Exp. Brain Res. 38, 103–108 (1980)

Experimental Brain Research

# Development of Binaural Input, Response Patterns, and Discharge Rate in Single Units of the Cat Inferior Colliculus

D.R. Moore and D.R.F. Irvine

Neuropsychology Laboratory, Department of Psychology, Monash University, Clayton, Victoria 3168, Australia

**Summary.** The binaural input to single neurones in the inferior colliculus of barbiturate- and ketamine-anaesthetised kittens was tested using pure tones. Stimuli were presented to each ear independently via sealed sound-delivery systems. Cells were classified according to the predominant type of input (excitatory or inhibitory) from each ear. There was no significant difference between age groups in the proportions of cells showing each type of binaural input. For all ages, cells excited by monaural stimulation of either ear (EE cells) tended to be of low best frequency (BF) and cells excited by monaural stimulation of one ear, but inhibited by simultaneous stimulation of the other ear (EI cells), had higher BFs. Units for which quantitative spike count data were obtained were also categorised according to their response pattern. Cells categorised as "onset", "pauser" and "burst-type" were found in approximately equal proportions in animals of all age groups. "Primary-like" units were not found in animals less than 20 days old. Unit discharge rate was significantly higher for adults than for any of the three kitten groups. These data suggest that (1) binaural connections are not subject to postnatal developmental alteration and (2) the development of excitatory responses after 20 days consists of an increase in the number of discharges rather than a change in the pattern of these discharges.

**Key words:** Cat – Auditory – Binaural – Development

The development of neuronal response properties in the central auditory pathway of the cat has received considerable attention in recent years (Aitkin and Moore, 1975; Aitkin and Reynolds, 1975; Brugge et al., 1978; Moore and Irvine, 1979; Pujol, 1969; Pujol, 1972). With one exeption (Aitkin and Reynolds, 1975), these studies have been restricted to monaural stimulation. Since the majority of cells in the central auditory pathway receive binaural input (Aitkin and Dunlop, 1968; Aitkin et al., 1975; Goldberg and Brown, 1968; Hall and Goldstein, 1968) the characteristics of binaural interaction during development also require consideration.

Two major classes of central auditory neurone have been distinguished on the basis of the nature of their input from the two ears (Goldberg and Brown, 1968, 1969). One class receives predominantly excitatory input from each ear. The other group receives excitatory input from one ear and inhibitory input from the other. The inhibitory input can be manifested either as an inhibition of spontaneous activity by monaural stimulation (EI cells) or by a response to binaural stimulation that is weaker than the excitatory monaural response (EO(I) cells; Aitkin et al., 1975). It is probable, though not certain, that the absence of spontaneous activity is the only factor that prevents EO(I) cells being classified as EI; these two groups are therefore commonly combined into a single EI category.

An association between these binaural input patterns and best frequency (BF) has been established at various levels of the adult cat central auditory pathway. EE cells tend to have low BF and EI cells higher BF (Aitkin and Webster, 1972; Boudreau and Tsuchitani, 1968; Brugge et al., 1970; Guinan et al., 1972; Roth et al., 1978). It has been suggested (Goldberg and Brown, 1968, 1969) that these two classes of neurone are associated with the coding of interaural intensity difference (EI cells) and average binaural intensity (EE cells). The primary aim of this study was to examine the development of binaural input and its relationship with BF in

---

*Offprint requests to:* D.R. Moore, Ph.D. (address see above)

0014-4819/80/0038/0103/$ 1.20

neurones in the kitten inferior colliculus (IC). These results provide a necessary foundation for the investigation of kitten IC unit responses to interaural intensity differences to be reported elsewhere.

The quantitative spike count data collected in the present study also provide a basis for an examination of the development of the rate and pattern of neuronal discharges in the IC. Pujol (1969) has reported that discharge patterns of IC neurones undergo a period of post-natal maturation. In the present study, an examination of the development of discharge rate and pattern in IC units of kittens aged 11–40 days is presented and these results are discussed with reference to the possible mechanisms underlying development of excitatory input to IC neurones.

## Methods

### *Subjects and General Procedure*

Forty kittens in three age ranges from 11–40 days and seven adult cats were used in this study. Data concerning development of peripheral responses, and threshold and tuning of IC units in these animals have been presented elsewhere (Moore and Irvine, 1979). Kittens were anaesthetised with ketamine hydrochloride (Ketalar, 35 mg/kg, i.m.) and sodium pentobarbitone (Nembutal, 10–20 mg/kg, i.p.). Adult cats were anaesthetised with Nembutal (i.v. to effect). Supplementary anaesthetic (Nembutal) was administered whenever the animal showed a withdrawal reflex to a pinch of the paw. Rectal temperature was monitored throughout and maintained at 37° C (kittens) or 37.5° C (adults). Surgical methods and techniques of stimulus presentation, calibration, and recording have been reported in detail previously (Irvine and Huebner, 1979; Moore and Irvine, 1979). Tungsten-in-glass microelectrodes 2–3 MΩ at 1 kHz) were used to isolate single units in the central nucleus of the IC (ICC).

### *Binaural Classification*

Following determination of BF, neurones were classified with respect to laterality of input on the basis of their responses to tone bursts (250 ms duration, 10 ms rise/fall time) at BF presented independently to each ear via sealed, sound-delivery systems. Classification was based on computer-generated response histograms (73% of units) or on audiovisual monitoring of the cells' response (27% of units) to BF tones 20 dB above the contralateral ear threshold.

Cells were classified as EE or EI according to the criteria elaborated above, the latter category including both EI and EO(I) cells. Cells exhibiting excitatory response to stimulation of one ear but no modification of either spontaneous activity or the excitatory response by stimulation of the other ear were classified as monaural. Cells classified as EE were further categorised with respect to their binaural interaction pattern. The response to simultaneous, equal-intensity stimulation of the two ears was compared to the sum of the responses to monaural stimulation of each ear, each measure being corrected for the spontaneous discharge level of the cell. A binaural response greater than the sum of the monaural responses was termed facilitation; a response less than the sum was termed occlusion (Hind et al., 1963).

Units for which quantitative spike-count data were collected were also categorised according to their response pattern to a 20 db suprathreshold contralateral stimulus. Four categories of response pattern were used for this classification and a description of each type of pattern is presented in the 'Results'.

### *Location of Units*

Electrode penetrations were made in a dorso-ventral direction through the IC. At the conclusion of the single penetration in each animal an electrolytic lesion (10 μA for 10 s) was made, the animal was decapitated and its head placed in formol-saline. Following several months fixation, the brains of 11 of the animals were removed and frozen 50 μ serial sections of the IC were cut in the sagittal plane and stained with thionine. Data from areas other than ICC were discarded. For the remaining 36 animals, judgment of unit location was based on physiological criteria established by Aitkin and his colleagues (Aitkin and Moore, 1975; Aitkin et al., 1975) and confirmed in the first series of animals. These criteria were (a) that the BF of the unit fitted into the dorso-ventral tonotopic sequence through ICC (b) that the unit responded consistently to a suprathreshold excitatory stimulus (c) that the response was restricted to a limited portion of the frequency spectrum (in the case of adult cats).

## Results

### *Binaural Interaction*

A total of 187 cells, predominantly from rostrodorsal ICC, were classified with respect to the nature of input from the two ears. Only a small proportion (approximately 10%) of neurones displayed spontaneous activity and such cells were found in cats of each age group. No acoustically unresponsive cells were isolated. The numbers of cells of each type in the various age groups are presented in Table 1. EI cells were, with only three exceptions, excited by the contralateral and inhibited by the ipsilateral ear. Cells classed as "other" were not clearly distinguishable as EE, EI, or Monaural. Three of these cells were not excited by monaural stimulation of either ear, but responded to simultaneous stimulation of both ears. All remaining cells classified as "other"

**Table 1.** Numbers of each cell type in the four age groups

| | Age Group (Days) | | | | |
|---|---|---|---|---|---|
| | 11–20 | 21–30 | 31–40 | Adults | Total |
| *Cell Type* | | | | | |
| EE | 10 | 17 | 15 | 17 | 59 |
| EI | 18 | 26 | 20 | 29 | 93 |
| Monaural | 5 | 6 | 7 | 4 | 22 |
| Other | 4 | 7 | 2 | 0 | 13 |
| Total | 37 | 56 | 44 | 50 | 187 |

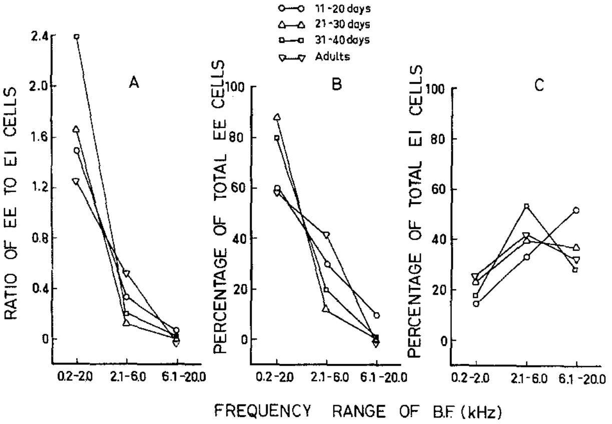

**Fig. 1A–C.** BF ranges for cells in each age group. **A** Ratio of EE to EI cells. **B** Percentage of EE cells. **C** Percentage of EI cells

were excited by monaural stimulation of the contralateral ear and showed no response to ipsilateral stimulation. The response to binaural stimulation, however, was larger than that to stimulation of the contralateral ear alone. It is apparent from Table 1 that there is no marked variation in proportions of cells showing different binaural input between age groups. A chi-square test ($\chi^2$; Siegel, 1956) confirmed the stochastic independence of these two factors ($\chi^2 = 9.90$, df = 9, $0.5 > p > 0.3$).

The relationship between binaural input pattern and BF is shown in Fig. 1A. Among units with low BFs (less than 2 kHz) EE cells outnumber EI cells in all age groups, whereas almost all cells with high BFs are EI. For high BF units the relationship between binaural input and BF is almost identical for all age groups. The ratio of EE to EI units having low BF varies somewhat between age groups, but there does not appear to be any systematic developmental trend in this variation. Examples of monaural cells having BFs in each of the ranges shown in Fig. 1 were found in all age groups.

The relationship illustrated in Fig. 1A could result from a variety of distributions of EE and EI cells with BF. The actual distributions are presented in Figs. 1B and C. It is apparent that the great majority of EE cells have low BF, with almost none exceeding 6 kHz. EI cells are distributed more homogeneously, but with larger proportions having BFs in the middle-high frequency range. Again, there are no differences between age groups in these relationships.

The numbers of EE cells having the two forms of binaural interaction are shown in Fig. 2. In adult cats, occlusion and facilitation are exhibited by approximately equal proportions of EE cells. In the three kitten groups, however, occlusion is by far the more common form of interaction. A chi-square analysis revealed that this difference in binaural interaction patterns was significant ($\chi^2 = 7.04$, df = 2, $0.05 > p > 0.02$).

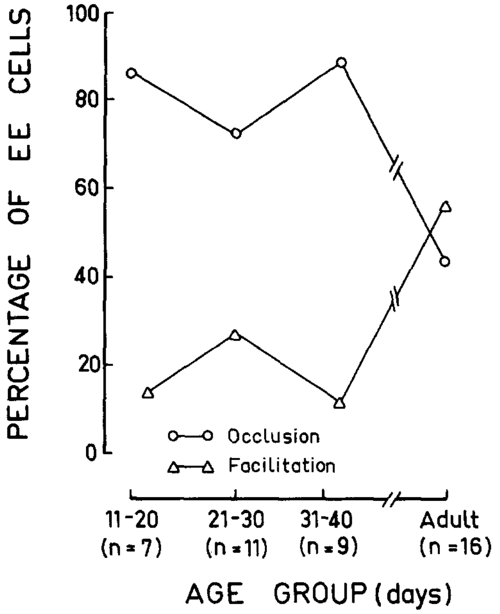

**Fig. 2.** Binaural interaction in EE cells. Percentages of EE cells in each age group characterised by facilitative or occlusive binaural interaction. Terms defined in text

### *Response Patterns*

One Hundred thirty-six cells were classified with respect to their discharge pattern in response to a 20 dB suprathreshold contralateral stimuli. Four categories were employed for this classification, and response histograms representative of these categories are shown in Fig. 3. Three of the categories (onset, pauser, primary-like) have been used by Kiang et al. (1965) and Pfeiffer (1966) to classify units in the adult cat cochlear nucleus. Onset units (e.g., Units 21-6, 28-3; Figs. 3A, E) displayed only a phasic burst of activity following stimulus onset. Pauser units (e.g., Units 21-5, 68-1; Figs. 3B, F) had an initial burst of activity followed by a short silent period, and a sustained level of activity that was usually lower than the initial burst. Primary-like unit response patterns (e.g., Units 22-8, 89-10; Figs. 3C, G) were similar to those found in auditory nerve fibres (Kiang, 1965; Kiang et al., 1965). This pattern consisted of a brief transient increase in discharge rate followed by a decline to a steady, lower level of activity. The fourth discharge pattern was similar to that previously described by Pujol

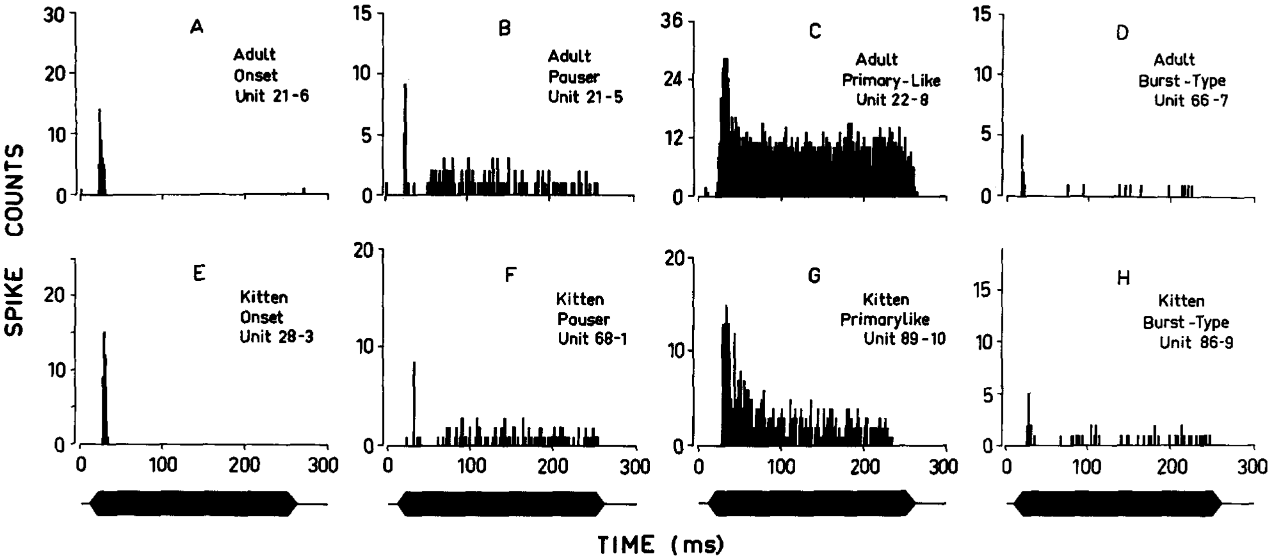

**Fig. 3A–H.** Examples of response histograms. **A–D** Units from adult cats. **E**, **F**, **H** Units from the youngest (i.e., 11–20 days) group of kittens. **G** A primary-like unit from a 24-day-old kitten. The tone-burst envelope is shown beneath the kitten histograms. Ordinate: Number of spikes in response to 20 stimulus presentations. Abscissa: Elapsed time following stimulus trigger pulse. Each histogram bar represents the number of spikes per 1.5 ms sampling bin

**Table 2.** Numbers of cells having each discharge pattern in the four age groups

| Discharge Pattern | Age Group (Days) 11–20 | 21–30 | 31–40 | Adult | Total |
|---|---|---|---|---|---|
| Onset | 6 | 6 | 7 | 6 | 25 |
| Pauser | 13 | 19 | 14 | 23 | 69 |
| Primary-like | 0 | 11 | 3 | 11 | 25 |
| Burst-type | 5 | 5 | 5 | 2 | 17 |
| Total | 24 | 41 | 29 | 42 | 136 |

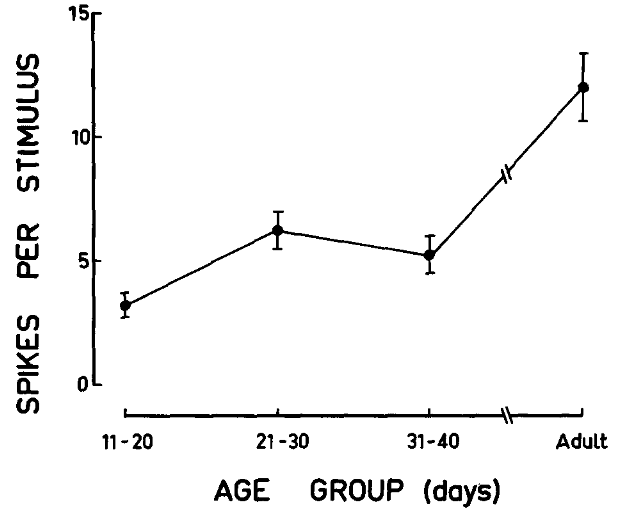

**Fig. 4.** Discharge rate. Mean number of spikes elicited by a 20 dB suprathreshold contralateral stimulus in units of each age group. The standard error of each mean is indicated by the vertical bars

(1969) for IC units in the young kitten. This category, which is here designated "burst-type", was used because of Pujol's (1969) claim that some response histograms in 4-day-old kittens consisted of an onset response followed by bursts of discharges with intercalated silent periods. Although a number of cells were classified as burst-type, the discreteness of this catogory was not at all clear. Most of the cells so classified had low discharge rates (e.g., Units 66-7, 86-9; Figs. 3D, H) and might well have been weakly driven pausers or primary-like cells. No cells in this category, even in the youngest age group where the proportion of units displaying this pattern was highest, had the regularly timed phasic bursts of activity observed by Pujol (1969) in 4-day-old kitens.

It is apparent from Table 2 that cells categorised as "onset", "pauser" and "burst-type" were found in animals of all age groups. Moreover, the proportion of these three categories of discharge pattern did not vary markedly between age groups. "Primary-like" units were not found in the youngest group of animals, but had reached the adult proportion in the 21–30 day group. The fact that units responding throughout the stimulus period were found in the latter group of kittens is contrary to Pujol's (1969) suggestion that "continuous" responses only appear near the end of the first post-natal month.

**Table 3.** Q-values obtained in Newman-Keuls comparisons of discharge rate for each age group with those of the adult group

| Age Group (days) | 11–20 | 21–30 | 31–40 |
|---|---|---|---|
| | 174.0 | 137.7 | 112.7 |
| Criterion Qs ($p = 0.01$) | 101.7 | 94.9 | 83.6 |

### *Discharge Rate*

It was found that the number of spikes elicited by a 20 dB-suprathreshold contralateral stimulus was considerably higher for units from adult cats than from any of the three kitten groups (Fig. 4). An analysis of variance (Winer, 1971) performed on these data showed that the difference between groups was highly significant ($F_{3,130} = 11.89$, $p < 0.001$). Newman-Keuls comparisons (Winer, 1971) revealed that the adult discharge rates were significantly higher than those for any of the kitten groups (Table 3), whereas none of the differences between kitten groups were significant.

## Discussion

The proportion of EE to EI cells reported here is similar to that previously found in the adult cat (Aitkin et al., 1975) and kitten (Aitkin and Reynolds, 1975) ICC. The relationship between binaural input and BF in the adult IC is in general accord with recent results of Roth et al. (1978), and presumably reflects the association of these properties in nuclei of the superior olivary complex (Boudreau and Tsuchitani, 1968; Goldberg and Brown, 1968; Guinan et al., 1972; Tsuchitani, 1977). As for the adult cats, kitten EE cells tended to have low BFs whereas EI cells were more homogeneously distributed with respect to BF. The stability of this relationship with age provides support for Aitkin and Reynolds' (1975) suggestion that binaural connections are not subject to postnatal developmental alteration. The possibility remains that some finer aspects of binaural interaction might be subject to developmental change and postnatal plasticity.

Binaural interaction in the kitten auditory pathway has not been examined previously. In this paper it has been shown that EE cells in the three age groups examined here display an almost exclusively "occlusion" pattern of interaction. In adults, on the other hand, roughly equal numbers of "occlusion" and "facilitation" interactions were obtained. Although it is possible that these data reflect a real developmental change in binaural interaction, an alternative explanation is suggested by the striking resemblance between the curves plotting development of "facilitation" (Fig. 2) and strength of contralateral, excitatory responses (Fig. 4). It is possible that some cells in young kittens have the binaural input characteristics of facilitatory cells but exhibit occlusion because of the cells' inability to fire at other than low rates. These cells would be expected to undergo a transition to facilitation as they became capable of firing more strongly. If the inability of neurones in young kittens to fire at other than low rates reflects processes intrinsic to the neurone, this argument would support the notion of a stability of connections with age. However, it is also possible that an increase in the number of excitatory connections occurs during the first few postnatal weeks. These two alternatives might be resolved by intracellular recordings, or by electron microscopic evaluation of synaptic terminals.

The data presented here on response patterns and discharge rate represent the first attempt to compare quantitatively the development of these response parameters. It has been shown that three types of discharge pattern are found in approximately the same proportions in young kittens and adult cats. "Primary-like" patterns, on the other hand, were not found in the youngest group of kittens tested, but the proportion of these cells after the third week was the same as for the adults. It has also been shown that the neuronal firing rate to a given suprathreshold stimulus increases significantly between the kitten groups and the adults. Taken together, these data demonstrate that the development of contralaterally evoked responses after 21 days consists of an increase in the number of discharges rather than a change in the pattern of these discharges.

*Acknowledgements.* We wish to thank Dr. L.M. Aitkin, Mr. D.P. Phillips, and Mr. R.S. Gumby for helpful comments; Mr. T. Crowle, Mrs. C. Kenyon, Mr. V. Kohout, Mrs. J. Sack, and Miss P. Ward for technical assistance.

## References

Aitkin, L.M., Dunlop, C.W.: Interplay of excitation and inhibition in the cat medial geniculate body. J. Neurophysiol. **31**, 44–61 (1968)

Aitkin, L.M., Moore, D.R.: Inferior colliculus. II. Development of tuning characteristics and tonotopic organization in central nucleus of the neonatal cat. J. Neurophysiol. **38**, 1208–1216 (1975)

Aitkin, L.M., Reynolds, A.: Development of binaural responses in the kitten inferior colliculus. Neurosci. Lett. **1**, 315–319 (1975)

Aitkin, L.M., Webster, W.E.: Medial geniculate body of the cat: Organization and responses to tonal stimuli of neurons in the ventral division. J. Neurophysiol. **35**, 365–380 (1972)

Aitkin, L.M., Webster, W.R., Veale, J.L., Crosby, D.C.: Inferior colliculus. I. Comparison of response properties of neurons in central, pericentral, and external nuclei of adult cat. J. Neurophysiol. **38**, 1196–1207 (1975)

Boudreau, J.C., Tsuchitani, C.: Binaural interaction in the cat superior olive S-segment. J. Neurophysiol. **31**, 442–454 (1968)

Brugge, J.F., Anderson, D.J., Aitkin, L.M.: Responses of neurons in the dorsal nucleus of the lateral lemniscus to binaural tonal stimulation. J. Neurophysiol. **33**, 441–458 (1970)

Brugge, J.F., Javel, E., Kitzes, L.M.: Signs of functional maturation of peripheral auditory system in discharge patterns of neurons in anteroventral cochlear nucleus of kitten. J. Neurophysiol. **41**, 1557–1579 (1978)

Goldberg, J.M., Brown, P.B.: Functional organization of the dog superior olivary complex: An anatomical and electrophysiological study. J. Neurophysiol. **31**, 639–656 (1968)

Goldberg, J.M., Brown, P.B.: Response of binaural neurons of dog superior olivary complex to dichotic tonal stimuli: Some physiological mechanisms of sound localization. J. Neurophysiol. **32**, 613–636 (1969)

Guinan, J.J., Jr., Norris, B.E., Guinan, S.S.: Single auditory units in the superior olivary complex. II. Locations of unit categories and tonotopic organization. Int. J. Neurosci. **4**, 147–166 (1972)

Hall, J.L., Goldstein, M.H.: Representation of binaural stimuli by single units in primary auditory cortex of unanesthetized cats. J. Acoust. Soc. Am. **43**, 456–461 (1968)

Hind, J.E., Goldberg, J.M., Greenwood, D.D., Rose, J.E.: Some discharge characteristics of single neurons in the inferior colliculus of the cat. II. Timing of the discharges and observations on binaural stimulation. J. Neurophysiol. **26**, 321–341 (1963)

Irvine, D.R.F., Huebner, H.H.: Acoustic response characteristics of neurons in nonspecific areas of cat cerebral cortex. J. Neurophysiol. **42**, 107–122 (1979)

Kiang, N.Y.-S.: Stimulus coding in the auditory nerve and cochlear nucleus. Acta Oto-Laryngol. (Stockh.) **59**, 186–200 (1965)

Kiang, N.Y.-S., Watanabe, T., Thomas, E.C., Clarke, L.F.: Discharge patterns of single fibers in the cat's auditory nerve. Research Monograph No. 35 Cambridge: M.I.T. Press 1965

Moore, D.R., Irvine, D.R.F.: The development of some peripheral and central auditory responses in the neonatal cat. Brain Res. **163**, 49–59 (1979)

Pfeiffer, R.R.: Classification of response patterns of spike discharges for units in the cochlear nucleus: Tone-burst stimulation. Exp. Brain Res. **1**, 220–235 (1966)

Pujol, R.: Dévelopment des réponses à la stimulation sonore dans le colliculus inférieur chez le chat. J. Physiol. (Paris) **61**, 411–421 (1969)

Pujol, R.: Development of tone-burst responses along the auditory pathway in the cat. Acta Oto-Laryngol. (Stockh.) **74**, 383–391 (1972)

Roth, G.L., Aitkin, L.M., Andersen, R.A., Merzenich, M.M.: Some features of the spatial organization of the central nucleus of the inferior colliculus of the cat. J. Comp. Neurol. **182**, 661–680 (1978)

Siegel, S.: Nonparametric statistics for the behavioral sciences. Tokyo: McGraw-Hill Kogakusha 1956

Tsuchitani, C.: Functional organization of lateral cell groups of cat superior olivary complex. J. Neurophysiol. **40**, 296–318 (1977)

Winer, B.J.: Statistical principles in experimental design, 2nd. Ed. New York: McGraw-Hill 1971

Received May 8, 1979