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Electrophysiological Studies of the Nervous System

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This is the final report on the above project originally funded for the period January 1970 - June 1971 and finally completed in May 1972.

As initially conceived the electrophysiological studies to be performed fell under 3 headings, all pertinent to the mechanisms by which potentials are evoked in a brain by sensory stimulation:

1. The effects of chloralose on the evoked potential;
2. Studies on the evoked resistance shift that accompanies evoked potentials;
3. The relationship of eye movements to potentials aroused by visual stimulation.

As the following report will make clear, two of the above sets of experiments were completed (numbers 1 and 3), while the experiments on the evoked resistance shift were actually done on the cochlea, not upon the brain, as originally intended. In addition, several new types of studies not envisaged in the original project description were undertaken, and in some cases completed and published.

1. Effects of Chloralose on the Nervous System

We have studied some 10 cats under chloralose anesthesia in various tests of this general hypothesis: chloralose may impair the ability of

glial cells to clear K+ ion extruded during normal neuronal activity, thus prolonging the recovery of neurons that have already fired and lowering the threshold of those that have not. Using cats with electrodes implanted throughout the classical auditory pathway we simultaneously established the so-called click recovery curve at the cochlear nucleus, inferior colliculus and auditory cortex. As compared to the situation in the same cat when unanesthetized, the electrical response to the second of a pair of clicks was profoundly depressed at the cortex, but not at the cochlear nucleus or inferior colliculus; furthermore, we could collect no evidence that, under the drug, two subthreshold or subminimal stimuli would summate differently than they did in the normal animal. Both aspects of the hypothesis were thus disconfirmed and the project was abandoned. This negative result was not considered of sufficient general interest to warrant publication (Hillyard, Galambos).

2. Resistance Shifts and Other Electrophysiological Measurements on the Cochlea

These experiments are designed to measure the resistances and capacitances between the 3 fluid-filled compartments of the cochlea (scala media, tympani and vestibuli) under 2 conditions: when the basilar membrane is at rest and when it is active.

According to the most popular modern theory, the cochlear microphonic response is the result of a resistance change in the hair cell membrane that follows bending of the hair cells; this resistance change alters the flow of current moving across the basilar membrane from the electropositive Scala Media (+80 mv) to the scala tympani, and

is recorded externally by an electrode on, say, the round window.

As yet, however, no direct measurements exist to validate what is at the crux of this theory - the assertion that hair cells behave as variable resistance elements. Recent developments in methodology make such measurements feasible now, and we are in the midst of making them. We are attempting to approximate accurately the actual impedance of the cochlea fluids and partitions; such measurements are an essential first step for establishing how much current flows through the hair cells at rest, before it is modulated by acoustic stimulation.

This attempt to determine the distributive electrical properties of the cochlea is presently under way in the laboratory of Dr. Vincente Honrubia at the University of California at Los Angeles. The collaborative effort has already yielded some highly reproducible values for impedance and capacitance at the basal turn in the resting guinea pig cochlea, and should shortly be extended to analysis of the dynamic state, with various tones being impressed upon the ear to drive the basilar membrane (Steven Sitko).

3. Lambda Waves Evoked by Retinal Stimulation

Lambda waves appear in the human occipital EEG about 80 msec. after the onset of eye movement across a structured visual field. Since their discovery in the early 1950s, they have been discussed and studied as possible useful central correlates of visual perception, eye movement control, and similar events related to visual processing. Our studies under this heading were initiated in order to clarify in cats the conditions under which lambda waves appear.

Unanesthetized and flaxedil-immobilized cats with chronically implanted electrodes were used. Retinal stimulation comparable to that produced by eye movements was accomplished by moving vertical black and white stripes past their immobilized eyes during 200 msec periods. Potentials identical to human and feline lambda waves were elicited not only at the cortex, but at lateral geniculate and optic tract as well. This means that lambda waves originate at the retinal level, not at the cortex, as has hitherto been thought. Cellular mechanisms responsible for these phenomena can be hypothesized, and the lambda waves can be differentiated from other eye-movement related potentials such as the PGO wave, calcarine cortex potential, corollary discharge and efference copy.

The following report on this work has been submitted to the editor of Electrophysiol. clin. Neurophysiol. for consideration for publication:

> Ebersole, J. and R. Galambos. Lambda waves evoked by retinal stimulation in the absence of eye movements.

4. Human Electrophysiological Studies

A. Studies completed.

A list of 8 papers published during the past two years in this area is appended.

B. Manuscripts covering the following experiments are currently in press:

Picton, T. W. and S. A. Hillyard, Cephalic skin potentials in electroencephalography. Electroenceph. clin. Neurophysiol.

This study undertook to map the skin potentials recordable from the scalp and to differentiate them from potentials originating in the underlying brain. Large skin potentials timelocked to auditory stimuli were recorded under conditions where they could seriously contaminate EEG recordings made during perceptual tasks. Simple methods are described for completely eliminating these unwanted skin potential artifacts which several experimenters seem to have been confusing with responses from the brain.

'Picton, Terence W., Steven A. Hillyard & Robert Galambos. Cortical evoked responses to omitted stimuli. Major Problems of Brain Electrophysiology. Ed. M. N. Livanov. USSR Academy of Sciences, 1972.

The click evoked response in man shows a large positive wave (the P3) at 300-400 msec. which appears during decision-making, attentiveness, and similar states where the signal has special significance for the listener. In this study the listener is required to report correctly on how many clicks are absent in a long train of them

being presented at 1/sec; a positive wave is also shown to be time-locked to the moment a click is expected but does not occur. This electrical event shares so many latency, amplitude, scalp-distribution and wave-shape features with the P3 as to make it probable that the two waves represent the same underlying cortical processes. If this is so, the omitted-stimulus paradigm should prove of great use in perceptual studies, since the "decision-complex", as we have come to call these waves, is entirely uncontaminated by any stimulus-evoked electrical activity.

This paper also advances and develops the idea that the P3 waves represent, or reflect, the comparison of 2 separate neuronal "models" of a stimulus that is being detected, evaluated or attended. One model consists of the actual processing achieved in the classical auditory pathway and its nuclei; the other model, representing the expectations of the listener, and therefore related to memory and attention, is taken to be the output of the reticular formation, medial thalamus and association cortex, at least. The primary auditory cortex appears to analyze and display incoming data, whereas the secondary system seems to anticipate and recognize the specific acoustic signals which are being attended. This

view, which is not unlike that of Sokolov, E. Roy John and others, has the human brain make a comparison between the sensory input processed by the primary auditory system and the possibilities proposed by the secondary auditory system. "Between the reality and the prophecy rests the judgement of perception," to quote the final sentence of the paper in press.

5. Psychophysical Studies on Loudness Enhancement in Man

The following abstract of a paper presented at the October 1971 meeting of the Acoustical Society of America summarizes some new experiment to which we have given increasing attention over the past 6 months.

> Galambos, R., J. Bauer, T. Picton, K. Squires and N. Squires. Loudness enhancement following contralateral stimulation.
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> The apparent loudness of a tone pip can be increased by 15 dB or more if it is preceded by a tone burst to the contralateral ear. The experiment is done by delaying the pip, S_1, by a variable time, ΔT, after the offset of a contralateral tone; the listener assesses the loudness of S_1 by adjusting the intensity of a second tone pip, S_2 that follows S_1 by 1500 msec. Some parametric explorations of the phenomenon are reported here.

A paper covering this material has been accepted for publication by J. Acoust. Soc. Amer.

In subsequent studies by Robert Elmasian the parametric exploration of this interesting phenomenon was continued, and it has been established that the monaural and binaural conditions yield at least as large a loudness enhancement as does the dichotic case first explored.

Our purpose in undertaking these experiments was to look into the possibility that the human olivo-cochlear bundle or efferent auditory tract, might be activated by a sound, and thus alter the perceptability of a second sound following closely thereafter. While the hypothesis seems to have been confirmed, we have not yet been able to establish by electrophysiological recordings at the ear canal that the auditory nerve response to the enhanced signal covaries with it in amplitude, as it should do if the cochlear efferents are involved.

These experiments are to be continued under a grant from NIH (NS 10482-01).

Publications

Hillyard, S.A. and R. Galambos. Eye movement artifact in the CNV. Electroenceph. clin. Neurophysiol. 28: 173-182, 1970.

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Hillyard, S.A., K.C. Squires, J.W. Bauer and P.H. Lindsay. Evoked potential correlates of auditory signal detection. Science, 172: 1357-1360, 1971.

Gazzaniga, M.S. and S.A. Hillyard. Language and speech capacity of the right hemisphere. Neuropsychologia 9: 273-280, 1971.

Hillyard, S.A. The psychological specificity of the contingent negative variation and late evoked potential (P300). Electroenceph. clin. Neurophysiol. 31: 302-303, 1971.

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Nottebohm, F., M. Konishi, S. Hillyard, and P. Marler. Auditory templates and the ontogeny of birdsong. In: F. Worden and R. Galambos (Eds.). Auditory processing of biologically significant Sounds. Neurosciences Res. Prog. Bull. 10: 34-59, 1972.