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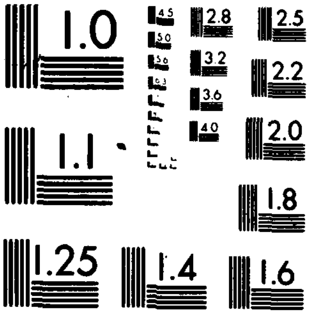

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(9) PROGRESS REPORT,

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(6) Animal Preparations to Assess Neurophysiological Effects of Bio-Dynamic Environments",

~~Contract No~~. NR207-234

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Biological Sciences Division of the
Office of Naval Research

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July 17, 1980

Dr. Donald H. Reid
Aerospace Physiologist
Biophysics Program
Office of Navel Research (440B)
800 N. Quincy Street
Arlington, VA 22217

Dear Dr. Reid:

The enclosed application "Dissecting Visual, Visuomotor and Vestibular Contributions to the Effects of Bio-Dynamic Environments" constitutes a progress report and proposal for continuing studies.

I would like to bring to your attention that a paper "Contributions of eye-muscle afference and efference to visual-motor development," authored by me, will be included in a book "Development and Maintenance of Visually Coordinated Behavior," Alan Hein and Marc Jeannerod, editors. Springer and Co. will be publishing the book. In addition, a paper describing the effects of eye paralysis is in preparation for submission to the journal Vision Research. Both of these papers will cite the support of the Biological Sciences Division of the Office of Naval Research Contracts #NR207-234.

The appendix to our progress report and proposal describes a miniature E.K.G. monitor which we developed to provide continuous information on cardiac function during surgery on cats and kittens. The apparatus utilizes a unique approach to the problem of monitoring heart activity. The advantages to the Navy of this design, as I view it, are three. First, it can easily be used to telemeter cardiac function. Second, the essential device, which can be used for humans without modification, weighs less than 1/2 ounce. Third, the output can be digital, providing a single signal for each heart beat or can be analogue, so that the complete wave form is available for display or recording. The estimate of weight does not include the batteries, plastic case or speaker, items which would not be necessary if the device were used where power could be provided and access to the output were available via external monitoring. These advantages make our E.K.G. monitor ideal for use in aircraft, trainers, human centrifuges, etc. The appendix, in the form of an article, has been submitted for publication in the journal Behavior Research Methods and Instrumentation. Support by ONR Contract #NR207-234 is acknowledged.

I hope that the proposal meets with your approval. If you have any questions. please call me at (617) 253-5759.

Sincerely,

Alan Hein

Alan Hein, Ph.D.
Professor of Psychology

AH:mca

DISSECTING VISUAL, VISUOMOTOR AND VESTIBULAR CONTRIBUTIONS TO THE EFFECTS OF BIO-DYNAMIC ENVIRONMENTS

Submitted by:

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GENERAL INTRODUCTION

Veridical perception of the visual world and motor performance which respects the location of objects in space is essential to survival. Mechanisms of some complexity support the development and maintenance of the capacity for perceptual-motor coordination. The evolution of these mechanisms has been accomplished in a terrestrial environment. Thus, it is not surprising that their operation is imperfect in specialized environments as are encountered in high performance aircraft. The altered gravitational-inertial forces encountered in such environments may disturb equilibrium, degrade motor performance and generate visual and postural illusions. Our efforts are directed towards understanding the operation of the mechanisms which normally support efficient performance and which, if perturbed, degrade such performance.

Spatially-directed behaviors depend on two broad categories of accomplishments: to locate objects through one or more perceptual channels and the ability to monitor one's own position in space. The outcome is the ability to move toward targets either with the whole body or with a part such as head or limb. ~~We will here be concerned primarily with~~ the visual and vestibular systems as sources of information about the location of objects in space, ARE THE PRIMARY CONCERN OF THIS REPORT.

Much information about the visual system and about the maintenance of posture has come from studies of parts of the relevant systems, in isolation. Since 1963, studies of the visual system have frequently focused upon the response properties of single units. Extensive documentation has been provided for the selectivity of such units with respect to input variables (e.g., Hubel & Wiesel, 1963; Hubel & Wiesel, 1968; Pettigrew & Freeman, 1973; Hirsch & Spinelli, 1971). However, the relation between response characteristics of single units and the perceptual capacities of the organism have not yet been clarified despite recent attempts to do so (e.g., Blakemore, Von Sluyters, Peck & Hein, 1976).

Our method is to dissect the mechanisms that on the sensory side provide information, and to examine performance of actual, albeit simple, behaviors. The means at our disposal to carry out this dissection include comparison of the behaviors of intact animals with those prepared surgically so as to interfere with specific components of the oculomotor and vestibular systems. In addition, these components can be interfered with either in adult animals or in the neonate, and the effects on performance compared.

REPORT OF PROGRESS AND PROPOSED STUDIES

A. Contribution of Eye Movement to Visual-Motor Coordination

1. Immobilization of the eye.

Experiments with visually-naive kittens had identified a constraint on the sequence in which two components of visual-motor coordination may be acquired. Visually-guided reaching with the forelimb cannot develop prior to the acquisition of the capacity for visually-guided locomotion (Hein & Diamond, 1972). Recently we examined the possibility that development of all visually-coordinated movement is constrained with relation to one component, movements of the eye. We hypothesized that these movements provide an innate link between the visual and motor systems essential to utilization of other sources of motor-visual feedback.

Fixating movements of the eyes provide a basis for the mapping of the posture of the eye in its orbit. The correspondence between each point in visual space and the retinal locus to which it will project, given a particular posture of the eye, forms a basis for the representation of visual space. Eye movements come to elicit orienting movements of the head toward visual targets. When this eye-head link has been established, exposure with visual feedback from locomotion permits the construction of a body-centered representation of visual space. This representation supports locomotion with respect to visual objects. Subsequently, when a limb has been localized within this map, visual feedback from limb movements permits acquisition of visually-guided reaching (Hein & Diamond, 1972).

This hypothesized sequence suggested that, in the absence of eye movements, opportunity to locomote in light would not support development of visually-guided locomotion. To investigate this possibility we have employed two surgical techniques to immobilize the eye of a kitten. In each case, cranial nerve III, IV and VI, which innervate the ocular musculature, are sectioned on one side. One procedure is a modification of a technique which Berlucci, Munson and Rizzolatti (1966) used in the adult cat. A ventral approach through occipital bone between the acoustic bullae is made to nerve VI and it is cut. Nerves III and IV are approached laterally in the fossa cranialis media, ventral to the temporal lobe. In a second technique the nerves are approached through the roof of the mouth. The soft palate is sectioned and the overlying bone removed with a rose burr to reveal the optic chiasm together with portions of one side of the optic nerve and optic tract. Lateral to these structures, cranial nerves III, IV, V and VI appear just caudal to the orbit. Careful dissection permits isolation of nerve V and section of III, IV and VI.

The first technique was used to produce monocular paralysis in five dark-reared kittens 6-8 weeks of age. While the kitten was anesthetized, the eye contralateral to the side of cranial nerve section was sutured shut. The animals recovered from surgery in light and were kept in a normal laboratory environment thereafter. Observations during the next 12 weeks confirmed the absence of eye movements. Eye movements could not be elicited in response to moving high-contrast targets and attempts to elicit post-rotary nystagmus also failed.

The kittens were tested repeatedly for the capacity to make visually-guided movements under control of the immobilized eye. Visually-guided locomotion was tested in an obstacle course; visually-guided reaching was tested in the bridge box (Hein & Diamond, 1971b). The kittens remained unable to perform these behaviors, repeatedly colliding with objects and failing to step across a gap onto a pier when it was not straight ahead. During the next week (13 weeks after surgery) eye movements began to appear indicating re-innervation of the eye muscles. One week after the eye movements were first observed visually-guided behaviors were re-examined. At this time the kittens traversed the obstacle course rapidly without collision and stepped accurately on to the pier of the bridge box.

The technique in which cranial nerves III, IV and VI are sectioned just caudal to the orbit results in permanent immobilization of the eye. This technique was used with four dark-reared kittens in which the contralateral eye was sutured shut at the time of cranial nerve section. The animals were kept in light continuously following surgery. Visually-guided behaviors were absent one month after surgery and had not been acquired when the animals were re-tested one year later. The lack of visually-guided behaviors in these animals is consistent with the failure of eye movements to re-appear. All subsequent eye paralysis surgery used this second technique to assure permanent immobilization.

We have confirmed that the retina of the immobilized eye remains responsive to light. If the immobilized eye alone is stimulated with a bright light (the intact eye being shielded), the pupil of the intact eye is observed to constrict. Immobilizing the eye by cranial nerve section produces emmetropia and mydriasis. These changes in the optical properties of the eye degrade the retinal image for nearby objects. Decreased acuity might disrupt acquisition of visually-guided behavior regardless of the effects of the absence of eye movement. We examined the contribution of reduced visual acuity to visual-motor development in a new group of four dark-reared kittens. One eye was sutured shut. The animal locomoted in light with the contralateral eye exposed in a state of mydriasis and emmetropia induced by the topical application of atropine. Ophthalmic atropine was applied 20 minutes before exposure in light. While paralyzing accommodative and pupillary reflexes, atropine does not interfere with eye movements. When tested after one week, these kittens were able to use the exposed eye to traverse an obstacle course and to mediate guided reaching in the bridge box. We concluded that the absence of eye movement rather than degredation of the retinal image had been the effective deprivation in preventing the acquisition of visually-guided behaviors.

The next study examined acquisition of visually-guided behaviors in six animals with one eye immobilized and the other mobile. Surgery was performed when the animals were six weeks old. Kittens were exposed daily in light with each eye occluded on alternate days. For three of these animals, the mobile eye was exposed with atropine; for the remaining three, the mobile eye was untreated. Within a week, all six kittens displayed visually-guided behaviors when tested using the mobile eye. The group in which the mobile eye had been treated with atropine during exposure and the group left untreated did not differ in these tests. All six animals failed to display visually-guided behaviors when tested using the immobilized eye. Two conclusions were drawn from these results. First, the interference with acquisition of visually-guided behaviors was not the result of a general inhibition of response to visual input. Second, the capacities mediated by the mobile eye were not accessible to the immobilized eye; under the condition of alternating monocular exposure visual-guidance of movement did not transfer interocularly.

It remained possible that some unknown effect of denervation surgery provented the animal from responding to visual input to the immobilized eye. The display of a consensual pupillary response of the intact eye to changes in illumination of the immobilized eye, along with the capacity of the denervated eye to mediate visually-triggered extension of the forelimb (Hein & Held, 1967) made this unlikely. Moreover, if the contribution of eye movement to visual-motor coordination is made during the formation of a representation of visual space, guided behaviors acquired before eye immobilization might be spared after denervation. This result would also show that the surgery per se does not preclude guidance.

To explore this possibility, light-reared kittens were tested while using only one eye. The presence of visually-guided locomotion and visually-guided reaching prior to surgery was confirmed. Subsequently, the tested eye was immobilized by unilateral section of cranial nerves III, IV and VI. After the animals recovered from surgery, guided behaviors were mediated by the immobilized eye. Thus, denervation of the ocular muscles did not prevent the eye from controlling visually-guided behaviors. The outcome of this study is consistent with the readily made observation that eye movements need not occur during execution of visually-guided behaviors. The contrasting effects of eye immobilization in animals reared preoperatively in dark and in light specify that it is in the initial acquisition of those behaviors that eye movements play a critical role.

It was possible that the effects of immobilization could also be produced if eye movements were not prevented but merely perturbed. To examine whether this might be the case, four dark-reared kittens were subjected to unilateral section of cranial nerves IV and VI at four weeks of age. (The contralateral eye was sutured shut.) This surgery paralyzes the superior oblique and lateral rectus muscles while all other extraocular and intraocular muscles remain innervated. Therefore, while eye movements are perturbed, they occur. Moreover, hyperopia and mydriasis are avoided. These animals were kept continuously in light following recovery from surgery. They were tested in an obstacle course and bridge box after two weeks and failed to display visually-guided behaviors at the time. Perturbation of eye movements appears to have prevented acquisition of these capacities. However, it seems likely that prolonged exposure of these animals might permit development of visual-motor coordination. The cats are being maintained in light to permit later re-testing.

2. Eye muscle deafferentation.

In cats dark-reared prior to eye immobilization, a period of binocular exposure while locomoting was required for mediation of visually-guided behavior by the immobilized eye. This suggests that visual feedback to the mobile eye during locomotion was essential to the development. This inference raised a number of issues suggesting further experiments which are now in progress. First, is information about the orbital position of the (occluded) mobile eye essential to localization of targets viewed by the immobilized eye? Evidence will be obtained from a preparation in which immobilization of on eye is combined with binocular exposure in light. This exposure, whether proceeding or following surgery, yields an animal which can use the immobilized eye for guidance. Enucleation of the mobile eye may eliminate guidance by the paralyzed eye. If this occurs, afference from the mobile eye is suggested as the source of information about that eye's posture. The role of afference in specifying eye posture has been discussed by Maffei and Bisti (1976), Maitin (1976), Skavenski (1972) and Steinbeck and Smith (1976). We will attempt to confirm this in a new group of animals provided binocular exposure either prior or subsequent to immobilization of one eye. After the kittens have demonstrated mediation of visually-guided behaviors by the immobilized eye, the mobile eye will be deafferented.

The procedure for deafferenting the extraocular muscles of the eye is as follows: an approach is made through the soft palate and sphenoid bone just caudal to the area where cranial nerves III, IV, V and VI appear. The ophthalmic branch of V is sectioned at the point where it emerges from the semilunar ganglion. In the cat, the extraorbital course of proprioceptive fibres is known to be carried by this branch (Batini & Buisseret, 1974).

It may be that the two preparations, kittens provided binocular exposure prior to immobilization of one eye and those provided this exposure following eye immobilization, behave differently with respect to enucleation of the mobile eye. In particular, afference from the mobile eye may be less important to mediation of guided behaviors by the immobilized eye in the case of kittens provided binocular exposure prior to immobilization.

Dark-reared kittens failed to mediate visually-guided behaviors with an immobilized eye when postoperative exposure while locomoting was provided to that eye alone (the mobile eye being sutured shut). Monitoring of the output, or motor command (which in an intact animal would produce an eye movement toward an eccentric target), evidently does not provide sufficient information for target localization in such animals. A role for afference from the extraocular muscles as a necessary source of information about eye posture is therefore suggested. Experimental examination of this issue has been begun.

Following the procedures described above, unilateral section of the ophthalmic branch of cranial nerve V is employed to eliminate afference from the extraocular musculature.

In a preliminary study, two dark-reared kittens had one eye enucleated when they were four weeks old and then were allowed to recover in the dark. When the animals were eight weeks old the ophthalmic branch of nerve V serving the intact eye was sectioned and the kitten was permitted to recover in light. Exposure in light was maintained for two weeks during which time eye movements appeared normal. Testing at this time revealed no visual guidance of behavior. This finding indicates that the capacity to locate the eye in its orbit utilizes information from eye muscle afference.

Eye muscle afference may be essential for the initial calibration of motor commands to the extraocular muscles. This suggestion receives support from a preliminary study with dark-reared intact kittens that had one eye deafferented and the other sutured shut. In this preparation eye muscle afference is available from the sutured eye. The animals are allowed monocular exposure in light for two weeks and then tested. In contrast to results obtained with dark-reared animals that have one eye enucleated prior to deafferentation of the fellow eye, these animals display guided behavior using the deafferented eye. Subsequent enucleation of the intact eye did not interfere with the capacity of the deafferented eye to mediate guided behavior. Again, afference from the intact eye appears necessary in the initial acquisition of guidance by the deafferented fellow eye. However, when later enucleation of the intact eye removes this source of information, the behavior is maintained. The same result would be predicted if, instead of enucleating the intact eye, it were to be deafferented.

A further issue is the role of visual input in maintaining the calibration of efferent commands to the extraocular muscles, in the absence of muscle afference. To address this, the kittens able to guide behavior with a deafferented eye in which the other eye is enucleated are placed in the dark. An initial failure to guide after a prolonged period in the dark has been found in preliminary work. These studies are continuing. A possible mechanism for degredation of the efferent program in the dark is suggested by the report of Fiorentini and Maffei (1977) that cats in which the eye muscles have been deafferented show pendular nystagmus in the dark. The absence of visual feedback from eye movement might (in the absence of afferent feedback) allow an undamped oscillation.

B. Contribution of Vestibular Input to Coordination

Our initial studies of animals in which the eye is immobilized included a series of kittens subjected to bilateral vestibulectomy. Because eye immobilization interferes with the vestibulo-ocular reflex, it appeared possible that instability of the retinal image was the cause of the failure to acquire visually guided behaviors with an immobilized eye.

To examine this possibility, a group of four visually naive kittens was subjected to vestibulectomy. The vestibular apparatus is reached by a ventral approach through the acoustic bulla. The entire area between the oval and round windows, including the petrous portion of the petromastoid bone, is excised with a bone curette. A concentrated solution of streptomysin, which is toxic to the VIIIth cranial nerve was applied to the area to assure degeneration of the vestibular nerve. Following recovery from surgery, the kittens were kept continuously in light. They were examined repeatedly for evidence of post-rotatory nystagmus. These observations were made with the animal restrained in a cat bag. The cat was positioned on a horizontal turntable with the head in various postures with respect to the surface of the turntable. They were rotated both clockwise and counterclockwise. Three observers confirmed that post-rotatory nystagmus was absent after rotation in either direction and with the head in any position. This test indicates total bilateral destruction of the vestibular apparatus.

Initially, these kittens appeared somewhat ataxic and hyperactive. However, within four months these problems subsided sufficiently so that visually-guided behaviors could be tested. At this time the animals were able to traverse an obstacle course without collision and reached accurately with the paw when tested in the bridge box. The acquisition of visual-motor coordination in the absence of vestibular input indicates that interference with the vestibulo-ocular reflex does not preclude acquisition of these capacities. Therefore, we concluded that the failure of the immobilized eye to mediate visually-guided behvaior could not be attributed to this factor.

The vestibulectomized kittens not only eventually displayed visually-guided behavior but soon after the surgery were able to stand upright. This suggested an inquiry into the source of information about the direction of gravity that they utilized and experiments to examine this question are ongoing.

An increase in the gain of afference from neck muscles has been shown to contribute to recovery of head-eye coordination in the vestibulectomized monkey (Dichgans et al., 1973). Recovery appears to require several weeks of exposure in light. While this mechanism might also contribute to the coordination of movements of the head and body in the kitten, it does not appear to offer a basis for the assumption of a posture appropriate to gravity. Rather, joint and cutaneous inputs might, in the absence of vestibular input, serve to provide information permitting the animal to stand. This information could be available on an innate basis. Particular patterns of pressure sensations in the joints might specify the upright posture and deviations from those patterns lead to postural adjustment. The cutaneous senses might play an auxiliary role. For example, equality of cutaneous input on the four paws might be informative of the direction of gravity. However, it appears more likely that these inputs come to specify the upright posture only after a period during which they can be associated with changes in vestibular input. Since in the group of animals already studied, the vestibular apparatus was intact during the first six weeks of life, ample opportunity was present for such associations to form. These kittens' postoperative exposure in light might also have contributed to their development of the ability to stand upright.

If a post-natal period with vestibular input is essential for development of the upright posture, there may be a critical period for its contribution. Perhaps only when the neonatal kitten is beginning to stand upright is the relevant association between vestibular input and joint-cutaneous sensations formed. To examine whether a post-natal period with the vestibular apparatus intact is essential to the ability to assume the upright posture, kittens will be vestibulectomized early in the neonatal period and their subsequent development followed. The surgical procedure will be that already described.

Surgery on kittens as young as one day old has been successfully performed in our laboratory using several types of anesthesia. Our preferred technique is intravenous injection of Brevital. Crucial to a good survival rate is pre and postoperative administration of a steroid (dexamethasome) to avoid shock. Surgical destruction of the vestibular apparatus requires a maximum of 20 minutes. Following this surgery the kittens require special handling, including hand feeding. As part of their post-surgical care the kittens are supplied colostrum, harvested from the mother, to provide normal protection against infection. They are intubated for this purpose. A milk substitute (KMR) and supplementary vitamins are also given by this route during the immediate postoperative period. The animals are kept in filter cages with glass fronts, permitting close observation. While the kittens move about, in some cases they tend to maintain postures which might interfere with normal growth. When this is observed, the kittens are moved frequently by hand.

Experiment 1: elimination of post-natal vestibular input.

Kittens will be taken at the moment of emerging from the birth canal, anaesthetized and then immediately subjected to vestibulectomy. Some of the animals will also have both eyelids sutured shut at this time. An incision will be made in the unopened lid from inner to outer canthus. The tissue which would normally form the margins of the lids will be removed and the lids sutured shut.

Destruction of the vestibular apparatus will be inferred from the absence of post-rotatory nystagmus of the eye, as described previously. This can be confirmed even when the lids are sutured shut. The animals will subsequently be maintained in our laboratory for a prolonged period. In addition to observing any spontaneous attempts to stand, we will place the kittens on their side on a suitably textured surface (the rough side of a piece of masonite) and observe any attempts to move to the prone position. If all of these indications remain negative during a period of six months, the experiment will be terminated. A negative outcome would imply that joint and cutaneous sensations do not innately specify the direction of gravity and will also indicate that, in the absence of vestibular information, visual input does not support development of the ability to stand upright. Experiment 2, described below, would then be carried out, to determine the possible critical period for vestibular input.

The kittens provided visual input following vestibulectomy may come to stand while those with eyelids sutured do not. This would imply that while joint and cutaneous sensations do not innately specify the upright, visual input can substitute for vestibular input in supporting development. This is not expected to occur. The procedure of eyelid suturing is appended here to check on the remote possibility that the original vestibulectomized animals succeeded in standing not because of their preoperative exposure but because postoperatively they received visual input.

Experiment 2: critical period for vestibular input.

Newborn kittens living with their mothers in the special filter cages will be observed closely. At the time that they first begin to stand (at approximately ten days of age), one group will be vestibulectomized. Another group will be vestibulectomized when standing has become well established (at approximately three weeks of age). Postoperative care of the animals will follow those procedures of Experiment 1 appropriate to their age.

All of these kittens may fail to stand upright. This would imply that a more prolonged period of opportunity to relate vestibular input to joint and cutaneous input is required for sparing of the ability to assume the upright posture. The critical period would lie within the range 3-6 weeks of age. It is also possible that both groups (those vestibulectomized at ten days and those vestibulectomized at three weeks) eventually stand, indicating that the critical period is within the first ten days of life. Standing in the three week group and failure to stand in the ten day group would imply a critical period between these two ages, and also suggests that it is not until the kitten is making frequent efforts to stand that input from joint receptors and from the cutaneous senses may become informative.

Experiment 3: relation of orientation discrimination to vestibular input.

We plan to examine the capacity of vestibulectomized animals to discriminate the orientation of visual targets. We will begin by determining the threshold for discrmination of vertical from oblique gratings using the modified jumping stand apparatus described by Mitchell, Kaye and Timney (1979). This apparatus is now under construction. Normal controls will be used. We expect an elevation of threshold to accompany vestibulectomy and will be interested in whether this elevation is decreased over time.

Experiment 4: segregating the contribution of vestibular from other proprioceptive input.

The question of what permits vestibulectomized animals to assume the upright posture (in the absence of visual input) will be addressed by restricting the potential source of information to input from joint, tendon and muscle. To accomplish this an attempt will be made to eliminate cutaneous input from the soles of the paws by deafferentation of the cutaneous receptors without damage to motor neurons. The relevant neuroanatomy has been described for the dog but, while the pattern of innervation is likely to be similar for the cat, this project has required a great deal of preliminary work. We have been refining the microsurgical techniques for selective section of the appropriate nerve fibers first in adults cats and, more recently, in kittens.

C. EKG Monitoring

The surgeries we perform on very young animals often compromise cardiac function, making it essential to monitor heart rate. We have designed and constructed a miniature EKG monitor which uses only one high performance integrated circuit, a readily available Pieso-electric sound element and two standard 9v batteries. With the aid of this monitor we have reduced mortality in our operated animals, so that death during, or soon after, surgery has become an exceedingly rare event. The monitor is described in Appendix I in the form in which it has been submitted for publication in "Behavior Research Methods and Instrumentation."

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HONORS:

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1979	Whitaker Health Sciences Foundation Award

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American Association for the Advancement of Science
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American Society of Zoologists
Association for Developmental Psychobiology
Animal Behavior Society

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PUBLICATIONS

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Appendix 1

A MINIATURE EEG MONITOR

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A number of procedures used in animal research are likely to compromise cardiac function. Among these are surgery on very young animals, in which the risk of the operative procedure itself is compounded by variability in response to anesthesia, and preparations in which brain stem or vagus nerve may inadvertently be stimulated. In all such cases, it is essential to monitor heart rate. Ideally the monitor should be small, battery powered and emit an unmistakable telltale coincident with the heartbeat. In addition, for some purposes it is desirable that the complete wave form be available for display or recording. In this article a solution to those requirements is presented.

The device uses only one high performance integrated circuit, a readily available piezoelectric sound element and two standard 9 v batteries. The design eliminates the effects of electrode offsets, while providing a gain of 10^4 and low frequency bandwidth limiting. It emits a brief tone which can easily be discriminated from the ambient noise in a laboratory or operating room. The heart of the monitor is an Analog Devices instrumentation amplifier (AD521)[1]. The performance characteristics of this monolithic instrumentation amplifier are listed in Table 1. Although the design, illustrated in Figure 1, appear simple, it is dependent upon the inherent sophistication available in the AD521. Two aspects of this sophistication have previously been exploited in our laboratory[2]: first, the device is capable of operating with gains up to 10^5 (utilizing suitable DC offset adjust) and second, a capacitor inserted into the input gain loop effectively AC couples the amplifier, without using capacitors at the input leads which tend to imbalance them and degrade the Common Mode Rejection(CMR).

The unit and its controls are depitcted in Figure 2. Placement of the offset adjust at the front panel allows convenient compensation for the inevitable signal variations due to electrode placement. The capacitor in the input loop of the AD521 compensates for all electrode offsets and drift parameters for a particular electrode placement. Another feature of the AD521, permits isolation of the output amplifier from the input and gain stages. This capability is utilized to make the last stage a zero crossing comparator which goes into positive or negative saturation depending upon the amplified heart signal fed to it by the gain stage (see Fig. 3). When the output goes into positive saturation, indicating the presence of the QRS segment of the heart signal, power is applied to the piezoelectronic buzzer which emits a clear, easily discernible tone.

DC coupling of the input stages preserves high CMR at the input; this feature enables the device to function even with the simplest of electrodes, while eliminating interference from 60 Hz or other periodic wave forms which may be present due to long electrode leads or poor grounding. The output of the amplifier is basically in digital form containing information on the duration of the QRS and can be counted digitally or viewed on an oscilloscope. For the circuit parameters shown, the low frequency cut-off is approximately 8Hz.

Although the amplifier can provide a gain up to 10^4, due to its bipolar input construction the applications are limited to low impedence electrodes (less that 20 $K\Omega$).

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