Auditory Evoked Brain Stem Potentials in a Case of "Locked-in" Syndrome

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 Auditory evoked brain stem potentials were measured in a patient with occlusion of the basilar artery about 7 mm above its origin, resulting in the "locked-in" syndrome due to infarction at the junction of the lower one third and upper two thirds of the pons. The first three waves of the evoked response originating from the acoustic nerve and auditory nuclei in the caudal pons were normal in wave form, peak latency, and voltage level. Waves IV and V, generated in the region of the lateral lemniscus and inferior colliculus in the rostral pons and caudal midbrain, demonstrated prolonged peak latency and reduced voltage, indicative of slowed neural conduction in the pons above the level of the superior olivary complex. These findings suggest that auditory evoked potential recordings may have considerable value in the localization of brain stem disorders.

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Chort-latency auditory click-evoked **D** potentials are measures of electrical activity generated from various auditory centers in the brain stem. Depth and scalp electrode recordings in animals with experimental lesions have shown that the "Jewett waves" I. II, III, and the IV-V complex are reflections of electrical activity from the acoustic nerve (wave I), the cochlear nuclei (wave II) and the superior olivary complex (wave III) in the caudal pons, and the nuclei of the lateral lemniscus and inferior colliculus (waves IV and V) in the rostral pons and caudal midbrain.1-3 The origin of waves VI and VII have not been determined from studies with experimental animals, but clinical findings indicate that wave VI may reflect activity from the region of the rostral midbrain or caudal thalamus (medial geniculate bodies) and wave VII from the thalamus or thalamocortical auditory projections.⁴

This report describes the procedures we have used in recording auditory evoked potentials in normal subjects and in a patient with an acute infarction of the pons. The findings provide further clinicoanatomical correlations of these click-evoked responses and demonstrate the potential value of this procedure in the diagnosis of brain stem disorders.

METHODS

All patients and normal volunteer subjects were studied in the Neuroaudiology Laboratory of the Department of Neurology, Wayne State University, in Harper Hospital, Detroit. Electrical activity from auditory centers in the brain stem was evoked using 0.1-msec clicks presented monaurally via earphones. Click intensity was usually 76 dB above the average hearing threshold for clicks for young adult subjects with normal hearing. Other click levels were also used (66 and 86 dB) when it was necessary to aid in the identification of various components of the evoked response. The electrical activity, recorded from a pair of EEG disk electrodes positioned at the vertex (C_z) and mastoid ipsilateral to the ear stimulated, was amplified 200,000 times and filtered through a lowand high-band pass of 100 to 3,000 Hz. Evoked responses were averaged with a computer (Nuclear Chicago model 7100) over a 15-msec analysis interval with 400 data points and a 37.5-µsec sampling rate. A total of 1,500 clicks were presented at a repetition rate of 10/sec for each averaged response. Evoked potentials were recorded at least twice in each ear at each intensity level used and recorded on an X-Y plotter

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Normal Peak Latencies of Auditory Evoked Brain Stem Potentials at 86-dB Hearing Level						
Re	Latencies Relative to Click Stimuli			Latencies Relative to Wave I		
Wave	Mean	SD	Wave	Mean	SD	
1	1.3	0.1	1-11	1.1	0.1	
H	2.4	0.1	1-111	2.0	0.2	
111	3.3	0.2	I-IV	3.1	0.2	
IV	4.4	0.2	I-IV/V	3.9		
IV/V	5.2		I-V	3.9	0.2	
v	5.2	0.3	I-VI	5.2	0.1	
VI	6.5	0.1	I-VII	7.2	0.3	
VII	8.5	0.2				

for a permanent record. The latencies of the evoked response waves I through VII relative to onset of the click stimuli, as well as interwave latencies, were measured to the nearest 0.1 msec. Data obtained in our laboratory from ten healthy adult subjects with normal hearing, aged 23 to 31 years, served as the references for evaluating the responses from our patients.

DATA FROM NORMAL SUBJECTS

Auditory click-evoked brain stem potentials obtained from our normal hearing subjects usually showed seven distinct waves with well-defined peaks. Mean normal latencies and standard deviations for all the waves relative to both the click stimuli and wave I obtained with click intensity at 86-dB hearing level are shown in the Table. Latencies of the various waves were consistent among repeated recordings. In one subject, waves IV an V fused into a single wave, which was then identified as the wave "IV-V" complex. Responses from three subjects did not show clearly formed waves VI and VII. These normal latencies and standard deviations are in good agreement with the data of Starr and Achor⁵ at comparable hearing levels. An increase in latencies of the positive peak responses of more than 2.0 SD from these mean normal values is considered abnormal. Amplitudes of the various waves in the averaged response are measured from the highest point on the positive peak of the wave to the subsequent negative trough. Even though peak-topeak voltage may vary considerably among normal subjects and even from one recording to the next, the amplitude of wave V (or the IV-V complex) is always greater than that of wave I. Thus, as Starr and Achor⁵ have pointed out, V/I amplitude ratio (or IV-V/I) of less than 1.0 is considered abnormal and indicative of brain stem auditory pathway disorder.

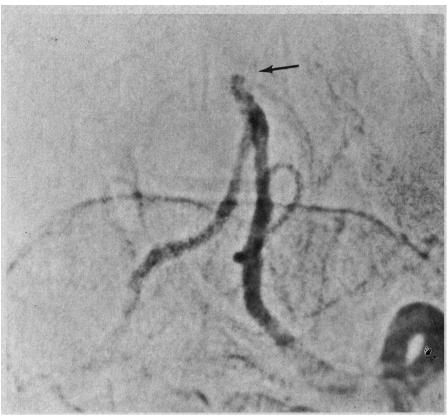


Fig 1.—Left vertebral arteriogram showing occlusion of basilar artery 7 mm beyond origin (arrow). Note retrograde filling of terminal portion of right vertebral artery.

REPORT OF A CASE

A 34-year-old man was admitted to the Neurology Service of Wayne State University, at Harper Hospital, Detroit, on Oct 29, 1976. He had been well until Oct 24, 1976, when he began to complain of bifrontal headaches. The headaches continued until Oct 26, when he became light-headed and developed a mild left-sided weakness. This led to admission to another hospital on that day.

Examination at that time disclosed a lethargic patient complaining of headaches. He had bilateral horizontal nystagmus, a mild left-sided facial weakness, ataxia involving the left upper limb, generalized hyperreflexia, and bilateral extensor plantar responses. Over the next 48 hours his condition deteriorated and he became quadriplegic and comatose. Fluid obtained by lumbar puncture was clear, and there were no cells. Protein level was normal and cultures and serologic tests were subsequently negative. An echoencephalogram was normal and a bilateral retrograde brachial arteriogram showed apparent poor filling of the basilar artery, which was not clearly defined.

At this point he was transferred to the Neurology Service at Harper Hospital for further evaluation. On admission he was found to have a blood pressure of 180/130 mm Hg. He would not respond to verbal stimuli; however, he would withdraw his extremities to noxious stimuli, with the right side moving less than the left side.

Respirations were of the Cheyne-Stokes type. There were no bruits heard over the neck or cranium.

Cranial nerve examination disclosed grade II hypertensive retinopathy without papilledema or hemorrhage. The pupils were equal, round, 4 mm in diameter, and reacted directly and consensually to light. The eyes were centrally positioned, with occasional pendular nystagmus in the vertical direction and ocular bobbing. The oculocephalic response could be obtained, but irrigation of the external auditory canal with ice water did not produce any oculovestibular response. The corneal reflexes were present but slightly depressed bilaterally. Very slight facial movement could be obtained on painful stimulation. The patient was severely quadriparetic with very little movement of the extremities on painful stimulation. The muscle stretch reflexes were increased and symmetrical bilaterally. There was a bilateral extensor plantar response.

A transfemoral arteriogram showed

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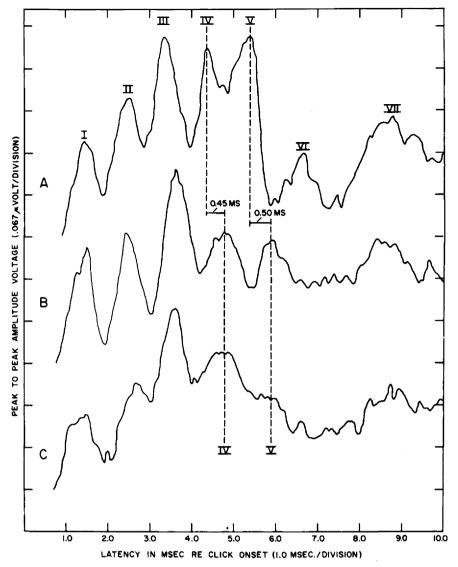


Fig 2.—Auditory evoked brain stem potentials with click stimuli (86-dB hearing level) presented to left ear of normal subject (A) and left (B) and right (C) ears of patient with locked-in syndrome. "Jewett waves" I through VII are based on average of 1,500 clicks presented at rate of 10/sec. Positivity at vertex is up in these recordings.

complete obstruction of the basilar artery approximately 7 mm rostral to the vertebral arterial junction (Fig 1). The posterior inferior cerebellar arteries were visualized bilaterally. Right and left internal carotid artery injection did not disclose any significant retrograde or collateral filling of the basilar system.

On Nov 2, 1976, six days after the onset of symptoms, the patient appeared to be alert with eyes open, conjugate, and directed straight ahead. The respirations were now regular and an endotracheal tube was in place. The patient was able to turn his head slightly to one side or the other on command. Examination of the cranial nerves showed no papilledema. Pupils were round, equal, 4 mm in diameter, and reacted briskly to light, both directly and consensually. The involuntary eye movements had now disappeared, and the patient could move his eyes in a vertical direction, either up or down, on command. He was able to answer questions correctly by looking up for "yes" and down for "no." No lateral movement, however, was possible by command, and the oculovestibular and oculocephalic reflexes were absent in the horizontal plane. There was no ptosis, enophthalmus, or exophthalmus. Corneal reflexes were brisk bilaterally. Bilateralupper and lower-facial weakness was observed. There was no voluntary or spontaneous involuntary movement of the extremities and no withdrawal movement on painful stimulation. The muscle stretch

reflexes remained hyperactive bilaterally and there was a bilateral extensor plantar response.

Serial electrocardiograms in this patient were within normal limits. Serial electroencephalograms revealed a background activity of 7 to 8 cps of low amplitude, intermixed with low- or medium-voltage 4- to 6-cps theta activity. There were no focal, lateralizing, or paroxysmal features.

The patient's condition was believed to represent the result of an infarction occurring at the junction of the lower one third and upper two thirds of the pons, resulting in the "locked-in" syndrome.

On Nov 1, 1976, auditory evoked potentials were recorded monaurally at the patient's bedside with click stimuli at 86dB hearing level. Responses from the left and right ears are shown in Fig 2, together with evoked responses from a normal subject shown at the top of the figure for comparison. For each ear, the first three waves showed normal latencies, with sharp, well-defined peaked wave forms. Latencies for wave IV (4.8 msec) were slightly prolonged relative to the click stimuli in each ear (2.0 SD) with somewhat reduced voltage. Wave V latency relative to the click stimuli (5.9 msec) was increased 0.7 msec beyond the normal mean value of 5.2 msec, which represented a significant shift of more than 2 SD. Latency shift of wave V relative to wave I was 4.4 msec. which was 0.5 msec greater than the average shift of our normal subjects (> 2SD). The significant delays in peak latencies occurred above wave III. Furthermore, even though wave V was easily identified in the recordings, it was significantly decreased in voltage level in the left ear and almost completely absent in the recording from the right ear. Moreover, the wave V/I amplitude ratio was less than 1.0 in both ears. Wave VI could not be identified at its normal latency of 6.5 or 6.6 msec. Whether the response was of such low voltage that it could not be identified or whether it had shifted instead to the latency where wave VII normally occurs (8.5 to 8.9 msec) could not be ascertained in these recordings.

The auditory evoked potentials recorded in this patient with monaural clicks at 86dB hearing levels showed normal waves I through III with no evidence of peripheral shift, slightly delayed wave IV latency with decreased amplitude, and a significantly prolonged wave V response with depressed voltage. These findings suggested slowed neural conduction velocity in the ascending pontine auditory pathways above the level of the superior olivary nuclei in the caudal pons affecting neural transmission along the lateral lemniscus bilaterally. The presence of wave V, even though delayed in onset and diminished in voltage, would seem to suggest that auditory nuclei in the inferior colliculi were not completely disconnected from auditory centers located in the caudal pons.

COMMENT

The "locked-in" syndrome is usually seen with infarction of the ventral pons. This produces tetraplegia or severe tetraparesis due to interruption of the descending corticobulbar and corticospinal motor pathways.⁶⁻⁹ However, the reticular activating system is preserved in the tegmentum of the pons, and the patient appears to be alert but completely paralyzed except for eye movements used for communication.

The syndrome has also been reported in one case of midbrain infarction¹⁰ and one in which tumor infiltrated the pons and midbrain as high as the thalmus.¹¹ In our case, the arteriographic findings of occulsion of the basilar artery 7 mm rostral to the vertebral artery junction clearly indicates infarction of the ventral pons at the junction of the lower one third and

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upper two thirds. In this location, an infarct to the ventral pons would spare the reticular activating system and the central auditory connections in the pons, including the cochlear nuclei, trapezoid bodies, and the superior olivary nuclei. These central auditory structures at the pontomedullary junction and caudal pons would in fact tend to be below the level of the infarction. The sparing of these structures is reflected in the normal latencies and amplitudes for waves I through III in the auditory evoked potentials.

The ascending auditory system from the caudal pons to the midbrain (lateral lemniscus) is a multisynaptic pathway that travels in the lateral portion of the tegmentum of the pons. Ischemia or extension of infarction into this area at the junction of the lower one third and upper two thirds of the pons would interrupt some of the fibers in this tract. This should produce alteration in the latency. amplitude, or wave form of the auditory evoked potential arising at the level of the next principal nuclear mass in the auditory pathway, which is the inferior colliculus. The finding of increased latency and reduced amplitude of wave V in this case supports this hypothesis.

Similar findings of increased latency of wave V has been described in another case of "locked-in" syndrome.¹² The syndrome occurred in a patient with central pontine myelinolysis, a condition in which demyelination in the basis pontis can extend into the tegmentum of the pons, producing some interruption of the ascending auditory pathway. The similarity in the abnormalities in auditory evoked potentials in two cases of "locked-in" syndrome resulting from two entirely different pathological processes is startling.

The abnormality in the auditory evoked potentials recorded in the "locked-in" syndrome suggests that this noninvasive procedure, which can be performed in conscious or comatose patients at the bedside or in the laboratory, is a useful indicator of brain stem disease. In addition, the discrete abnormality in wave V described suggests that this test may have considerable value in localizing the level of disordered conduction within the brain stem.

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