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THE EFFECT OF THE ACOUSTIC NERVE CHRONIC ELECTRIC STIMULATION UPON THE GUINEA PIG COCHLEAR NUCLEUS DEVELOPMENT

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Abstract. 14 newborn guinea pigs have been deafened three days after birth by bilateral destruction of the organ of Corti, and among them 8 have been supplied with a chronic auditory electric stimulation by means of an intracochlear implanted electrode. The histological study and the anatomical reconstructions of these animals' cochlear nuclei demonstrate that this chronic stimulation prevents, at least partially, these auditory pathway medullary formations from atrophy due to the cochlear destruction.

Our studies on surgical rehabilitation of total deafness by means of multichannel cochlear implant (Chouard et al., 1981) allowed us to demonstrate that clinical results depend on two principal parameters: (*a*) the functional value of the electrode–cochlear nerve interface (which may be appreciated as an inverse function of the electrical threshold level of the round window stimulation test); (*b*) the prelingual or post-lingual status of the deafness.

Moreover, in case of prelingual deafness presenting an effectual electrode–nerve interface (it means a low electrical threshold level to the round window stimulation test), it clearly appeared to us (Chouard et al., 1982) that the audiologic and phoniatric performances depended directly on the age of the patient. Our children, who were 9 to 17 years old, presented after 12 or 24 months very much better results than adults after the same delay, as if the lack of hearing during youth or adolescence had involved some trouble in the development of the auditory pathway.

Even if only a few histological reports of the brains of congenitally deaf humans (Brower et al., 1914; Castex et al., 1906; Zancia, 1908) describe abnormalities of cochlear nuclei, there is evidence that neonatal sound deprivation adversely affects central auditory mechanisms of the animal. Physiological effects have been described by Tees (1967) in the rat, Batkin et al. (1970) in the rat, McGinn et al. (1973) in the mice, Clopton et al. (1977) and Silverman et al. (1977) in rat. Anatomical data have been reported by Webster et al. (1979) and Trune (1982) who demonstrated the effects of neonatal conductive hearing loss on brain stem auditory nuclei of the CBA/J mice.

Our clinical data suggested to us that, on the contrary, a chronic electric stimulation of the deaf cochlea during the postnatal period could be able to prevent this atrophy produced by an early deafness. This supposition was supported by the constatations of Blakemore et al. (1975) who demonstrated that the development of the visual cortex of the cat depended on the visual experience of the animal. The aim of this study is to determine if the same phenomenon is encountered as far as the cochlear nerve and brain stem cochlear nuclei are concerned.

MATERIAL AND METHODS

22 guinea pigs have been histologically studied. 14 of them have been surgically deafened three days after birth by bilateral destruction of the organ of Corti. This destruction has been performed by means of drill opening the basal turn and an injection of neomycine inside the scala vestibuli. The efficacity of this destruction has been verified by means of brain stem evoked auditory response registra-

Table I. *Description of the status of the studied animals*

N=normal; I=implanted; D=deaf; vertical bars indicate animals of the same litter

	Guinea pig name	Status	Age when died (in days)	Stimulation duration (in days)	Cochlear nuclei volumes (in mm^3) Right	Left	Total
1	2	N	2		1.940	2.421	4.361
2	780	I	32	20	4.760	3.367	8.128
3	781	N	32		3.680	4.274	7.954
4	785	D	45		3.438	3.681	7.119
5	786	I	45	15	4.627	4.353	8.980
6	787	N	45		5.461	4.698	10.159
7	819	D	58		3.564	4.609	8.173
8	820	I	58	30	5.621	5.361	10.982
9	949	D	60		2.819	1.912	4.731
10	950	N	60		5.213	6.148	11.361
11	951	I	60	32	5.224	5.044	10.268
12	936	D	75		3.831	4.078	7.909
13	937	N	75		6.551	6.945	13.496
14	938	I	75	50	5.088	4.841	9.929
15	918	I	75	51	5.150	4.728	9.878
16	246	I	78	58	6.135	5.008	11.143
17	811	N	150		3.770	4.860	8.630
18	931	I	150	126	4.991	4.580	9.571
19	932	N	150		5.162	4.905	10.067
20	933	D	150		2.875	2.819	5.694
21	770	D	240		3.260	3.122	6.382
22	647	N	390		4.912	4.823	9.735

tion prior to and immediately after the destruction. Of these 14 new-born deafened guinea pigs, 8 received a 125 microns bare diameter platin 90% iridium teflon coated electrode, unilaterally driven into the scala vestibuli of the right ear, and coupled to a skull connector. After weaning, 3 weeks later, these 8 implanted young guinea pigs were supplied with a chronic electric stimulation driven by a Philips classical hearing aid. The amplification of this prosthesis was selected to obtain a Preier response (head and shoulder deviation) by means of a 60 db stimulation. Thus these implanted guinea pigs benefited with a normal sound environment during the remainder of their life in the regular animal quarter.

After variable delays described in Table I all these deafened implanted (called "implanted") and non-implanted animals (called "deaf") and 8 normal guinea pigs (called "normal") of different ages (see Table I) were anaesthetized and sacrificed. Before death each brain stem was fixed by opening the skull and administering an intrameningeal injection of formaldehyde in order to avoid tissue destruction as a result of the dissection. The cochleas had been separately embedded for another study concerning the intracochlear damages due to chronic implantation; these cochlear data shall not be described here. The brains were dehydrated with ethanol, cleared in toluene, embedded in paraffin, and coded in order that the examiner would not know on which animal he was working. Serial 11 μm sections cut in a horizontal plane were mounted and colored with hemalun-eosine. Sections were studied using cochlear nuclei cell nomenclature described by Osen (1969) in the cat, used by Webster (1979) and Trune (1982) in the mice and Noda et al. (1974) in the guinea pig.

The limits of the cochlear nuclei have been, slide by slide, traced on a graph paper at ×90 using a Nachet projector. In order to measure the volume of nuclei, areas have been calculated by a Kontron image analysis system con-

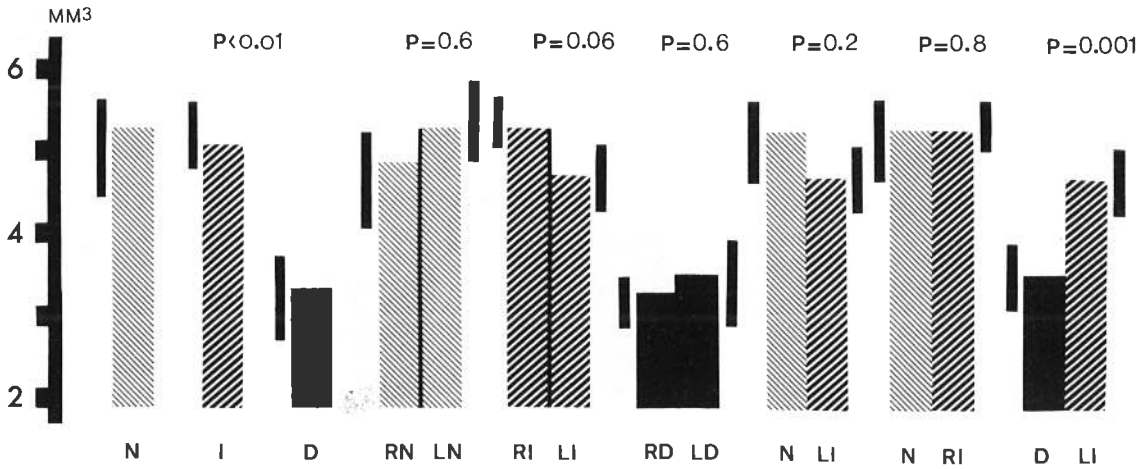

Fig. 1. Mean value of cochlear nuclei volumes in mm^3 ($p<0.01$). Vertical bar=stand. dev. RN=right side of normal group; LN=left side of normal group; N=both sides of normal group. Same code for I=implanted and D= deaf.

nected to a microcomputer. In some cases dorsal cochlear nucleus (DCN) and ventral cochlear nucleus (VCN) have been separately measured, but in most cases, because of the difficulty in precisely determining the limits between these two formations, measurements have only been performed on the totality of the cochlear nucleus (CN); therefore only these global measurements of CN have been studied.

Using the same image analysis system three auditory cell groups have been examined in nine cases concerning 3 brothers of 3 different litters (see Table I): octopus cells (OCT), lateral superior olivary nucleus (LSO) and medial nucleus of the trapezoidal body (MNTB). These particular groups have been selected for their easy identification. For each group the limits of 10 cells of several different sections have been traced at ×950 and measured. Moreover for each of these 9 animals the whole cell population of the VCN of one section, selected in the largest part of the nucleus, has been traced at ×950, and areas and perimeters measured to obtain some idea of the cell forms and of the number and volume of the cell population regarding the nucleus dimensions. Regarding the smallest size of auditory cells described by Osen, Webster and Trune, only areas up to 50 $microns^2$ have been counted. All these measurements and their data will be detailed in the Thesis of one of us (Buche, 1983).

RESULTS

A. If we consider separately each of the 3 groups (normal, implanted and deaf) and do not include the animal n' 2 which is only 2 days old, the volume of each CN does not depend on the age of the guinea pig. For this reason this animal n' 2 is not included in the following results.

B. *Cochlear nuclei volume.* Results are summarized in Fig. 1 A. There are significant differences in the sum of the CN volumes of both sides between normal implanted and deaf ($p<0.01$), whatever the age of the animal. If we consider normal or deaf subjects there is no difference between the mean volume of right and left side ($p>0.05$). Within the implanted group there is a difference between the mean volume of left and right side which is almost significant ($p=0.06$). Using the same measurement significant differences appear between the left side of the implanted group and the deaf group ($p=0.01$), but no significant difference between left or right side of im-

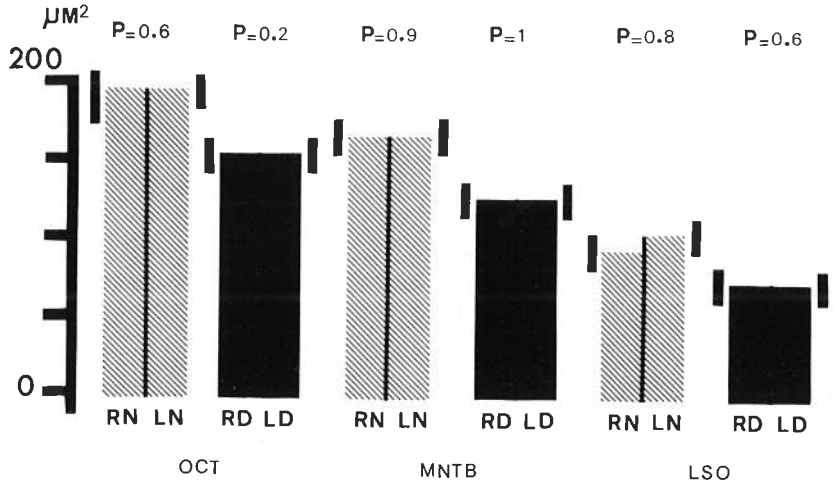

Fig. 2. Mean value in microns^2 of group cell areas of normal and deaf animals. Same legend as in text and Fig. 1.

planted group and normal group ($p=0.2$ and $p=0.8$).

C. *Auditory cell areas.* If each type of cell is considered, there is no difference, in normal or in deaf animals, between left and right mean areas (Fig. 2). If we consider the implanted animals, results depend on the type of the cell.

1. OCT: in the implanted group there is a significant difference between the left and right side ($p<0.01$); that means that in this group the OCT cell area of the side which has been supplied with electric stimulation is larger than the non-stimulated side. The OCT mean area of this non-stimulated side is not significantly different from the OCT deaf group; on the other hand the OCT mean area of the right electrically stimulated side is not different from the OCT normal group (see also Fig. 3).

2. MNTB: in the implanted group there is no difference between left and right side; this implanted group is significantly different from the deaf group, and different from the normal group (Fig. 4).

3. LSO: the results are quantitatively the same (Fig. 5).

D. *Whole cell population areas.* The frequency distribution of CN cell areas of one section of each 3 animals of the 3 litters, and the ratio whole cell population area/cochlear nucleus section area of these nine sections are summarized in Fig. 6 and Table II. Regarding the ratio area/(perimeter)^2, no significant differences have been found between the different groups of animals.

DISCUSSION

Our data suggest that the effects of the early bilateral destruction of the ear consist of: (A) a diminution of the CN volume; (B) a diminution of the size and number of auditory cells; (C) a diminution of the ratio cell area/CN area; this particular result probably signifies a diminution of the dendritic field and intercell con-

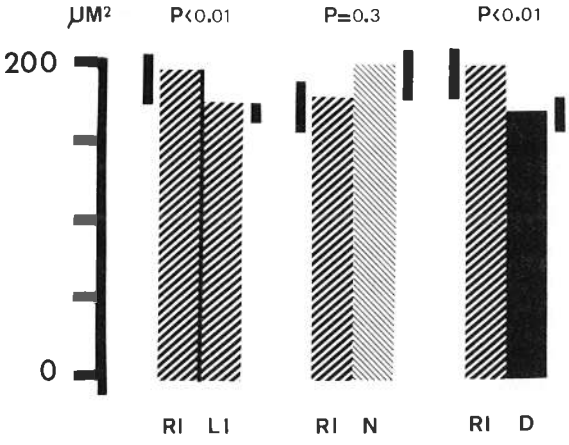

Fig. 3. Mean value in microns^2 of OCT group cell areas. Same legend as Fig. 2.

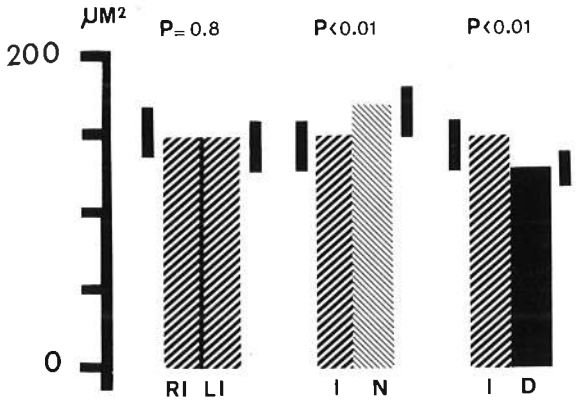

Fig. 4. Mean value in microns² of MNTB group cell areas. Same legend as Fig. 2.

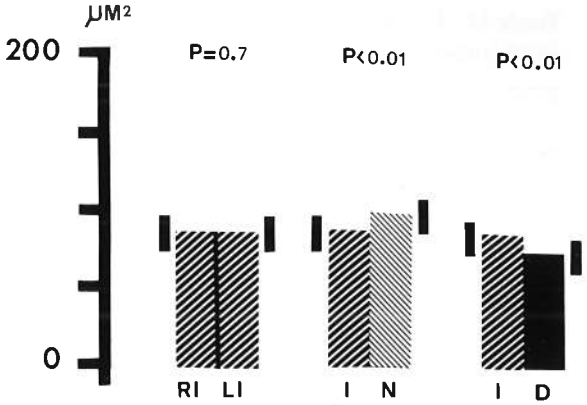

Fig. 5. Mean value in microns² of LSO group cell areas. Same legend as Fig. 2.

nections, that our histological colorations did not allow us to demonstrate. All these results are consistent with the studies of Webster (1979) and Trune (1982) who demonstrated in mice that the neonatal conductive bilateral hearing loss produced an atrophy of auditory brain stem nuclei.

But the most important result of our study is the fact that the electrical stimulation is able to at least partially prevent the pontine auditory formations from this atrophy. That this is so indicates that in cases of congenital deafness it would be worthwhile performing a multichannel cochlear implantation as early as possible.

Some particular points must be discussed:

A) If we except animal n' 2 which was sacrificed on day 2, we did not find any correlation between the age of the animal, the duration of the stimulation and the importance of the atrophy protection induced by the electric stimulation. Two reasons may explain that: 1) Webster et al. (1979) described in the development of the CN of mice a critical period, before 45 days of age, during which acoustic stimulation has a more pronounced effect on neural maturation than the same stimulation given between 45 and 90 days; our electrical stimulation always began before day 21, a long time before this critical period. 2) Moreover Dobbing et al. (1970) showed that the brain weight and the relative brain weight of the guinea pig do not consistently vary after 20 days of age. It would be interesting to observe what kind of results would be obtained if the electrical stimulation was provided at a later stage than we did.

B) We must also discuss the fact that in the implanted group the development of the implanted side is almost normal, whilst the atrophy of the non-stimulated side is hardly prevented. Besides, this difference is not found in LSO and MNTB cell groups. These facts are probably due to the bilateral connections of

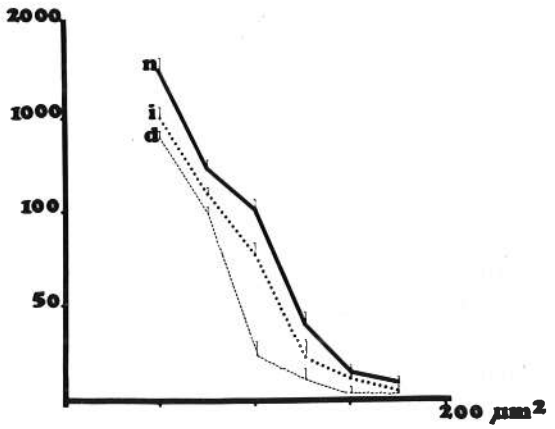

Fig. 6. Diagram of cell numbers (ordinate) as a function of cell areas (abscissa). Mean value of the nine animals of three litters (see Table II). Because of non-linear ordinates only positive part of unbiased standard deviation is designed in vertical bar. N=normal; I=implanted; D=deaf.

Table II. *Results of the whole cell population measurements (areas in microns^2) of one slide of each guinea pig (see explanations in text and Fig. 6)*

	Normal			Implanted			Deaf		
Animal ref. ...	787	937	932	786	938	931	785	936	933
Cell numbers	2 128	2 111	2 002	1 287	1 465	1 263	848	1 239	901
Cell areas	113 276	126 803	105 503	73 814	75 312	64 240	46 907	51 802	44 820
C.N. area	2.6E+9	2.8E+9	2.5E+9	2.5E+9	2.6E+9	2.4E+9	2.1E+9	2.1E+9	2E+9
Cells/C.N. area	4.3E−5	4.5E−5	4.2E−5	2.8E−5	2.8E−5	2.4E−5	2.2E−5	2.4E−5	2.2E−5

the auditory system, which are important for LSO and MNTB if we consider their particular location on the auditory pathway. That is in accordance with the results of Trune who showed that after unilateral ear destruction the controlateral CN development is almost normal. One may ask if a bilateral implantation would be able to suppress this difference. Anyway, even if actually implanting both ears of human patients would appear unreasonable, this fact seems to us a supplementary argument for selecting for implantation the right ear in a right-handed patient, especially when no particular reason drives us to another choice.

C) If we consider on one hand the length of life of a guinea pig, the age at which this animal is able to reproduce itself, the date of this critical period of 45 days in maturation of auditory nuclei and the date on which the relative brain weight does not yet vary, and on the other hand the same dates concerning the life of the human and the maturation of his brain and auditory formations, one may think that the critical period before which the acoustic stimulation is indispensable for auditory nuclei development is approximately 4 to 5 years.

That signifies that congenitally and totally deaf children must probably be implanted before this date. Our purpose is not to discuss here the problems of child implantation, but these results we are reporting will be interesting to consider when this discussion is opened.

RÉSUMÉ

14 cobayes nouveau-nés ont été assourdis, trois jours après leur naissance, par destruction de l'organe de Corti, et 8 d'entre eux ont requ une stimulation auditive électrique chronique grâce à une électrode implantée dans la cochlée. L'étude histologique et la reconstruction anatomique des noyaux cochléaires de ces animaux ont permis de montrer que cette stimulation chronique empêchait au moins partiellement l'atrophie de ces formations centrales secondaire à la destruction cochléaire. Ceci est vrai aussi bien du coté implanté que du coté opposé à l'implantation.

ZUSAMMENFASSUNG

14 neugeborene Meerschweinchen wurden durch die Zerstörung des Organs von Corti drei Tage nach der Geburt taub gemacht. Acht unter ihnen bekamen durch eine in der Cochlea implantierte Elektrode eine chronische elektrische Hörreizung. Das histologische Studieren und die anatomische Wiederherstellung der Cochleariskerne jener Tier zeigten, dass diese chronische Reizung die Atrophie der Zentralbildungen hinderte, die von der Cochlearisziserstörung hervorgerufen wird, auch sowohl für die eingefügte Seite als für die Einfügung entgegengesetzten Seite.

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DISCUSSION

Ruben – Johnstone – Tonndorf – Pujol – Chouard