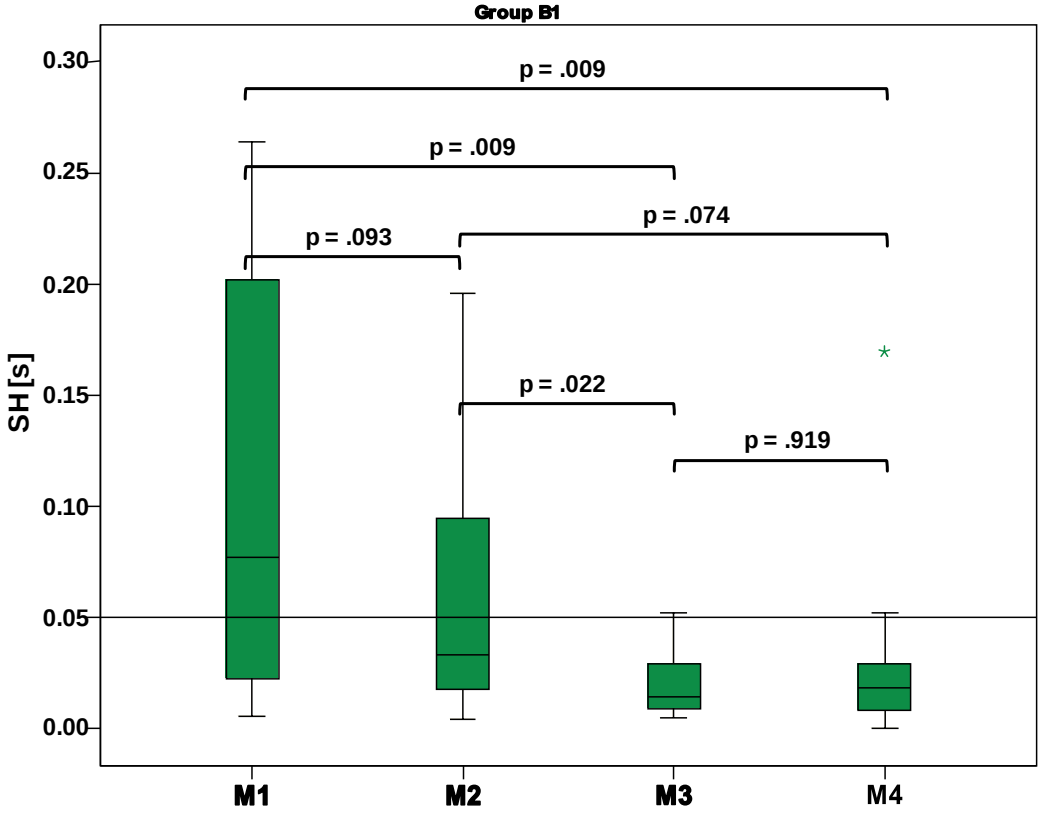



Figure 42: Box plot showing monthly results of SH in group B1

Applying the Friedmann's test our mean monthly values for SH were compared to each other, resulting in a significance within M1 and M4 (p= .003).

A summary of our comparisons using the non parametric test from Wilcoxon is displayed on Tab. 38.

Tab. 38: Wilcoxon's test comparing paired samples

| Mean SH pair | M1-M2 | M1-M3 | M1-M4 | M2-M3 | M2-M4 | M3-M4 |
|---|---|---|---|---|---|---|
| **Sig. (p)** | .093 | .009 | .009 | .022 | .074 | .919 |

### 3.4.3.3 Group B2

Tab. 39: Descriptive statistic summary for mean monthly SH

| | Months | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|---|
| | | | | 25% [s] | 75% [s] |
| Infants N=10 | M1 | < .0001 | .067 | .041 | .125 |
| | M2 | .754 | .047 | .029 | .072 |
| | M3 | .677 | .029 | .017 | .061 |
| | M4 | .001 | .037 | .032 | .045 |

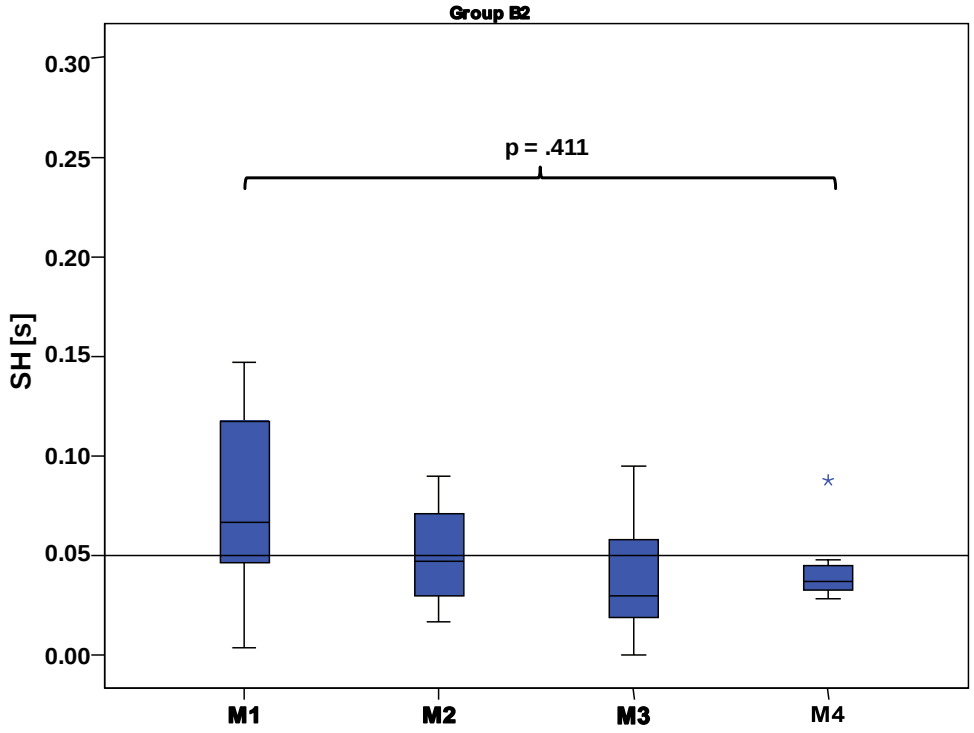



Figure 43: Box plot showing monthly results of SH in group B2

Applying Friedmann's test our mean monthly SH values were compared to each other in this group, resulting in a non-significance within M1 and M4 (p= .411).

### 3.4.4 Analysis of mean signal length (SL)

Distribution Analysis: The distribution analysis (Shapiro-Wilk test) for each group was the condition ruling which statistical test we applied. In group A and B1 there was no statistical significant difference, but a significant difference was found in group B2.

#### 3.4.4.1 Group A

Tab. 40: Descriptive statistic summary for mean monthly SL

| | Months p | Mean [s] | Std. Dev. [s] | Std. Error [s] | Median [s] | Min [s] | Max [s] |
|---|---|---|---|---|---|---|---|
| Infants N=10 | M1 p= .925 | 1.229 | .323 | .102 | 1.275 | .752 | 1.831 |
| | M2 p= .337 | 1.077 | .303 | .096 | .976 | .740 | 1.661 |
| | M3 p= .195 | 1.391 | .557 | .176 | 1.332 | .782 | 2.647 |
| | M4 p= .255 | 1.375 | .491 | .155 | 1.393 | .799 | 2.196 |

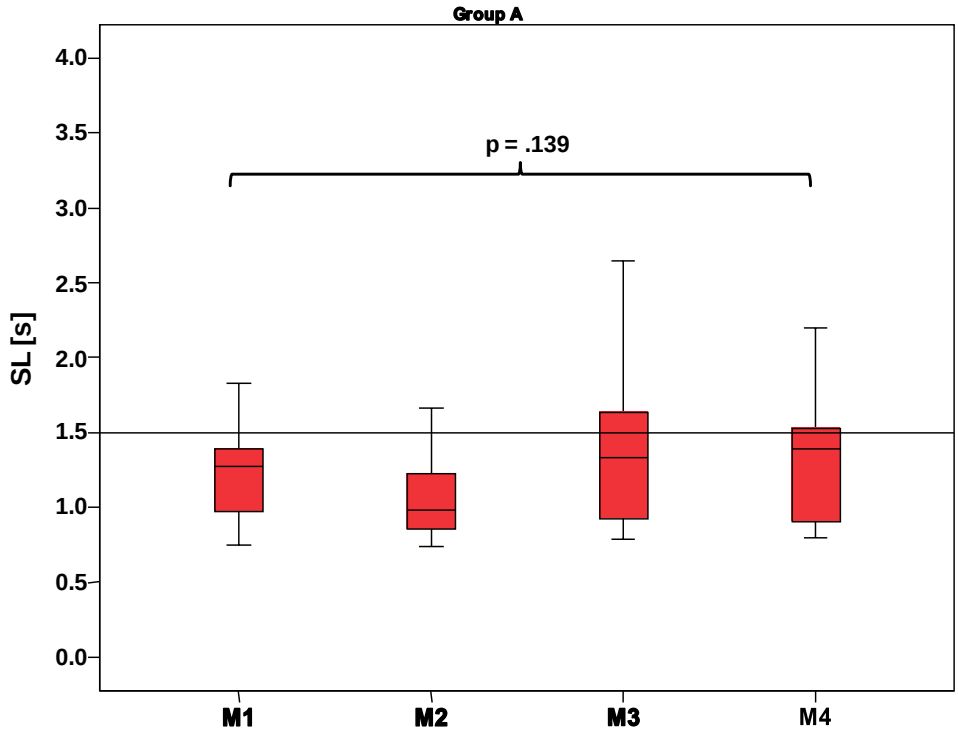



Figure 44: Box plot showing monthly results of SL in group A

Applying a one-way ANOVA for repeated samples there was no statistically significant difference obtained (p= .139). The effect size, eta squared was .181.

### 3.4.4.2 Group B1

Tab. 41: Descriptive statistic summary for mean monthly SL

| Infants N=10 | Months p | Mean [s] | Std. Dev. [s] | Std. Error [s] | Median [s] | Min [s] | Max [s] |
|---|---|---|---|---|---|---|---|
| | **M1 p= .279** | 1.409 | .538 | .170 | 1.385 | .734 | 2.607 |
| | **M2 p= .549** | 1.835 | .814 | .257 | 1.737 | .743 | 3.582 |
| | **M3 p= .787** | 1.552 | .409 | .129 | 1.565 | .991 | 2.298 |
| | **M4 p= .326** | 1.579 | .349 | .111 | 1.533 | .921 | 2.109 |

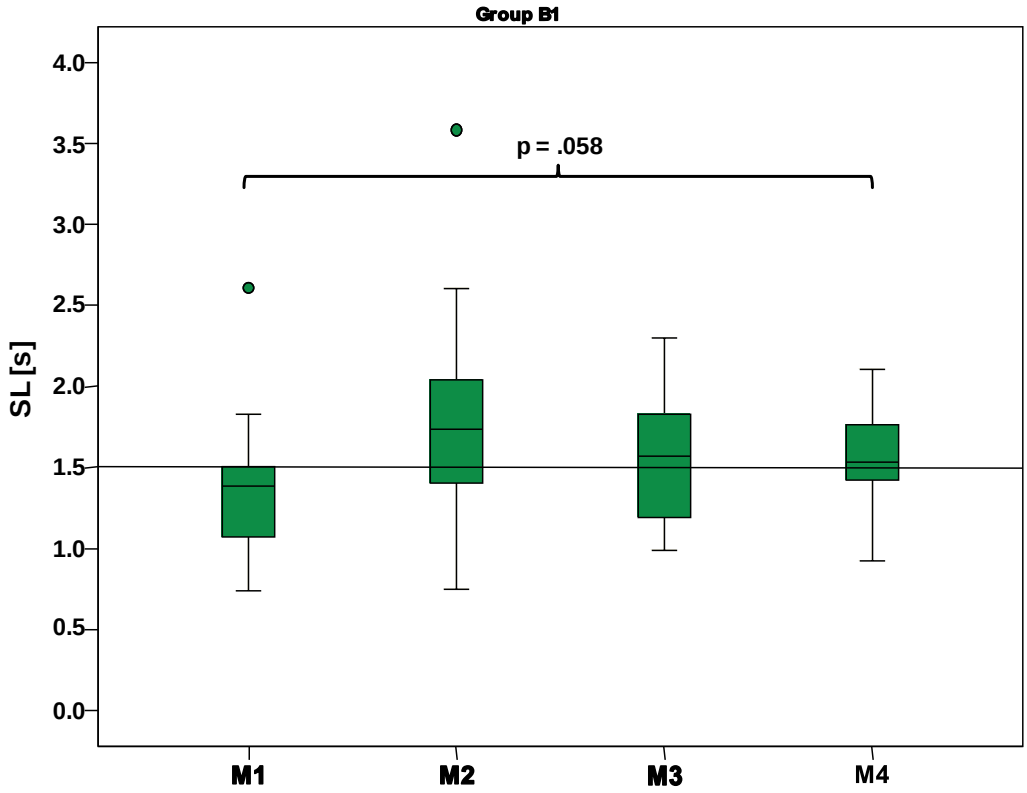



Figure 45: Box plot showing monthly results of SL in group B1

Applying a one-way ANOVA for repeated samples no statistically significant difference was obtained (p= .058). The effect size, eta squared was .238.

### 3.4.4.3 Group B2

Tab. 42: Descriptive statistic summary for mean monthly SL

| | Months | Shapiro-Wilk Test significance (p) | Median [s] | Percentile | |
|---|---|---|---|---|---|
| | | | | 25% [s] | 75% [s] |
| Infants N=10 | M1 | .005 | 1.063 | .806 | 1.280 |
| | M2 | .033 | 1.182 | .951 | 1.683 |
| | M3 | .008 | 1.456 | .926 | 1.640 |
| | M4 | .010 | 1.322 | 1.091 | 1.401 |

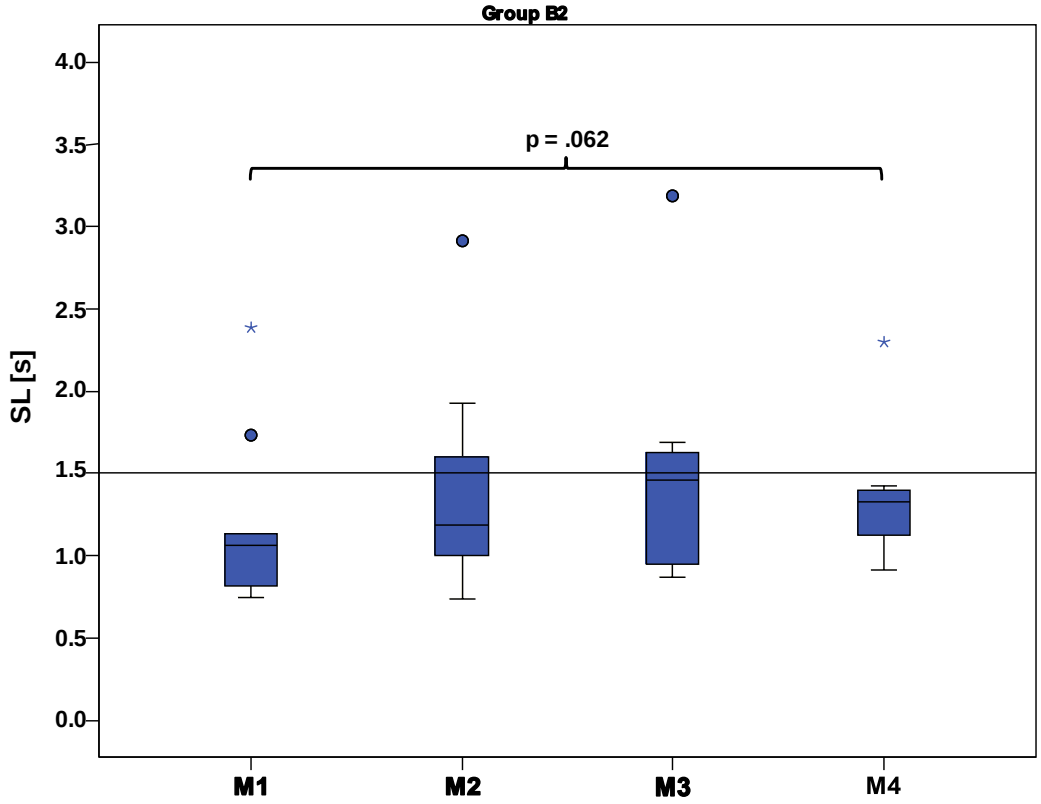



Figure 46: Box plot showing monthly results of SL in group B2

A non-parametric test (Friedmann's test or paired test) compared the mean monthly SL values, resulting to a non-significance (p= .062).

## 3.5 Two-weekly analysis of four children from group B1

We were able to make more compact calculations in this part of our analysis due to the data distribution for 4 infants (Tab. 5 and Tab. 6) consisting of 2 females (AE/AK) and 2 males (AL/BZ). Averages of the data in two-weekly intervals were calculated and we named these intervals P1 - P10. Therefore P1 contained data for the first 14 days of life and P2 from the $15^{th}$ till $28^{th}$ days respectively. With this procedure we were aiming to have a better objectivity in our calculations for the first 20 weeks of life.

The average results of the variables in two-weekly intervals were calculated for 20 weeks, therefore in 10 two-week periods. These periods P1 to P10 were compared for these 4 children using grouped bar graphs (histograms). The legends on the top right side indicate what colours we used for the representations of the 4 infants respectively. The value of the dependent variable is shown on the y-axis and this corresponds with the periods and the children (independent variables) represented on the x-axis. Our results being displayed in this manner, visual comparisons can be made by examining the heights of the graphs.

Statistical analysis for each variable was carried out from P1 - P10, and comparisons were made using a non-parametric test (Friedmann's test). We further constructed box plots showing the differences between the periods for each variable, thus making more comparisons possible. There are no outliers in these cases because our data originates from two-weekly average values of these variables.

### 3.5.1 Analysis of the two-weekly interval results of NI 1

For the analysis of the two-weekly averages (means) of the NI 1 in ten periods (P1-P10), we made bar graphs showing the corresponding independent and dependent variables. The legends on the right side correspond to the children represented during each period respectively, see Figure 46. Therefore, differences in the behaviour of NI 1 can be identified for each child in each period by looking at the bars. The level of the average NI 1 produced had a maximum of 0.54, from AE during P1. We found an average minimum NI 1

value from AK during P5. We obtained the lowest values from all 4 children during P5 and P6, which was not above 0.15. After P6, the average NI 1 from the children did not exceed 0.2. An exception was AK, with values during P7 and P10 which were higher than 0.2.

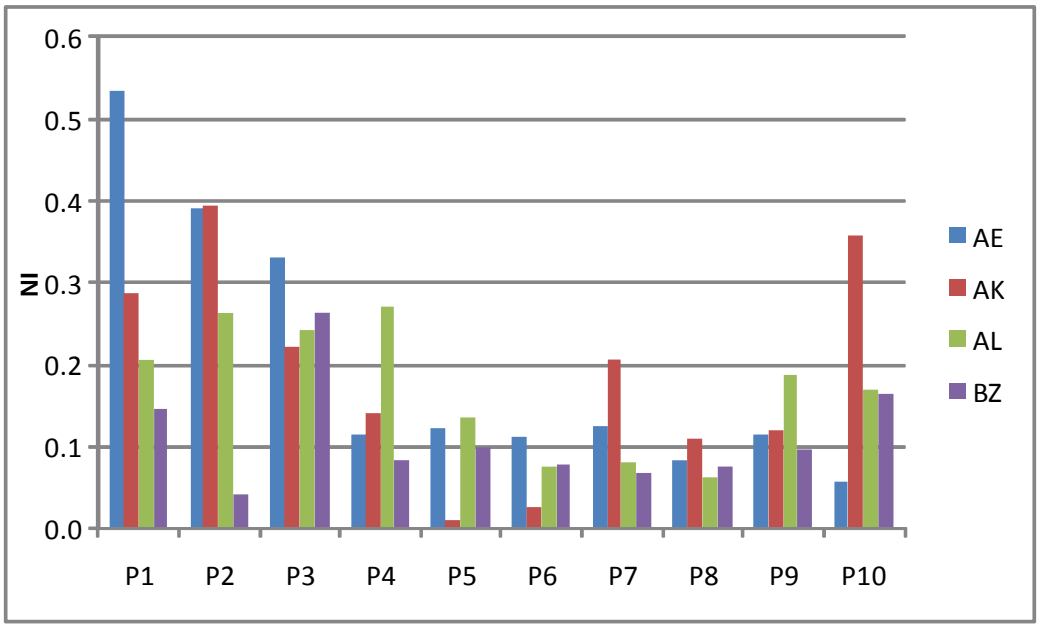



Figure 47: Bar graph showing two-weekly interval results of NI 1

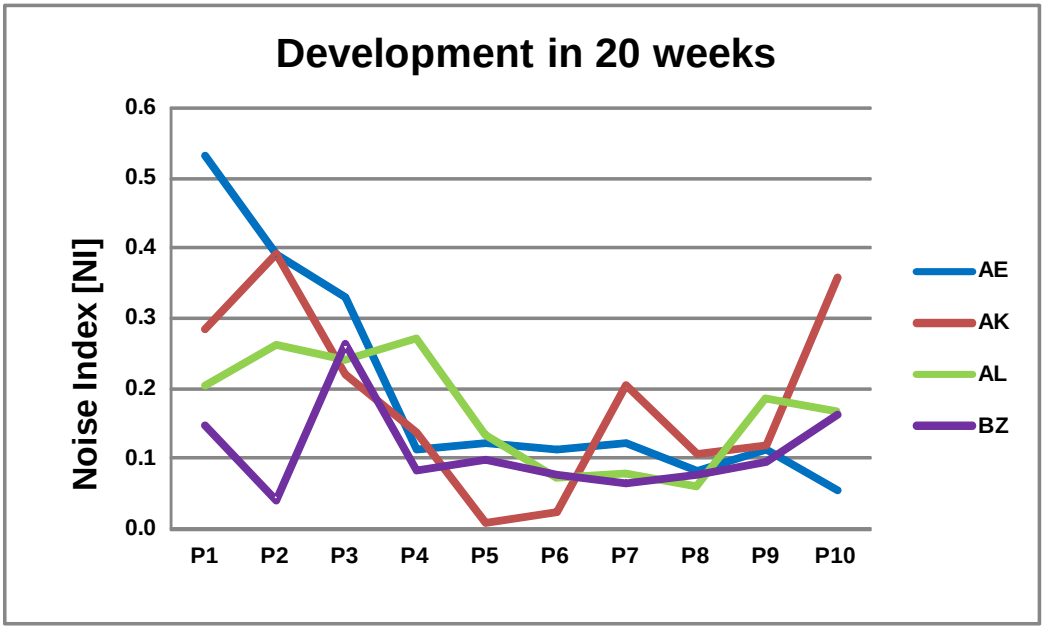



Figure 48: Noise Index (NI) Development Curve

With a Friedmann's test or paired test, we compared the two-weekly results of NI 1 from P1 - P10 and obtained a significant difference (p= .046).

Therefore applying the Wilcoxon`s test (paired test), we compared the periods to one another, resulting in non-significant differences. In this part of our analysis, we only compared neighbouring periods and the significance (p) for each compared pair is shown on Tab. 43.

Tab. 43: Significance of NI 1 during the periods

| NI 1 | P1/P2 | P2/P3 | P3/P4 | P4/P5 | P5/P6 | P6/P7 | P7/P8 | P8/P9 | P9/P10 |
|---|---|---|---|---|---|---|---|---|---|
| **Sig. (p)** | .715 | .715 | .144 | .465 | .273 | .465 | .144 | .068 | .465 |

Constructing side-by-side box plots with the periods (P1 - P10) on the x-axis, the average values of our dependent variables can be compared.

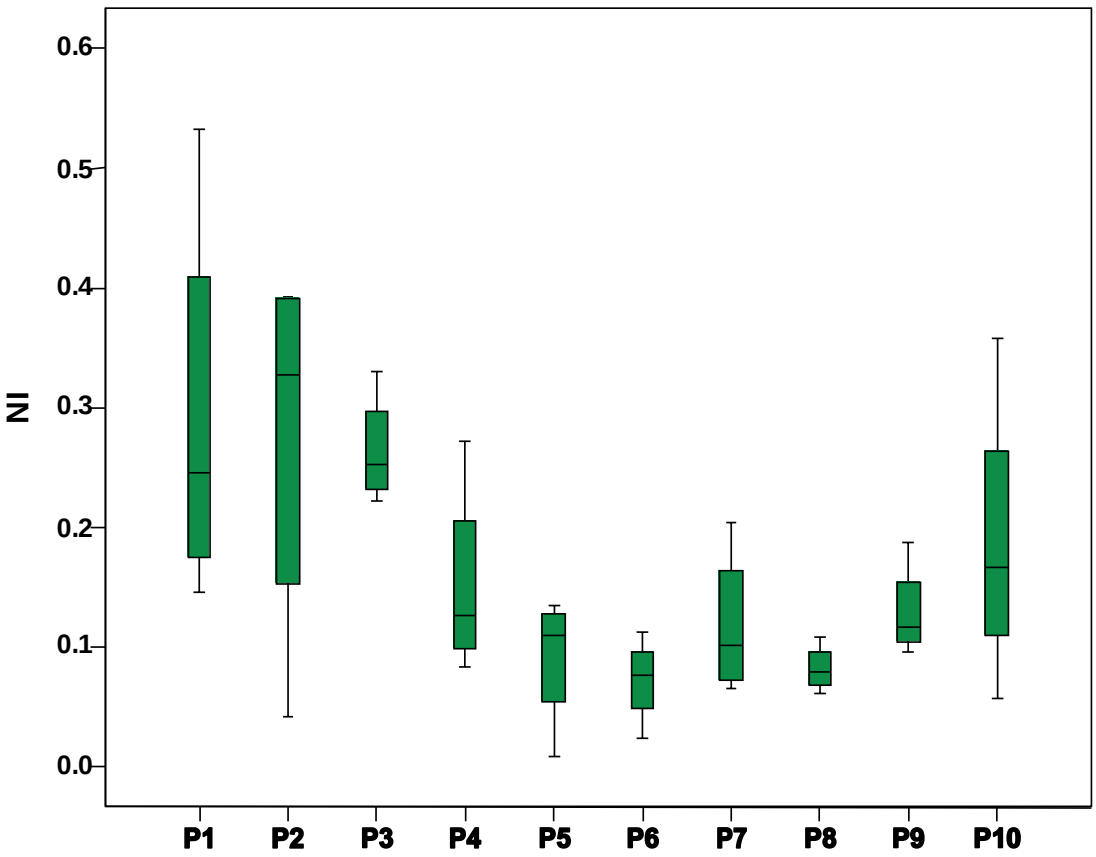



Figure 49: Box plots with results of NI 1 from P1 - P10 for 4 children

Despite obtaining a significant difference (p= .046) for the two-weekly average of NI 1 from P1 - P10, there were no paired significant differences (see Tab.

43). However, the box plots show visual differences between the periods, and their IQR varied. The influence of the children AE and AK are significant and this corresponds to their unusual behaviour during P1 and P2 as well as during P7 and P10. This caused a wider IQR during P1, P2, P7 and P10 but generally a reduction in the median value is evident. From P1 to P6, there is a drop in the median and this rises again in P7. The median drops from P7 to P8 and later rises again from P8 to P10. Despite the rise and fall of the two-weekly averages for NI 1, the values at P10 never reached the high levels we measured during P1 or P2.

### 3.5.2 Analysis of the two-weekly interval results of NB

For the analysis of the NB in two-weekly intervals or periods, we were able to compare the 4 children across 10 periods using bar graphs. Figure 49 shows the parameter NB in seconds (y-axis) over the entire period of analysis (P1 - P10 on the x-axis). The legends on the right side represent the children during the periods respectively. A minimum value was registered during P6 which correlated to the results in chapter 3.5.1. A maximum value was calculated during P10, this was however above 0.7 s, whereas during P1 only an average of about 0.23 s was registered.

The Friedmann’s test (or paired test) compared the two-weekly results of NB from P1 - P10, producing a non-significant difference (p= .468).

Despite the non-significant difference obtained, constructing box plots made visual interpretations possible. Our box plots during P2, P3 and P10 are characterised through a wider IQR. The median value rises from P1 to P3 and falls to P6, rises to P7 and falls to P8. The values rise again to P10; therefore describing an 'up and down waveform' (pendulum) as a whole, see Figure 51.

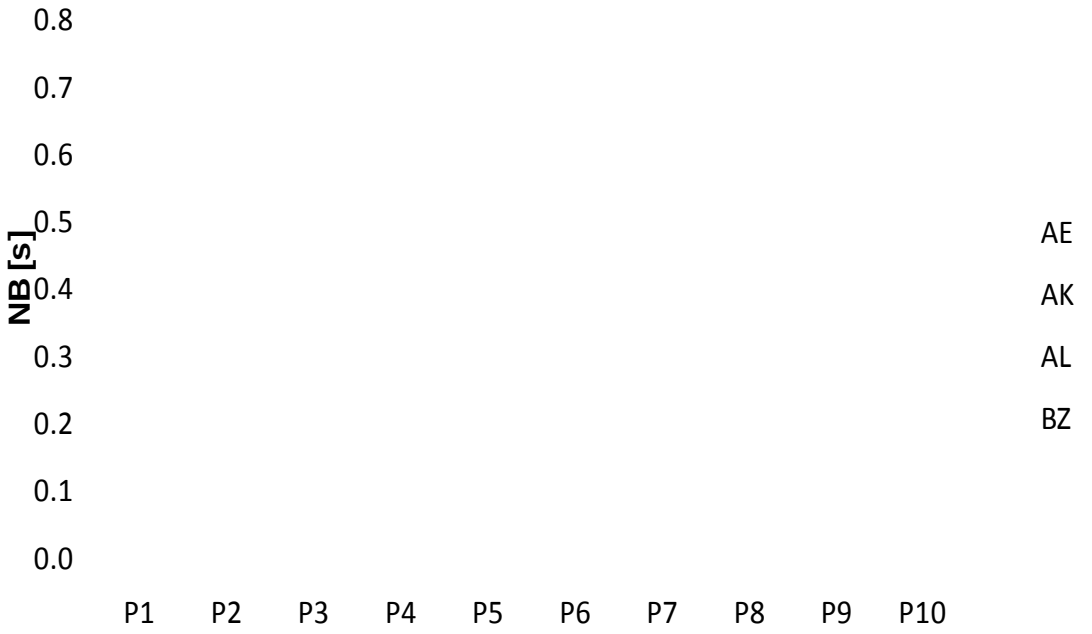



Figure 50: Bar graph showing two-weekly interval results of NB

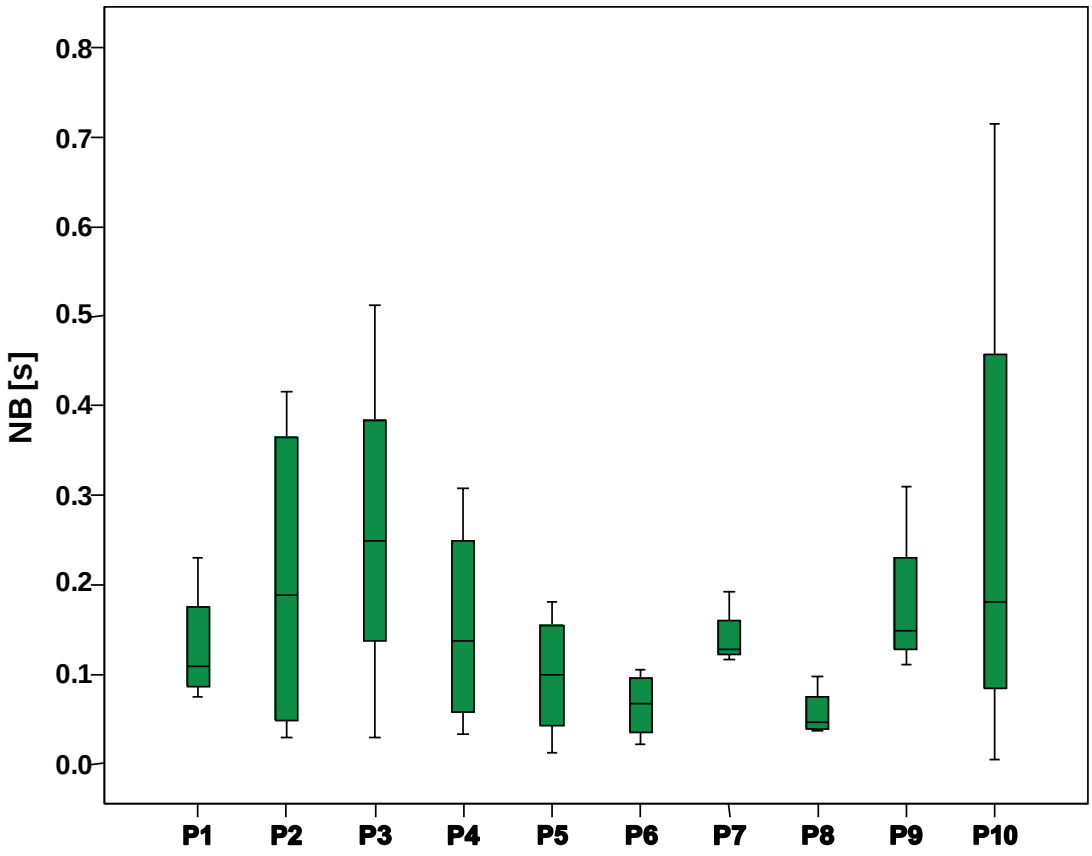



Figure 51: Box plots with results of NB from P1 - P10 for 4 children

### 3.5.3 Analysis of the two-weekly interval results of SH

Analyzing the SH in two-weekly intervals or periods, we were able to compare the 4 children again using bar graphs. The histograms show the levels of SH in seconds (y-axis) and their corresponding periods (x-axis) for each of the children as shown in Figure 52. A maximum value was obtained from AE (about 0.28 s) during P1 and we noticed that after P4, no value exceeded 0.10 s. AK as an exception produced an average SH of about 0.22 s during P8.

The Friedmann's test or paired test compared the two-weekly results of SH from P1-P10 producing a non-significant difference (p= .132).

Despite this non-significant difference, our box plots from P1 to P10 in Figure 53 differ visually from each other. During P8, we notice a positive skewness of our data and a widening of the IQR, caused by AK.


Figure 52: Bar graph showing two-weekly interval results of SH

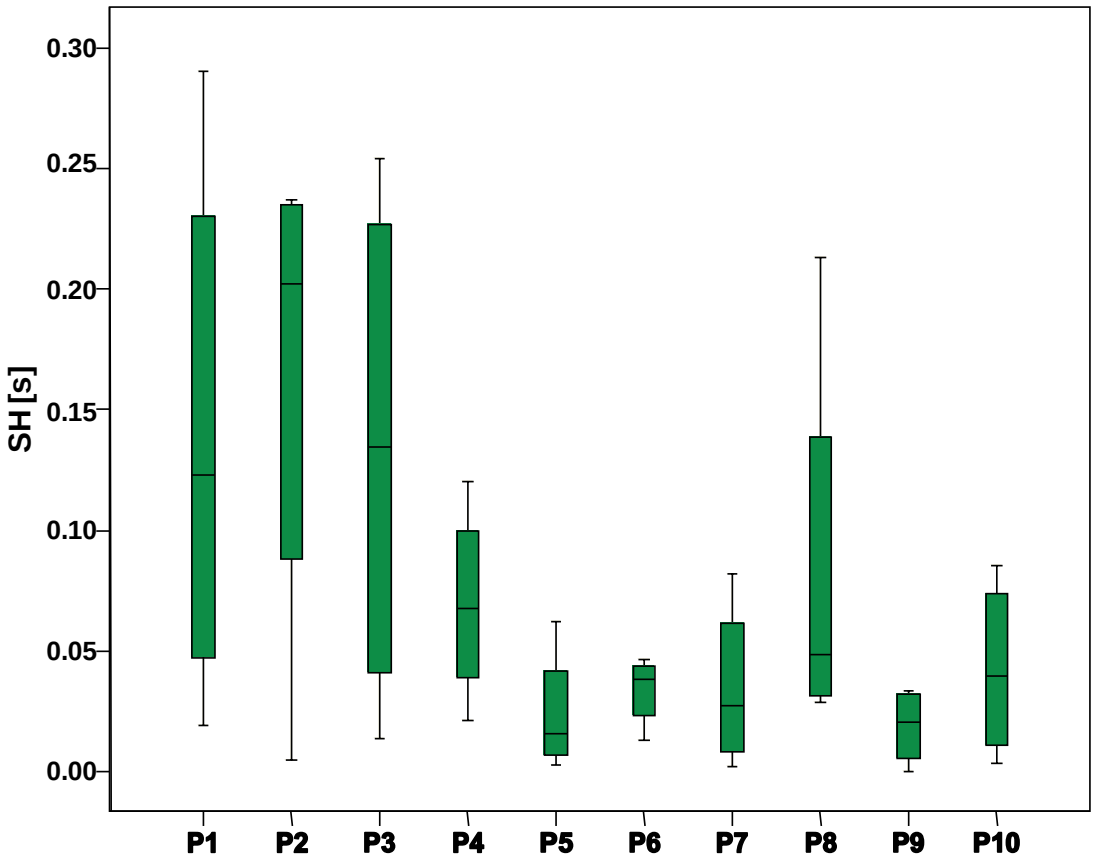



Figure 53: Box plots with results of SH from P1 - P10 for 4 infants

### 3.5.4 Analysis of the two-weekly interval results of SL

Analyzing the SL in two-weekly intervals or periods, we were able to compare the 4 infants again using bar graphs. The graphs show the levels of SL in seconds (y-axis) and their corresponding periods (x-axis) for each of the children as shown in Figure 54 below. The bar graphs show an interesting pattern that we could observe during the period of analysis, with maximum values coming from AL and minimum values from AE. During the first three periods, the average SL from AE did not exceed 1.0s; meanwhile the other children produced averages above 1.0 s from P1 - P10. We noticed that at P10, the average SL from all 4 children was slightly above or below 1.5 s.

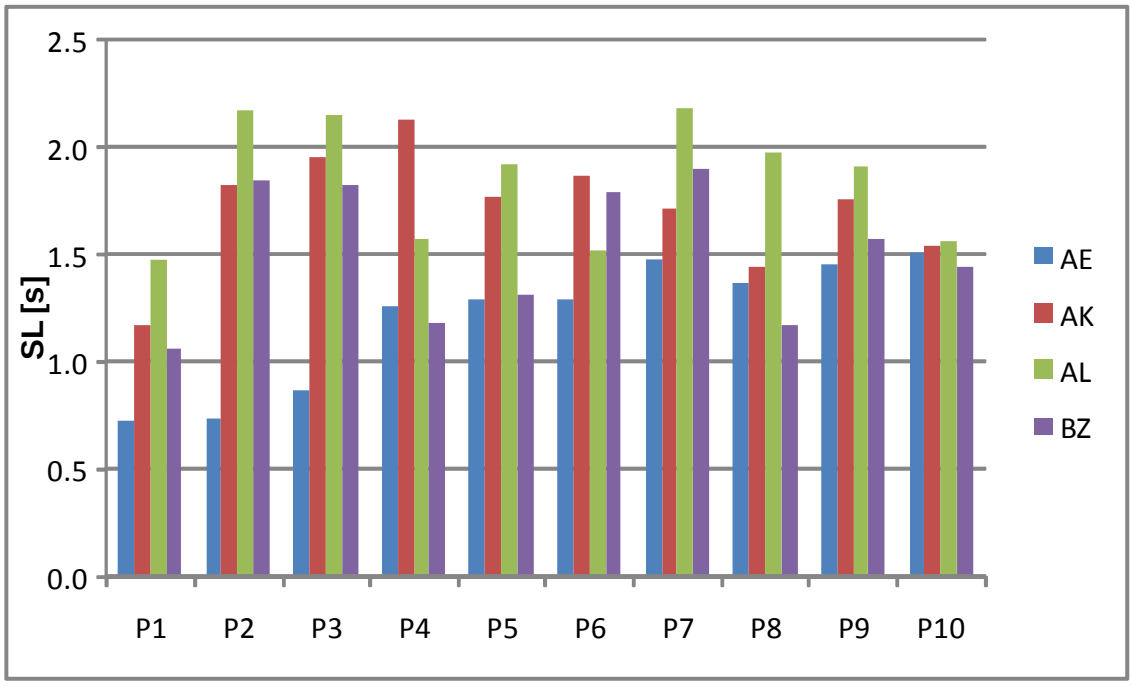



Figure 54: Bar graph showing two-weekly interval results of SL

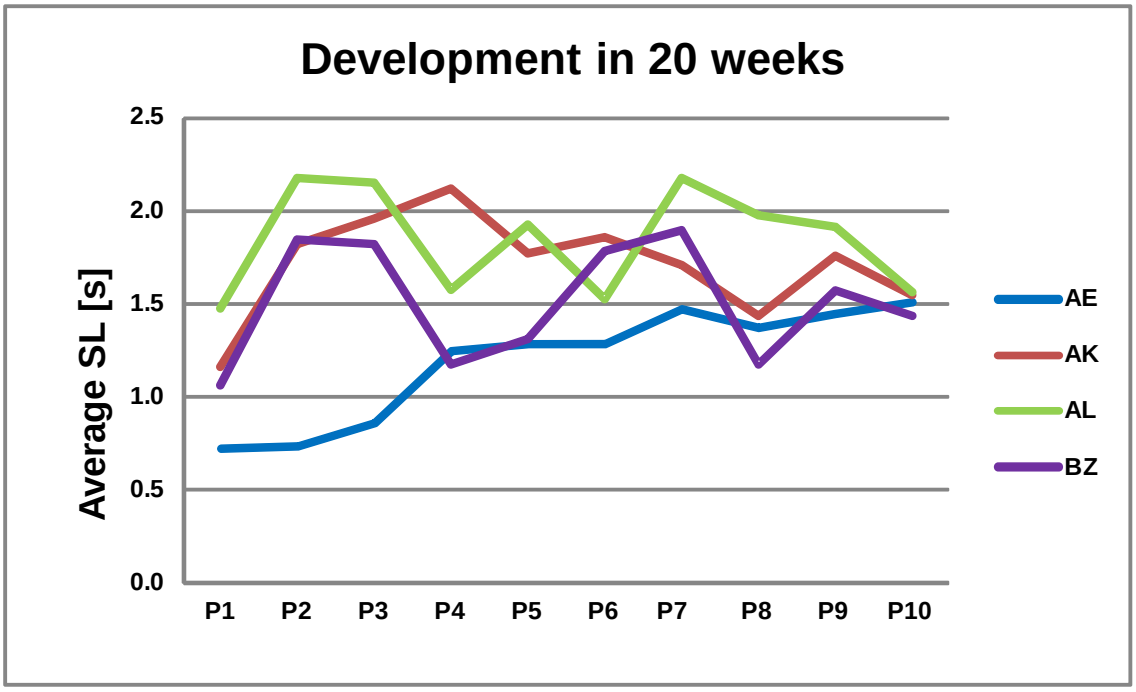



Figure 55: Average signal length (SL) Development Curve

The Friedmann's test or paired test compared the two-weekly results of SL from P1-P10, producing a non-significant difference (p= .109).

We created box plots, again showing the behaviour of the average SL during the periods P1 - P10 for these 4 infants. As we see in Figure 56, the average

values of SL are negatively skewed during (P2 and P3) and positively skewed in P4. Meanwhile reaching P10, we obtained a small dispersion of our average SL for the 4 children with a median value of about 1.5 s.

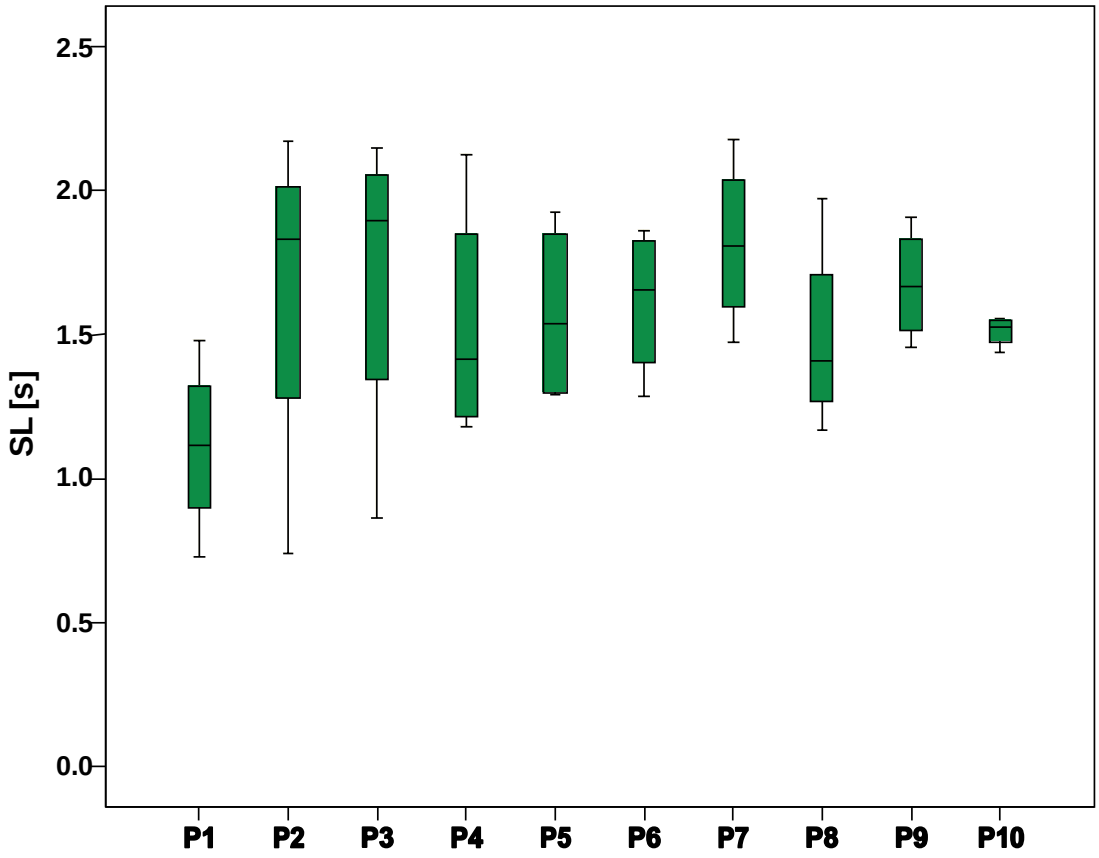



Figure 56: Box plots with results of SL from P1 - P10 for 4 infants

## 3.6 Interrelationship between analysed variables

We investigated the interrelationship of our variables in each group for the first four months using a non-parametric correlation test (Spearman-rho). The influences of our variables on each other as the infant grew older differed between the groups, and their correlation coefficients (R) are given in the tables shown below.

### Group A

In group A, there was no significant correlation between the infant's ages and the variables SL, NB, SH and NI 1.

Tab. 44: Non-parametric correlation test in group A

| | | | Age | SL | NB | SH | NI 1 |
|---|---|---|---|---|---|---|---|
| Spearmann`s rho | Age | Correlation coefficient | 1.000 | .153 | -.095 | -.235 | -.095 |
| | | S g. (2-tailed) | | .346 | .560 | .145 | .560 |
| | | N | 40 | 40 | 40 | 40 | 40 |

* Correlation is significant at the .05 level (2-tailed)

As we noticed in all groups, there were negative correlations between the SL and the NI 1. A negative correlation was also observed between the degrees of SH and the NB within the infant's in group A.

### Group B1

In group B1, there was no significant correlation between the infant's ages and the length of the signals (SL) they produced, but there was a very significant negative correlation between the child's age and the degree of SH (r= -.424, p= .01). We also registered a significant negative correlation between their ages and the values of NI 1 (r= -.366, p= .05). The correlation in this group between age and NB was also negative and not significant.

Moreover, a very significant correlation was found between SL and NB, which was not the case in the other two groups. With an increasing SL, there is a tendency to observe noise segments within the cries. However, NI 1 was not affected by SL.

Tab. 45: Non-parametric correlation test in group B1

| | | | Age | SL | NB | SH | NI 1 |
|---|---|---|---|---|---|---|---|
| Spearmann`s rho | Age | Correlation coefficient | 1.000 | .130 | -.190 | -.424** | -.366* |
| | | S g. (2-tailed) | | .425 | .241 | .006 | .020 |
| | | N | 40 | 40 | 40 | 40 | 40 |
| | SL | Correlation coefficient | .130 | 1.000 | .431** | .021 | -.263 |
| | | S g. (2-tailed) | .425 | | .005 | .898 | .101 |
| | | N | 40 | 40 | 40 | 40 | 40 |

** Correlation is sig. at the .01 level (2-tailed) * Correlation is sig. at the .05 level (2-tailed)

### Group B2

In group B2, there was also no significant correlation between the age of the infants and the length of the signals (SL) they produced. A trend for a negative correlation between age and the variables NB, SH and NI 1 (in Tab. 46) existed but it was not significant.

Tab. 46: Non-parametric correlation test in group B2

| | | | Age | SL | NB | SH | NI 1 |
|---|---|---|---|---|---|---|---|
| Spearmann`s rho | Age | Correlation coefficient | 1.000 | .252 | -.008 | -.312 | -.126 |
| | | S g. (2-tailed) | | .117 | .962 | .050 | .439 |
| | | N | 40 | 40 | 40 | 40 | 40 |
| | SL | Correlation coefficient | .252 | 1.000 | .207 | -.029 | -.154 |
| | | S g. (2-tailed) | .117 | | .200 | .858 | .343 |
| | | N | 40 | 40 | 40 | 40 | 40 |

** Correlation is sig. at the .01 level (2-tailed) * Correlation is sig. at the .05 level (2-tailed)

In group B2, with an increase in SH a significant correlation was observed with the resulting chaotic segments, a phenomenen which was however more significant in group B1.

# 4 Discussion

Subharmonics and chaotic segments (see chapter 2.2) were first identified in the vocalizations of infant's using narrow-band spectrograms (Sirviö & Michelsson, 1976; Kelman, 1981; Robb and Saxmann, 1988; Mende et al., 1990a). It was anticipated by some earlier researchers (Sirvio & Michelsson, 1976) that subharmonics might serve as a differential indicator of neurological or structural pathologies. Meanwhile it has become apparent that these phenomena are also prevalent in the cries of normally developing young infants (Hirschberg, 1999).

Cry production in infants requires a good functioning laryngeal/vocal system as well as a good neurophysiological coordination through the CNS (Newman, 2007). Failure in achieving this balance leads to an unstable neuro-muscular activity and consequently to the appearance of "noise-like elements" in visible sound spectrograms.

The fundamental frequency ($F_0$) and related parameters of cry signals play an important role in infant cry research. $F_0$ depends on various laryngeal factors (muscle tension and mucosa consistence) as well as the subglottal pressure. Voice intensity is regulated through the subglottal pressure which equally influences the $F_0$ (Titze, 1988). Many researchers could prove that increased values of $F_0$ may reflect a neuro-physiological at-risk status of the child; and particularly when coupled with other risk factors (orofacial clefts and insufficient larynx innervations) more serious cognitive disabilities are evident (Wasz-Höckert et al., 1968; Michelsson, 1971; Tenold, 1974; Michelsson & Sirvio, 1976; Michelsson et al., 1977; Zeskind and Lester, 1978; Lester et al., 1985; Wasz-Höckert et al., 1985; Fuller & Horii, 1986; Lester, 1987; Wermke et al., 1987; Corwin et al., 1992; Mende et al., 1990b; Pearce & Taylor, 1993; Michelsson & Michelsson, 1999). Preliminary results on spectral analysis of pre-speech sounds of orofacial cleft infants compared to a control group showed how $F_0$ and PPQ are influenced in patients with UCLP (Wermke et al., 2002a). Other studies were able to show the relationship between $F_0$ and the presence of certain noisy segments in spectrograms of the infant cry (Hauschildt, 2006; Steck-Walter, 2007; Kempf et al., 2008). These studies implied that the mean

fundamental frequency in the infant cry does not depend on the infants' age during the first 132 days, however at age $5^{1/2}$ months the mean $F_0$ in the cry signals from the UCLP- infants began to rise significantly (Wermke et al., 2002a).

Further implications resulting from such changes in $F_0$ (noise segments and frequency jumps) were not yet considered in these studies, however in a pilot project (Hauschildt, 2006) orofacial cleft infants were analysed from this perspective. Developing a noise index NI (a mean value of the noise portion within a cry sequence), Hauschildt tested infants during the first six months of life. The effect of wearing the palate plate and of not wearing it on the mean $F_0$, PPQ and appearance of noise segments were analysed. Supporting the positive effects the palate plate has on cleft infant's phonation; Steck-Walter (2007) found a stable mean $F_0$ observed with and without using the palate plate, except during the 3rd and 5th months. Since the infants wear the plate day and night, some adaptation of the cry production system is assumed, whereby short interruptions for cleaning purposes were compensated. The 3rd month is very important as it is here that the larynx begins to descend (Lieberman, 1985) accompanied with neurobiological changes in the brain (Herschkowitz et al., 1997). During this time a reorganisation in the neuronal control mechanism of vocal control is assumed which is also accompanied with changes in acoustic cry properties (Mende et al., 1990a; Wermke and Mende, 1992). There was a significant increase in vocalizations from cleft infants with noisy segments when they did not wear a palate plate during sound production in the first six months of life (Hauschildt, 2006). The compensatory effect of the palate plate in reducing these noisy segments as well as keeping a stable mean $F_0$ correlated significantly in this study. However, noisy segments have also been found in spectrograms from children born without any disorders (Wasz-Höckert et al., 1968; Lester, 1987; Mende et al., 1990a). More often in younger infants, the appearance of noise segments is explained with the higher constraint of their primitive and small vocal cords in overcoming high sub-glottal pressure especially when screaming.

In my study, comparisons were made over a period of 15 weeks between cleft and non-cleft infants as a longitudinal study, using a NI defined here as an objective method in accessing vocal cord regularity and hence diagnosing potential pre-speech development disorders. Extending this analysis until the 20th week in group B1 (non-cleft infants) was done to help further projects in understanding and interpreting the present results.

## 4.1 Evaluating the noise index (NI)

The noise index as a factor characterising the noise expansion in pre-speech utterances can be used as an objective method in accessing 'risk markers' on spectrograms during infant vocalisation (Hauschildt, 2006). In non-cleft and in orofacial cleft infants, the reduction of such noisy segments on sound spectrograms is important during pre-speech development, enabling them to train melodic properties better and acquire crucial prosodic features of their native language (Steck-Walter, 2007; Wermke et al., 2007; Wermke/Mende, 2010 in press). Dysphonation in sound spectrograms from orofacial cleft infants may be explained with the turbulences during airflow which result from open oro-nasal connections. This phenomenon is supported by the incapability of their incomplete muscle tissues to withstand such high subglottal pressure, and so the vocal folds vibrate asynchronically. Without surgery, the infants seem to compensate the energy lost through this open connection by generating more subglottal pressure, therefore increasing the fundamental frequency $F_0$ (Mühler et al., 1996; Wermke/Mende et al., 2002). This false compensatory regulation is believed to be avoidable when the patients wear a palate plate shown by the fact that more noisy segments were visible on spectrograms when they did not wear a palate plate (Hauschildt, 2006). In Hauschildt's pilot study the NI correlated with the severity of the deformation, hence the present study recruited more children in order to discover whether there is a significant correlation between the recorded NI and the degree of malformation in cleft infants (see Tab. 2).

In this study, only pre-speech utterances recorded from orofacial cleft infants wearing a palate plate were recruited for analysis (group A). This simulated the

conditions for the infants in group B1 and B2 (see chapter 2.1). To support Hauschildt`s hypothesis that a NI could represent a suitable tool for accessing the intensity of noisy elements in daily medical practice, it was necessary to develop an objective NI which could also be used in healthy infants. After modifying Hauschildt's original index, the results of both NI 1 and NI 2 (explained in chapter 2.3.2) were compared for group A (in chapter 3.1).

There was a significant difference between NI 1 and NI 2 in the orofacial cleft group (p= .036) over the period of 4 months. As seen in Tab. 8, despite there being no eminent differences in the descriptive statistic summary there was a difference in the maximum value (0.64 for NI 1 and 0.68 for NI 2). This can be explained through the effect of a filter which we implemented in the excel calculations and moreover by the exact quantitative measurements applied here (see chapter 2.3.2) A paired test between NI 1 and NI 2 (correlation .937) produced supporting evidence of our chosen modifications (see Tab. 9). This showed that on the one hand both methods are roughly comparable and that on the other hand the quantitative analysis provided more reliable results.

Analysing the relative frequency of the occurrence of cries belonging to a noise class 0-V (number of cries within a cry sequence) as Hauschildt (2006) did in her analysis may not provide all necessary data and some reliable information might get missing. Considering the total cry time and therefore calculating individual factors for each cry could be a better approach as is shown by the differences we obtained while comparing NI 1 and NI 2 ( in chapter 3.1). When comparing NI 1 and NI 2 on a group basis over a period of 4 months, significant differences were found only in the infant LA. The results of NI 1 and NI 2 from the infants AN, EA and SE only had the tendency of showing a significant difference (p= .075). However, on comparing the results of NI 1 and NI 2 on a child basis over a period of 4 months (see Figure 14) other differences became transparent. The IQR`s of the box plots from the infants AN, DL, LU and SH while comparing NI 1 and NI 2 showed marking differences. Probably, this was due to the effect of the more reliable calculations we made while calculating NI 1 contrasted to, Hauschildt`s (2006) more visual approach calculating her NI 2.

In the present study over 7000 cry signals from 30 infants (Tab. 5) were analysed regarding the contents of noise segments shown during the first 15 months of life. There was a significant difference (see Figure 15) in the appearance of noisy segments (NI 1) between the non-cleft groups B1 and B2 (p= .021), differing with respect to familial history of language impairments (see chapter 2.1). Also the cleft infants (group A) differed significantly from the control group B1 (p= .008), whilst no difference was found overall between group A and group B2 (p= .625).

Analyses between the groups on a monthly basis showed no significant group differences in mean NI values during the first 4 months of life. Nevertheless some trends could be observed.

In the cleft group (A) the mean NI value decreased continuously from M1 through to M3 but it rose again in M4 and the same trend was observed in group B2. In contrast, group B1 showed a clear continuous development over the first 4 months with a decreasing NI 1 value. An increase in the value of NI 1 in the $4^{th}$ month did not occur in this group. The monthly decrease of NI 1 was also statistically significant (see chapter 3.4.1.2). These results suggest a development of vocal control during the first month characterized by a stabilisation of vocal cord activity. The stability of vocal control is not disturbed by the production of more advanced vocal types, as these do not occur until about 4 months of age (e.g. babbling). Babbling production requires the tuning between laryngeal and vocal tract activity (Kempf, 2008). As could be demonstrated here, the tuning was well managed by group B1 without exhibiting an NI 1 rise. At this pre-speech phase contrary to group B1, group A and B2 manifested a disturbed vocal control.

As possible candidates for contributors to irregularity in vocal fold vibration, "Titze (1993, p. 153 - 156) formulated the following:

1. Unsteadiness in muscle contractions in the laryngeal and respiratory system. Particularly the incomplete summation of muscle twitches in an attempt to form a "smooth tetanus" brings about a fundamental frequency jitter (Baer, 1981b; more recently, the process has been modelled by Titze, 1991).

2. Turbulence in the glottal airstream.
3. Vortex shedding and instability in the jet emerging from the glottis (this differs from the turbulence above). The jet may flip-flop from side to side, even if turbulence does not exist.
4. Asymmetry in the mechanical or geometrical properties of the two vocal folds. Usually, a dominant oscillation mode exists due to synchronization of two similar oscillators by the airflow, but excessive asymmetry may create desynchronization.
5. Nonlinearity in the mechanical properties of vocal tissues (the constitutive equation) and the pressure-flow relations. Nonlinearities complicate the mode structure of a vibrating system.
6. Coupling between the vocal folds and the vocal tract. Acoustic pressures in the subglottal and supraglottal region may play a part in driving the vocal folds. If these pressures change dynamically, oscillation may be pertubated.
7. Mucus riding on the surface of vocal fold tissue. The mucus could reorient itself from cycle to cycle, causing disturbances in the vibration pattern".

Titze (1993) points to the fact that several of these sources of irregularity can exist in combination with others. Some of them, like mucus and air turbulence, may result in high-dimensionality chaos; others, like left-right asymmetry, may lead to low-dimensionality chaos. It is important to study the sources one at a time to get a better understanding of their effect on vocal fold vibration. Some of this work can be done with physical models and excised larynges, where the effects of neural inputs, the vocal tract, or mucus can be selectively eliminated.
Low-dimensionality chaos, as found in infant cries may be caused by a left-right asymmetry of the vocal cords (Titze, 1993).
Parametrically, the bifurcations may relate to dynamically changing tissue stress. In newborns, the amplitude to length ratio we already mentioned in chapter 1 is extremely large, resulting in strong nonlinearities in the restoring forces.

Assuming that a genetic factor (a physiological condition) influences the NI, this hypothesis can be supported by the similarity between the cleft infants and the $FH^+$ infants. Infants born with a familiar risk for a language developmental disorder ($FH^+$ infants) were found to produce more vocalizations with noisy segments and subharmonics (Blohm, 2007, Wermke at al., 2010).

The results of similar phenomena in group A and B2 are very interesting and will be also discussed in chapter 4.2. Although on first sight a cleft is very different from a specific language impairment disposition, there seem to exist developmental neuro-physiological similarities. Infants in groups A and B2 were still below 2 months of age when these similarities became apparent. Since oral-motor movement patterns associated to articulation are not yet relevant in infants below 2 months, there must be another reason for the similarities in group A and B2. Also, due to an immature vocal tract in young infants the influence of such cleft malformations on articulatory activities is not manifested before the 3$^{rd}$ or 4$^{th}$ month (Oller, 2000), however our results show similarities even at this time. Therefore in both groups (cleft and $FH^+$) there is a similar deviation in the temporal organization of laryngeal sound production. This may reflect either a delayed intra-uterine or a genetically influenced developmental process engaged in brain organisation. Our interpretations also correlate with findings that most cry parameters directly reflecting laryngeal control deviated in cleft infants (group A) and infants with a positive family history for language developmental disorder (group B2); cf. Wermke et al., 2002a; Hauschildt, 2006; Steck-Walter, 2007; Blohm, 2007; Kempf, 2008 for details.

In contrast to the evidence from control group B1, our results in the other groups suggest a strong relationship in the appearance of noise segments in vocalizations between cleft infants (group A) and those with a positive family history of language developmental retardations (group B2). Blohm (2007) already found some deviations in the prosodic elements produced from babbling in infants with $FH^+$ analysed between the 16$^{th}$ and 70$^{th}$ week of life compared to a control group of age-appropriates ($FH^-$). She also suggested that a high coordination of phonation, articulation and respiration is necessary for a continuous speech development. Kempf (2008) compared cleft infants to a

control group of normal infants and her results supported Blohm`s assumption that normal infants co-ordinate phonation and respiration better, thus tuning these mechanisms more successfully. However, in order to enable better interpretations more comparative longitudinal investigations covering the development of the children until approximately the age of 2 ½ years would be required.

Results from another study by Denner (2007) in which the investigated parameters in pre-speech utterances from $FH^+/FH^-$ infants were compared within and between the groups on a monthly basis: show why it is necessary to make cry analysis from different perspectives. Although the occurrences of the spectral features were normally distributed between the groups during this period, some differences were found. The infants in the $FH^+$ group produced more pre-speech vocalizations, with a dominance of single arc (SA) melodies, as compared to the infants in the $FH^-$ group. Also, the infants with a family disposition for speech acquisition disorders ($FH^+$) had a poor content of utterances with short noises. These short noises are potentially believed to be the beginning of non cry vocalizations in infants (cf. Papousek, 1994). Looking at all the investigated months some differences between the groups become apparent, especially those which were gender-specific.

## 4.2 Evaluating the signal length (SL)

As shown in Figure 6, the expiratory phase during a breathing cycle was the basis of our analysis in this study. It has been proven that for vocalisation, non-primates exhibit less respiratory control than primates (Wilder & Baken, 1974). The human infant's respiratory cycle develops continuously during the first eight months and its expiratory phases become longer (Wilder & Baken, 1974). During speech the infants need an intentional control of their breathing cycle so as to obtain longer phases of expiration and shorter inspiratory phases accompanied by pauses. Therefore this functioning network of participating muscles and their co-ordination through the CNS in the 3 groups was considered in my study.

Recruiting only utterances recorded spontaneously, we created a solid platform for analysing the average signal lengths (SL) during the first 15 - 20 weeks. Very little has hitherto been published on the subject of the average signal lengths of spontaneous utterances. Many researchers have analysed pain cries (Lester and Boukydis, 1985) but these have different characteristics and are much longer. Signal lengths of about 1.0 s till 6.5 s were reported in these studies. Lind (1999) made an analysis of spontaneous cries in a concentrated appointment mode during the first 100 days of life. Although only one child was considered in her analysis, during the relevant age of 9 - 12 weeks, she reported an average signal length of 1.64 s. Borschberg & Ruppert (1998) made reports of similar average signal lengths (1.7s) by analysing twin infants between the 4$^{th}$ and 6$^{th}$ months.

The average signal lengths from orofacial cleft infants has also been analysed in other cry researches. Massengill (1969) submitted reports of an average signal length of 1.4 s during the 4$^{th}$ month from orofacial cleft infants. Three children with orofacial clefts were analysed by Zeipert (2004) between the 1$^{st}$ and 6$^{th}$ month, she reported an average SL from 1.9 s - 2.7 s. Massengill (1969) and Zeipert (2004) never compared their findings with results from normal born infants. Mühler (1996), however, made such comparisons and he postulated an increasing average signal length in cries from orofacial cleft infants (1.25 s - 1.9 s) until the 4$^{th}$ week. Between the 5$^{th}$ and 8$^{th}$ week, the average signal length

(about 1.2 s) almost reached the values he found in non-cleft infants (1.29 s). Therefore, he did not find any existing differences in the average signal length of cry signals recorded after the second month in both groups of children. Mühler compared results of cries evoked through pain unlike to our analysis and other recent studies which focussed on spontaneous utterances. Kempf (2008) compared average SL from 12 orofacial cleft infants (5 female and 7 male) between the 9$^{th}$ and 16$^{th}$ week to those of a control group. Despite the different conditions during signal recordings (2 cleft infants did not have palate therapy and there were recordings of the other infants with and without their wearing the palate plate); there were no significant differences to the control group. Kempf reported an average SL of 1.4 s (1.35 s from the cleft infants; 1.43 s from the control group). The capacity of the lungs determines the length of cry signals (Sutherland & Rattcliff, 1961; Ginet, 1969; Chiswick, 1976). In these children no breathing problems had been diagnosed and therefore these results met the author`s expectations.

As the present study compared three groups during a period of 15 weeks, there were statistically significant differences found in the average SL. The orofacial cleft infants (group A) differed significantly from the control group B1 (p= .000). Although our control group B1 differed significantly from B2 (p= .001), there was no difference between group A and B2 (p= .980). See Figure 16 for explanations.

By making an analysis between and within the groups on a monthly basis, very interesting observations could be made (see Figure 30 - Figure 33). There was no significant difference in the monthly average SL between the groups from M1-M4, except during the second month between group A and B1 (p= .016), see Figure 31. During M1 the median average SL in group A was 1.28 s and this decreased to 0.98 s during M2. On the other hand, the median average SL from our control groups increased from 1.39 s – 1.74 s (in group B1) and 1.06 s - 1.18 s (in group B2). During M2 there was a significant difference in the average SL between group A (cleft infants) and the control group B1 (FH-) but no significant differences in average SL existed either between group A / B2 or between groups B1 / B2 (see Figure 31). This result therefore may support

findings made by Wermke et al. (2010) after analysing the cry melody in vocalizations from two month old infants born with and without clefts. In their research, significant differences in the MCI[11] and SI[12] were found at the age of two months between infants with and without clefts. Therefore, taking the results of both studies (Wermke at al., 2010 and the present one) into consideration there are reasons to believe that a cleft malformation or a family history for language developmental disorders ($FH^+$) may influence the cry melody. This may occur due to a disturbed regulation in the neuromuscular co-ordination of respiratory and laryngeal structures. This assumption is supported by the results Denner (2007) published comparing pre-speech utterances between $FH^+$ and $FH^-$ infants from birth until the age of 4 months. Her results postulated that the period between the 2nd and 3rd month is very decisive for whether an infant with $FH^+$ develops a normal or a delayed speech acquisition at the age of 24 months. There was a fall in the MCI for the $FH^+$ infants from 0.52 during the 2nd month to 0.48 during the 3rd month compared to $FH^-$. When reduced amounts of complex structures on cry spectrograms suggest a delayed speech development (Wermke et al., 2007), then this similar behaviour in the MCI from infants with orofacial clefts and those with $FH^+$ may be a further indicator that their speech could be modified and not be undergoing a normal developmental pattern.

During the third month, while the median average SL in our control group B1 decreased to 1.57 s, the value in the cleft group (1.33 s) and control group B2 (1.46 s) increased. Observations from Lind (1999) already proposed a similar average signal length (1.64 s) in spontaneous utterances between 9 - 12 weeks of age in a normal born infant, and our findings may support her assumption.
Despite the median average SL in group A (1.39 s) and group B1 (1.53 s) being almost stable at M4, the median average SL in group B2 decreased to 1.32 s. Although very little is known from the literature on the average SL of spontaneous utterances, these results may support assumptions that despite morphological differences in infants, development in SL never advances linearly

[11] MCI is a Melody Complexity Index calculated with the formula MCI= MA/ (MA+SA).
[12] SI is a Segmentation Index calculated with the formula SI= S/MA (see Wermke et al., 2010)

(see Figure 34). This becomes clear in the orofacial cleft group during the second month, seen in a fall in the average signal length. More effort is required from the infants to produce cry sounds and therefore to maintain these longer expiratory phases in the cry cycle (see Figure 6). For sound production expired air is needed to flow at an optimal pressure at a certain period of time (Fiukowski, 1992). This can be achieved by increasing the subglottal pressure; hence much better neuromuscular coordination is needed. Other parameters beside NI = [f (SL)] for the examination of voice production in clinical settings include the analysis of the maximum phonation time (MPT) [Yumuto, 2004]. As a simple indicator of phonatory ability, the MPT (average SL) becomes shorter when airflow (measured clinically as MFR) is inefficiently consumed at the glottis (Yumuto, 2004; p. 168). MFR and PQ (vital capacity divided by the MPT) have a positive relationship such that PQ may be a clinical substitute to the maximum flow rate (MFR) [Hirano et al., 1968] when no airflow measurement is available. Therefore inefficient consumption of airflow at the glottis occurs not only in patients with dysphonia as a result of laryngeal disabilities (UVFI) but also in cleft infants and in $FH^+$ infants, as our results show. In order to classify these phonatory disabilities by considering the voice profile, it may be necessary for further studies to analyse the frequency and intensity ranges in vocalisations from these three groups of children.

Comparisons between orofacial cleft infants and normal born ones (Mühler, 1996), already proposed a higher average SL for the cleft infants during the first month. Despite his comparisons being based on evoked pain cries, on one hand his assumptions cannot be supported from our results because in our analysis the control group B1 produced the highest average SL during each month. However, on the other hand Mühler's assumption that the average SL from the orofacial cleft infant's drops during the second month (4 - 8 weeks) can be supported by our findings (see Figure 34). Only our control group B1 maintained median SL above 1.4 s after M1 and this development tendency can be supported by looking at Figure 44 - Figure 46. This result also supports our Hypothesis 2, since phonatory control over a cry time period was achieved only by our control group B1. In contrary, the median SL in cleft infants and control

group B2 infants never extended our control marker point set at 1.5 s (in Figure 44 - Figure 46) during M1 - M4.

## 4.3 Evaluating the control group B1

In the present study more steps have been taken towards exploring morphologic-acoustic interdependencies. Biological changes with certain relevant neuronal maturation (neurophysiological condition) during development are reflected through variable acoustic properties in cry signals. Many studies have made comparisons between acoustic properties in cry signals from cleft and non-cleft infants but no standardized method has yet been established. Analysis of selected cry characteristics from 4 healthy infants from our control group B1 (2 females and 2 males) were made at a very close time interval (every two weeks). Our results may serve as a platform of reference for other researchers comparing spontaneous cry sounds from non-cleft and / or cleft infants during the first 5 months of life. Besides identifying potential risk markers for later speech and language disturbances, already known markers for neurophysiological retardation can be exploited. Therefore, determining suitable relevant clinical indicators in cry signals from children, more objective comparisons are possible and contradictory results from other studies can be explained.

### 4.3.1 Noise Index 1 (NI 1)

Although there existed a significant difference (p= .046) for the two-weekly results of NI 1 from P1-P10, no significant differences were obtained by conducting pair wise tests between the periods (see Tab. 43). Comparing Figure 47 and Figure 49, we notice that the female infants (AE and AK) were responsible for high NI 1 values during P1, P2 and P10. For all 4 children, the lowest NI 1 values were recorded during P6 (12 weeks old). We may assume that an adaptation to different utterance patterns is trained while more complex melodies are produced. Many noise like sounds were produced during P7 and P9 from AK and AL respectively, leading to rising NI 1 values. At 5 months of age (P10), AK had NI 1 values already existing at P3 which we did not expect at

this age of development (see Figure 48). Therefore making clear distinctions between the NI 1 value in female and male infants cannot be possible from our findings, as much more representative data is needed.

Nevertheless, it becomes clear that all 4 children except AK have the tendency to produce NI 1 values below 0.2 towards P10. The implications of inter-individual "anatomic restructuring" and therefore variable sound properties may be responsible for the different curve patterns. The assumption that irregular patterns (noisy segments) are present in spontaneous utterances from healthy children has been supported by our analysis. Our data also show that these noise segments are still present in cry sounds from infants at 5 months of age.

### 4.3.2 SH and NB

NI as defined by Hauschildt (2006) is an average value for noise portions in cry sequences. Comparing Figure 50 and Figure 52, the SH and NB were visible on sound spectrograms at variable periods. While during the first four periods (P1-P4) mainly SH dominated, NB were found distributed throughout the entire analysis. The high SH value from AK at P8 did not increase the NI value but increasing NB value resulted in a high NI value at P10 from AK. This means that the influence of the SH and NB in the value of NI can be very different in compared periods.

### 4.3.3 Signal length (SL)

Detailed analysis of the two-weekly averages from 4 normal born children showed individual differences during a period of 20 weeks (5 months). On the one hand, AE only produced cries with an average SL below 1.0 s during P1-P3 (Figure 54) but towards P10 all 4 children developed similarly. This data may support the assumption that the average SL from spontaneous utterances in infants should be shorter than the average SL from pain cries. Reports from other analysis of spontaneous cries during the first six months postulated an average SL ranging from 1.2 s - 1.7 s (Massengill, 1969; Borschberg & Ruppert, 1998; Lind, 1999; Kempf, 2008) which can be supported from our findings.

Looking at the average SL development curve in Figure 55, there should have been a problem with AE during P1 - P3 as she produced averagely shorter cries (below 1.0 s). Nevertheless our expectations were met as she got older, therefore producing signals within an accepted average SL after P3.

During this analysis many differences between the 4 infants were obvious and resulted in an "up and down movement" of the development curve (Figure 55). The SL depends on the control of the respiratory mechanism and the tuning capability also varies individually in healthy infants (Kempf, 2008). More complex cries are registered at about 10 weeks of age (about P5) and their melodies are less coupled with the air produced during expiration (Wermke/Mende, 1992), through which an intentional tuning with resonant frequencies can be reached. From the 3$^{rd}$ month (about P5), the vocal tract structure changes and new vocalisation types are registered (Vihman, 1996). At about this age some pre-articulatory phenomena have been proven in infant vocalisations (Wermke/Mende et al., 2002). Therefore, this also shows how important pre-speech analysis may be for detecting risk markers for later language development disorders.

### 4.4 Influence of analysed variables

In this study we analysed how our variables influenced the level of the NI within the three groups during a four month period (see chapter 3.6).

The orofacial cleft infants (group A) showed a negative correlation between their ages and measured average NB, SH and NI 1. Also, their ages did not play a great role on the average SL as seen in Tab. 44.

The values of NI 1 from children in all the three groups were not necessarily dependent on their signal lengths. We therefore obtained negative correlations between SL and the NI 1 in all three groups. Negative correlations existed between SH and NB in the cleft group (A), meanwhile significant correlations were found in our control groups (B1 and B2).

As we already assumed, there were some similarities between the orofacial infants (group A) and FH$^{+}$ infants (group B2). With age, there was a negative correlation to NB, SH and NI 1 in group B2 as well. There was no influence of

their age on the length of signals they produced as well. However, our methods of analysis were confirmed since we noticed correlations between the measured SH as well as amount of chaotic segments (NB) and the NI 1 levels from infants in groups A and B2 (see Tab. 44 and Tab. 46).

In infants born without any disorders (group B1), there was also a negative correlation between their ages and measured average NB. However, unlike the other two groups (A and B2), the normal born children showed a very significant negative correlation between their ages and the degree of SH (R= -.424, p= .01) see Tab. 45). Also, when these infants get older, there exists a significant negative correlation to NI 1(R= -.366, p= .05) as well. We only found in normal born infants a very significant positive correlation between SL and the appearance of NB (R= .431, p= .01). These results may further support the assumption that physiological conditions play a role in speech development.

In cry analysis it is assumed that subharmonics are precursors of chaotic episodes and therefore should strongly correlate with the NI 1. Our observations can confirm these assumptions and our methods of analysis are also ratified.
Group A and B2 were similar on certain observations as explained above but we also noticed some similarities between group B1 and B2. In group A, there was a significant correlation between SH and NB on the measured NI 1 value. Meanwhile in both groups B1 and B2, the correlation between SH and NB was very significant to the measured NI 1 value (see Tab. 44 - Tab. 46).
The hypothesis that the age of the infants may affect the levels of measured NI 1 can be confirmed by this analysis. In all three groups, as the infants get older the level of NI 1 is reduced with a negative correlation (groups A/B2) and a significant negative correlation (group B1).
These results may be important for further researchers analysing spontaneous cry sounds from infants, since we have proven for the first time that NI may be influenced by the physiological background of these infants. In spectrographic analysis of the infant cry, other researchers might have to make more comparisons based on the infants individually because considering only group based analysis may hide certain realities and lead to unreliable conclusions.

# 5 Summary and Conclusion

The delicate anatomical structures involved in infant cry production require intricate neurophysiological control especially in premature infants or those with a reduced respiratory or laryngeal function. Certain features like phonatory noise or subharmonics can be observed in infant cries using spectrograms. These features have a certain indicative valence for characterising the maturation stage of vocal control or its performance. One possible cause of deviation in neurophysiological coordination during voice production is disturbed CNS mechanisms, finally the consequences of orofacial clefts. Another is the influence of a familiar disposition for speech development disorders.

The present paper studied the latter two relationships. For the evaluation and interpretation of a noise index (= average value of the noise portion within a cry) in infant's pre-speech utterances, we analysed 1423 voice-signals emitted during the first 15 weeks of life by 10 orofacial cleft infants (5 females and 5 males), comparing these with a control group. The control group B of healthy infants was subdivided into B1 ($FH^-$ infants with a negative family history of speech developmental disorders) and B2 (FH+ infants with a positive family history of speech developmental disorders).

Infants born with orofacial clefts are substantially exposed to severe difficulties for speech and language acquisition. Coupled with a premature muscle network, cleft infants are deprived in various ways (vocal nasality, limited consonant repertetoire, backward articulation etc) and their coordination of respiration, phonation and articulation is limited from a very early age. From birth until about 2 months of age, an infant's cry is characterised by a tuning phase between respiration and phonation. After training the production of more complex cry melodies with different rhythms, infants begin at 3 - 4 months of age (Wermke et al., 2005) to tune their phonation and articulation. Successfully absolving these stages of development is presumably a prerequisite for later acquisition of inconspicuous speech and language competence. The development of articulation is based on the tuning of melodies produced in the larynx and resonant frequencies from the vocal tract (Kempf, 2008).

For an objective evaluation of pre-speech development in healthy and sick infants, this study produced comparable data on the appearance of selected parameters in age-appropriate control groups.

In order to examine the connection between these selected cry properties and the physiological condition in infants, we made comparisons to 2623 voice-signals from 10 $FH^+$ infants and 3002 voice-signals from 10 $FH^-$ infants (all without orofacial clefts and age-appropriates). For interpretations of future results, we also analysed 2684 voice-signals from 4 infants in the control group B1 ($FH^-$) taken at closer time intervals until the $20^{th}$ week of life. Until today, no research team has ever made detailed analysis of noisy elements in this manner; therefore for the daily clinical analysis of pre-speech vocalizations from non-cleft and cleft infants it was necessary to evolve a new objective method.

This study showed that the appearance of noise-like elements (NI) in the vocalizations of orofacial cleft infants and $FH^+$ infants were identical during the first 15 weeks of life. Also, we could show that in both these groups (A and B2) there was a delayed development in the average signal length (phonation time). Although cleft infants and $FH^+$ infants differ from each other physiologically, our results may propose a common neurophysiological retardation. Comparing prosodic elements in cries from $FH^+$ and $FH^-$ infants showed differences (Blohm, 2007; Denner, 2007). Therefore, future research could apply this knowledge to a larger sample of infants in order to establish a better therapy concept, thus preventing late interventions.

Infants from our control group B1 ($FH^-$) met our expectations because when they got older, a development in their pre-speech capability was noticed. Our results support the hypothesis that in cry research, physiological differences (orofacial clefts or a family history for speech development disorders) in infants may encourage the appearance of noise-like elements in their vocalisations. However we believe that a period of training enables the infants to reduce their mean NI. The production of more complex melodies with age was better managed by the $FH^-$ infants and they also produced longer cries.

To avoid a developmental retardation in speech and learning capabilities, it may be necessary in future to make more compact studies considering many other parameters and making comparisons with age-appropriates. Further studies also have to correlate these findings while investigating the consequences of these maturation processes on sound production.

Despite physiological differences in the three groups of infants, the noise index (NI) as applied in this study can be used as an objective parameter for daily clinical diagnosis during the first four months of life.

# 6 Zusammenfassung

Die vorliegende Arbeit befasst sich im Rahmen einer prospektiven Studie zur Analyse und Interpretation eines Rauschindex (RI) oder mittlerer Rauschbandanteil über eine Schreisequenz in der Vokalisation junger Säuglinge. 1423 Lautaufnahmen von 10 orofazialen Spaltkinder (5 weiblich und 5 männlich) während der ersten 15 Lebenswochen wurden analysiert. Säuglinge mit einer orofazialen Spaltbildung sind bezüglich vieler Aspekte in ihrer sprachlichen Entwicklung benachteiligt (hypernasale Resonanz, eingeschränktes Konsonantenrepertoire, Rückverlagerung der Artikulation usw.) sowie bei der Koordination von Respiration, Phonation und Artikulation vor der chirurgische Behandlung. Ab Geburt bis zum Alter von 2 Monaten sind Säuglingslaute durch ausgeprägte Frequenzmodulationen charakterisiert, die auf einer Abstimmung von Respiration und Phonation beruhen. Nachdem Säuglinge in den ersten Wochen die Produktion komplexer Schrei-Melodien mit unterschiedlichen Rhythmen geübt haben, beginnen sie im Alter zwischen 3 - 4 Monaten die Phonation und die Artikulation fein abzustimmen (Wermke et al., 2005).

Das erfolgreiche Absolvieren dieser Entwicklungsstadien ist möglicherweise eine Voraussetzung für einen späteren unauffälligen Sprech- und Spracherwerb. Die Artikulation beginnt sowohl mit einen intentionalen Tuning der Melodien, die laryngeal erzeugt werden, als auch mit der Bildung von Resonanzfrequenzen des Vokaltraktes (Kempf, 2008).

Diese Entwicklungsprozesse sind bei Säuglingen mit orofazialen Spaltbildungen gestört. Die erhöhte nasale Impedanz führt durch einen rückgekoppelten Regelkreis zu einem Anstieg des subglottischen Druckes (Hauschildt, 2006). Die winzigen Stimmlippen der jungen Säuglinge sind diesem Druck nicht ausreichend gewachsen, so dass es regelmäßig zu phonatorischen Rauschphänomenen in deren erzeugten Lauten kommt. Dies verhindert das "Trainieren" melodisch-rhythmischer Elemente als Vorstufe für die spätere muttersprachliche Prosodie. Für eine objektive Auswertung solcher Phänomene in den vorsprachigen Entwicklungen wurden in dieser Studie das Auftreten und der Grad ihrer Ausprägung anhand ausgesuchter Parameter bei Säuglingen

mit orofazialen Spalten (Gruppe A)) und bei solchen in einer altersähnlichen Kontrollgruppe (B) untersucht.

Die Kontrollgruppe B bestand aus gesunden Säuglingen ohne (FH- oder B1) bzw. mit (FH+ oder B2) einem familiären Risiko für eine spezifische Spracherwerbsstörung. Letztere wurden einbezogen, da Säuglinge mit orofazialen Spalten (A) und Säuglinge mit einer familiären Disposition für Spracherwerbsstörungen ($FH^+$) ähnlichen Abweichungen in der neurophysiologische Koordination der Lautproduktion aufweisen (Denner, 2007). In der Kontrollgruppe wurden 2623 einzelne Laute von 10 $FH^+$ Kindern und 3002 Laute von 10 $FH^-$ Kindern miteinander verglichen. Um Entwicklungstrends besser beurteilen zu können, wurden in dichteren Intervallen (wöchentlich statt monatlich) 2686 Laute aus der Gruppe B1 ($FH^-$) bis zur 20 Lebenswoche analysiert.

Diese Studie konnte zeigen, dass während der ersten 15 Lebenswochen sehr identische, geräuschähnliche Phänomene (RI) in der Vokalisation von Spaltkindern und $FH^+$ Kindern auftreten. Außerdem konnte gezeigt werden, dass in diesen beiden Gruppen eine verzögerte Entwicklung der durchschnittlichen Signallänge (Phonationszeit) einzelner Laute auftrat. Trotz allen physiologischen Unterschieden zwischen den Spaltkindern und den $FH^+$ Kindern deuten unsere Ergebnisse auf eine gemeinsame neurophysiologische Entwicklungsverzögerung hin. Ein Vergleich prosodischer Elemente in der Vokalisationen von älteren $FH^+$ und $FH^-$ Kindern ergab auch Unterschiede (Blohm, 2007; Denner, 2007). Die vorliegende Studie bestätigt dies und die Erkenntnisse könnten zukünftig verwendet werden um geeignete Therapieverfahren zu entwickeln.

Säuglinge aus der Kontrollegruppe B1 ($FH^-$) bestätigen die gestellten Hypothesen, da mit zunehmendem Alter eine signifikante Reduktion von Rauschphänomenen beobachtet wurde. Keine andere Studie hat bis heute eine vergleichbare objektive und detaillierte Analyse der Rauschelemente in Säuglingslauten durchgeführt.

Die Ergebnisse bestätigen die Hypothese, dass neurophysiologische Besonderheiten, die auf eine orofaziale Spalte oder eine familiäre Disposition

für eine Spracherwerbsstörung zurückzufuhren sind, das Auftreten von rauschähnlichen Elementen in der Vokalisation von Säuglingen beeinflussen könnten. Ganz offenbar gehört eine 'Trainingphase' dazu, um den mittlere RI zu reduzieren. Komplexere Melodien konnten mit zunehmendem Alter von den $FH^-$ Kindern besser beherrscht werden, da sie wohl auch längere Schreie koordinierter erzeugten.

Die Arbeit bestätigt auch, dass der Rauschindex (RI), wie er in dieser Studie angewandt wurde, geeignet ist, um bei der klinischen Betreuung von orofazialen Spaltkindern, insbesondere während der ersten vier Lebensmonate, als Entwicklungsstandindikator dienen kann.
Um einem Entwicklungsrückstand in der Spracherwerbsfähigkeit gefährdeter Säuglinge zu belegen, wird es in Zukunft nötig sein, umfassendere Studien durchzuführen, wobei weitere akustische Parameter berücksichtigt werden sollten.

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# Declaration

1. This thesis with the title "Quantitative analysis of subharmonic and noise phenomena in vocalizations of young infants - comparing infants with and without orofacial clefts" is not identical to any other thesis or dissertation.

2. I did this thesis myself and did not have any help apart from the references which have been attached to this work.

3. I have never presented this study at any other faculty in order to receive a grade which makes me carry the doctorate title.

Wuerzburg on the, 14th of March 2011

……..

(Ndemazeh Arnold Fuamenya)