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RECORDING OF SHORT LATENCY VESTIBULAR EVOKED POTENTIALS TO ACCELERATION IN RATS BY MEANS OF SKIN ELECTRODES [1]

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Vertigo is one of the most common complaints in clinical medicine. Very often the patient is suspected of having a vestibular disorder and he is referred to the otolaryngology service for vestibular evaluation. However, in spite of the importance of this subject and the large number of vestibular tests conducted, none of these tests can localize the site of pathological lesions in the vestibular system, i.e. none of these tests can differentiate between a vestibular end organ lesion (vestibular labyrinth) and a vestibular nerve lesion, and most of the tests cannot differentiate between a peripheral vestibular lesion and central lesions in the vestibular pathways (the vestibular nuclei, the cerebellum, the thalamus and its cortical projections). For example, the bithermal caloric test and the various rotation tests, which are the most important in the evaluation of vestibular function, demonstrate vestibular hypofunction, without localizing the lesion to the labyrinth, vestibular nerve, ganglion or nucleus. Therefore, these tests (and others) cannot differentiate between Meniere's disease, vestibular neuritis and acoustic neurinoma (Coats 1977).

A similar problem which existed with respect to the determination of the sites of lesions in the auditory, visual and somatosensory systems has been resolved by the development over the past few years of evoked potential techniques, and these have become routine clinical tests of sensory function (auditory, visual and somatosensory evoked potentials) (Feinmesser and Sohmer 1976; Desmedt 1977; Pratt et al. 1979).

By means of these non-invasive techniques, evoked potentials from several levels in the central nervous system can be recorded, permitting the demonstration of the sites of lesions along the neural pathways from the sense organ to the cerebral cortex. This has been especially refined with respect to the auditory system, where responses of the receptor cells, auditory nerve fibres, brain stem pathways and cortex can be recorded. For example, the auditory brain stem potentials are based on the presentation of repetitive sound stimuli (clicks) which synchronously excite many hundreds of auditory nerve fibres. An average response computer and electronic filtering permit the recording with surface electrodes of a series of 7 compound action potentials within 10 msec after stimulus presentation. The principal component of each of these 7 waves probably represents sequential activation of the auditory nerve and brain stem pathways (Feinmesser and Sohmer 1976). The short duration of the acoustic stimulus (less than 1 msec) permits the recording of a response without smearing the responses of individual fibres,

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since most of the fibres respond within a very short time interval (i.e., synchronously).

Even though brain stem potential testing has been established as a reputable routine test of auditory function, there have been only limited attempts to develop an analogous test of vestibular function (Spiegel et al. 1968; Schmidt 1979). There seem to be practical difficulties in the development of such a vestibular test since it is difficult to use the natural, adequate stimulus (acceleration) because the long durations of stimulation used clinically would prevent synchronous activation of a sufficient number of nerve fibres, a situation which is required in order to record a clear, sharp compound action potential with surface electrodes and averaging technique. For the same reason, a caloric stimulus would be inappropriate. There is a single report in the literature (Schmidt 1979) on the recording with far-field techniques of a 'vestibular' response in the cat to electrical stimulation in the external auditory canal, which was ascribed to vestibular nerve activation. The disadvantages of this technique include: (a) the stimulus is not a natural one; (b) the source of the response is not clear; (c) the exact site of excitation is not clear. The electrical pulse probably stimulated the nerve directly, bypassing the end organ.

The purpose of this study was to attempt to develop a technique analogous to the auditory brain stem evoked potential which would permit the recording of vestibular evoked potentials to a natural stimulus of short duration and high intensity (e.g., angular acceleration) using far-field recording techniques.

Techniques

This project was conducted on rats. A special apparatus was designed and constructed by the mechanical workshop. This apparatus [2] includes two main parts: (a) a body holder; and (b) a head holder which firmly holds the animal's head at the proper angle for maximal stimulation of a pair of semicircular canals. This apparatus delivers repetitive and short acceleration stimuli (clockwise or counterclockwise) with maximum intensity of 5000°/sec [2] for 1.5 msec. The rats were anaesthetized by intraperitoneal injection of urethane (1200—1500 mg/kg), tracheotomized, and attached to the apparatus in the presumed proper position for maximal stimulation of the lateral semicircular canals (the axis of rotation was perpendicular to the plane of the lateral semicircular canals).

The electrical activity was recorded by needle electrodes attached to one pinna and vertex, with the contralateral pinna as ground. The response to acceleration stimuli was recorded, and the signal-to-noise ratio improved by using filtering (80—10,000 Hz) and averaging techniques (N = 128 or 256). The evoked potentials were displayed vertex positive up.

Results

Fig. 1a shows a typical potential which was recorded from a rat using the above technique with clockwise rotation. The potential is composed of 3 downward going waves (vertex negative (A, C, E)) and 2 upward going deflections (vertex positive (B, D)). The latency of the first trough (A) is about 7 msec measured from the onset of the trace, which was synchronous with the mechanical stimulus. In some experiments not all of these components were apparent in the traces; occasionally the first downward and upward going waves were absent or unclear (Fig. 1c) and in these cases the latency of the first trough (C) was about 12 msec (from the onset of the trace).

This evoked potential changed markedly with changes in direction of rotation (clockwise or counterclockwise) (Fig. 1b), and its

[2] Patent pending application.

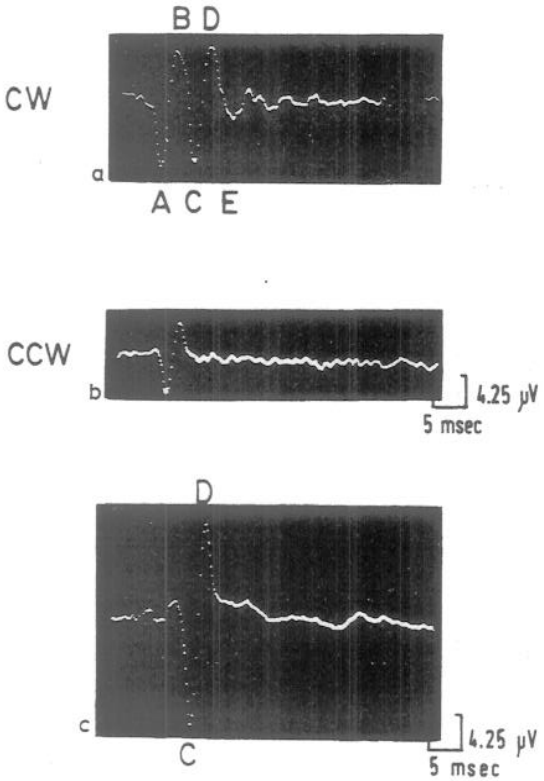

Fig. 1. a (upper trace): a typical vestibular evoked potential composed of 5 waves (A—E) (clockwise rotation — CW, 256 stimuli). b (middle trace): with the opposite direction (counterclockwise rotation — CCW) there is a marked change in the wave form of the vestibular evoked potential. c (lower trace): vestibular evoked potential — the first two waves (A, B) are absent (CW rotation, 256 stimuli).

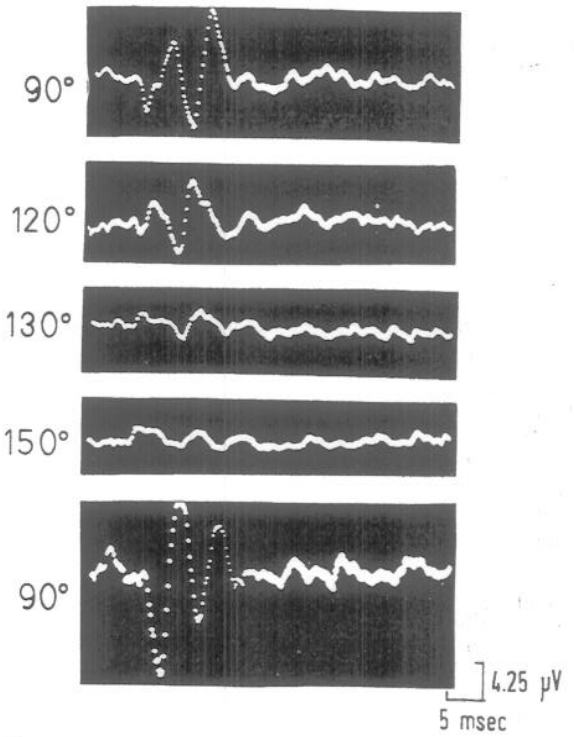

Fig. 2. Changes of wave form and amplitude of the vestibular evoked potential as a function of the head angle (CW rotation, 256 stimuli).

wave form and magnitude were highly dependent on the angle of the head. Fig. 2 demonstrates this dependency and shows that the largest potential was recorded when the angle of the head with respect to the axis of rotation presumably gives the maximal stimulation to the pair of semicircular canals tested (in these experiments, the lateral pair).

At the end of each experiment the animal was killed by an overdose of pentobarbital. On repeating the test on the dead animal, no evoked potential was recorded, even with a large number of consecutive acceleration stimuli (Fig. 3).

In another control experiment the tracheotomized animals were paralysed with succinylcholine and respired with a small respirator. The evoked potential was still present after

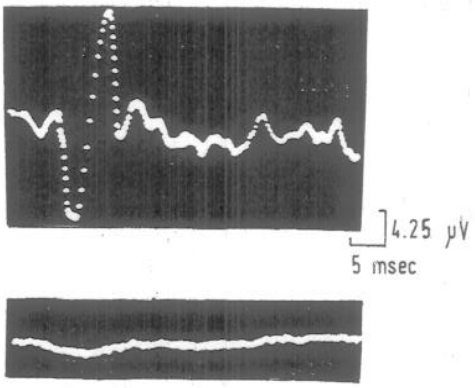

Fig. 3. Records from a rat before and after death. No response is evident after death (lower trace).

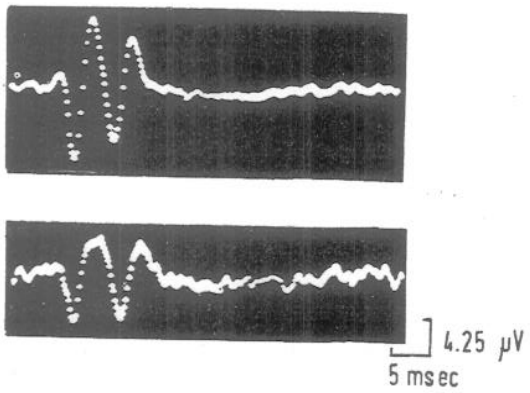

Fig. 4. Vestibular evoked potentials before (upper trace) and after (lower trace) paralysis following injection of succinylcholine. Note that the wave forms are almost identical.

paralysis (Fig. 4) though somewhat reduced in amplitude.

Another set of experiments was conducted on labyrinthectomized rats. Labyrinthectomy was done, using a surgical microscope and the transmeatal approach, by opening the oval window and injecting 96% alcohol into the inner ear. Recording of the response to acceleration stimuli was carried out before and after labyrinthectomy. Destruction of the inner ear in this way caused the evoked potential to disappear completely while typical potentials could still be recorded from the intact contralateral ear.

In a few animals we performed the experiments before and after sectioning the 8th nerve in the cerebello-pontine angle. Section of the 8th nerve caused the ipsilateral evoked potential to disappear.

Discussion

This study has successfully demonstrated that a potential evoked by repetitive acceleration stimuli can be recorded and that its source is in the vestibular system. This potential is not an artifact since it disappears with the animal's death. The finding that it is so strongly dependent on the direction of rotation and on the angle of the head points to its vestibular source. Moreover, destruction of the inner ear and sectioning of the 8th nerve cause it to disappear, confirming that the sensory end organ is the inner ear. It is not a myogenic response since it is still evident after paralysis of the animal. The relatively short latency of the evoked potential also excludes the possibility of a myogenic response and supports the conclusion that the site of generation of this potential is in the peripheral part of the vestibular pathway, most probably the vestibular nerve and ganglion. It is obvious that an acceleration stimulus in a particular direction excites one lateral semicircular canal, while it inhibits the contralateral semicircular canal. Most probably the potentials which were recorded from one side were composed of synchronous electrical events in both vestibular pathways. Additional experiments should be conducted to evaluate the unilateral vestibular evoked potentials.

The experiments of Goldberg and Fernandez (1971) on single units of the vestibular nerve showed that the response to strong acceleration stimuli is composed of a very rapid rise in the discharge rate within a few milliseconds of the onset of the stimulus. This sharp response can explain our success in recording vestibular evoked potentials by surface electrodes using intense and short acceleration stimuli.

Additional experiments should be carried out in order to determine the exact generators of each component of this evoked potential, but even at this stage the importance and the significance of the possibilities of recording a vestibular evoked potential in man using acceleration stimuli is apparent. Following its further development and application to man, this technique should be able to make very important clinical contributions by facilitating the diagnosis of vestibular pathology and the localization of the lesion in the vestibular pathway.

Summary

Short latency (less than 15 msec) vestibular potentials evoked by short and intense acceleration stimuli were recorded in rats by surface electrodes, using electronic filtering and with averaging techniques. The evoked potential is strongly dependent on the direction of rotation and on the angle of the head, and it disappears after labyrinthectomy or sectioning the 8th nerve. All these facts point to its vestibular origin. Although these results were obtained in rats, the importance and the significance of recording a vestibular evoked potential in man is obvious. It would lead to the possibility of objective verification of a vestibular disorder and localization of the lesion.

Résumé

Enregistrement, par électrodes cutanées, de potentiels évoqués vestibulaires à courte latence à l'accélération, chez le rat

On a enregistré chez le rat, par électrodes de surface, des potentiels vestibulaires de courte latence (inférieure à 15 msec), évoqués par des stimulus brefs et intenses d'accélération, en utilisant des techniques de filtrage électronique et de moyennage. Ce potentiel évoqué dépend étroitement de la direction de rotation et de l'angle de la tête; il disparaît après labyrinthectomie ou section du nerf VIII. Toutes ces données indiquent son origine vestibulaire. Bien que ces résultats aient été obtenus chez le rat, l'importance et la significativité de l'enregistrement du potentiel évoqué vestibulaire chez l'homme sont évidentes. Il débouche sur la possibilité d'une vérification objective d'un trouble vestibulaire, ou de la localisation d'une lésion vestibulaire.

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