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Research Paper

The Optimal inter-implant interval in pediatric sequential bilateral implantation

Angelika Illg [a, *], Carolin Sandner [a], Andreas Büchner [a, b], Thomas Lenarz [a], Andrej Kral [a], Anke Lesinski-Schiedat [a]

[a] *Department of Otorhinolaryngology, Hannover Medical School, Hannover, Germany*
[b] *Cluster of Excellence, Hearing4All, Hannover Medical School, Hannover, Germany*

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ABSTRACT

An increasing number of children receive bilateral cochlear implants (CIs) sequentially. Outcomes of bilateral implantation show high variability. This retrospective analysis investigates the optimal inter-implant interval. For this purpose, speech comprehension results of 250 children who underwent sequential bilateral cochlear implantation were evaluated. All individuals underwent periodic speech perception testing in quiet and noise. The most recent unilateral data for each side were statistically analyzed. Speech test outcomes were evaluated with reference to age at first implantation and interval between implantations.

A statistically significant difference for speech test performance was obtained between the first-implanted ear and the second-implanted ear for all children (expressed as a mean). These outcomes were dependent on the inter-implant interval. There was a significant correlation ($r = -0.497$; $p = 0.000$) between speech test results and the inter-implant interval. Nevertheless, one subgroup of 27 children had the same or better results for the second side as compared with the first.

In conclusion, the evaluation of the inter-implant interval and age groups at first implantation showed a preferred interval of up to four years in children under the age of 4 at first implantation. The older the children were at first implantation, the shorter the inter-implant interval had to be. It is as a direct consequence of this interval that children for whom it was longer were also older.

1. Introduction

Compared with unilaterally implanted individuals, bilateral implant recipients show better speech comprehension in noisy conditions, better directional hearing and improvement with regard to binaural mechanisms such as the head shadow and squelch effects, and better binaural summation (Brown and Balkany, 2007; Ching et al., 2007; Galvin et al., 2008; Sparreboom et al., 2011). Children and adolescents who underwent sequential bilateral cochlear implantation show poorer speech comprehension outcomes for the second-implanted ear than for the first side (Gordon et al., 2014; Illg et al., 2013) although these children also benefit in terms of binaural listening. As an example, Steffens et al. (2008) describe the effect of binaural advantages after sequential bilateral cochlear implantation. The authors emphasize that both those children with high- and low-level monaural speech recognition scores for the first-implanted ear had a significant binaural advantage subsequent to the second implantation. Other studies (Chadha et al., 2011; Galvin et al., 2007a, b, 2008, 2010; Sparreboom et al., 2010, 2012a, b; Wolfe et al., 2007; Zeitler et al., 2008) describe similar results for lateralization or for speech recognition in quiet or noise (Smulders et al., 2011).

The age at which children receive a cochlear implant (CI) is one of the strongest predictors of hearing and speech skills after cochlear implantation (Connor et al., 2006; Lesinski-Schiedat et al., 2004; Nikolopoulos et al., 1999; Sharma et al., 2002). Long-term studies have also shown that performance improves slowly over time and requires years to approach the final outcome (Beadle et al., 2005; Uziel et al., 2007). This long-term progress likely reflects the complexity inherent in the development of the auditory system that is largely dependent on auditory input.

Cortical development continues until adulthood, with extensive

* Corresponding author. HNO-Klinik der MHH – Deutsches HörZentrum, Karl-Wiechert-Allee 3, 30625 Hannover, Germany.
E-mail address: illg@hoerzentrum-hannover.de (A. Illg).

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Table 1
Characteristics of CI users.

	Mean ± SD [years]	Median [years]	Min. – max. [years]
First CI	2.33 ± 1.66	1.96	11.07–0.43
Second CI	6.18 ± 3.53	5.37	15.57–1.04
Inter-implant interval	3.92 ± 3.10	3.17	14.08–0.08
Duration of experience with first CI	9.09 ± 3.45	8.46	17.32–2.95
Duration of experience with both CIs	5.22 ± 1.87	4.98	14.38–1.78

developmental changes both at the cellular and microcircuitry levels (Kral and O'Donoghue, 2010; Kral and Sharma, 2012). In animal experiments, absence of hearing experience alters these developmental processes extensively and demonstrates their dependence on auditory input (Kral et al., 2013). With unilateral implantation in animals, plastic reorganization of the "aural preference" in favor of the implanted ear within an early sensitive period has been described (Gordon et al., 2015; Kral et al., 2013).

In children with unilateral CIs, a modifying influence of unilateral hearing on the auditory system has been shown that induces auditory maturation; however, at an implantation age of 6.5–7.0 years, developmental maturation is less likely to be initiated (Kral and Sharma, 2012). Sharma et al. (2005) assumed that a second, 'late' implant would stimulate cortical areas and also that there would not be normal connections either within cortical layers or to higher-order auditory and language areas, which may lead to inferior outcomes for the later-implanted ear.

Nonetheless, speech recognition improves in children who undergo sequential bilateral cochlear implantation. Systematic studies on the effects of stimulation of the second-implanted ear are rare and include only limited numbers of individuals (Gordon and Papsin, 2009; Gordon et al., 2015; Graham et al., 2009).

Therefore, although mechanisms for aural preference have been described and implications for speech comprehension results are known, this is not the case for the optimum inter-implant interval in children and adolescents. We therefore investigated the speech comprehension of young children after sequential cochlear implantation, involving a large population, to calculate the optimum inter-implant interval. For this purpose, data for 250 congenitally deaf individuals were analyzed according to two predictors: inter-implant interval, and age of first and second implantation.

2. Material and methods

2.1. Subjects

Two hundred and fifty children and adolescents who underwent sequential bilateral cochlear implantation at our center between 1995 and 2011 were included in this retrospective study. During the 1990s, it was customary to implant children predominantly in one ear only. As adolescents, many of these unilateral CI users requested a second, contralateral implant. Therefore, 157 children received their second implant with an inter-implant interval of less than four years, and 93 children were provided with theirs after a period of more than four years.

First implantations were carried out between 1995 and 2010. All children were diagnosed with profound hearing loss under the age of 2. Descriptive data of the demographic variables for all CI users are provided in Table 1. One hundred and fifteen children had some residual hearing within the range 125–750 Hz on the second side prior to implantation (Fig. 1). The remaining 135 children had no residual hearing confirmed by objective audiometry (automated auditory brainstem response, AABR) at the time of first preoperative clinical diagnostics. Additional cognitive developmental disorders were not observed amongst this group of children. All patients with cognitive developmental disorders such as autism, other syndromes or any suspected cognitive participation were excluded.

The breakdown for etiology of deafness for the 250 children was as follows: unknown (64%); genetic (17.6%); premature birth (5.6%);

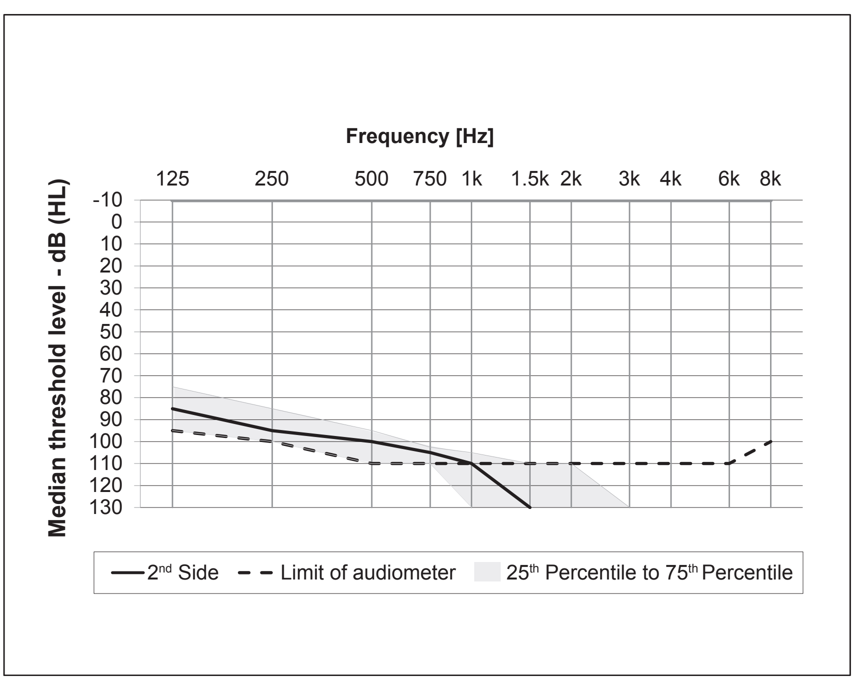

Fig. 1. Preoperative median sound levels of the second ear. The solid line shows the residual hearing of the second ear preoperatively, the dashed line the audiometer limit and the grey area the upper and lower quartiles.

syndromic (3.6%); caused by a cytomegalovirus (3.6%); ototoxic drugs (2.8%); periportal hypoxia (1.6%), inner ear dysplasia (0.8%); other infections (sepsis) (0.4%).

The individuals were implanted with multichannel CIs manufactured by Cochlear, Advanced Bionics or MED-EL. Because their bilateral implantation was sequential, 50.4% (n = 126) of the children received different implants; of this subgroup, implants from different manufacturers were used in 3.2% (n = 4) of cases. A total of 124 children (49.6%) (n = 124) were provided with the same implants on both sides.

2.2. Speech comprehension tests

All 250 children were periodically tested using the German-language Freiburg monosyllabic word test (FMT) in quiet and the German-language Hochmair-Desoyer, Schulz, Moser sentence test (HSM) in quiet and in noise (10 dB S/N ratio, SoNo). All tests were performed in free field at 65 dB SPL and for each side, with bilateral hearing also tested separately. The most recent data for each implanted side were evaluated.

2.3. Evaluation and statistics

The speech test results were evaluated with reference to two predictors: inter-implant interval and age at first implantation. Because the analysis was retrospective, not all data were available for all comparisons. Where the total number of data sets was not 250, this number is given together with the relevant results.

To evaluate the optimum inter-implant interval for second implantation, the 137 FMT data sets for the second-implanted ear were divided into six inter-implant interval groups of equal duration (two years) (Table 2).

All data were analyzed statistically using IBM SPSS Statistics, version 22, 23 and 24 (Pallant, 2010). The tests performed were one-factor analysis of variance (ANOVA) followed by the Scheffé post-hoc test. The Wilcoxon test with Bonferroni correction was used to statistically compare the mean of the data between the first and second side. The *t*-test and Mann- Whitney *U* test were used to compare age differences and speech comprehension between the main group and the group with the same or better outcomes for the second-implanted ear. To correlate two variables, the Spearman's rho correlation coefficient was applied. Furthermore, the effect of inter-implant interval was statistically evaluated using the Kruskal-Wallis test by ranks in MATLAB R2016b (Mathworks, Natick, USA). The significance level for post-hoc comparisons was corrected by applying the Bonferroni method. Statistical-significance level was set to $p < 0.05$ (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$).

Table 2
Inter-implant interval: evaluation groups.

Group	Number of children	Inter-implant interval
1	23	<2 years
2	37	3–4 years
3	25	5–6 years
4	27	7–8 years
5	12	9–10 years
6	13	>11 years

3. Results

There were 144 FMT data sets with scores for the first side (FMT1), 137 for the second side (FMT2), and 167 for the bilateral condition (FMTbi). Mean scores and standard deviations for these children were as follows: first side: 66.13% ± 22.17%; second side: 41.89% ± 29.84%; bilateral: 69.70% ± 23.36%. Significant differences were found between all test conditions (FMT1 vs. FMT2; FMT1 vs. FMTbi; FMT2 vs. FMT bi: p = 0.000) (Fig. 2). Availability of complete data for HSM sentences in quiet was as follows: first side: for 112 children (HSM1); second side: for 117 children (HSM2); bilateral: 135 (HSMbi). Mean scores and standard deviations are as follows: first side: 74.87% ± 29.69%; second side: 45.03% ± 36.85%; bilateral: 74.46% ± 31.26%. Significant differences were found between all test conditions (HSM1 vs. HSM2; HSM2 vs. HSMbi: p = 0.000; HSM1 vs. HSMbi p = 0.001). Availability of complete data for HSM sentences in noise was as follows: first side: for 111 children (HSM_n1); second side: for 105 children (HSM_n2); bilateral: for 135 children (HSM_nbi). Mean scores and standard deviations are as follows: first side: 30.55% ± 25.11%; second side: 12.98% ± 21.64%; bilateral: 34.97% ± 27.93%. Significant differences were found between all test conditions (HSM_n1 vs. HSM_n2; HSM_n1 vs. HSM_nbi; HSM_n2 vs. HSM_nbi: p = 0.000).

3.1. Speech comprehension as a function of inter-implant interval and chronological age at second implantation

Because of the difference between results for the first- and

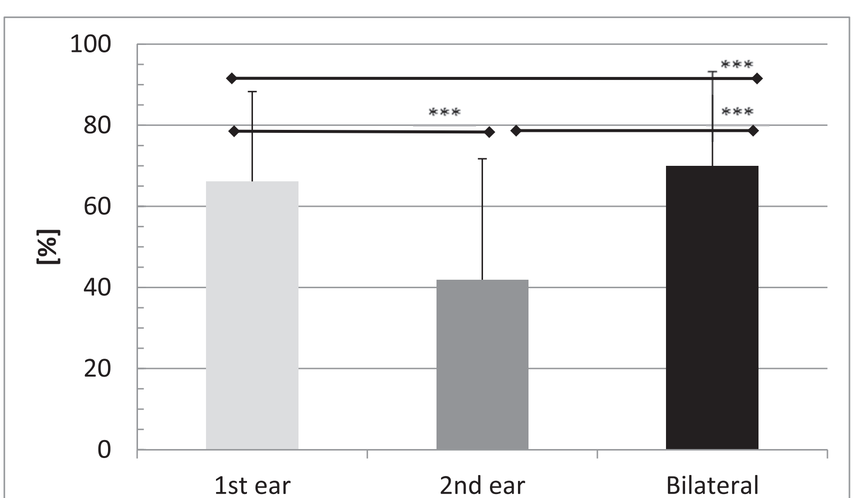

Fig. 2. Results of Freiburg monosyllabic tests: first side (FMT1), second side (FMT2), and bilateral (FMTbi). The data shown are means ± SD.

second-implanted ear, correlation between speech comprehension and inter-implant interval was investigated. Only FMT scores are analyzed in the following section; outcomes for HSM sentences in quiet and noise exhibited the same tendency (not shown). The data reveal a negative correlation (Spearman's rho) between speech comprehension test performance and inter-implant interval (r = - 0.497; p = 0.000) (Fig. 3).

The Kruskal-Wallis test by ranks confirmed that there were differences between groups ($p = 2.7*10^{-9}$). The mean scores for each interval group were compared using the post-hoc Wilcoxon-Mann-Whitney test and corrected for multiple comparison by applying the Bonferroni correction (Fig. 4). Significant differences were found when comparing the mean ranks of groups 1 and 6 (p = 0.000), groups 1 and 5 (p = 0.004), groups 1 and 4 (p = 0.012), groups 2 and 6 (p = 0.000), groups 2 and 5 (p = 0.006), groups 2 and 4 (p = 0.014), and groups 3 and 6 (p = 0.000). Thus, the data revealed that the first two and last three groups were similar in terms of the relationships between them: the first two groups differed from groups 4, 5 and 6 but were not different from each other. Group 3 was in between: while it did not differ from groups 1 and 2, it also did not differ from groups 4 and 5. The corresponding FMT2 means (±standard deviation) showed a downward trend: from 58.69% ± 26.08% (group 1) and 56.90% ± 25.67% (group 2) to 46.20% ± 26.90% (group 3), 30.41% ± 26.15% (group 4), 21.25% ± 17.85% (group 5), and 3.46% ± 8.26% (group 6). This, taken together, allows the conclusion that children with an inter-implant delay of more than four years exhibit poorer performance associated with the second-implanted ear (see Fig. 5).

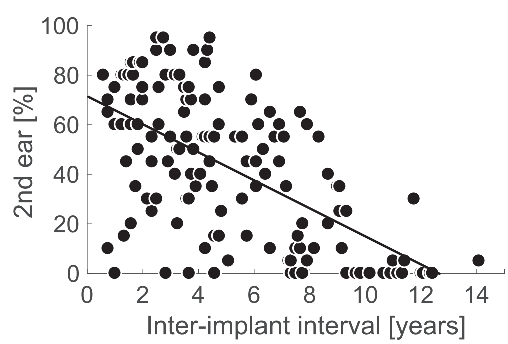

Fig. 3. Results of Freiburg monosyllabic tests: second side (FMT2) in relation to inter-implant interval.

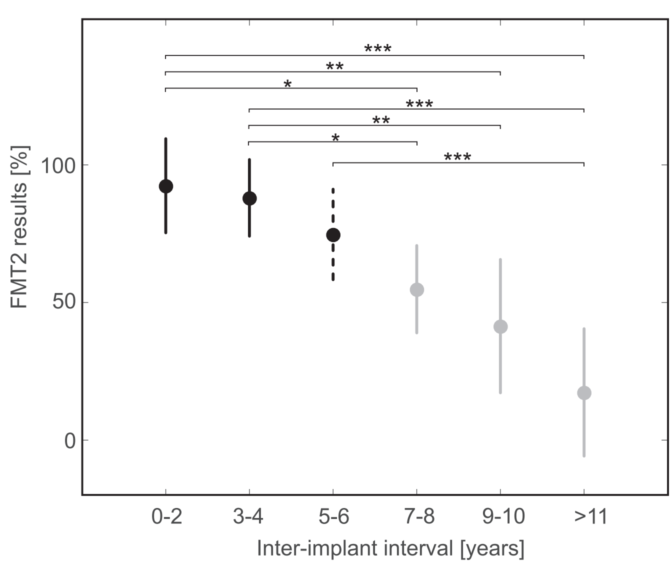

Fig. 4. Mean ranks (±SEM) derived from the Kruskal-Wallis test by ranks based on FMT scores for the second-implanted ear as a function of inter-implant interval with post-hoc statistical comparison (Wilcoxon-Mann-Whitney test, Bonferroni-corrected). Beginning at an inter-implant interval of 5 years, performance starts dropping off significantly. Means FMT scores show a corresponding decrease; see text for details.

As with inter-implant interval, a difference also emerges relating to chronological age at first-side and second-side implantation. The correlation between speech comprehension and chronological age at second-side implantation was determined. The data show a negative correlation (Spearman's rho) between speech comprehension test results and the chronological age at second-side implantation (r = - 0.500; p = 0.000) which is similar to the correlation between speech comprehension test outcomes and the inter-implant interval.

3.2. Children who obtain the same or better results with the second-implanted ear

There was a group of 27 children whose speech comprehension of monosyllabic words with the second-implanted ear was equal to, or better than, that with the first-implanted ear. Their mean ages at the first CI intervention were 1.70 ± 0.71 years [min. 0.56 years – max. 3.25 years] and 5.01 ± 2.06 years [min. 2.02 years – max. 10.19 years] for the second CI. The mean inter-implant interval was 3.31 ± 2.03 years [min. 0.58 years – max. 7.92 years].

Mean scores and standard deviations were as follows: first side: 64.00% ± 17.04% (FMT1); second side: 74.07% ± 15.57% (FMT2); bilateral: FMTbi 83.11% ± 11.58%. Significant differences were found between mean scores for the first and second side (p = 0.000), the second side and the binaural conditions (p = 0.001), and the first side and the bilateral condition (p = 0.000) (Fig. 6).

Mean HSM sentence scores and standard deviations were as follows: first side; 80.18% ± 25.46%; second side: 79.34% ± 24.98%; bilateral: 85.83% ± 22.59%. Significant differences were found between the mean results for the first side and for the bilateral condition (p = 0.022), and for the second side and for the bilateral condition (p = 0.002).

Mean scores (and standard deviations) for HSM sentence scores in noise were as follows: first side: 41.47% ± 30.05%; second side: 35.35% ± 29.64%; bilateral: 47.89% ± 29.58%. Significant differences were found between the mean results for the first side and for the bilateral condition (p = 0.005), and between those for the second side and for the bilateral condition (p = 0.005).

No correlation was found between speech comprehension (FMT2) and inter-implant interval in children with same or better results for the monosyllabic test (second side) (r = - 0.121;

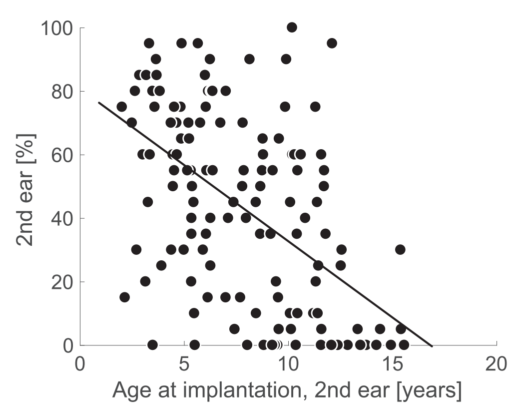

Fig. 5. Results of Freiburg monosyllabic tests: second side (FMT2) in relation to age at second implantation.

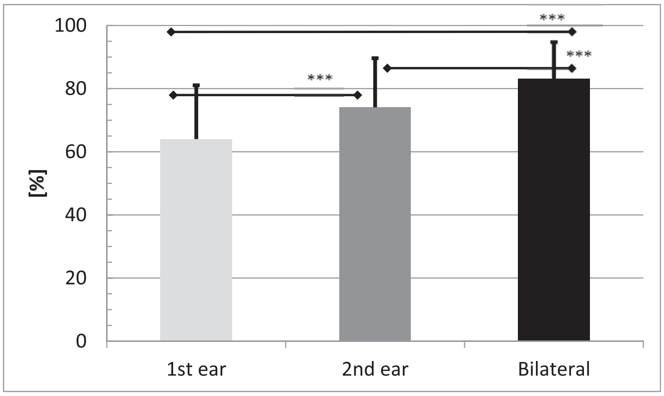

Fig. 6. Results of Freiburg monosyllabic tests on children who achieved the same or better outcomes with the second-implanted ear: first side (FMT1), second side (FMT2), and bilateral (FMTbi). The data shown are means ± SD.

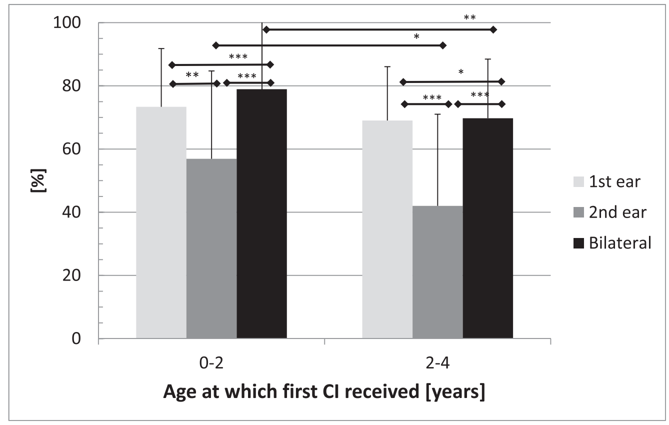

Fig. 7. Results of Freiburg monosyllabic tests: first side (FMT1), second side (FMT2), and bilateral (FMTbi) divided into two different age groups depending on age at first implantation. The data shown are means ± SD.

$p = 0.549$); this differs considerably from the results for the entire sample.

A *t*-test comparison of individuals' age at implantation between the main group and this 27-strong group of children revealed no significant difference between age at first-side implantation ($t(275) = 1.93$ $p = 0.055$) and second-side implantation ($t(275) = 1.71$ $p = 0.088$). The inter-implant interval for these 27 children is not significantly shorter than that for the main group ($t(275) = 0.99$ $p = 0.322$).

3.3. Speech comprehension based on age at time of first implantation

To investigate the influence of age at first implantation, data was evaluated for the 97 children 4 years old or younger at the time of implantation. To aid evaluation, the subjects' data were divided into two age groups based on age at first implantation. These were group A: 0–2 years at first implantation (55 children), and group B: 2–4 years at first implantation (42 children). In group A, mean duration (with standard deviation) of experience with the first implant was 8.75 ± 3.00 years and that with both implants was 5.67 ± 1.74 years. In group B, mean duration (with standard deviation) of experience with the first implant was 9.95 ± 3.62 years and that with both implants was 5.48 ± 1.96 years.

Mean FMT scores and standard deviations for the younger of the age groups (A: 0–2 years at first implantation) were as follows: first side (FMT1): 73.37% ± 17.51%; second side (FMT2): 56.91% ± 28.67%; bilateral (FMTbi): 78.93% ± 20.51%. Significant differences were found (Fig. 7) between the first and second side ($p = 0.003$), the second side and the bilateral condition ($p = 0.000$), and the first side and the bilateral condition ($p = 0.000$).

Mean FMT scores (with standard deviation) for group B (2–4 years at first implantation) were as follows: first side: 69.03% ± 16.65%; second side: 42.00% ± 32.74%; bilateral: 69.74% ± 22.28%. Significant differences were found between the first and second side ($p = 0.000$), the second side and the bilateral condition ($p = 0.000$), and the first side and the bilateral condition ($p = 0.014$).

In the monosyllabic test, significant differences between the two age groups were found for the second side ($p = 0.031$) and for the bilateral condition ($p = 0.007$).

As before, this grouping confirms that even if first implantation is performed within the sensitive period for therapy of deafness (<4 years), the outcome may be better if implantation is performed earlier rather than later (i.e. within the first two years as opposed to the third and fourth years of life). Furthermore, even though within this subgroup performance with the second-implanted ear was worse than that with the first-implanted ear, these children also showed binaural advantages in terms of speech perception. Here, too, performance was superior if the first implantation was performed at an early stage.

3.4. Speech comprehension as a function of inter-implant interval and age at first implantation

Data for the two groups based on age at first implantation were compared with reference to the inter-implant interval. For this purpose, each of the age groups A and B was subdivided into two groups based on inter-implant interval. Because of the correlation between inter-implant interval and FMT2 score in the group as a whole (Figs. 3 and 4), four years of elapsed inter-implant time was chosen as the basis for this subdivision.

Results for group A were as follows. For the first side, mean FMT scores (with standard deviation) obtained by the youngest children were 72.41% ± 18.56%, where the inter-implant interval was less than four years, and 75.00% ± 15.91% where this interval exceeded four years. For the second side, mean FMT scores (with standard deviation) were 65.00% ± 22.29% where the inter-implant interval was less than four years, and 42.64% ± 33.54% where this interval exceeded four years. Significant differences were found between the mean scores for the second side ($p = 0.009$), and between the first and second side in those children with the greater inter-implant interval (i.e. >4 years ($p = 0.000$)) (Fig. 8).

Results for group B were as follows. For the first side, mean FMT scores (with standard deviation) obtained by the youngest children were 72.86% ± 14.4% where the inter-implant interval was less than four years, and 66.79% ± 17.76% where this interval exceeded four years. For the second side, mean FMT scores (with standard deviation) were 66.54% ± 21.25% where the inter-implant interval was less than four years, and 27.5% ± 29.75% where this interval exceeded four years.

Significant differences were found between the mean scores for the second side ($p = 0.000$), and between the first and second side in those children with the greater inter-implant interval (i.e. > 4 years ($p = 0.000$)) (Fig. 9).

4. Discussion

This retrospective study investigated the speech comprehension

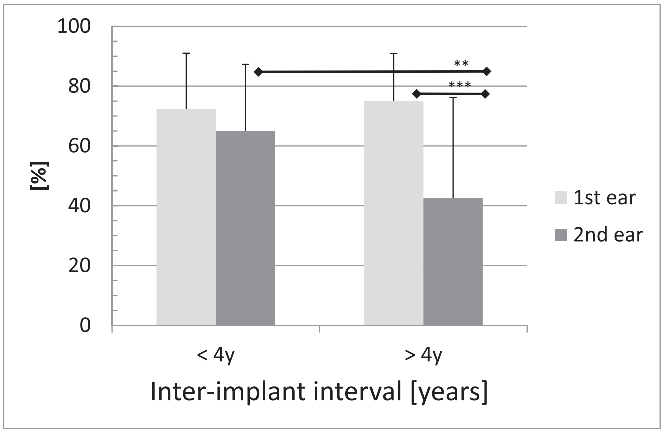

Fig. 8. Results of Freiburg monosyllabic tests in children who received their first implant at the age of between 0 and 2 years: first side (FMT1), second side (FMT2) divided into two different age groups depending on age at first implantation. The data shown are means ± SD.

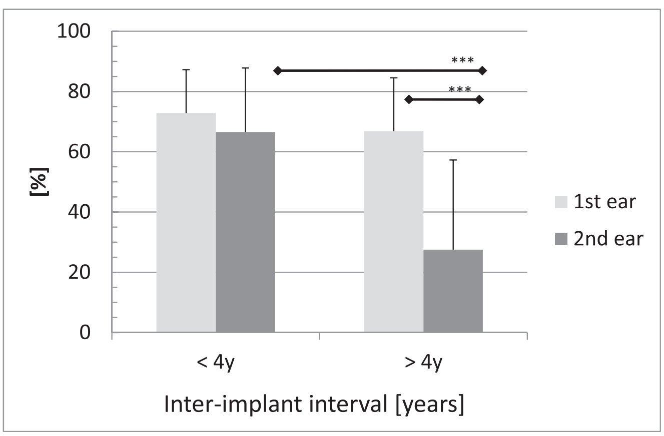

Fig. 9. Results of Freiburg monosyllable tests in children who received their first implant at the age of between 2 and 4 years: first side (FMT1), second side (FMT2) divided into two different age groups depending on age at first implantation. The data shown are means ± SD.

of young individuals after sequential cochlear implantation to predict the optimum inter-implant interval or the optimum age for the second implantation. All subjects were implanted in the first ear at an early stage, i.e. within the first four years (this being the critical period for therapy of deafness). Second implantations took place both within and outside this critical period.

The study demonstrates, with reference to a small group, that good performance is possible even if the child undergoes second-side implantation outside this critical period. It is highly probable that speech comprehension achieved with the second ear was not learned *de novo*. Rather, the second-implanted ear's 'access' to the already established language networks was facilitated. In this sense, information learned through the first ear could be 'transferred' to the input received via the second-implanted ear. Such learning transfer (generalization) from one ear to the other is well known in normal-hearing subjects (review in Wright and Zhang, 2009). Most cortical neurons are binaural and remain so even in congenital single-sided deafness (even though differences in binaural interaction can be found) (Tillein et al., 2016); inputs through the left and right ear thus converge on the same neuronal population. Under this assumption, new learning of phonetic analysis is not necessary: it is sufficient that interaction between the two inputs is reorganized to facilitate transfer of learned speech comprehension to the second-implanted ear. This explains why the effects can be observed even beyond the end of the critical period. However, this was possible only if sequential implantation was performed with an inter-implant interval of less than four years; implantations beyond this interval compromised the effect and lead to persisting detrimental effects for speech comprehension on the second-implanted ear. This effect was more pronounced if the first implantation was in the second half of the critical period (2–4 years).

Our results agree with the general finding for sequential bilateral implanted children that speech perception scores obtained with the second implant are poorer than the performance for the first-implanted side (Fig. 2) (Peters and Litovsky, 2007; Steffens et al., 2008). Speech comprehension achieved with the first-implanted side may be influenced by the high degree of plasticity in central auditory pathways in early childhood and the 'sensitive period', a topic frequently described by different authors (Gordon et al., 2015; Kral and O'Donoghue, 2010; Kral and Sharma, 2012; Kral et al., 2013; Lesinski-Schiedat et al., 2004; Sharma et al., 2002, 2005). Correspondingly in the present study, when considering results obtained relative to the first implant alone, speech comprehension outcomes tend to be poorer with increasing age at second implantation. Although most children received hearing aids before first implantation, speech perception outcomes in the older group (2–4 years) were slightly poorer than in the younger age group (0–2 years) (Fig. 7). Also, with respect to those children who developed language skills to some extent after previously receiving hearing aids, children implanted at a younger age showed superior speech comprehension results, which again support the notion of early implantation. Speech test performance obtained with the second implant also indicates a link between speech comprehension in quiet and age at the time of first-side implantation (Fig. 7); this corresponds to findings reported by Zeitler et al. (2008), a rare study with data available for comparison relating to first implants.

The results of the present study also showed that there is a small group of 27 children (10.8% of the main group) with same or better speech comprehension outcomes obtained using the second implant. Myhrum et al. (2017), too, report some participants who obtained good speech perception results with their second CI, even when inter-implant intervals were long and without the use of effective hearing aids during the inter-implant interval. However, the authors did not evaluate this subgroup any further.

The 27 children in our study were of significantly younger age at first implantation ($p = 0.055$), but age at implantation was not different for the second ear. While they did not show significantly smaller inter implant-intervals compared with the whole group, this subgroup also exhibited a tendency for negative correlation between speech comprehension and inter-implant interval.

Speech comprehension outcomes could also be influenced by residual hearing or duration of hearing aid use. However, no significant differences were found between the main group and this small subgroup. Additionally, the use of different devices for first- and second-side implantation may influence speech performance; nevertheless, the distribution of implants was similar to that in the main group. The proportion of the group that uses different implants is 40.74% ($n = 11$); 59.25% ($n = 16$) use the same implants. Other factors explaining differences in speech comprehension could be the angle of insertion, the number of inserted electrodes or the length of the cochlear duct, which were not investigated in this study. O'Connell et al. found 2016 that a greater angle of insertion leads to better speech comprehension.

These data in general confirm the influence of inter-implant interval (Fig. 4) and demonstrate that, where age at second implantation is well beyond the sensitive period for the first implantation, performance may still be as good as, or better than, that obtained with the first implant and be unusually high for children implanted at or beyond the age of 5 for the first time. This provides evidence that – unlike the case with the first implantation – it is not the absolute age at second implantation that crucially influences outcomes in these cases. These children were able to benefit from the early first implantation and, in part, 'transfer' performance to the second side; additionally, they exhibited binaural advantage in terms of speech comprehension. This shows that, in children implanted at a very young age, inter-implant interval and higher age at second implantation are, in combination, the most important influencing variables in sequential bilateral implantation.

Performance achieved with the second-implanted side was affected by the duration of the inter-implant interval. The auditory cortex is differentially driven by both ears and ongoing deprivation for the second ear may have degenerative ear-specific consequences, leading to abnormal 'aural preference' of the hearing ear (Kral et al., 2013; Tillein et al., 2016). Therefore, speech comprehension outcomes may worsen in children and adolescents with increasing inter-implant interval (Fig. 3) although the duration of CI experience had the greatest effect on CI performance (Blamey et al., 1996). With long inter-implant intervals, even very lengthy experience with the second implant was not able to compensate for poor scores in the speech tests, with no significant increase in these scores seen over time (Illg et al., 2013). Thus, there was no transfer of plastic changes induced through the first-implanted ear (Kral et al., 2013). Additionally, in children and adolescents with long inter-implant intervals (five or more years), a similar observation was made: speech performance results achieved with the second-implanted ear were very poor even after long periods (>5 years) of binaural hearing (Illg et al., 2013).

Despite the differences between the two sides, all of these children continue to use both implants. The lower level of input from the second implant does not interfere with the better performance achieved with the first-implanted side; rather, it assists the bilateral hearing mode (Fig. 2). We observed no detrimental effects from using both implants; this corresponded with Ramsden et al.'s (2005) findings.

Furthermore, in the combined evaluation of speech perception scores as a function of age at first implantation and inter-implant interval, a positive relationship between speech comprehension and this interval was found and statistically verified (Fig. 8), thus confirming the importance of inter-implant interval as a predictor. A positive effect on speech comprehension with decreasing inter-implant interval was clearly demonstrated. Speech perception scores of children with a longer inter-implant interval and higher age at second implantation were significantly poorer than for the children with shorter intervals (Fig. 7).

Some authors (Gordon and Papsin, 2009; Sparreboom et al., 2010) have proposed that inter-implant interval has a major influence on hearing and speech comprehension, but without being able to substantiate this because of the small numbers of children involved and because their samples included only children with short inter-implant intervals. Wolfe et al. (2007) concluded that an improvement in speech recognition seems to be possible for children who received their first CI before the age of three and a second CI by the age of 10 at the latest. This implies that the inter-implant interval should not exceed seven years. The results of the present study show that, in children under the age of 4 at first implantation, inter-implant intervals of more than four years lead to poorer outcomes being obtained with the second implant. This is confirmed by outcomes for young children who performed just as well or better with the second-implanted ear. It seems likely that, the older the children are at first implantation, the shorter the inter-implant interval needs to be age at second implantation increases commensurately with the inter-implant interval. Obviously, it is a direct consequence of the inter-implant interval that children with longer intervals are also older, and this is a co-determinant of outcomes.

The present data recommend inter-implant intervals no longer than four years in prelingually deaf children who derive no significant benefit from hearing aids. Gordon and Papsin (2009) and Gordon et al. (2015) also indicate that, for sequentially implanted children with a shorter inter-implant interval (<2 years), interaural performance differences were not statistically significant. The authors describe the detrimental impact of unilateral implants on bilateral auditory development and conclude that deprivation of the second side can be avoided by early implantation of both ears simultaneously or with limited delay (Gordon et al., 2013).

Given our large sample of children and their inter-implant intervals, the results of the present study validly demonstrate differences between speech comprehension achieved with the first- and second-implanted side. This study confirms the hypothesis that unilateral cochlear implantation reorganizes the brain and generates a "stronger" and a "weaker" ear, resulting in an abnormal "aural preference" of the stronger ear (Gordon et al., 2015; Kral et al., 2013). While this may evoke comparison with presbyopia in the visual system, the condition is significantly different in that the 'representation' of the weak ear in the cortex is preserved (Kral et al., 2013; Tillein et al., 2016); training techniques may, therefore, provide help in overcoming the aural preference. At present, however, the easiest means of preventing abnormal auditory preference may be through simultaneously cochlear implantation or by using hearing aids to take advantage of residual hearing (Illg et al., 2013; Wolfe et al., 2007).

5. Conclusion

Inter-implant interval correlates significantly with speech comprehension results obtained with the second-implanted side. To avoid abnormal aural preference in pediatric implantation, this interval should – in children first implanted under the age of 4 – be limited to less than four years. The older the children were at first implantation, the shorter the inter-implant interval needed to be. It is a direct consequence of the inter-implant interval that children for whom this interval was longer were also older.

Conflict of interest statement

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

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.heares.2017.10.010.

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