UC Irvine

UC Irvine Previously Published Works

Title

Temporal relationship between single unit activity in superior olivary complex and scalp-derived auditory brainstem response in guinea pig.

Permalink

<https://escholarship.org/uc/item/8090n3fj>

Journal

Brain research, 419(1-2)

ISSN

0006-8993

Authors

Kano, Y
Starr, A

Publication Date

1987-09-01

DOI

10.1016/0006-8993(87)90592-0

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at <https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

Temporal relationship between single unit activity in superior olivary complex and scalp-derived auditory brainstem response in guinea pig

Yuji Kano* and Arnold Starr

Department of Neurology, University of California at Irvine, Irvine, CA 92717 (U.S.A.)

(Accepted 3 February 1987)

Key words: Single unit activity; Superior olivary complex; Auditory brainstem response (ABR); Timing of unit discharge; Timing of the ABR component; Latency/intensity function

Single unit activities in the region of the superior olivary complex were recorded from 8 guinea pigs concurrently with the recording of auditory brainstem potentials from the scalp. At any one anatomical site, be it a fiber tract (e.g. trapezoid body) or a nucleus (e.g. medial nucleus of the trapezoid body), the modal latency of the onset discharge of the units encountered corresponded in time with the latencies of several different waves (waves P2–P5) of the auditory brainstem response (ABR). Moreover, at the time of occurrence of just one of the ABR waves, single units in several diverse anatomical sites in and around the superior olive were found with modal latencies of onset discharge at that same time period. The slopes of the latency/intensity functions for both the peaks of the ABR and the modal latency of the onset discharge for most of the single units studied in the superior olive and its adjacent fiber tracts were remarkably similar. These data support the hypothesis of multiple rather than single generator site(s) for components of the ABR, at least, for waves P2–P5 in the guinea pig. These data do not distinguish whether the ABR are generated in part by travelling nerve action potentials or graded synaptic events.

INTRODUCTION

A sequence of short-latency potentials to auditory stimuli, known as auditory brainstem response (ABR) can be recorded from the scalp of human and animals, using signal averaging^{11,20}. The potentials are thought to be the far field reflections of electrical events arising from the brainstem auditory pathway.

There have been several studies attempting to define the generator sites of the ABR components using pathological correlations in patients^{21,23}, and both lesion^{2,4,6,7,9,26,27} and intracranial recording^{1,9,11,15} methods in animals. The generators of the ABR are presumed to be as follows: wave I, VIII nerve within the cochlea; wave II, cochlear nucleus in animals and/or proximal VIII nerve in humans; wave III, contralateral superior olive in animals; ipsi-

lateral cochlear nucleus in humans; waves IV–V, the rostral pons bilaterally both in animals and humans^{3,16,19,27}. The principle limitation of the intracranial recording technique is the limitation in matching the 'far field' ABR components to the electrical activity occurring intracranially. The results, however, suggest that there are multiple brainstem sites that are active at the time of each of the ABR components after wave I¹. The major limitations of the lesion methods is that the lesion may affect the output from the lesioned structure as well as the structure itself, complicating the establishment of a causal relationship between the lesioned structure and the loss of a particular component.

In this study, we recorded single unit responses in the region of the superior olivary complex while monitoring the ABR on the scalp to define the rela-

* Present address: Department of Oto-Rhino-Laryngology, Teikyo University School of Medicine, Kaga 2-11-1, Itabashi-ku, Tokyo, Japan.

Correspondence: A. Starr, Department of Neurology, University of California at Irvine, Irvine, CA 92717, U.S.A.

tionship between the timing of unit discharges in and around a particular brainstem auditory structure, the superior olive, and the timing of the ABR components

MATERIALS AND METHODS

Preparation

Eight guinea pigs, 0.6–1.0 kg in weight, were used in these experiments. They were anesthetized with an intramuscular injection of ketamine hydrochloride 100 mg/kg and xylazine 3 mg/kg. In addition, all surgical fields and pressure points were infiltrated locally with 1% procaine. Anesthesia was maintained thereafter by repeated administration of procaine and ketamine. The heart rate was continuously monitored and rectal temperature was maintained at 38–39 °C by a heating pad beneath the guinea pig. The animals were secured in a stereotaxic head holder and hollow ear bars, and mounted prone in a stereotaxic apparatus. A small recording electrode screw was fixed at the midline, 3 mm posterior to the bregma on the skull, and a needle was placed in the midline at the back of the neck to serve as a reference electrode. Spinal fluid was drained by opening the dura mater between the skull and the first cervical vertebra. The animals were changed to a supine position and the head positioned to place the ventral surface of the brainstem approximately horizontal in position. A tracheostomy was performed, and the animal immobilized by gallamine triethiodide and artificially respired with room air. The bone overlying the ventral aspect of the brainstem was exposed using an operating microscope and removed with a dental drill. The dura mater covering the brainstem was incised and removed, and a small hole was made in the pia mater for insertion of a micropipette electrode. Agar was then placed in the bony opening overlying the brainstem and bilateral thoracotomies performed to reduce brain pulsations.

Stimulus generation

Acoustic stimuli (click) were delivered to the ears of the guinea pigs by activating Beyer transducers with a square wave pulse, 2 V peak to peak, 100 μ s duration and 39 ms interstimulus interval. The earphones were coupled to the hollow ear bars located inside the ear canals. The maximum intensity of click

was 94 dB SPL peak equivalent.

Recording techniques

Auditory brainstem responses. The potentials between skull and neck electrodes were amplified 100,000 times and filtered between 30 and 3,000 Hz. The amplified potentials were led to the analog-to-digital converter of the computer and to an FM tape recorder (0–2,500 Hz frequency response). The potentials were sampled at a rate of 40 kHz (25 μ s bin width) over a 12.8 ms analysis time and 500 trials were averaged. The averaged data were then stored in the computer. There were no significant latency or amplitude differences between the averaged ABR potentials recorded during the experiments and those obtained later from the tape.

The ABR was recorded in 4 epochs; the first was at the starting point of the experiment, the second was just prior to opening the dura mater, the third was just after opening the dura mater and exposing the ventral surface of the brainstem, and the fourth was during unit recordings. There were no significant changes in the ABRs between these epochs.

Units. Glass micropipettes filled with 2 M NaCl solution or 3 M KCl solution saturated with Fast green FCF (6–25 M Ω resistance) were used. The electrodes were mounted on a stereotaxic micromanipulator and inserted stereotaxically at an angle of 0–10° mediolaterally in the frontal plane, and lowered through the trapezoid body towards the region of the superior olive in the pons by a hydraulic micromanipulator located outside the sound attenuating room. Single unit activity was amplified 500 times and recorded on tape along with the ABR recorded from the scalp. The tape-recorded unit activity was analyzed by a window discriminator, and the output pulses digitized by the computer to create the post-stimulus onset time histogram (PSTH) and latency distributions of the responses to each click trial.

Recording procedures

The microelectrode was advanced through the brainstem while presenting clicks over a 50-dB range. When a single unit responsive to clicks was isolated, its responses to monaural and binaural click stimuli were recorded as the intensity range was reduced in 10-dB steps from 94 dB SPL. Of the more than 150 units encountered, only 46 were systemati-

cally examined over at least 3 intensity levels. The other units were lost before this protocol could be completed. At least 200 click trials were tested at each intensity and for each mode of stimulation; monaural and binaural. Twenty-eight of the 46 units were held sufficiently long to allow analysis of their responses to the complete range of intensities. After recording from a single unit, dye was ejected electrophoretically through the recording microelectrode ($20 \mu\text{A}$ 10 min)²⁴. Up to 3 marks were made in each experiment and the locations of the other unit recording sites were estimated from the scale of the micromanipulator with reference to the stained sites.

Histological investigation

The animals were sacrificed after recording and perfused with Ringer's solution through a catheter inserted into the arch of the aorta followed by 10% formalin. Frozen transverse serial sections ($50 \mu\text{m}$ thick) were made and the location of the stains defined from Nissl-stained sections. The locations of the units were ascribed to the various divisions of the superior olive and adjacent fiber connections as shown in Fig. 1.

Analysis

The simultaneously recorded brain potentials and unit activities were analyzed by the computer from the tapes. The peak latencies of the ABRs averaged to the click stimuli were measured from the computer display. Excitatory and inhibitory characteristics of the units were determined from the unit firing patterns displayed on an oscilloscope and confirmed by

the PSTH. The timing of occurrence of the first unit discharge in each of the 200 single trials was measured to provide the mean and standard deviation of latency of the onset discharge for each unit. The modal latency of the initial discharge of the unit was determined from the PSTH sampled with a $60\text{-}\mu\text{s}$ bin width over a 30-ms timebase using 200 click stimuli. Examples of the measurements of the onset latency and standard deviation, and the modes of the PSTHs of two units with different variations in their onset discharges are illustrated in Fig. 2. Classifications of the PSTHs, according to the nomenclature of Pfeiffer¹⁸ and Tsuchitani²⁵, were determined from the PSTHs of unit discharges using a 30-ms analysis time and a $150\text{-}\mu\text{s}$ bin width to click stimuli at 94 dB SPL. Examples of the patterns of the PSTHs are shown in Fig. 4.

Fig. 1. An illustrative drawing of the region of the superior olivary complex in guinea pig. TB, trapezoid body; MNTB, medial nucleus of the trapezoid body; VNTB, ventral nucleus of the trapezoid body; LNTB, lateral nucleus of the trapezoid body; MSO, medial superior olivary nucleus; LSO, lateral superior olivary nucleus; VLPO, ventrolateral periolivary nucleus.

Fig. 2. The mean (A) and modal (B) latencies of two units (left, a fiber in the trapezoid body and, right, a cell in the VNTB) with different means and variabilities (small and large) of onset discharge. The mean latency of the unit and its standard deviation at each stimulus intensity was obtained by averaging the latencies of the first spike for 200 successive clicks (A). The modal latencies of the units are depicted in (B). The bin width of the PSTH was $60 \mu\text{s}$. Calibration: left unit 2.0 mV, right unit 0.7 mV.

RESULTS

Auditory brainstem potentials recorded from the guinea pig consist of 5 positive and 4 negative waves in the initial 10-ms after click stimulation. The amplitudes and latencies of these waves remained constant throughout the experimental procedures as long as body temperature was steady. In approximately 2/3 of the animals, wave P4 separated into two smaller subcomponents, particularly at high stimulus intensities (see Fig. 3A). The discreteness of these subcomponents was enhanced by extending the low-pass filter from 100 to 30 Hz (Fig. 3B). The absolute latencies and intercomponent times of the brainstem potentials as a function of signal intensity are included in Table I.

Brainstem single units were classified according to several parameters: (1) Type of unit (predominantly monophasic positive; fibers, or biphasic polarity; cells). (2) Excitation pattern according to the ear stimulated (ipsilateral and/or contralateral excitation with or without inhibition). (3) Discharge patterns (on-type, chopper-type, pause-type). (4) Latency of initial discharge. (5) Anatomical location.

(1) *Type of unit and anatomical location.* A total of 46 units were studied: 15 were fibers, 12 of which

were located in the trapezoid body (TB) and 3 located between the medial nucleus of the trapezoid body (MNTB) and the medial superior olivary nucleus (MSO). There were 31 cells studied, 12 located in the ventral nucleus of the trapezoid body (VNTB), 12 in the MNTB, 5 in the MSO, and 2 in the lateral superior olivary nucleus (LSO) (Table II).

(2) *Excitation types* were classified according to (a) excitation by inputs from only the contralateral ear (O/E type, 24 units), (b) excitation by inputs from only the ipsilateral ear (E/O type, 12 units), and (c) bilateral excitation (E/E type, 4 units). Contralateral excitation was characteristic of cells in both the ventral and medial nuclei of the trapezoid body (20 of the 24 units with this pattern), while ipsilateral excitation characterized trapezoid body fibers (10 of the 12 units with this pattern). There were 6 cells showing inhibition (3 E/I and 3 I/E units), 3 in the MSO, 2 in the LSO, and 1 in the VNTB.

(3) *Discharge patterns* revealed by the PSTHs (Fig. 4) were of two major types (Table II): an on-pattern (21 of the 46 units), characterized by discharges occurring at short latency after stimulation and a chopper-pattern in which the discharges were spaced in a periodic manner (21 units). The on-type was further subdivided as on-narrow or on-wide based on the

Fig. 3. A representative ABR from the guinea pig over a 70-dB intensity range. A: the recordings are derived between a scalp electrode and a neck reference electrode. The ABR shows two subcomponents of P4, (labelled a,b), at the two highest stimulus intensities. The effect of changing the low-pass filter on the subcomponents of P4 is in B and demonstrates their enhancement by extending the low-pass filter from 100 to 30 Hz.

TABLE I

Latency (ms) of auditory brainstem response in guinea pig $\bar{X}$ is sign for mean; S.D. is sign for standard deviation.

Component	Intensity (dB SPL)									
	94		84		74		64		54	
	$\bar{X}$	S.D.	$\bar{X}$	S.D.	$\bar{X}$	S.D.	$\bar{X}$	S.D.	$\bar{X}$	S.D.
A.										
P1	2.01 ± 0.22		2.05 ± 0.25		2.10 ± 0.23		2.21 ± 0.27		2.34 ± 0.32	
N1	2.49 ± 0.24		2.55 ± 0.26		2.63 ± 0.28		2.74 ± 0.34		2.87 ± 0.41	
P2	2.81 ± 0.26		2.88 ± 0.29		2.94 ± 0.29		3.09 ± 0.36		3.25 ± 0.40	
N2	3.06 ± 0.26		3.11 ± 0.26		3.14 ± 0.24		3.20 ± 0.31		3.36 ± 0.39	
P3	3.51 ± 0.27		3.56 ± 0.29		3.64 ± 0.30		3.77 ± 0.36		3.92 ± 0.43	
N3	4.07 ± 0.31		4.12 ± 0.32		4.17 ± 0.39		4.29 ± 0.49		4.43 ± 0.47	
P4a	4.51 ± 0.36		4.57 ± 0.34		4.59 ± 0.40		4.70 ± 0.47		4.77 ± 0.47	
N4a	4.59 ± 0.67		—		—		—		—	
P4b	4.85 ± 0.23		—		—		—		—	
N4b	5.48 ± 0.39		5.55 ± 0.41		5.55 ± 0.47		5.65 ± 0.53		5.74 ± 0.50	
P5	6.42 ± 0.53		6.45 ± 0.56		6.59 ± 0.63		6.76 ± 0.68		6.87 ± 0.68	
B.										
Intensity	Interval									
	P1---N1		P1---P2		P1---N2		P1---P3		P1---N3	
	$\bar{X}$	S.D.	$\bar{X}$	S.D.	$\bar{X}$	S.D.	$\bar{X}$	S.D.	$\bar{X}$	S.D.
94 dB SPL	0.49 ± 0.09		0.81 ± 0.12		1.06 ± 0.12		1.51 ± 0.13		2.06 ± 0.18	
24 dB SPL	0.56 ± 0.28		0.97 ± 0.23		1.06 ± 0.24		1.61 ± 0.18		2.27 ± 0.33	

TABLE II

Location, excitation characteristic and PSTH pattern of single units in and around the superior olivary complex

Units	Location	n	Excitation	n	PSTH pattern				
					On-	On-	Chopper	Chopper-	Pause
						wide		pause	
Cells (31)	Ventral nucleus of trapezoid body (VNTB)	12	Ipsilateral	0	—	—	—	—	—
			Contralateral	10	5	1	1	1	2
			Bilateral	2	0	1	0	0	1
	Medial nucleus of trapezoid body (MNTB)	12	Ipsilateral	2	0	1	1	0	0
			Contralateral	10	5	2	3	0	0
			Bilateral	0	—	—	—	—	—
	Medial superior olivary nucleus (MSO)	5	Ipsilateral	1	0	0	0	0	1
			Contralateral	2	0	0	2	0	0
			Bilateral	2	0	0	1	1	0
	Lateral superior olivary nucleus (LSO)	2	Ipsilateral	2	0	0	2	0	0
			Contralateral	0	—	—	—	—	—
			Bilateral	0	—	—	—	—	—
Fibers (15)	Trapezoid body (TB)	12	Ipsilateral	10	5	0	1	4	0
			Contralateral	2	1	0	1	0	0
			Bilateral	0	—	—	—	—	—
	Fiber tract between MNTB and MSO	3	Ipsilateral	0	—	—	—	—	—
			Contralateral	3	0	0	3	0	0
			Bilateral	0	—	—	—	—	—
n		46		46	16	5	15	6	4

Fig. 4. Examples of the most common types of PSTHs encountered. The firing pattern was defined by the PSTH to 200 click stimuli at 94 dB SPL, with a 30 ms total analysis time and a 150 μ s bin width.

temporal dispersion of the onset discharges in the PSTH. Sixteen of the 21 on-type units had their onset discharges concentrated in a narrow time period while 5 units' onset discharges were dispersed. The chopper-patterns were subdivided according to whether the periodicity of the discharges continued for 3 or more repetitions (15 units) or whether the periodic discharges were curtailed (chopper-pause type, 6 units). The intervals between the modes of the periodic repetitive discharges in the chopper-pattern units ranged from 1.7 to 4.2 ms. A third type of discharge pattern, pause type, showed a relative suppression of activity after the onset discharges (4 units), 2 of which had a short suppression and 2 had a long suppression.

(4) *Latency of the initial discharge* was measured for 200 click trials (Fig. 2) and the mean, standard deviation, and mode calculated. Fig. 5 plots the number of units that were encountered as a function of the standard deviation of latency of the onset discharge with the stimulus intensity set at 94 dB SPL. The majority of the units studied (36 of 46) had a standard deviation of the initial discharge that was less than 1.0 ms. This included 21 of the 31 cells and all 15 fi-

Fig. 5. Illustration of the number of units that were encountered as a function of the standard deviation of the onset discharge latency in 250- μ s increments with the stimulus intensity at 94 dB SPL. The majority of the units studied had a standard deviation of the initial discharge that was less than 1.0 ms.

bers. All of the units with initial discharge latencies that varied by more than 1.0 ms were cells located in the ventral (5 units) or medial (5 units) nuclei of the trapezoid body. The units with largest variation in latency (>2.0 ms) were those with absolute onset latencies of more than 8 ms. There were no significant latency differences in the 4 units responsive to stimuli from each ear (bilateral excitatory) as a function of the ear stimulated.

Correspondence between the latency of ABR components and the latency of single units. The relationship between the latency of the peaks of the auditory brainstem potentials and the modal latency of the onset discharge of brainstem units to click signals at 94 dB SPL are depicted in Fig. 6 and Table III. Note that the latency of the units have all been adjusted to be relative to wave I of the ABR obtained during the sampling of that unit to correct for differences in middle ear transmission characteristics between animals that could affect the intensity of the sound signal reaching the cochlea. The timing of the unitary discharges in any single brainstem structure does not bear a simple relationship to the latency of any single component of the ABR. For instance, among the population of 12 trapezoid body fibers studied, the

Fig. 6. Illustration of the relationship between the latency of the peaks of the ABR and the modal latency of onset discharge of brainstem units to click stimuli at 94 dB SPL. The modal latencies were adjusted to be relative to P1 of the ABR recorded at the same time as that unit. The location of the units in the superior olivary complex is indicated in the legend. Abbreviations as in Fig. 1.

timing of the onset discharges corresponded to the occurrence of waves P2 (4 units), N2 (2 units), P3 (3 units), N3 (2 units) and P4 (1 unit). Similarly, while approximately 1/2 of the cells in the medial nucleus of the trapezoid body (5 units) discharged at the time of P4, the temporal coincidence of activity of the other units in this structure corresponded to waves P3 (3 units), N4 (1 unit) and to even the period after P5 (3 units). Another way of realizing the complexity of relationship between the timing of the components of the auditory brainstem response and the discharge of single brainstem units is to recognize that at the time of one of the components, P3, for instance, units in 4 different brainstem structures were active (trapezoid

body, medial nucleus of the trapezoid body, medial superior olive, and ventral nucleus of the trapezoid body). Only the time period of N4 had a paucity of unit activity with just 1 cell located in the contralateral MNTB active during this period. The laterality of the acoustic input relative to the site of single unit recording affected the relationship between the timing of unit discharges and the occurrence of ABR components. Of the 5 cells active at the time of P3, 4 were excited contralaterally and one bilaterally, whereas the 3 fibers in the trapezoid body active at the time of P3 were excited ipsilaterally. Of the 13 cells active at the time of P4, 11 were excited contralaterally and 2 ipsilaterally (1 each in the MNTB and MSO). Of the 4 cells active at the time of P5, 2 were ipsilaterally excited (LSO), 1 excited contralaterally (MSO) and 1 bilaterally excited (MSO).

There were 3 chopper-pattern units (in the TB) whose first discharges corresponded in latency with P2 of the ABR, 1 unit (in the TB) corresponded in latency with N2 and 3 units (2 in the MNTB, 1 in the MSO) with P3. The discharge intervals of these chopper-pattern units ranged from 1.7 to 4.2 ms, allowing the synchronized second and perhaps third discharges of these chopper units to coincide with other peaks and troughs of the ABR. However, those units with a chopper discharge pattern whose onset occurred at P4 or later (14 units) were unlikely to contribute further to the ABR.

Latency relations between single unit activity and ABR components as a function of signal intensity. The peak latency of the ABR waves decreased in an or-

TABLE III

Correspondences between the onset latencies of units relative to the period of the ABR waves as a function of location in and around the superior olivary complex

Location of units	n	ABR waves							
		II		III		IV		V	
		P2	N2	P3	N3	P4	N4	P5	>P5
VNTB	12	0	0	1	0	6	0	0	5
MNTB	12	0	0	3	0	5	1	0	3
MSO	5	0	0	1	0	2	0	2	0
LSO	2	0	0	0	0	0	0	2	0
n	31	0	0	5	0	13	1	4	8
TB	12	4	2	3	2	1	0	0	0
MNTB-MSO	3	0	0	0	0	1	0	2	0
n	15	4	2	3	2	2	0	2	0

derly manner as signal intensity was lowered; for a 70-dB change, the latency increased from 0.75 ms for P1 to 1.08 ms for P4 (Table I). The timing of the onset discharges of many of the single units in the brainstem nuclei, using the model latency of the onset discharge, showed a similar degree of latency shift with changes in signal intensity. Fig. 7 contains plots of the modal onset latency for brainstem auditory units along with the latency of ABR components as a function of signal intensity to show that the slopes of these latency/intensity functions for most of the units and the ABR waves are remarkably similar. The correlation coefficients between the slopes of these two types of functions were similar for 90% of the units ($P \leq 0.05$).

Fig. 7. Latency/intensity functions of the modal onset latency for brainstem auditory units along with the ABR components.

DISCUSSION

The various components comprising the auditory brainstem potentials recorded from scalp in humans and animals reflect electrical events originating at different levels of the auditory brainstem pathway extending from the cochlea to the midbrain^{11,20}. There are 3 major areas of uncertainty concerning the relationship between the scalp-recorded events and their generation within the auditory pathway. First, does one^{4,15} or do several^{1,12,27} anatomical sites along the auditory pathway contribute to the generation of a single peak of the ABR? Second, what are the homologies between the ABR components in different species^{16,22}? And third, what neural processes account for the generation of the ABR: graded synaptic potentials or all-or-none potentials of nerve fibers^{3,5}?

The present study involving the recording of single unit activity in the region of the superior olivary complex of guinea pig provides data relevant to the first and third of these issues. At any one anatomical site, be it a fiber tract (e.g. trapezoid body) or a nucleus (e.g. medial nucleus of the trapezoid body), the modal latency of the onset discharge of the units encountered corresponded in time with the latencies of several different waves of the ABR. Moreover, at the time of occurrence of just one of the ABR waves, single units in several diverse anatomical sites in and around the superior olive were found with modal latencies of onset discharge occurring at the same time. In addition, the well-synchronized second and third discharges of the units with a chopper-pattern in and around the superior olivary complex whose first discharges corresponded in latency with P2–P3 of the ABR could also contribute to the generation of the later ABR components. There was one on-wide and one pause unit which showed bimodal with the first discharge. The second peak of the unit with bimodal first discharge could contribute to the generation of the later ABR components. This temporal dispersion may be reflected by the dispersion of the unit firing of the previous auditory pathway, especially in the VIII nerve. These data would favor the hypothesis of multiple sites rather than a single site being the generator for a particular component of the ABR, at least, for waves P2–P5 in the guinea pig. These single unit data are different from those described by

Huang and Buchwald¹⁰ who found, in the cat, that single units with constant latency (S.D. <0.1 ms) in the superior olive, as well as other brainstem recording sites, had a very narrow latency range for the onset discharge that was different for each nucleus and had a close relation to just one component of the ABR. In our study, the population of units with small variations in onset latency (i.e. <0.1 ms or even <0.25 ms) were temporally related not to just one but rather to several components of the ABR. The discrepancy between the data reported in the present study in guinea pig and Huang's and Buchwald's results¹⁰ in cat could represent a species difference or a unit sampling difference due to the different electrodes employed or to the different anesthetic used. However, previously published single unit studies of the superior olive in the cat^{8,25} described a fairly broad range of onset latencies (2–11 ms) rather than a restricted latency range, which is similar to our findings. Therefore, we conclude that cells in the superior olivary complex discharge in temporal coincidence with ABR peaks ranging from P3 to P5.

The present results suggest that at the time of the P3 component, cell populations located in the contralateral medial and ventral nuclei of the trapezoid body and in both MSO fire coincidentally. At the time of the P4 component, cell populations located in the contralateral VNTB, bilateral MNTB (contralateral dominant) and MSO are active. At the time of the P5 component, cells located in both MSO and ipsilateral LSO fire coincidentally. Thus, at the times of both P3 and P4, units located primarily contralateral to the ear stimulated are active, suggesting that these components are generated contralaterally to the ear stimulated. This result corresponds to the results of lesion studies in animals^{4,26,27}.

The slopes of the latency/intensity functions for both the peaks of the ABR and the modal latency of the onset discharge for most of the single units tested in this study were statistically similar. This finding suggests that the same processes leading to the generation of the ABR probably also account for the timing of single unit discharges in the auditory pathway. However, the wide range of absolute latencies encountered in the units from one restricted portion of the auditory brainstem pathway (superior olive and its fiber connections) makes it difficult to ascribe the generation of any one component to a particular

subgroup of units in the superior olive without invoking special circumstances. Alternatively, one could propose that since the units with time-locked activity in the superior olive and its adjacent fiber tracts are distributed over a time period from 2 to 11 ms, the neural elements in just this area alone could be capable of participating in the generation of waves P2–P5.

Kimura has provided a working model to account for the far-field potentials recorded from the scalp during activation of peripheral nerves¹³. A standing positivity occurs at a distance when the traveling nerve action potential traverses a transition border between two conductive medias that differ either in volume or impedance^{14,17}. Thus, for stimulation of the median nerve, a standing positivity is observed in the far field when the nerve impulse traverses the boundaries between the palm and forearm and again between the palm and the digit. A similar process might also be considered for the generation of some of the positive components of the ABR recorded from the vertex. Transition borders of conductive differences ought to occur, for instance, where the VIII nerve exits the bony cochlea, where the VIII nerve enters the brainstem at the cochlear nucleus, and where the trapezoid body fibers turn rostrally from the pons to ascend towards the midbrain. For a positive potential to occur at each of these proposed transition points of possible conductance change, there must be a significant number of nerve fibers having synchronous time-locked activity. However, inspection of Fig. 7 containing plots of the units encountered in the region of the superior olive does not reveal such a clustering of units into distinct groups, except for the period of N4 that is associated with the converse, i.e. activity in relatively few units. Thus, the results from the present study do not distinguish whether the far-field auditory brainstem responses are generated by traveling nerve action potentials or synaptic graded potentials of neurons. Nevertheless, the study does demonstrate that the majority of neural elements encountered in the region of the superior olivary complex of the brainstem discharge with a temporal precision (i.e. a kind of 'time-keeper') considered essential for generating the ABR. Additional studies are needed to distinguish whether any of these unit events actually contribute to the generation of far-field ABR components.

ACKNOWLEDGEMENTS

We would like to thank Jay K. Manago for the ex-

REFERENCES

- 1 Achor, L.J. and Starr, A., Auditory brainstem responses in the cat. I. Intracranial and extracranial recordings, *Electroencephalogr. Clin. Neurophysiol.*, 48 (1980) 154–173.
- 2 Achor, L.J. and Starr, A., Auditory brainstem responses in the cat. II. Effects of lesions, *Electroencephalogr. Clin. Neurophysiol.*, 48 (1980) 174–190.
- 3 Buchwald, J.S., Generators. In E.J. Moore (Ed.), *Bases of Auditory Brainstem Evoked Responses*, Grune and Stratton, New York, 1983, pp. 157–195.
- 4 Buchwald, J.S. and Huang, C.-M., Far-field acoustic responses: origins in the cat, *Science*, 189 (1975) 382–384.
- 5 Caird, D., Sontheimer, D. and Klinke, R., Intra- and extracranially recorded auditory evoked potentials in the cat. I. Source location and binaural interaction, *Electroencephalogr. Clin. Neurophysiol.*, 61 (1985) 50–60.
- 6 Gardi, J., Merzenich, M. and McKean, C., Origins of the scalp recorded frequency-following response in the cat, *Audiology*, 18 (1979) 353–381.
- 7 Goldenberg, R.A. and Derbyshire, A.J., Averaged evoked potentials in cats with lesions of auditory pathway, *J. Speech Hear. Res.*, 18 (1975) 420–429.
- 8 Guinan Jr., J.J., Guinan, S.S. and Norris, B.E., Single auditory units in the superior olivary complex. I: Responses to sounds and classifications based on physiological properties, *Int. J. Neurosci.*, 4 (1972) 101–120.
- 9 Henry, K.R., Auditory brainstem volume-conducted responses: origins in the laboratory mouse, *J. Am. Aud. Soc.*, 4 (1979) 173–178.
- 10 Huang, C.-M. and Buchwald, J.S., Interpretation of the vertex short-latency acoustic response: a study of single neurons in the brainstem, *Brain Research*, 137 (1977) 291–303.
- 11 Jewett, D.L., Averaged volume-conducted potentials to auditory stimuli in the cat, *Electroencephalogr. Clin. Neurophysiol.*, 28 (1970) 609–618.
- 12 Kevanishvili, Z.Sh. and Kjaia, O.A., On the origin of the auditory averaged evoked responses recorded from the scalp in the anesthetized cat, *Acta Otolaryngol.*, 76 (1973) 98–108.
- 13 Kimura, J., Mitsudome, A., Beck, D.O., Yamada, T. and Dickins, Q.S., Field distribution of antidromically activated digital nerve potentials: model for far-field recording, *Neurology*, 33 (1983) 1164–1169.
- 14 Kimura, J., Ishida, T., Suzuki, S., Kudo, Y., Matsuoka, H. and Yamada, T., Far-field recording of junctional potentials by median nerve volleys at the wrist, *Neurology*, 36 (1986) 1451–1457.
- 15 Lev, A. and Sohmer, H., Sources of averaged neural responses recorded in animal and human subjects during cochlear audiometry (electrocochleogram), *Arch. Ohren, Nasen, Kehlkopfheilkd.*, 201 (1972) 79–90.
- 16 Moller, A.R. and Jannetta, P.J., Neural generators of the auditory brainstem response. In J.T. Jacobson (Ed.), *The Auditory Brainstem Response*, College-Hill, San Diego, 1985, pp. 13–31.
- 17 Nakanishi, T., Origin of action potential recorded by fluid electrodes, *Electroencephalogr. Clin. Neurophysiol.*, 55 (1983) 114–115.
- 18 Pfeiffer, R.R., Classification of response patterns of spike discharges for units in the cochlear nucleus: tone-burst stimulation, *Exp. Brain Res.*, 1 (1966) 220–235.
- 19 Scherg, M. and Von Cramon, D., A new interpretation of the generators of BAEP waves I–V: results of a spatiotemporal dipole model, *Electroencephalogr. Clin. Neurophysiol.*, 62 (1985) 290–299.
- 20 Sohmer, H. and Feinmesser, M., Cochlear action potentials recorded from the external ear in man, *Ann. Otol. Rhinol. Laryngol.*, 76 (1967) 427–435.
- 21 Starr, A. and Hamilton, A.E., Correlation between confirmed sites of neurological lesions and abnormalities of far-field auditory brainstem responses, *Electroencephalogr. Clin. Neurophysiol.*, 41 (1976) 594–608.
- 22 Starr, A., Auditory pathway origins of scalp-derived auditory brainstem responses. In C. Morocutti and P.A. Rizzo (Eds.), *Evoked Potentials. Neurophysiological and Clinical Aspects*, Elsevier, Amsterdam, 1985, pp. 133–143.
- 23 Stockard, J. and Rossiter, V.S., Clinical and pathological correlates of brainstem auditory responses abnormalities, *Neurology*, 27 (1977) 316–325.
- 24 Thomas, R.C. and Wilson, V.J., Precise localization of Renshaw cells with a new marking technique, *Nature (London)*, 206 (1965) 211–213.
- 25 Tsuchitani, C., Physiology of the auditory system. In E.J. Moore (Ed.), *Bases of Auditory Brainstem Evoked Responses*, Grune and Stratton, New York, 1983, pp. 67–108.
- 26 Wada, S. and Starr, A., Generation of auditory brainstem responses (ABRs). II. Effects of surgical section of the trapezoid body on the ABR in guinea pigs and cat, *Electroencephalogr. Clin. Neurophysiol.*, 56 (1983) 340–351.
- 27 Wada, S. and Starr, A., Generation of auditory brainstem responses (ABRs). III. Effects of lesions of the superior olive, lateral lemniscus and inferior colliculus on the ABR in guinea pig, *Electroencephalogr. Clin. Neurophysiol.*, 56 (1983) 352–366.