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June 15, 1966

Dear Dr. [Name]

Please find enclosed for your review and transmission an unsolicited proposal entitled, "Psychophysiological and Verbal Correlates of Altered Consciousness during Amytal Interview."

The proposed research will correlate electrophysiological, psychological and verbal measures of both patients awaiting trial at the male psychiatric prison ward and normal control subjects in the amytal interview situation. It is believed that the approach described in the proposal will further elucidate the effects of amytal with regard to behavioral aspects of emotion, deception, and memory.

A starting date of October 1, 1966 (alternate November 1, 1966) with the project to extend for one year is requested; two additional years are recommended. Direct cost support in the amount of $ is requested for the first year, estimated budgetary requirements are $ for the two succeeding years. The principal investigator is and the co-principal investigator is [Name].

I may be contacted at [Address] August 18th, 1966. Dr. [Name] will be out of the United States from July 28th through his current residence address is.

His temporary residence address is.

Your consideration in this matter is appreciated and I look forward to a favorable reply.

Sincerely yours,
PSYCHOPHYSIOLOGIC AND VERBAL CORRELATES OF ALTERED CONSCIOUSNESS

and

ABSTRACT

The proposed research is an experimental exploration of altered consciousness during an amobarbital interview in order to more accurately define and evaluate clinically observed changes in verbal behavior. Hypotheses basic to this research and derived from several years of clinical experience with amytal interviews are:

1. The primary and predominant effect of intravenous amyotil is on "anxiety-tension" and the usually associated constriction of off behavior. Hypotheses basic to this research and derived from several years of clinical experience with amytal interviews are:

2. While imminent and focal issues of the patient's attention (e.g., the crime for which he awaits trial, malingered hemiplegia, cerebrovascular, etc.) remain particularly impervious to the effects of amyotil, more peripheral material is dealt with in greater detail, elaboration and indescretion as though the patient were confiding the material without constriction or caution due to appropriate apprehension pre-programmed under stress prior to the amyotil interview, i.e., the subject consciously or unconsciously decides how to deal with certain questions before the interview. (3) Amnesia for the contents of the interview may be due to an impairment of "consolidation" processes of memory associated with disconjugate eye movements.

Experimental and control subjects will be selected from patients at the male psychiatric prison ward of the additional control subjects will be recruited from the student population. Additional control subjects will be recruited from the student population. Psychiatric interviews and psychological tests will be employed to evaluate personality structure, anxiety levels, intelligence, and suggestibility of the subjects. Verbal responses will be recorded to equated word association, biographical data, and test questions before, during, and after amyotil interview administered in double-blind control procedure. Electroencephalograph, EEG, and GSR will be monitored and correlated with the interview and verbal test material. Verbal responses will be evaluated against independently verifiable control material, psychophysiological and psychological variables in a double-blind fashion.
I. RESEARCH PLAN

A. Introduction

(1) Current status of work in this area

Intravenous sodium amytal has long been observed to exert a significant influence on an individual's mental state. The most dramatic effect was the temporary resolution of catatonic stupor in schizophrenia and reactive depression (Blackween, 1930; Lorenz, 1932). As "amytal interview" intravenous amytal has formed the basis of special diagnostic and therapeutic techniques, "Narcanalysis" (Horsley 1943), "Narcosynthesis" (Grinker & Spiegel, 1945). Underlying principles and theoretical bases in regard to clinical application remain obscure. At the same time its established clinical use over the past three decades enables one to avoid unexplored pharmacologic pitfalls.

Many early theories explain the effect of amyta based on Hugling Jackson's concept of the release of lower centers resulting in "release of unconscious material as in dreams" Hennan (1938); Delay (1949) attempted to give this a structural basis by claiming that amyatal narcosis "led to a temporary depression of activities of cortical cells". Lindemann (1932) stated that the drug in turn permits an "inCREASE in neuropsychological activities in older parts of the brain". Freed (1946) felt that the release of strong effects occurred frequently enough to justify the localization of the site of action to the diencephalon. Grinker (1945) also suggested that the action was on the diencephalon, and was depressive in nature, so that anxiety producing impulses "no longer bombard the cortex". Kubie & Margolin (1945) agreed that the drug by its "psychologically analgesic" action lessening the patient's need to defend protective symptomatologic structures permitted exploration of painful areas of experience which had been repressed. Masserman (1956) stressed the commonality of the action of amytaL and all drugs, and concluded, "there is no doubt that alcohol, morphine, barbiturates and bromides and most so called ataractics, and similar drugs used in 'psychopharmacologic doses' act as cortical depreSSANT causing impairment of finer perceptions and discriminations, constrictions of the interpretive field an progressive disorganization of adaptive responses". Weinstein (1954) saw the shift in behavior as "in symbolic expression" representing an adaptive and more effective defense in a situation of greater stress. Brickner (1954) felt that verbal material elicited under amytaL was as systematic as any oth-ermentation and demonstrated underlying mental mechanisms of fractionalization, reuniting and compa-words. These underlying verbal structures were not generally evident in the waking state.

Gottschalk (1969) summarized the effect of barbiturates on human behavior as characterized "(a) decreased attention to stimuli; (b) warmer, more appropriate mood; (c) decreased anxiety; (d) increased contact and communication; (e) reduction of psychic manifestation". Despite the work of Meuhlinger (1951) and Lorenz (1932), Gerson and Victoroff (1948) demonstrated the falliib of amytaL as a truth serum.

Recent experimental investigation has revealed that the affective changes due to amytaL are readily measurable with a standardized rating scale technique (Trent, 1962). Likewise, no evidence has been found for specific or general effects of differing pentobarbital dosages on six different measure (pausing time, talking time, total elapsed time, fluency, total power, and mean pitch) of verbal bel (Starkweather and Hargreaves, 1964). Moreover, although Chlorpromazine affected pausing time and related verbal content, Amytal had no selective effect on these constituents of spontaneous speech (Goldman-Eisler, 1965). Nonetheless, it is important that Amytal was found to increase the subject certainty of recall in the perception of geometric figures (Breslow, 1958). Kelley, et al. (1964) using Amytal as an aid to the Rorschach method found an increase in the number of responses and le constriction and stereoty. Sato (1962) examined students under Amytal and found increased produc...
in affective responses on the Rorschach while the GSR revealed diminished levels of autonomic excitement. Miller (1964) studied escape and avoidance in rats and attributed the behavioral effect of Amytal to a "differential effect on the fear mechanism." The findings of the above studies as well as our own clinical impressions suggest that Amytal influences behavior by a reduction of "anxiety-tension."

(2) Rationale of approach to problem

It is well known that the evaluation of drug effects is difficult due to individual differences in psychological, biological, physical and social status. Thus, the dosage administration of drugs usually is regulated by the physician according to the patient's response. In general, the amobarbital interview has been conducted on the basis of the clinician's skill in monitoring and detecting the patient's state of consciousness. It is proposed here that psychophysiological responses during amobarbital interview may index the patient's affective-cognitive status.

The general hypothesis of this proposal is that intravenous amyotal affects behavior through the mitigation of anxiety and an alleviation of tension. An independent measure of the drug effect on the level of consciousness is required. Shagoss (1954) introduced measures of EEG and behavioral response as indicators of sedative tolerance. However, other investigators have reported difficulty in determining the sedation threshold according to Shagoss' criteria (Acknor & Pampiglione, 1959). More recently, inhibition of the galvanic skin reflex by sodium thiopental has been demonstrated to indicate both sedation and sleep thresholds and differences in these measures between psychotic and psychoneurotic depressed subjects (Perez-Reyes, Shands, and Johnson, 1962). It would seem pertinent to employ the GSR in addition to the EEG as a monitoring response during the amyotal interview.

Current research on dreaming has produced definitive data linking eye movements to dream material (Kleiman, 1963). Likewise, the subject's lack of attention to the environment associated with reverie has been related to the appearance of wandering eye movements during conditions normally eliciting a vestibular nystagmus (Wendt, 1941; Collins, 1963). Ront and Mazza (1965) found the disconjugate eye movements occurred during anesthesia and were correlated with a loss of memory for pictorial material. Westheimer and Rabboss (1961) provide evidence that barbiturates interfere with eye vergence movements. The value of using eye movements to ascertain the patient's altered state of consciousness in the amyotal interview must be explored. Apart from the possible relation to the verbor's qualitative aspects of the patient's altered state of consciousness, eye movement monitoring may also provide an effective index of both sedation and sleep thresholds. In summary, the psychophysiological variables in the proposed research on the amobarbital interview are the galvanic skin response (GSR), electroencephalogram (EEG), and electrooculogram (EOG).

Another aspect and the primary focus of this problem will be in the delimiting and characterization of altered consciousness. Artusio, (1955) has shown that there is a stage during ether anesthesia at which patients are unable to form new memories although their mental function is intact as measured by responses to spoken words, problem solving, old memory, etc. This area has been traditionally handled through clinical interpretation of the patient's verbalizations vis-a-vis the interviewer's cues. Gottschalk (1961) emphasized that different methods of sampling the verbal behavior of a subject and drugs may give somewhat different information about the psychopharmacologic effect of the drug. In order to obtain additional evidence of both affective and cognitive changes, it would be appropriate to employ a standardized verbal test, in equated forms, previous to, during, and following the amyotal interview. The earliest used and most fruitful verbal test has been that of word association (Woodworth, 1938). Responses in word association tests are regulated by both affective and cognitive processes. T
proposed study will employ a standard free association test and a special variant. In the first, stimuli word lists will be prepared from established norms (Palermo & Jenkins, 1964) into sets matched for associative "preference" (Moran, et al., 1964). In the second, both stimuli and responses are available in a forced-choice item. A more complete description of these tests is presented below in the procedure section.

An important aspect of our project is the "non-laboratory" subject. In essence, the artificiality of experimental work with contrived and difficult to manage laboratory stress is absent. The experimental subjects are to be selected from among those indicted for serious charges under observation at the psychiatric prison ward of the.

These subjects are living under realistic stress of overwhelming personal significance. The immense annual admission rate of 1500 permits selection of the "higher-caliber", cunning criminal without gross personality deterioration or psychosis.

The approach to the evaluation of the subject's state of consciousness during amytal interview consists of: (a) subjects under real-life stress, (b) psychophysiological indices of EEG, GSR, and e movements, (c) psychological tests of personality, anxiety, intelligence and suggestibility, (d) psychiatric-clinical interpretation of the subject's state of consciousness, and (e) interview and word association tests to index affect and content of thought processes.

(3) Specific Aims

a. To explore cognitive and affective verbal patterns in individuals under stress during altered states of consciousness resulting from intravenous amobarbital.

b. To correlate and monitor alterations in consciousness as indicated in verbal responsiveness under intravenous amytal by means of EEG, EEG, and GSR.

B. Methods of Procedure

(1) Subjects

The experimental subjects for this project will be the patients of the male psychiatric prison of the. These subjects will be selected at random to include 20 criminals 16 years or older, of average or better intelligence and without overt psychosis. The first control group will consist of 10 criminals, approximately matched to the experimental group as to age, alcohol or drug addition, and psychiatric diagnoses. Concomitantly, a second control group consisting of 10 paid, normal volunteer subjects will be recruited from the student population of personnel office. Fifteen subjects, the first control group and five of the second control group, will receive, independent of the experimenter's knowledge, only saline during the supposedly amytal interview. It is planned that the study should continue for three years to complete a total sample of 120, i.e. 60 experimental and 60 control subjects.

(2) Apparatus and tests

a. Psychological Variables. All subjects will be initially screened and evaluated along the following dimensions: (1) Personality characteristics interpreted from the Minnesota Multiphility Personality Inventory (MMPI) on the clinical scales (Hathaway & McKinley, 1951), (2) Anxiety level estimated from the Taylor scale of manifest anxiety (Taylor, 1963) and the IPAT-8-para form anxiety battery (Scheier & Cattell, 1960), (3) Intellectual functioning as measured by
b. **Psychiatric interview**—This procedure involves a relatively exploratory, dynamically oriented, and open-end interview designed to elicit material on the person's basic personality pattern as well as material related to recent events leading to his crime and hospitalization on the prison ward. Interviews with control subjects will be aimed at the evaluation of their basic personality organization and their response to stress as altered by I.V. amytal. All interviews will be taped, transcribed, and then evaluated in light of corroborative material from eye witness accounts, arresting officer's report, parole and trial records. Control subject material will be assessed along similar personality dimensions by three independent raters.

c. **Word association tests**—Two different types of word association tests will be used, namely free association and binary forced-choice. In the free association test, critical words relating to the subject's recent crime and/or areas of personality conflict will be interspersed with standard "neutral" stimuli. Measurements will be made for response latencies, thematic content, associative "set" or preference, and commonality.

The binary forced-choice association test is designed to measure individual differences in semantic habits as different from syntactic or relational association habits (Nunnally, Flaugher, and Hodges, 1963). Four types of choices, evaluative-good (pleasant words), evaluative-bad (negative words, eg. ugly, sour), denotative (attributes, eg. long, sharp), and categorization (classificatory, eg. reptile, coed) are combined into subscales. For example, contrasting the evaluative-good and the denotative tendencies, *Orange:* sweet, round.

In this manner individual differences in the use of different modes of semantic response to objects in the human and material environment are measured. The test instrument subscales as now constructed have Kuder-Richardson formula 20 reliability coefficients ranging from .62 to .79. Measurements will consist of scores obtained on the combined evaluative and the categorization-denotative balance scales.

d. **Examination rooms**—Amobarbital interviews will be conducted in the seclusion room on the male prison ward.

e. **Psychophysiological Variables**—These variables will be recorded on a six-channel polygraph. Four channels will be used for EOG in the determination of eye movements by use of peri-orbitally placed surface electrodes. Electrodes will be located on each eye at the outer and inner canthus for horizontal movement and directly above the supraorbital margin and below the infraorbital ridge for vertical movement. The electrodes will be of the nonpolarizable silver chloride type. One channel will be used to record the galvanic skin response. Silver-silver chloride electrodes with a starch paste of 0.05 N sodium chloride solution will be used in measuring the GSR (O'Connell, et al., 1960; Edelberg & Burch, 1962). The apparent electrical resistance to an applied current of 8 microamps/cm² between the palm and the forearm reference site will be continuously recorded. The EEG will be monitored with a monopolar occipital electrode arrangement. These variables will be synchronized with the verbal material through the use of voice operated relays and event markers.

The experimental subjects will be allowed five days to adapt to the ward regime prior to the
psychological tests, psychiatric interview, and word association tests. Within the following week the amytal interview will be conducted with preselected material, equated for particular relevance, that earlier was or was not directly probed for by the interviewer.

The subject will recline in bed and be prepared for EEG, EEG, and GSR recordings that will be taken throughout the test period. After an initial test period of five minutes, a continuous drip of normal saline solution will start. A second five minute period will elapse to allow the subject to accommodate to the needle in his arm. During this interval, an eye fixation test and an abbreviated form of the binary forced-choice word association test will be administered. The eye fixation test will require the subject to fixate successively illuminated targets at varied but preset degrees of separation in horizontal, vertical and intermediate loci from a central reference point of fixation. The word association test will consist of a randomized sample of items from the subscales of the binary forced-choice test. At the end of this interval, a 2-1/2% sodium amytal solution will be injected at the rate of 1.6cc/minute. Or, in the case of certain control subjects, the normal saline will continue and no amytal will be introduced.

The amytal solution will be started without the subject's knowledge. Concurrently, the subject will be interviewed as to standard classificatory information, eg, age, residence, occupation, etc. The interview will continue until clinical signs of altered consciousness, eg, slurred speech, affective appear and the non-specific or spontaneous GSR activity has changed. This latter event is regarded as indicative of the drug effect threshold. The administration of the drug will now be slowed to maintain wakefulness in the subject. The subject will now receive taped word association tests (free and binary forced-choice) for a 15 minute period, and eye fixation tests before, between, and after the word association tests. Material for recall following the interview will be presented to the subject coregardless of the binary forced-choice test. Response profiles will attempt to elicit material of particular relevance to the individual's psychiatric-legal status. The entire session will be completed between from 45 to 60 minutes. All responses and interview material will be tape recorded for subsequent analysis.

The control subjects will receive identical tests. However, in the case of the normal volunteer group, no word adaptation time will be scheduled although the same testing intervals will be maintain; These subjects will be interviewed with respect to specially prepared factual material and items of personal information to be withheld unknown to the experimenter. Motivation of the subjects will be rejected by combinations of aversive consequences, eg, electric shock to the leg, decrements in monetary compensation. Standardized instructions and procedures will be used to control for any bias due to subject-experimenter relations and other social variables.

Test data will be treated by the following methods: Interview data will be summarized and related according to topics and stenotyped for independent rating of categories and affective content by qualified staff psychiatrists. Topic categories will be divided between spontaneous and nonsensational material relevant to central or focal issues and peripheral matters. Further subdivision will be made based upon detailed scrutiny of the obtained data, fitting such topics as illegal actions, sexual behavior, social relationships, etc, into standard units of subject matter, orientation (pro, con, and neutral), standards and values (premises of material), traits and subjective states (feelings). Each topical code will be checked for completeness, comprehensibility, consistency, uniformity of coding units, and inappropriate responses. All statements will also be classified as to factual, preference, and identified nature. Numerical ratings will be made of the coded statements as to the intensity of affect and the degree of closeness to focal issues. Amenable data will be transformed to mutually exhaustive class coded, and key punched for computer handling. Response profiles of psychological test scores, wall associations, GSR activity, (nonspecific and stimulus-elicited), EEG measures, and eye movement
parameters for individual subjects and distributions of these variables for groups and total sample studied will be prepared. Correlational procedures and where indicated multivariate analysis of variance and covariance will be carried out to establish the significance of findings. Comparisons will be made between the non-drug and amytal data within individuals and within and between the experimental and control groups.

Particular attention will be given to the analysis of eye movements during altered states of consciousness. This measure will be examined for changes in the rate and sequence of spontaneous and smooth tracking movements, the incidence and frequency of fixation change and blinking, the coincidence of "type" of eye motion with specific emotionally-toned interview material, the quality of directed eye vergence motions during target fixation tests, and the variations in binocular coordination (conjugate and disconjugate movement). Since preliminary tests have revealed that, visually observed, disconjugate and divergent eye movements are associated with amnesia, it is planned to incorporate real-time data reduction of this variable by an analog signal correlator after further confirmatory testing. The experimental design as described above is schematically given in Figures 1 and 2.

Significance

The results of these studies will add to basic knowledge on the mode of interaction between anxiety and thought as expressed through verbal productions. This has far reaching implications for the theoretical concepts of psychotherapy. An opportunity will be afforded to test clinically derived postulates formulated on the change of behavior under intravenous amytal and related drugs. In particular, a significant evaluation of the use of amytal in eliciting information during interrogation will be obtained. Standardization of these techniques will permit their application and comparison with the effects other pharmacologic agents have on verbal responses. Particular phenomena such as the dramatic resolution of catatonia and stress induced stupors will be further elucidated. Predictive methods to assess potential for explosive assaultive and homicidal behavior of habitual drug and alcohol users will be explored. This is of timely importance in view of the fact that fully half of the currently recorded homicides are associated with drug or alcohol use.

Facilities

The general ward facilities of the hospital are available for these studies. Included are personnel familiar with handling patients under stress as well as assisting in patient care during amytal interviews. Appropriate neuro-radiological and electroencephalographic studies of selected patients are performed as part of hospital care. In addition to the usual equipment and medication necessary for patient care there is available two Norelco tape recorders with special boom and microphones for recording the patients' productions during an amytal interview and foot pedal for transcribing afterward. There is also a Gray Audograph and Dictaphone to assist in handling the detailed biographical material. Office and laboratory space are provided by the

consultation and use of their equipment and personnel, Dr. of Anesthesiology, has also offered the use of his facilities.

General facilities at are available for control aspects of these studies. Office and laboratory space are provided by the Department of Psychiatry. Ready access to consultation with experts in electroencephalography in the Department of Neurology and liaison activities with the Department of Physiology and Pharmacology exist. The Department of Biomedical Engineering is available for consultation and use of their equipment and personnel, Dr. of Anesthesiology, has also offered the use of his facilities.
<table>
<thead>
<tr>
<th>Instrument</th>
<th>Measure</th>
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<tbody>
<tr>
<td>Psychological</td>
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<tr>
<td>WAIS</td>
<td>Profile and Standard score</td>
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<td>Taylor Scale and IPAT Battery</td>
<td>Standard Scores</td>
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<td>EEG</td>
<td>IQ; verbal; performance</td>
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<td>Psychiatric Interview</td>
<td>Categorized Topics, Content Analysis, Intensity and Relevancy Ratings</td>
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<td>Polygraph</td>
<td>Wave pattern, E alpha</td>
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<td>Recordings</td>
<td>conjugate-disconjugate, fixation and blinks, quality of vergence, sequence and rate of tracking movements etc.</td>
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<tr>
<td></td>
<td>conductance units, latency, amplitude changes, frequency of nonspecific responses</td>
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Figure 2. EXPERIMENTAL SEQUENCE AND DATA ANALYSIS

- Psychiatric Evaluation & Screening Interview
- Psychological Testing
- Word Association Tests & Interview
- Simultaneous EEG, EOG, & GSR Monitoring

No Amytal

Intravenous Amytal or Saline Control

No Amytal

Session 1

Session 2

Session 3

RAW DATA

All Parameters Measured, Scored, Coded, & Collated

Summary Statistics on Individuals & Groups by Session & Experiment

Correlation of Verbal and Psychophysiological Statistics

Inferential Statistical Analysis

Descriptive Qualitative Report of Findings
for consultation and limited use of varied equipment, e.g. analog computer. A Tandberg tape recorder, microphones, Edison Voice Writer, and office equipment are available for use through the Sub-Department of Behavioral Sciences. A computer unit and services are present for data reduction and analysis. A six-channel Grass-polygraph with appropriate preamplifiers is available, on a loan basis from the Department of Neurology, for use with the control subjects at

II Supporting Data

A. Previous work
References


Goldman-Eisler, F., Speech production and the predictability of words in context, Quart. J. Exp. Psychol., 1958, 10, 96.


Lindemann, E., Psychological changes in normal and abnormal individuals under the influence of sodium amytal. *Am. J. Psychiat.*, 1932, 11, 1083.


Miller, N. E., The analysis of motivational effects illustrated by experiments on amylobarbitone sodium, Chapter 1, in *Animal behavior and drug action*, 1954, Ciba Foundation Symposium.


Trent, C., Changes in the Clyde Mood Scale produced by a sleep threshold dose of amobarbital, Psychopharm., 1962, 3, 468-472.


### BUDGET ESTIMATE FROM OCTOBER 1, 1966 (ALTERNATE NOVEMBER 1, 1966) THROUGH SEPTEMBER 30, 1967 (ALTERNATE OCTOBER 31, 1967)

<table>
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<td>30</td>
<td>$</td>
<td>(sub-total)</td>
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</table>

Fringe Benefits (9% of total salaries)

Consultation Services
- Engineering Psychiatrists - Independent ratings of qualitative data in Research Pharmacologist

Equipment
- Polygraph recorder, 6 channels with preamplifiers and accessories

Consumable Supplies
- Electrodes
- Electrical parts (relays, timers, stimulus lights)
- Polygraph paper
- Magnetic sound recording tape
- Office Materials
- Psychological Testing Materials

Travel
- Domestic, (estimated 30 round trips)

Hospitalization
- None

Iterations
- None

Subject Costs
- Ten paid volunteers at $ per experiment (total of 3 sessions)

Publication Costs
- Data Preparation and Processing (includes computer services)

Sub-Total $ Overhead (47.8% of salaries) $ TOTAL $
# DIRECT COST BUDGET ESTIMATE FOR FIRST YEAR AND CONTINUATION OF PROJECT

<table>
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<th>SECOND YEAR</th>
<th>THIRD YEAR</th>
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<td>Consultant</td>
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<tr>
<td>Equipment</td>
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<tr>
<td>Supplies</td>
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<td>Travel (Domestic)</td>
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<td>Subject Costs</td>
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<tr>
<td>Publication</td>
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<td></td>
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</tr>
<tr>
<td>Data Preparation and Processing</td>
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</tr>
<tr>
<td>TOTAL</td>
<td>$</td>
<td>$</td>
<td>$</td>
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</tbody>
</table>

Estimated Direct Cost Total for entire proposed project period: $ __________

Remarks

Equipment costs for the second year are for a more complete analysis of the degree of conjugate eye movements through the use of an analog signal correlator.

Equipment costs for the third year are not estimated at this time, but are contingent upon the results of the preceding two years work. It may be advantageous to examine other parameters of EOG and EEG with the aid of a scanner system (analog to digital data reduction) connected to IBM punched card output equipment.
All research carried out in this project shall include signed statements of informed consent by the subjects and also provide for confidentiality of data. These procedures will be carried out according to the standard policies of both