BRAIN-STEM EVOKED POTENTIALS AND THEIR GENERATIONS

RADHA SIMHADRI

Evoked potentials in response to auditory stimuli have been studied for many years. Fifteen individual potential wave-forms can be identified in the averaged responses (Picton *et al.,* 1974). Due to technological reasons, it is only since a decade that attention has been turned to study the early portion of the evoked response (waves having latencies less than 10m. Sees). This sequence of waves which are separated by intervals of approximately lm. Sec. have been tentatively correlated with activation of the brain-stem auditory nuclei and thus have been termed the Brain-stem Evoked Responses (BSER). This BSER could provide a sensitive and objective audio logical and neurological measure which would be particularly useful among populations unable to respond appropriately in conventional auditory testing. The BSER technique can also be used as a tool for observing the functional maturation within the brain-stem auditory pathway (Hecox and Galambos, 1974).

Previous work is based upon the concept that the evoked responses are generated by a progressive activation of the auditory pathway. The neural origin of this response has been established, however, the specific contribution of individual components in the auditory pathway has not been determined (Picton *et* a/., 1974). It has been postulated (Jewett and Williston, 1971, Picton *et ah,* 1974) that the 7 wave-forms (Waves I-VII) of the BSER observed within 10m. sees, after stimulus presentation have separate neural generators connected in series. Wave I represents activity generated by the auditory nerve, Wave II from the Cochlear nucleus, and Wave III from the Superior Olivary Complex (SOC), Wave IV from the lateral lemniscus (LL), Wave V from the inferior colliculus (IC) and Waves VI and VII from medial geniculate body (MGB) and auditory radiations respectively.

While it may be possible to associate a given wave with activity in a distinct portion of the auditory system, it seems unlikely that any but the earliest of waves (I and II) will represent exclusively the activity of a specific nucleus of tract. Several investigations have attempted to verify experimentally the neural generators of the BSER component waves. Literature in this area can be divided into two categories: (1) those investigating BSER neural generators in animals (E.g., Cat) either through lesion or through intra-electrcde studies, (2) those investigations aimed at obtaining human data to confirm wave sources.

Animal Studies: Jewett (1970) studied 18 anesthetised cats by taking direct recordings from the scalp and rostral brain locations. He observed 5 positive

Ms Radha Simhadri, University of Texas, U.S.A.

waves (P_1—P_5). P_1 recorded from the scalp occurred simultaneously with N_1 recorded from the round window. It was concluded that P_1. reflected activity of the VIII cranial nerve bi-polar cells. The remaining waves were suspected to be composite reflections of both slow and fast wave activity of multiple brain-stem generators. Increase in wave amplitude and/ or inversion of polarity was observed for P_2 near the cochlear nucleus, for P_3 near the SOC, and for P_4 in or about the IC or areas slightly rostral to it. These deeply anesthetised animals showed no evoked potentials when recordings were taken from the MGB and auditory context. Jewett's findings were confirmed later by Lev and Sohmer (1972) who used a similar technique on 23 anesthetised cats.

Buchwald and Huang (1975) produced histologically confirmed lesions throughout the auditory tract of the cat andobserved the related effects on the surface recorded BSER. Decerebration of the animal at the level of IC did not alter the BSER. Wave V disappeared when the IC was aspirated. When structures above cochlear nucleus (not including cochlear nucleus) were destroyed, only the first two waves of the BSER remained and subsequent waves disappeared. When structures above auditory nerve were damaged (not including auditory nerve), only Wave I remained. Buchwald and Huang concluded that the integrity of the auditory nerve and cochlear nucleus determined the observation of Wave I and II respectively.

Buchwald and Huang (1975) also produced lesions through the midline of the brainstem and observed that Wave III and V were dependent on crossed fibers, but Wave IV was dependent on both crossed and uncrossed fibers. They also observed that the integrity of MSQ was required for the observation of Wave III, and an intact ventral nucleus of the LL for the observation of Wave IV.

Starr and Achor(1978) also took direct recordings from sub-cortical auditory structures of anesthetised cats in a manner similar to Jewett and Williston's (1971) and Lev and Sohmer's (1972) study. They concluded that BSER components recorded with scalp electrodes reflect the composite activity of as many as 6 brainstem generators.

Starr and Achor (1978) also examined the effect of discrete lesions on surface recorded BSERs in the cat. A lesion at the ventral cochlear nucleus reduced the amplitude of Wave V but did not effect the latency of components beyond Wave II. Lesion in the inferior colliculus, lateral lemuiscus and dorsal cochlear nucleus, however had no influence on the scalp recorded BSER. Starr and Achor went on to suggest that their data contradicted the assumption that a specific neural generator was responsible for a given wave of the surface recorded BSER. They also added that these data did not compromise the reliable correlation between BSER component alterations and neurologic lesion sites in human. Lesion's in human are far more chronic and extensive than those produced in cats.

Human Studies: Lev and Sohmer (1972) speculated that the similarity between the cat and human BSER suggested that the human response may reflect similar neural generators. Subsequent studies (Sohmer *et al.,* 1974, Starr and

Achor 1978, Starr and Hamilton 1976, Stockard and Rossiter, 1977) examined alterations of the BSER in patients with confirmed eighth nerve and brainstem lesions. These studies demonstrate that Wave I was typically the only remnant when lesions involved the ponto-medullary junction or when the brainstem was extensively damaged. Alterations of Waves II and III were associated with lesions in the medulla and pons; i.e., the cochlear nucleus, trapezoid body and superior olive. Lesions affecting mid-brain auditory structures were associated with changes in Waves IV and V.

Topographical analysis of scalp distributions have been conducted by several investigations (Martin and Coats 1973, Martin and Moore 1977, Picton *et al.*, 1974). Picton *et al.*, (1974) found that Wave I was restricted to the ipsilateral (relative to the stimulated ear) mastoid, and it was very similar to the N_1 potential recorded with a trans-tympanic needle electrode. They concluded that this was reasonable proof that Wave I originated in the auditory nerve. Wave components between I and IV reversed polaiity between ipsi and contralateral mastoids; consequently these components appeared to reflect horizontally oriented diploles perhaps in the cochlear nucleus and superior olivary complex. Wave V appeared to be a far field reflection of lateral lemniscus or inferior colliculus components. Picton *et al.*, (1974) concluded that Wave I-IV represented activity of the auditory nerve and brainstem nuclei, but the BSER waves recorded from vertex to mastoid reflected the composite contribution of multiple generators.

Starr and Achor (1975) were unable to reveal any significant alterations in BSER wave-forms in comatose patients with deep sub-cortical involvements, thus contradicting the hypothesis of lemniscal and/or collicular origin of the BSER components.

Kevanishvilli (1980) stressed the importance of tapping the BSER generator mechanism in the light of its functional properties, as revealed in his investigations in man with intact CNS. He recorded (1) BSER to monaural stimulus from ipsi-lateral and contralateral scalp areas, and (2) BSER under monaural and binaural stimulations were compared. His hypothesis was that if Lev and Sohmer (1972) and Buchwald and Huang's schemes on the organisation of the auditory sub-cortex could be proved if (1) the earlier BSER components had greater amplitudes on ipsilateral, and the later components on the contralateral areas, and (2) if the later components were not duplicated in amplitude under binaural Vs monaural acoustic stimulation. Bilateral asymmetry of the BSER was studied (Kevanishvilli 1980) in 6 normally hearing adults and 12 patients with hearing loss in one ear and normal thresholds in the other ear.

Kevanishvilli concluded that his findings were in agreement with Lev and Sohmer and Buchwald and Huang Schemes that under monaural acoustic sti-mulation the initial two BSERs components would be larger on ipsilateral recordings, and the last two components on contralateral recordings. The stronger and earlier activation of generators of the later BSER com-ponents with ipsilateral stimulation is reasonable proof of their sub-lemniscal

origin. Two powerful acoustic nuclei, the ccchltar nucleus and superior olivary complex, and respective fibre bundles are located at this level, the trapezoid body being the greatest among the latter.

According to the animal data (Roseweig *et al.,* 1958), in the lateral lemniscus and inferior colliculus binaurally evoked effects are less than the sums of monaurally evoked, ipsi and contralaterally registered effects. The findings in Kevanshivilli's study support the leminscal and collicular origin of the later BSER components proving that the amplitudes of the BSER to binaural stimulus do not differ from those of the algebraic sum of the BSERs recorded to monaural stimulus from ipsi and contralateral scalp areas. Otherwise, with the lemniscal and/or collicular origin of the later BSER components the duplication of their amplitudes under binaural Vs monaural stimulation (Ipsi+Ipsi) should not be expected. Such a duplication can be observed only in sub-lemniscal structures because of the presence of the following afferent inputs (Goldberg, 1975).

(1) *Exclusively ipsilateral* (the 8th nerve, the cochlear nucleus) or contralateral (the nucleus of the trapezoid body), (2) *independent bilateral* (the trapezoid body, and some neuron populations of the nuclei of the SOC), and (3) ' *additive' bilateral* (unique excitatory—excitatory neurons characteristic of the nuclei of the SOC).

From the studies reviewed one can see the ambiguities in their findings. The difference in findings can be attributed to various factors. For e.g., 1. in Lev and Sohmer's conclusions concerning the BSER generating mechanisms, comparisons were made between scalp-derived BSER with evoked potentials from different brainstem loci. However, they made no comparisons between scalp-derived BSERs and evoked potentials of the trapezoid body, individual nuclei of the SOC, the lateral lemniscus and its nuclei etc. It is probable these evoked potentials could demonstrate temporal concordances with individual components of the scalp-derived BSERs. For these reasons their conclusions may be different.

2. In Lev and Sohmer's experiments the amplitude ratios of intra- and extra-cerebrally derived evoked potentials were also small, being less than 5 or 10. For the comparison, in Starr and Achor's (1978) experiment, these ratios exceeded 50. Thus, it cannot be excluded that in Lev and Sohmer's experiments the electrodes were always accurately placed in the respective auditory structures and which in turn probably produced distortions of the intrinsic waveforms.

3. Considering the absence of the effect of the brainstem section between the dorsal and ventral nuclei of the lateral lemniscus upon component 4 (Jewett and Williston's Wave V) after the previous midline splitting of the rhombencephalon, Buchwald and Huang concluded that it is generated in the ventral nucleus of the lateral lemuiscus and in the pre-olivary region. This conclusion could be different, since in such situations the other auditory nuclei would also be preserved, e.g., most of the nuclei of the SOC and half of the trapezoid body.

4. Other mechanisms which might (Achor and Starr) account for any differences in evoked potential findings following a lesion may be because—

(a) The lesion structure was indeed the generator of the component.

(b) There was damage to fibers passing through the lesioned structure which connect to the actual generator located some distance away.

3. There were physiological disturbances to the generator located in a region remote from the lesion due to circulation or pressure effects and

4. The lesion resulted in altered function of the remaining neural elements.

Conclusion

A composite impression of the literature reviewed shows how several investigators have been motivated to assign a specific correspondence between given BSER component waves and specific neural generators. It must however be stated that at this time the concept of a simple-one-to-one relationship between a given component of the BSER and a single auditory structure is unlikely. Also the designation.of a single auditory area as the primary contributor to a given component is also tenuous. Finally, as Davis (1973) has indicated ' the precise identification of specific structures underlying the later components of the response continues to pose an elusive problem'.

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