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AUDITORY BRAIN STEM RESPONSES IN THE CAT. II. EFFECTS OF LESIONS [1,2]

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The term auditory brain stem response (ABR) refers to the potentials recorded from scalp electrodes in humans and animals during the first 10 msec following an acoustic stimulus. Although this portion of the auditory evoked potential has been clearly demonstrated to be of eighth nerve and brain stem origin (Jewett 1970; Lev and Sohmer 1972; Buchwald and Huang 1975; Starr and Hamilton 1976), the specific auditory structures generating each of the components of the ABR are still uncertain.

Several investigators (Jewett 1970; Lev and Sohmer 1972; Buchwald and Huang 1975) have suggested that each peak of the ABR in the cat has a single main generator, even though there is evidence of substantial temporal overlap in the evoked potentials occurring in the individual brain stem auditory structures (Jungert 1958; Wicklegren 1968). In contrast, Achor and Starr (1980) concluded from the correspondence in latency between the ABR recorded at the surface and the evoked potentials recorded from the depth that most of the components of the ABR in the cat have major contributions from at least two brain stem sites. Furthermore, within the group of studies which have suggested that there is a single main generator for each of the components, there has been disagreement as to which structure is the principal generator for each of the components. For example, both Jewett (1970) and Lev and Sohmer (1972), using the correspondence between surface- and depth-recorded activity, found the region of the inferior colliculus to be the most active site in the brain stem at the latency of the fourth peak of the ABR. In contrast, Buchwald and Huang (1975), using the effects of transection of the brain stem on the ABR, found that destruction of the inferior colliculi did not affect the fourth peak.

The conflicting findings in the literature suggest that the capabilities and limitations of each experimental technique for defining the generators of surface-recorded activity must be evaluated very cautiously. For example, transection of the neuraxis may have profound effects in structures remote from the lesion, while the definition of a large amplitude voltage field in a brain stem site does not ensure that this field is reflected in the surface recording.

The hypothesis that each component of the ABR in the cat originates from a single main generator has important clinical implications as a comparable sequence of potentials is recorded in man and used in neurological diagnosis (Starr and Achor 1975; Stockard et al. 1976; Thornton and Hawkes 1976). The information gained in the cat could provide

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insight into the mechanisms of the ABR of man.

The purpose of the present study was to define the generators of the ABR in the cat from the effects of discrete lesions of the brain stem auditory pathway on the ABR recorded in both acute and chronic studies.

Methods

Subjects

Lesion effects were studied in 21 cats. Chronic effects were studied in 3 of these and acute effects in 20.

Surgery

The acute cats were anesthetized with an intraperitoneal injection of sodium pentobarbital (40 mg/kg) and placed in a stereotaxic frame with hollow earbars. Rectal temperature was maintained at 36—38°C by means of a circulating water pad. A screw electrode for recording the ABR was placed in the frontal sinus. A craniotomy was performed and the dura incised.

The chronic cats were anesthetized and a mount attached to the skull for fixing the head painlessly in a stationary position during subsequent recording sessions. A screw electrode for recording the ABR was placed in the frontal sinus and secured with dental cement. Insert earmolds were made for the presentation of acoustic stimuli during the recording sessions. An intramuscular injection of penicillin and dihydrostreptomycin was given and the cat allowed to recover for 1 week prior to the first recording session.

Stimulus generation

Monaural 'click' stimuli (produced by shielded transducers from 100 μsec square wave pulses) were presented at 25/sec. In the acute experiments, a 3.5 cm length of polyethylene tubing, containing fine steel wool for acoustic damping, was interposed between the transducers and the hollow earbars. The intensity of the click was 94 dB SPL peak equivalent and 65 dB above threshold for a jury of 3 normal hearing human subjects. The acoustic wave form and spectral energy of the click are presented in the companion paper (Achor and Starr 1980). In the chronic experiments, the transducers were connected to insert earmolds by polyethylene tubing. The effects of the earmolds on the acoustic output were not assessed.

Recording

The ABR was recorded between a screw placed in the frontal sinus 1 cm anterior to the intersection of the coronal and mid-sagittal sutures and a reference electrode (clip or needle) at the midline of the base of the neck (Achor 1978). A 125 μm diameter insulated tungsten electrode (also referenced to the neck) was used to monitor the activity in the brain stem while selecting the site to be lesioned.

Battery-operated amplifiers located inside the sound attenuating room amplified the ABR 10,000 times. The bandpass was 100—3000 Hz (—6 dB points, 12 dB/octave). The amplified signals were led to a computer and monitored on an oscilloscope. Positivity at the frontal sinus was displayed in an upwards direction. The evoked activity was averaged over 100 trials and the digitized data were stored on magnetic disks for subsequent analysis.

Discrete lesions (1—4 mm in diameter) were made by passing 400 μA or more of cathodal current (depth electrode negative) for 30 sec. In some animals several lesions were made in a single brain stem site.

In the acute experiments, recordings were obtained for at least 30 min prior to and following each lesion to define response stability.

For each of the recording sessions in the chronic experiments, the cats were immobilized with an intraperitoneal injection of

gallamine triethiodide (10 mg/kg), intubated and artificially respired. Rectal temperature was maintained at 36—38°C by means of a circulating water pad. Recordings were obtained on at least 4 occasions (separated by a week or more) prior to each lesion to define response stability and on at least 3 occasions following the lesion, except in one cat which was studied on only one occasion following the lesion. Lesions were made in the chronic animals using the same methods as in the acute studies with the exception that a small trephine hole was made for the passage of the depth electrode instead of a craniotomy. Following the lesion and recording, absorbent gelatin was placed over the exposed brain and the overlying tissues sutured close.

Perfusion and histology

The animal was deeply anesthetized with sodium pentobarbital and perfused through the heart with normal saline followed by 10% buffered formalin. The entire brain was removed, blocked and stored in 10% buffered formalin for 1 week prior to processing.

A reconstruction of the extent of the lesion was made from transverse 80 μm serial frozen sections stained with cresyl violet.

Determination of the lesion effects on the components of the ABR

The amplitudes and latencies of the components of the ABR were measured and compared for at least 4 pre- and 3 post-lesion tracings. Amplitudes were defined between the pre-stimulus baseline and the peak for each component. Amplitude effects were expressed as a percentage of the pre-lesion control values. Base-to-peak measurements were generally more useful than peak-to-peak measurements in determining whether a change in a given portion of the evoked potential was due to an effect on a peak or the following trough (or vice versa). However, a few of the lesion effects could not be adequately described by a per cent change in the base-to-peak values as the component shifted its position with respect to the baseline resulting in a change in the polarity of the peak. In these instances the effect was defined to be a 100% change in amplitude. A further description is given in the footnotes to Table I.

Latency was measured at the peak of each component and any change was expressed as an absolute value. Latency changes were not considered to be due to the lesion if they were associated with changes in body temperature (Williston and Jewett 1977).

In general, the ABR was very stable during the pre-lesion control recording period for the acute experiments. The variability in latency was limited to 150 μsec or less and the variability in amplitude was limited to 10% or less. The exceptions were for component N2.0 and most of the components after P5. In many instances these components were near the pre-stimulus baseline so that small absolute changes yielded large percentage changes. Furthermore, even when they were of large amplitude, they showed variations of up to 25%.

Although insert earmolds specifically fabricated for each cat were used to present the acoustic stimulus in the chronic studies, the ABR varied in both amplitude and latency from week to week. In the 3 chronic animals the variability in amplitude was 5—20% and the variability in latency was 100—300 μsec. Change in the acoustic coupling due to the earmold's placement did not account for these effects on the ABR since only minimal effects occurred when the earmolds were reinserted numerous times during a *single* recording session.

Results

Lesions were made in the eighth nerve, cochlear nucleus, dorsal and ventral acoustic striae, superior olivary complex, trapezoid body, lateral lemniscus and inferior colliculus. Tables I and II summarize the amplitude and

TABLE I

Per cent amplitude decreases in the ABR following lesions of the auditory pathway. CN, cochlear nucleus; DAS, dorsal acoustic stria; VAS, ventral acoustic stria; SOC, superior olivary complex; TB, trapezoid body; LL, lateral lemniscus; IC, inferior colliculus; I, ipsilateral; C, contralateral; L, left; R, right. Dashes indicate that the component was not evident in pre-lesion ABR. In several of the cats lesions were made in more than one area. The sequence of lesions in each of these cats is designated by the addition of a number to the letter or letters used to denote the cat. In Table I an ↑ indicates an amplitude increase and in Table II an ↓ indicates a decrease in latency.

Area	Cat	Stimulus	Component							
			P0.8—N1.5	P1.7	N2.0	P3	N3	P4	N4	P5
VIII	AW	I	100	100	90	90	95	95	95	
		C								
CN	Y	I				25	20	20	20	—
		C								
	QQ	I		40	48	40	74	76	64	—
		C								
	X	I,C								
	EE	I,C								
DAS	AJ	I,C								—
VAS	T	I				38		44	22	
		C								—
SOC	U1	I,C								—
	U2	I			100 **	45		12	17	
		C				36				—
	AZ	I			100 **	95	90	95	75	—
		C			100 ***	95	34	42	63	
	S	I,C								—
	FF1	I,C								
	AU	I,C								
TB	W	I				60	30	26		
		C				73	47	10		—
	AS	L			100 ***	36	89	33	50	
		R			67	37	78	32	41	—
	AT	L		22	100 **	74	62	35	30	—
		R		20	95	76	69	63	37	—
LL	TT1	I,C								
	TT2	I						17	14	40
		C								
	UU	I								
		C					44		29	42
	AF	I								
		C				20↑	95	23↑	25	
	RR	I								
		C *					40		27	50
IC	AH	I								
		C								50
	FF2,3	I,C								
	PP1,2	I,C								

* Temporary effects.

** The base-to-peak amplitude of this component changed from a negative to a positive value.

*** The base-to-peak amplitude of this component changed from a positive to a negative value.

TABLE II

Latency increases in the ABR following lesions of the auditory pathway. For explanations of abbreviations see Table I.

Area	Cat	Stimulus	Component							
			P0.8—N1.5	P1.7	N2.0	P3	N3	P4	N4	P5
VIII	AW	I								
		C								
CN	Y	I								—
		C								
	QQ	I								—
		C								
	X	I,C								
	EE	I,C								
DAS	AJ	I,C								—
VAS	T	I					100			
		C								—
SOC	U1	I,C								—
	U2	I				75	75	75	75	
		C								—
	AZ *	I			400	300	150	100		—
		C					250↓	125↓		125↓
	S	I,C								
	FF1	I,C								
	AU	I,C								
TB	W	I								
		C								—
	AS	L								
		R								—
	AT	L							300	—
		R							300	—
LL	TT1	I,C								
	TT2	I								
		C								
	UU	I								
		C								
	AF	I								
		C		75	100	100	150	100	150	200
	RR	I								
		C								
IC	AH	I								
		C								150
	FF2,3	I,C								
	PP1,2	I,C								

* These changes were questionable as there was not a clear indication of comparable pre- and post-lesion components.

latency effects of these lesions on the ABR in the acute animals. The effects of lesions in the chronic animals will be described in a later section.

Components P0.8 through N4 of the ABR (see Fig. 1 in companion paper) were evident

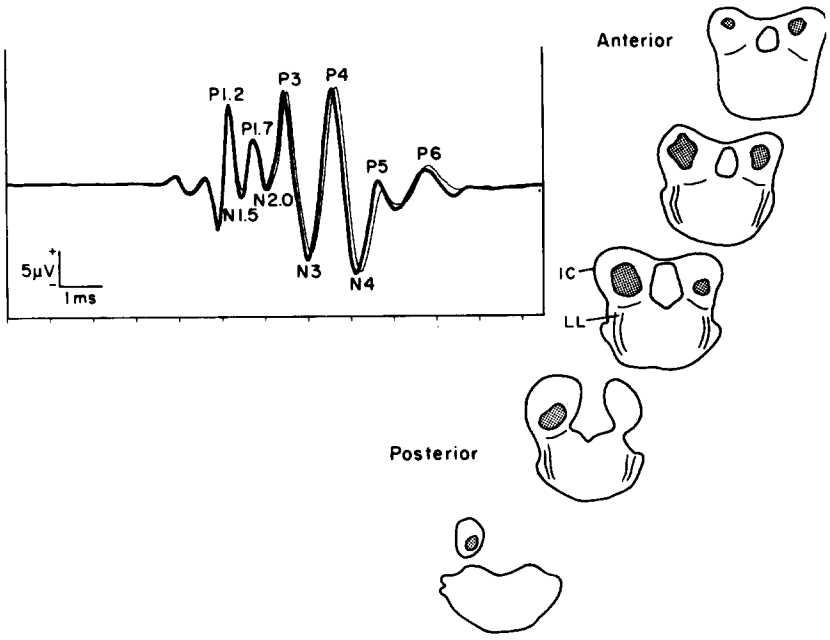

Fig. 1. Reconstruction of inferior colliculus lesions in cat PP and corresponding effects on the ABR. In this and subsequent figures the stippled area denotes the extent of the lesion. The bilateral lesions destroyed a large portion of the central nucleus of the inferior colliculus on each side. In this and all subsequent figures, the thin trace in the inset is the pre-lesion ABR and the thick trace is the post-lesion ABR. The click is presented 3 msec after the beginning of the trace. No effects were observed after either the first unilateral lesion or after the bilateral lesions. The slight latency changes in the ABR were correlated with an increase in body temperature.

in all of the responses to both ipsilateral and contralateral stimulation in the 21 cats. In contrast, P5 could be defined in only about half of the recordings. The components after P5 were evident in even fewer recordings and were therefore not evaluated.

Acute effects of eighth nerve and brain stem lesions on the ABR

Inferior colliculus. A unilateral lesion of the central nucleus of the inferior colliculus in one cat (AH) was followed by a 50% decrease in the amplitude of component P5 to contralateral stimulation and a 150 μsec decrease in latency. There was no effect on the ABR to ipsilateral stimulation. Unilateral followed by bilateral lesions in two other cats (FF and PP) had either no effect on the ABR or produced inconsistent changes in component P5. Fig. 1 contains a comparison of the pre- and post-lesion records for one of the two cats not having an effect. The small increase in the amplitude of component P5 was not consistently obtained. The decrease in latency for the ABR following the lesion was attributed to a slight increase in body temperature.

Because of the variable effects on component P5, the role of the inferior colliculus in the generation of this component could not be definitely established. However, it was clear that the integrity of the central nucleus of the inferior colliculus was not required for the generation of the components of the ABR up to and including N4.

Lateral lemniscus. Bilateral lesions restricted to the posterior portion of the lateral lemnisci in cat TT were not accompanied by any changes in the ABR.

A unilateral lesion of the posterior portion of the lateral lemniscus in a second cat (RR) was associated with decrements in the am-

plitudes of components N3 (40%), N4 (27%) and P5 (50%) of the ABR to contralateral stimulation. However, these effects lasted for only 20 min following the lesion. There were no transient or sustained effects on the ABR evoked by ipsilateral stimulation.

In contrast, unilateral lesions of the lateral lemniscus in two other cats which destroyed the anterior portion of the tract resulted in sustained decrements in the amplitudes of components N3 and N4 of the response to contralateral stimulation and inconsistent changes in P3, P4 and P5. There were no effects of these lesions on the ABR to ipsilateral stimulation. In one cat (UU) N3 decreased by 44%, N4 by 29% and P5 by 42%. The upper pair of traces in Fig. 2 shows the acute effects of the lesion on the other cat (AF). Components N3 and N4 decreased in amplitude (95% and 25%, respectively), components P3 and P4 increased in amplitude (20% and 23%, respectively), and P5 was unaffected. Latency increases of 75—200 μsec were evident in the ABR beginning with N1.0. This figure also contains the evoked responses recorded several weeks later (labeled 'chronic') showing the effects on the ABR to have diminished. A subsequent section of this paper discusses in detail the results of lesions on the ABR when followed over several weeks in chronic recordings.

In summary, lesions restricted to the posterior portion of the lateral lemniscus were either without effect or had only temporary influence on the ABR, whereas lesions restricted to the anterior portion of the tract were associated with a marked attenuation of component N3 of the ABR to contralateral stimulation and a smaller attenuation of N4.

Trapezoid body. A 2—3 mm partial lesion

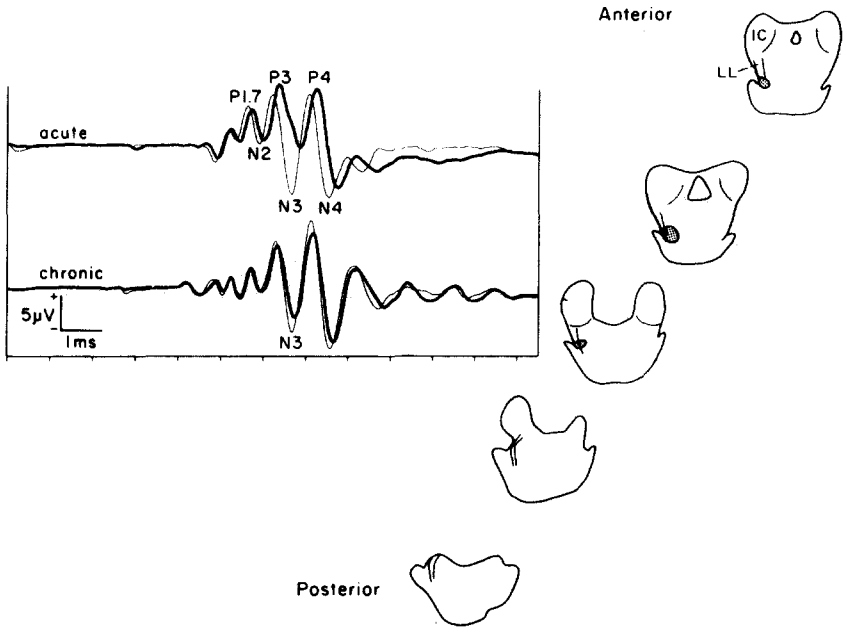

Fig. 2. Reconstruction of lateral lemniscus lesion in cat AF and corresponding acute and chronic effects on the ABR to contralateral stimulation. The unilateral lesion of the lateral lemniscus spared the posterior portion of the tract, but destroyed the anterior portion. In the acute recordings, components P3 and P4 increased in amplitude by 20% and 23%, respectively, and components N3 and N4 decreased in amplitude by 95% and 25%, respectively. Latency increases were correlated with a decrease in body temperature. In the chronic recordings obtained several weeks following the lesion the only statistically significant effect persisting was a decrease in the amplitude of component N3, which was not as marked as immediately following the lesion.

of the trapezoid body in cat W, just to the right of the midline and ventromedial to the superior olive, destroyed about 40% of the fibers decussating in the trapezoid body. The lesion resulted in amplitude decrements for components P3 (60%), N3 (30%) and P4 (26%) of the ABR to ipsilateral stimulation. The decrements were comparable for components P3 (73%) and N3 (47%) of the ABR to contralateral stimulation, but the decrement for P4 (10%) was within the variability of this component.

In cat AT a midline lesion destroyed approximately 50% of the decussating fibers in the trapezoid body (Fig. 3). The lesion effects on the ABR were fairly symmetrical to left and right stimulation and began at P1.7 (Table I).

In cat AS a similar midline lesion destroyed the anterior two-thirds of the trapezoid body. The lesion attenuated the components of the ABR to both left and right stimulation by 25—100%, beginning with N2.0. As with cat T the lesion effects were symmetrical (Table I).

In summary, lesions involving the trapezoid body in the midline consistently resulted in amplitude decreases for components P3, N3, P4 and N4 to stimulation of either ear. In 2 of the 3 cats effects were seen as early as N2.0 and in 1 of the cats as early as P1.7.

Superior olivary complex. Two lesions were made in cat U. The first lesion was approximately 2 mm in diameter and located just medial to the right medial superior olivary nucleus in the dorsal part of the trapezoid body. There were no effects of this lesion. The second lesion, located on the opposite side of the brain stem about 2 mm posterior to the first lesion, involved the lateral and medial superior olivary nuclei and the trapezoid body (Fig. 4). Component N2.0 of the ABR to stimulation ipsilateral to the second lesion ('left' in figure) shifted in a negative direction and components P3, P4 and N4 decreased in amplitude by 45%, 12% and 17%, respectively. All of the components

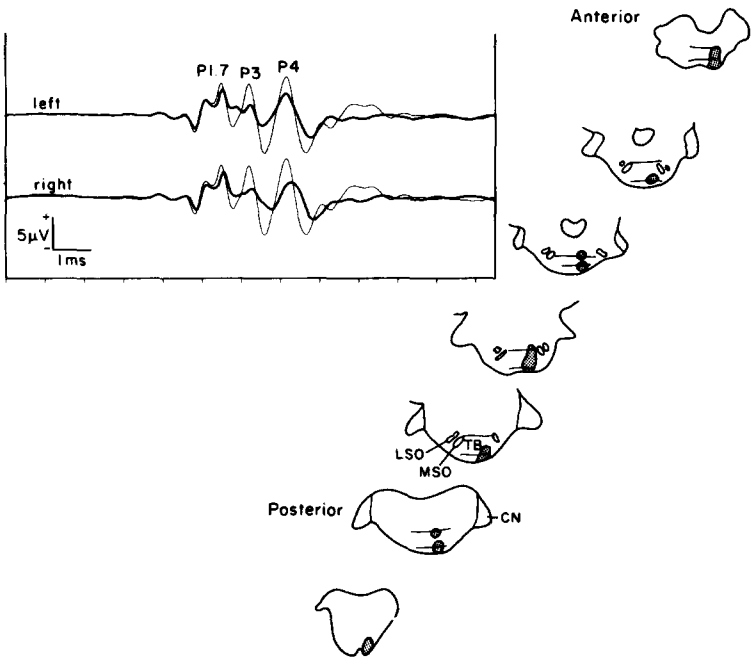

Fig. 3. Reconstruction of trapezoid body lesion in cat AT and corresponding effects on the ABR. The midline lesion destroyed approximately 50% of the decussating fibers in the trapezoid body. The lesion effects on the ABR were symmetrical for left and right stimulation and began with P1.7.

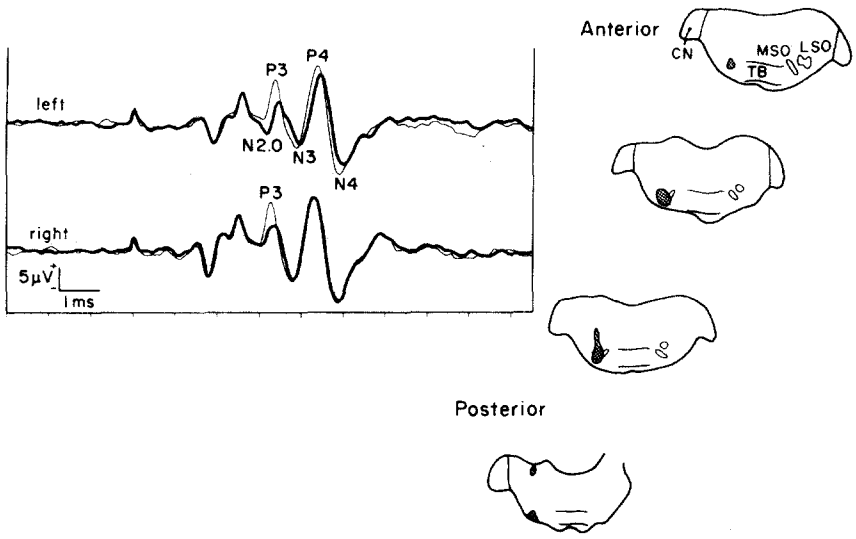

Fig. 4. Reconstruction of superior olivary complex lesion in cat U and corresponding effects on the ABR. The unilateral lesion involved the lateral and medial superior olivary nuclei and the fibers of the trapezoid body. Component N2.0 of the ABR to ipsilateral stimulation ('left' in figure) shifted in a negative direction and components P3, P4 and N4 decreased in amplitude by 45%, 12% and 17%, respectively. All of the components beginning with N2.0 showed small increases in latency. These changes were all greater than the variability of these components in this cat. The ABR to contralateral stimulation ('right' in figure) had only one lesion effect, a 36% decrease in the amplitude of component P3.

beginning with N2.0 showed small increases in latency. The ABR to contralateral stimulation (labeled as 'right') had an isolated effect on P3. This component decreased in amplitude by 36% without any change in any other portion of the ABR.

A large lesion in the superior olivary region of cat AZ destroyed a substantial part of the superior olivary complex, including most of the medial superior olivary nucleus. The lesion also interrupted most of the fibers decussating in the trapezoid body (Fig. 5). The ABR evoked by ipsilateral stimulation showed marked attenuation of *all* of the components following P1.7 (Fig. 5, 'right'). In the ABR evoked by contralateral stimulation (labeled 'left'), N2.0 changed polarity, P3 was eliminated, N3 both decreased in amplitude by 34% and shortened in duration, P4 and N4 decreased in amplitude by 42% and 63%, respectively, P5 shifted in a negative direction and N3, P4 and P5 decreased in latency by 125—250 μsec.

Lesions in the region of the superior olivary complex in 3 other cats had little or no effect on the ABR to either ipsilateral or contralateral stimulation. These included (1) a 2—3 mm lesion just dorsolateral to the superior olivary region in cat FF; (2) a small lesion restricted to the lateral superior olivary nucleus in cat S; and (3) multiple small lesions in the region of the superior olivary complex in cat AU, which spared the medial superior olive and all but the caudal part of the lateral superior olive.

In summary, extensive lesions of the superior olive which also involved the adjacent trapezoid body fibers were associated with (1) attenuation of the components beginning with P3, and (2) variable amplitude effects on N2.0. A unique finding was the isolated effect on component P3 of the ABR to contralateral stimulation in cat U. This was the only instance in which there was a clear effect on one component with no amplitude or latency effects on any of the subsequent components.

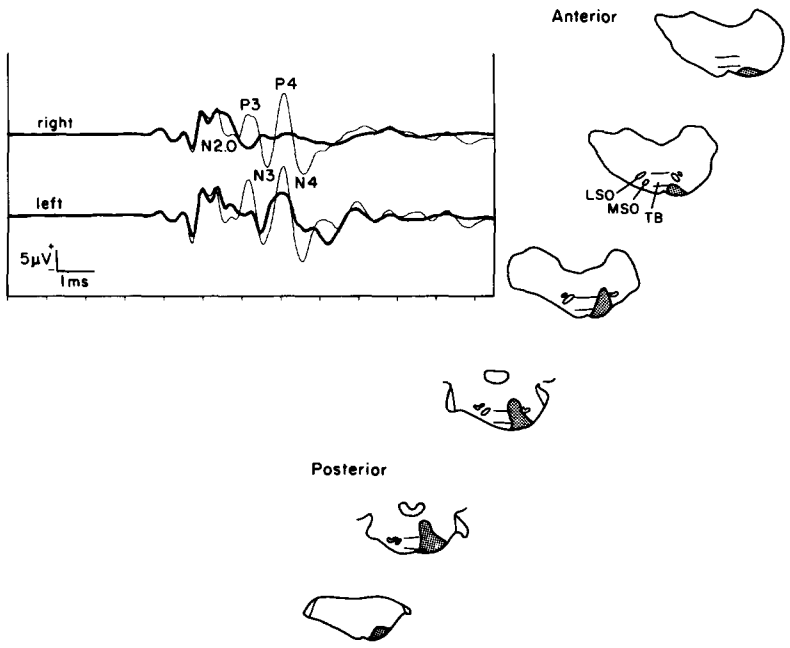

Fig. 5. Reconstruction of superior olivary complex lesion in cat AZ and corresponding effects on the ABR. The lesion destroyed a substantial part of the complex, including most of the medial superior olivary nucleus. The lesion also interrupted most of the fibers decussating in the underlying trapezoid body. All of the components of the ABR to ipsilateral stimulation ('right' in figure) beginning with N2.0 showed marked attenuation. In the ABR evoked by contralateral stimulation ('left' in figure), N2.0 changed polarity, P3 was eliminated, N3, P4 and N4 decreased in amplitude by 34%, 42% and 63%, respectively, P5 shifted in a negative direction, and N3, P4 and P5 decreased in latency by 125—250 μsec.

Dorsal and ventral acoustic stria. A 2—3 mm lesion ventrolateral to the superior olivary nuclei in the ventral acoustic stria in cat T had no effect on the ABR to contralateral stimulation, but changed the ABR to ipsilateral stimulation (Fig. 6). Components P3, P4 and N4 decreased in amplitude by 38%, 44% and 22%, respectively. The morphology of the wave form was also affected with the addition of a new trough and peak between components P3 and N3.

Lesions of the left and right dorsal acoustic stria in cat AJ, which completely transected this portion of the fiber output from the cochlear nucleus, had no effect on the ABR.

Cochlear nucleus. A small lesion in cat Y, which involved approximately 25% of both the ventral and dorsal divisions of the cochlear nucleus, reduced the amplitudes of components P3 through N4 of the ABR to ipsilateral stimulation by only 20—25% (Fig. 7). However, an extensive lesion affecting 75% of the cochlear nucleus in a second cat (QQ) produced much larger amplitude decrements (40—70%) beginning with component P1.7.

Eighth nerve. Crushing the eighth nerve in one cat (AW) attenuated all of the neural components of the ABR to ipsilateral stimulation by 90% or more (Fig. 8, upper traces labeled ABR). The wave form in this cat was unique in that the deflection normally labeled as P0.8 was composed of two parts, a main positive peak and a subsequent inflection point. The separation of the deflection just prior to component N1.0 into a neural component (hereafter labeled P0.8) and a cochlear microphonic component may have been due to

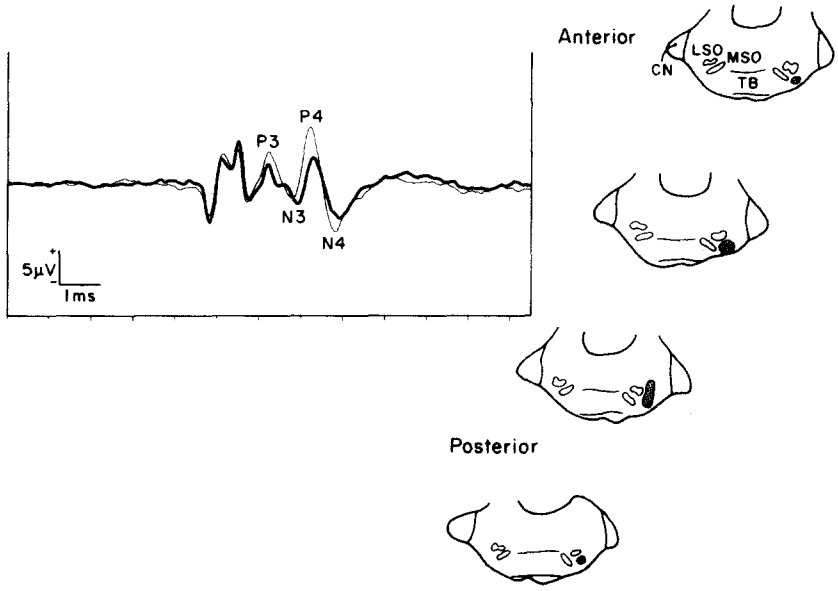

Fig. 6. Reconstruction of ventral acoustic stria lesion in cat T and corresponding ABR effects for ipsilateral stimulation. The lesion was located in the ventral acoustic stria ventrolateral to the superior olivary complex. The lesion had no effect on the ABR to contralateral stimulation but did have an effect on the ABR to ipsilateral stimulation. Components P3, P4 and N4 decreased in amplitude by 38%, 44% and 22%, respectively. A new trough and peak appeared between components P3 and N3.

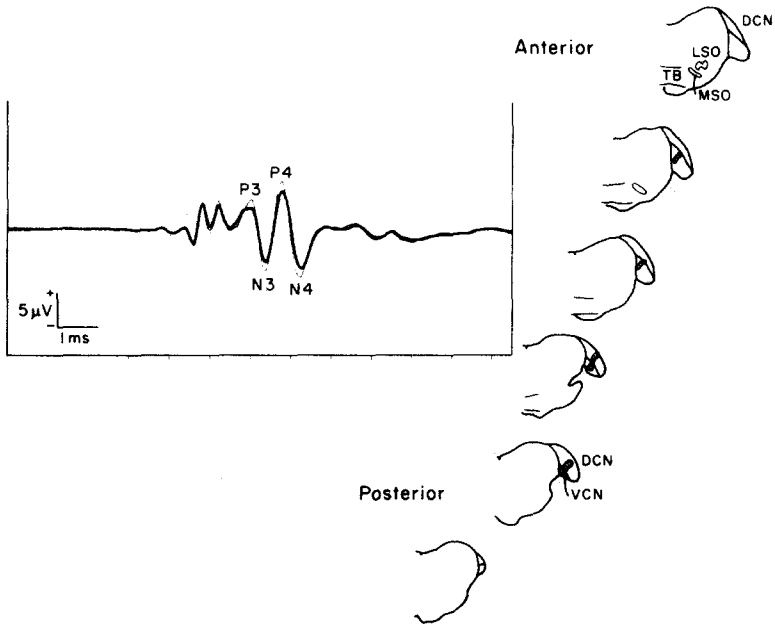

Fig. 7. Reconstruction of cochlear nucleus lesion in cat Y and corresponding effects on the ABR. The 2—3 mm lesion of the cochlear nucleus involved small portions of both the dorsal and ventral divisions. Components P3 through N4 decreased in amplitude by 20—25%.

the reduced body temperature of this animal (34.5°C). The inflection point (see vertical line d in (Fig. 8) was identified as a neural event and labeled P0.8 and the positive peak just prior to P0.8 (see vertical line c) was identified as part of the cochlear microphonic. Two observations aided in these determinations. First, decreasing the stimulus over a 40 dB range did not result in any latency changes for the positive peak, but did produce a latency increase for P0.8. This indicated that the inflection point labeled P0.8 was of neural origin and the earlier deflection was of cochlear microphonic origin. The second observation was that P0.8 occurred simultaneously with the first neural component of the evoked response recorded at the round window (N1 in bottom pair of traces). The cochlear microphonic origin of the components prior to the inflection point was also suggested by their correspondence in latency to the portion

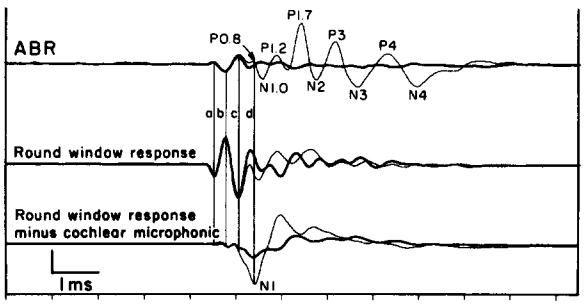

Fig. 8. Effects of the eighth nerve lesion in cat AW on the ABR, round window recording and N1 response of the round window to ipsilateral stimulation (upper, middle and lower pairs of traces, respectively). The N1 response was obtained by alternating the polarity of the click to cancel the cochlear microphonic. The vertical lines a, b, and c are aligned with components of the round window response which are purely cochlear microphonic in origin. The vertical line d is aligned with the neural component of the round window response N1 (bottom traces). The lesion greatly attenuated the ABR beginning with component P0.8, but only had a small effect on earlier activity. The N1 response of the round window was also sharply attenuated. Little effect was observed on the early portion of the cochlear microphonic (a—c in middle traces). The vertical calibration is 5 μV for the ABR and 250 μV for the other traces.

of the round window response which was purely cochlear microphonic in origin. The portion of the round window response which was determined by several tests to be purely cochlear microphonic is indicated by the vertical lines a, b and c. The conclusion is that the earliest portion of the ABR which is presumed to be neural in origin may instead be primarily cochlear microphonic activity.

A comparison of the cochlear microphonic and neural activity recorded from the round window indicated that the cochlear microphonic activity was unchanged following the lesion, but the N1 response was diminished by over 80%. The first 0.5 msec of the electrical activity recorded from the round window, which was cochlear microphonic, was unchanged following the nerve crush (see Fig. 8, 'round window response'). In contrast, the N1 component of the round window recording, which represents action potentials of the eighth nerve (Davis et al. 1952), was severely attenuated (see Fig. 8, bottom pair of traces). These wave form changes persisted for the 2 h they were measured following the eighth nerve lesion. Thus, crushing the eighth nerve abolished all of the neural components of the ABR. The potentials that persisted were of cochlear microphonic origin.

Chronic lesion effects

Chronic lesions of the lateral lemniscus and inferior colliculus were investigated in 3 cats.

Although a unilateral lesion of the anterior portion of the lateral lemniscus in cat AF resulted in substantial changes in several of the components of the ABR to contralateral stimulation in acute recordings (Fig. 2, 'acute'), only N3 was found to be affected in the chronic recordings and even the effect on this component was much reduced (Fig. 2, 'chronic'). In the acute recordings N3 was eliminated, but in the chronic recordings N3 was 75% of its pre-lesion value. The chronic effects on components P4 and N4 were not statistically significant.

The lesion of the central nucleus of the

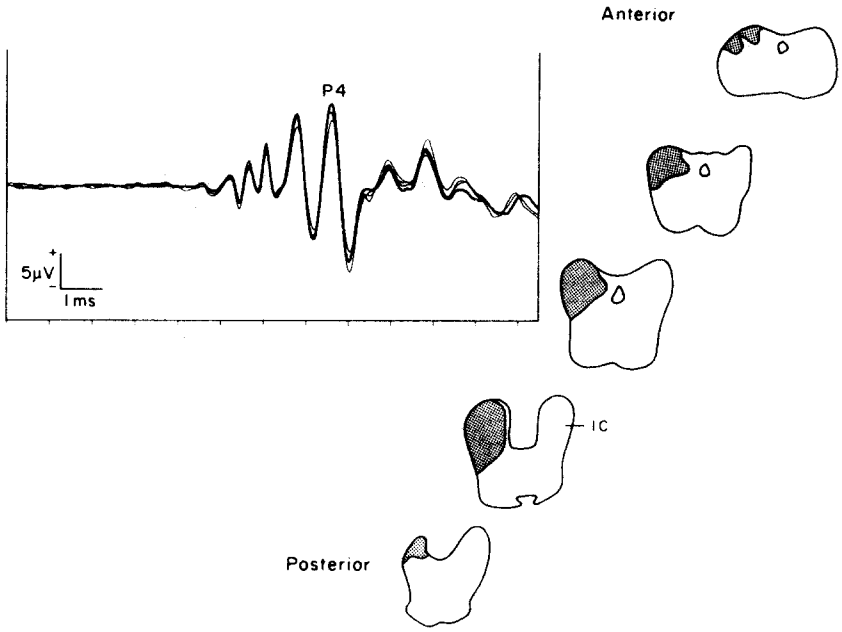

Fig. 9. Reconstruction of inferior colliculus lesion in cat AP and the corresponding chronic effects on the ABR to contralateral stimulation. The unilateral lesion destroyed the entire inferior colliculus without involving the lateral lemniscus. The ABR in this cat showed low variability across sessions as shown by the 3 overlapping pre-lesion records (thin traces). No effects of the lesion on the ABR were evident (thick trace).

inferior colliculus in cat AH that produced acute effects on the P5 component of the ABR to contralateral stimulation was not associated with any changes in the ABR in chronic recordings.

The inferior colliculus on one side of cat AP was completely destroyed, while the lateral lemniscus was spared (Fig. 9). This lesion had no effect on the ABR.

Thus, destruction of the inferior colliculus did not have any chronic effects on the components of the ABR. Moreover, the acute changes in the ABR noted in two cats immediately following lesions of the lateral lemniscus and inferior colliculus were either diminished or no longer present in chronic recordings.

Discussion and conclusions

The results presented in this study demonstrate that discrete brain stem lesions have complex effects on the ABR. (1) A lesion of a single brain stem auditory structure may affect only a single component of the ABR, but more typically the effect is on several components. (2) Lesions of certain portions of the classical primary auditory pathway (i.e., the dorsal cochlear nucleus, the dorsal acoustic stria, the lateral superior olivary nucleus, the posterior portion of the lateral lemniscus and the inferior colliculus) are not associated with changes in the ABR prior to component P5. (3) Except for midline lesions, the effects of brain stem lesions on the ABR are quite different for ipsilateral and contralateral stimulation. (4) The predominant effect of brain stem lesions on the ABR is an attenuation of the amplitudes of the components with only occasional increases in their latency. Opposite effects, i.e., increases in amplitude or decreases in latency, are rare. (5) The effects of some brain stem lesions on the ABR may only be transient.

There are at least 4 mechanisms which may

account for amplitude, latency, and/or morphology changes in a given component of an evoked potential following a lesion. First, the structure lesioned may be the site of generation of the component. Second, the lesion may damage fibers which course through the lesioned area and terminate in the generator sites located elsewhere. Third, the lesion may create physiological disturbances due to circulatory or pressure effects in regions remote from the lesion site. Fourth, the lesion may result in altered function of the remaining neural elements. While these alternative mechanisms limit the usefulness of the lesion method, there were several results in the present study which provided substantive information about the generator loci for the components of the ABR.

The virtual loss of all of the components of the ABR, except the first, following a lesion of the eighth nerve confirmed similar findings by Buchwald and Huang (1975). However, in the present study the first component was found to consist of both cochlear microphonic and neural activity. Crushing the eighth nerve abolished the neural events but had little or no effect on the cochlear microphonic. Although Buchwald and Huang (1975) interpreted the post-mortem loss of the first component as evidence of its neural generation, the cochlear microphonic also disappears post mortem, but over a long period of time. In fact, Wever et al. (1941) found that the cochlear microphonic dropped dramatically within a few minutes after death before declining slowly over the next 30 min. As Buchwald and Huang did neither indicate the time period before the post-mortem recordings were obtained nor provide evidence of an absence of change in the cochlear microphonic recorded from a round window electrode, the designation of wave 1 in their experiments as being generated only by the eighth nerve is uncertain.

The negligible changes following incomplete lesions restricted to the dorsal cochlear nucleus or complete lesions of its efferents in the dorsal acoustic stria suggest that the dorsal cochlear nucleus does not contribute to the far-field ABR recorded from the vertex.

The lesions of the ventral cochlear nucleus in cats Y and QQ were similar in placement but different in size and effect on the ABR. In QQ the lesion destroyed approximately 3/4 of the nucleus and the ABR was profoundly attenuated (>40%) beginning with P1.7. In cat Y the lesion was restricted to only 1/4 of the nucleus and the ABR was but slightly affected (20%) beginning at P3. The failure to demonstrate a change in P1.7 on the last animal indicates one limitation of the lesion method, i.e., if the lesion is too small there may be little or no effect even though correctly placed.

A surprising number of lesions of the superior olivary complex had no effect on the ABR and those which did have an effect also involved fibers of the trapezoid body. None of the lesions had an influence on any of the components prior to N2.0, but 3 of the lesions produced small changes in N2.0. The most consistent finding with lesions in the region of the superior olive was a marked decrease in the amplitude of component P3. In 2 of the 3 cats demonstrating an effect on P3, the ABR to both ipsilateral and contralateral stimulation was affected. It is interesting that in cat U component P3 of the ABR to contralateral stimulation was attenuated 36% with no effect on any of the subsequent components. This indicates that the generation of the components following P3 is not entirely dependent upon the integrity of the generator of P3. The findings from the changes in the ABR evoked by contralateral stimulation in cat AZ following a lesion of the superior olive support this hypothesis. Even though component P3 was virtually eliminated, components N3 and beyond were still present (although reduced in amplitude).

The lesion findings regarding component P4 suggest that it is generated by bilateral pathways. Following the lesion in cat AZ, which destroyed the medial superior olivary nucleus on one side and most of the fibers in

the trapezoid body on the same side, component P4 to an ipsilateral stimulus was eliminated. However, this component was reduced only 50% to a contralateral stimulus. Buchwald and Huang (1975) made a similar finding, but their results were more definitive because the lesion severed all of the decussating fibers in the trapezoid body. They determined that component P4 was equally of ipsilateral and contralateral origin.

In all 4 of the cats with lesions involving the trapezoid body (AZ, W, AS and AT) component P3 and N3 of the ipsilateral and contralateral ABRs were sharply reduced in amplitude and in most instances P4 and N4 were also sharply reduced. In 3 of the 4 cats component N2.0 was also clearly affected. As the trapezoid body is basically a midline structure, the changes in component N2.0 suggest that it depends upon the integrity of the trapezoid body and/or crossed projections. Components P3, N3, P4 and N4 also would appear to depend, in part, upon the integrity of the trapezoid body and/or crossed projections. In only 1 of the 4 cats was component P1.7 affected by the lesion of the trapezoid body and then the effect was small.

The most consistent findings with lesions of the lateral lemniscus were a marked decrease in the amplitude of component N3 and a smaller decrease in the amplitude of component N4 in the ABR to contralateral stimulation. These decrements were accompanied with little or no change in component P4. These findings suggest that the integrity of the contralateral lateral lemniscus is necessary in part for the generation of components N3 and N4.

The finding that the effects on the ABR from acute lesions failed to persist in chronic recordings is most puzzling. Two key differences were present in the procedures for obtaining acute and chronic records: anesthesia and the method of presenting the acoustic stimuli. For the acute recordings the cats were anesthetized and clicks were presented via hollow earbars, whereas for the chronic recordings the cats were unanesthetized and the clicks were presented via earmolds. As barbiturate anesthesia has only minor effects on the amplitudes and latencies of the components of the ABR (Achor and Starr 1980), it is unlikely that the discrepancy in acute and chronic recordings can be accounted for by this factor. It is also unlikely that slight differences in the acoustic stimulus imposed by the two methods of stimulus presentation were responsible for the reversal of the acute effects of the lesions on the ABR, since a similar transient change in the ABR was observed in one of the acute experiments when the stimulus was held constant. It is therefore likely that certain acute lesions may have remote and temporary effects on other portions of the brain stem auditory pathway and these may influence the ABR.

One implication of these results is that the sensitivity of the ABR in defining the presence of lesions in clinical populations may be influenced by the time separation between the onset of the lesion and the recording of the ABR. As a corollary to this, repeat testing of a patient's ABR may indicate a return to normal suggesting that the pathological process is resolving, when, in fact, the anatomical distribution of the lesion is unchanged.

Because of the lower intra- and inter-subject variability of latency measures of the ABR as opposed to amplitude measures, latency changes have been the main criteria used in the clinical assessment of ABR changes associated with neurological disorders (Starr 1977). The finding in the present study that lesions of the brain stem auditory pathway mainly result in amplitude changes and not latency changes runs counter to the current dependence in the clinical evaluation of the ABR on changes in inter-peak latencies (Starr 1977). Moreover, in at least one instance, a lesion of the brain stem resulted in a shorter latency, which is opposite to traditional views of the effects of a lesion. The smaller amplitudes and lower signal-to-noise ratio of the components of the ABR in man render amplitude determinations less reliable in humans than in cats. However, the results

of this study indicate that there is a need to devise adequate methods for defining amplitudes of the ABR in humans and their deviation with brain stem lesions.

Summary

Discrete lesions of the brain stem auditory pathway in cats were found to have complex effects on the auditory brain stem response (ABR). These effects ranged from an amplitude change on only a single component of the ABR to latency and amplitude changes for that component plus some or all of the subsequent components. Lesions of certain portions of the classical primary auditory pathway (i.e., the dorsal cochlear nucleus, the dorsal acoustic stria, the lateral superior olivary nucleus, the posterior portion of the lateral lemniscus and the inferior colliculus) were not associated with changes in the ABR prior to component P5. Except for midline lesions, the effects of a brain stem lesion on the ABR were quite different for ipsilateral and contralateral stimulation. The predominant effect of brain stem lesions on the ABR was an attenuation of the amplitudes of the components and only an occasional increase in their latency. Opposite effects, i.e., increases in amplitude or decreases in latency, were rare. The acute effects of brain stem lesions on the ABR could be transient and not persist in chronic recordings.

The components of the ABR were primarily affected by the following lesions. Component P0.8 was attenuated by a lesion of the eighth nerve. N1.0, P1.2 and N1.5 were unaffected by lesions of the cochlear nucleus but were affected by lesions of the eighth nerve, suggesting that the eighth nerve was the generator of these components. Except for one lesion of the trapezoid body component P1.7 was only affected by lesions of the cochlear nucleus or eighth nerve, suggesting its origin in one or both of these structures. N2.0 was affected by lesions of the ventral cochlear nucleus, the region of the superior olivary complex and the trapezoid body. P3 was affected by lesions in the region of the superior olivary complex and the trapezoid body. N3 and N4 were affected primarily by lesions of the lateral lemniscus, but also by lesions of the superior olivary complex and trapezoid body. The results suggest that except for the first few components (P0.8, N1.0, P1.2 and N1.5) each of the components has substantial contributions from more than one auditory brain stem structure. Component P0.8 was determined to have substantial contributions from both cochlear microphonic and neural activity.

Résumé

Réponses auditives du tronc cérébral chez le chat. II. Effets de lésions

Chez le chat, des lésions discrètes des voies auditives du tronc cérébral ont des effets complexes sur la réponse auditive du tronc cérébral (ABR). Ces effets vont de la modification d'amplitude d'une seule composante de l'ABR à des modifications de latence et d'amplitude de cette composante et de quelques unes ou toutes les composantes successives. Les lésions de certaines portions de la voie auditive primaire classique (i.e., noyau cocléaire dorsal, voie striée acoustique dorsale, noyau olivaire supérieur latéral, portion postérieure de lemniscus latéral et colliculus inférieur) n'entraînent pas de modifications de l'ABR avant la composante P5. A part les lésions de la ligne médiane, les effets d'une lésion du tronc cérébral sur l'ABR sont très différents si la stimulation est ipsilatérale ou controlatérale. L'effet prédominant des lésions du tronc cérébral sur l'ABR consiste en une atténuation des amplitudes des composantes et une augmentation occasionnelle seulement de leur latence. Des effets opposés, i.e., augmentation d'amplitude ou diminution de latence, sont rares. Les effets aigus des lésions du tronc cérébral sur l'ABR peuvent être transitoires et ne pas persister dans les enregistrements chroniques.

Les composantes de l'ABR sont principalement affectées par les lésions suivantes. La composante P0.8 est atténuée par une lésion du nerf auditif. N1.0, P1.2 et N1.5 ne sont pas affectées par des lésions du noyau cocléaire mais sont affectées par des lésions du nerf auditif, suggérant que le nerf auditif est le générateur de ces composantes. A l'exception d'une lésion de corps trapezoïde, la composante P1.7 n'est affectée que par des lésions du noyau cocléaire ou du nerf auditif, suggérant que son origine est dans l'une ou l'autre de ces structures. N2.0 est affectée par des lésions du noyau cocléaire ventral, la région du complexe olivaire supérieur et le corps trapézoïde. P3 est affectée par des lésions dans la région du complexe olivaire supérieur et du corps trapézoïde. N3 et N4 sont affectées principalement par des lésions du lemniscus latéral, mais également par des lésions du complexe olivaire supérieur et du corps trapézoïde. Ces résultats suggèrent qu'à part les toutes premières composantes (P0.8, N1.0, P1.2 et N1.5), chacune des composantes reçoit des contributions substantielles de plus d'une structure auditive du tronc cérébral. La composante P0.8 s'est avérée reçevoir des contributions substantielles à la fois de l'activité cocléaire microphonique et de l'activité cocléaire neuronale.

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