# THE BLACK VAULT

25.

January 11, 1966

Dear Dr.

As a follow-up to our conversation I am attaching an outline of a proposed research project designed (a) to elucidate the physiological mechanism(s) underlying the electrodermal response, and (b) based on such information to determine procedure for maximizing the information content of recordings from this system.

Since this represents only an informal proposal, I have attached only an approximate schedule of costs. I would expect these costs, including overhead, to amount to between for one year. The project would be handled administratively through the Business Office

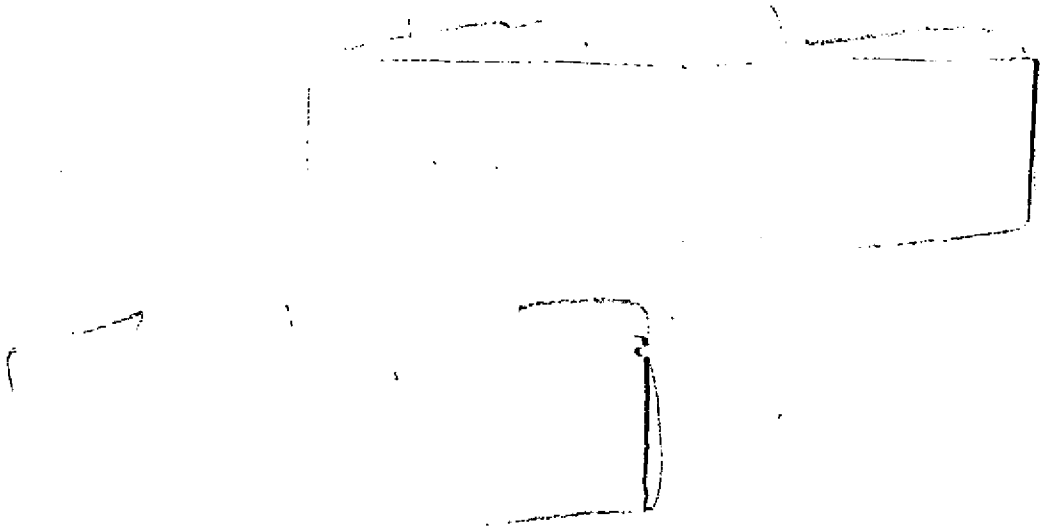
Any official correspondence in connection with possible negotiation of a grant or contract may be addressed to

If you require clarification or modification of various aspects of this proposal, please feel free to contact me further.

Sincerely yours,

Informal Proposal

# PHYSIOLOGICAL MECHANISMS UNDERLYING THE ELECTRODERMAL RESPONSE



Physiological Mechanisms Underlying the Electrodermal Response

## INTRODUCTION

The manifold uses to which electrodermal measurement has been applied testify to the respect held by a large number of investigators for its potential information content.

Various measures of this exquisitely sensitive system have, in fact, been used for several decades, hopefully, as indices of "emotional" activity.

On the other hand the highly controversial state of this area, and the distrust with which it is viewed by an equal number of competent investigators, are indications of major lacunae existing in this field of knowledge. In recent years several lines of evidence have to an extent revealed the explanation for this lack of agreement; namely that the electrodermal response amplitude and base level are multi-determined by a combination of relatively independent systems which combine in varying proportions according to the nature of the behavior taking place. Among systems experimentally implicated in this response are the sweat gland secretory tubule, the sweat gland duct, an epidermal barrier layer, the corneum and cutaneous blood vessels. Within these systems there are controversies over the nature of the physiological change giving rise to the electrical change. There is, furthermore, much argument over the relation between conductance measures and passive potential measures. Are these in fact independent as recently evidenced or are they different manifestation of a common process as claimed by a group of equally responsible investigators? If they are independent,

how do they interact? Is it possible that the skin potential response is in part of vascular origin?

Besides the limitation on our capability for meaningful, quantitative conversion of electrodermal data presented by this inadequate knowledge, it also prevents valid interpreatation on a psychological basis. If our inferences regarding higher level nervous (and emotional) activity of an individual are drawn from observation of his adaptive behavior, we must obviously be able to recognize the type of adaptation he is using. Cutaneous activity may biologically represent a preparation for aggressive muscular action, defense or flight or for information intake. The recent demonstration that the GSR is augmented on the side of the body involved in a muscular maneuver (33) lends further weight to its interpretation as adaptive behavior. The likely mechanisms involved in the various responses are vasomotor activity, thermal sweating, mechanical (moisturizing) sweating, water conservation (reabsorption) or sensitization of peripheral receptors. Recognition of the particular systems activated should enable qualitative identification of the gross behavior.

## STATEMENT OF THE PROBLEM

In using electrodermal activity as an indicator of central nervous system response to external stimuli, one would hope that its output can be in some manner calibrated in terms of quality as well as intensity of neural activity for use in qualitative as well as quantitative evaluation of central state. Distortions or lack

of reliability in this indicator can arise as a consequence of unacceptable technique or error in "neural calibration", that is in failure to recognize the considerations to be used in transforming from changes in conductance or potential to changes in central outflow. While our understanding of the principles of technique of measurement has already advanced to a point at which it need no longer constitute a major source of error, the same can not be said for our knowledge of the underlying physiological system or systems. Insofar as each primary suspected component (i.e. sweat gland, epidermis or vasculature) implies a different type of adaptive behavior, and insofar as they may interact in such a way as to present spurious information regarding the behavior of the individual, it is proposed that efforts shall be devoted to elucidation of the responsible systems and the means of separation. Particular attention will be paid to the potential measure which, because of its partially combined positive and negative components with their apparent stimulus response specificity, has a higher information than the conductance responses which are always unidirectional. In general the project will be directed toward calibration of electrodermal activity in terms of specific types and intensities of neural activity by elucidation of the various underlying mechanisms and their quantitative interrelations.

In the following discussion the entire group of reflex responses, whether they be change of resistance or conductance or a positive, negative or biphasic change in potential, will be collectively referred to as electrodermal activity.

The galvanic skin response or skin conductance response will be abbreviated SCR and skin potential response, SPR.

## EXPERIMENTAL BACKGROUND

### Areas of Agreement

There are several areas in which experimental evidence is currently in general agreement. Only key references are cited for each. (Many other aspects which have been experimentally demonstrated but not yet generally accepted are omitted). Areas of agreement are as follows:

1. That the electrodermal reflex depends on a sympathetic nervous supply (1).

2. That it is cholinergic, being completely blocked by the iontophoretic introduction of atropine (2).

3. That the sweat gland is functionally involved, at least in part, in this reflex (3).

4. That there is not a simple relation between sweat production and resistance change (4).

5. That amplitude of the resistance response falls off with increasing frequency of the excitation current (5).

6. That the resistance response can be potentiated or attenuated by various mild agents to which the skin surface is exposed (6).

7. That skin resistance is an apparent resistance, which in large part derives from a polarization potential (7).

8. That the "resistance" level falls with increasing current strength (6, 8).

9. That the resistance response and the negative SPR persist for a considerable period after arterial occlusion, while the positive wave is reduced (9).

10. That skin resistance falls with increasing temperatures (10).

11. That vascular reflexes have little effect on the skin resistance response (11).

12. That the GSR may be elicited by stimulation of area 5 of the pre-motor cortex which utilizes the pyramidal tract as a descending pathway, or by stimulation of portions of the hypothalamus or midbrain reticular formation. These two pathways are separate (12).

Controversies Posed by Experimental Findings

There are several basic contradictions or areas of uncertainity implied by other experimental data:

1. Skin potential responses (SPR) and skin conductance responses (SCR or GSR) had been considered by most workers as derived from the same functioning system. Both are eliminated by cholinergic blocking agents (13); they are highly correlated and are of highest amplitude on the palmar and plantar surfaces (14). Nevertheless, high SPR activity, without any SCR activity, has been found by , on the nail bed. Furthermore, has provided electrical and pharmacological evidence for the independent

origin of these effects. [redacted] have been able to abolish SPR but not GSR by exsanguination.

2. The sweat gland has long been considered as the source of electrodermal activity. Yet the nail bed noted above contains no sweat glands but produces potential responses very similar in form and occurrence to those from nearby skin. Furthermore, the output of sweat (vapor) from the skin has been shown under many circumstances to bear little relation to the level of electrodermal activity (4). It has also been possible using microelectrodes to obtain GSR's from slabs of epidermis which have been surgically and electrically isolated from adjacent sweat glands (18).

3. Both the positive and negative components of the SPR are abolished by atropine or hyoscyamine and are considered by many to be components of a single process (19). However, the positive component is more sensitive to ischemia (9). In the cat, [redacted] found only negative responses from the sweat glands, positive only from nearby epidermis. Moreover, reflex absorption of water through the skin (probably epidermal) is associated with the positive wave of the SPR (21). There is evidence for a stimulus response specificity in the positive and negative waves in that positive responses are associated with alert goal-oriented behavior (22). The negative wave appears to be relatively non-specific. The positive and negative waves also respond differentially to temperature change (23).

4. The skin conductance response has been generally assumed to be a single entity (12), but much evidence supports the view that it depends on two

different components (24). While the evidence for two components under separate control is strong, the case for the epidermis as one of these is presently on shaky grounds, especially as a result of the findings on the nail bed. The most likely alternative is another type of sweat gland, presumably thermal, since the palmar and plantar sweat glands are primarily non-thermal (25).

5. The almost abandoned notion that the SCR is produced by the increased conductivity of the corneum as it becomes permeated by a conducting electrolytes (sweat) has been revived by [redacted] on excellent experimental grounds. Postulation of a water barrier within the corneum allows retention of this hypothesis in the face of the observation that SCR's occur even in skin soaking in NaCl. [redacted] has argued that the inability of his model to explain many of the membrane-like properties of the skin is easily circumvented by assuming that the corneum itself may have membrane-like properties which change with hydration or electrolyte content (27).

Alternative Models

Several models of the electrodermal effector system are suggested by the experimental data and each of these will be used as a test vehicle for interpretation of experimental results in the proposed study. The consistancy of experimental results with each of these models will be considered in an effort to arrive at the most probable system.

The actual system may be, and likely is, a composite of two or more functional systems which may be listed for convenience as follows:

A. The Sweat Gland

1. The sweat gland body may undergo permeability changes which account for conductance or potential changes.

2. The sweat gland duct may undergo permeability changes which account for conductance change or potential change of the same or different nature as in (1).

3. The sweat gland duct may fill partially or completely and thereby create a channel of high conductivity. This in itself would normally cause only a conductance change, but in reducing the internal resistance of the sweat gland "generator", would result in a great contribution of sweat gland potential to total skin potential.

4. There is likely an active reabsorption process occurring in the sweat duct and this may be associated with characteristic potential waves.

5. Sweat gland secretion may function in moisturizing the corneum to protect it against abrasion during anticipated activity. It may alternatively function in thermoregulation in anticipation of a heat load. The level of this latter function would in all likelihood depend on the general state of thermostasis.

B. The Corneum

The corneum may act as a series resistor whose value is altered by degree of hydration occasioned by sweat glands and possibly epidermal transpiration.

C. The Epidermis

1. The epidermis may behave as a capacitor of essentially unchanging structure in parallel with the sweat gland. Leakage of this capacitor may be

insignificant or it could account for a conductance even exceeding that of the sweat glands.

2. It may behave as a barrier whose permeability is altered relatively slowly by humoral mechanisms.

3. It may behave as a barrier whose permeability is reflexly altered. This alteration may

a) function in insensible perspiration

b) function in reabsorption of water secreted by the sweat glands

c) be a by-product of the release of a chemical mediator by nerve endings whose function is to sensitize tactile receptors (28).

4. It may behave as a double-layered barrier, the outer layer contributing to the base potential and base conductance but static in nature, the inner one also contributing but subject to reflexly induced changes in permeability and therefore responsible in part for the GSR and SPR (23).

D. Blood Vessels

1. Alteration in blood volume is known to contribute to conductivity changes, though normally to an insignificant degree. In some cases, namely when electrodermal activity is of low level and the tissue is highly vascular, this could represent a significant relative effect.

2. Smooth muscle activity, either arterial, arteriolar or venous, constitute another source of potential. Inhibition could give rise to a different potential than contraction.

EXPERIMENTAL APPROACH

Attention will be given to possible resolution in the foregoing areas of controversy or uncertainty. Five primary questions may be used as the basis for formulation of research efforts:

1. Does the skin conductance response depend upon activity in the sweat gland alone, or does it (in addition) depend upon activity in an epidermal layer or in blood vessels.

2. Do the positive and negative components of the skin potential response depend upon activity in separate areas, e.g. sweat gland and epidermis (or blood vessel) or do they simply represent two phases of a process in a single effector organ?

3. Which component, epidermal or vascular, most likely accounts for the skin potential responses observed in a sweat gland-free area such as the nail-bed?

4. What is the biological (psychological) significance of each component? Are they qualitatively different? Do they vary in sensitivity?

5. How do separate elements in the skin combine to account for a given conductance level or a given potential? To what extent are elements in parallel and in series, and to what extent does the internal resistance of one component influence the manifestation of activity in another? What is the most rational approach to the correction of observed response amplitude for differences in base level?

Method

Each of the above postulated mechanisms represents a target for experimental evaluation as to its actual role in the electrodermal reflex. As

the tenability of each of these is experimentally indicated, attention will be given to the relative magnitude of contribution both to base level and response amplitude, and to the manner in which its contribution interacts with contribution of the other components. In each case skin conductance, skin potential, SCR and SPR will be simultaneously observed for quantitative test of interaction effects as well as consistancy with each proposed model. Specific experiments designed to aid in the answer to each primary question are outlined below.

1. Is the sweat gland alone involved in the skin conductance response?

a) Microelectrode experiments based on the isolated epidermal slab technique (18) will be continued in an effort to establish whether the observed SCR activity is real or is an artifact of sweat gland activity. This will primarily involve close examination of phase and wave-form relations of simultaneous recordings from the slab and nearby sweat glands.

b) All sweat glands in a micro field will be selectively inactivated by the iontophoretic introduction of silver ion (method already established by principal investigator) and observations made of recordings from this area and from nearby intact areas.

c) Efforts will be made to selectively reduce pick-up from non-sweat gland areas by infiltration of the upper layers of the corneum with paraffin. Preliminary experiments reveal that sweat glands continue to secrete after this procedure. The effect of this treatment on conductance and on conductance response will be examined.

d) The average sweat gland (microelectrode) response amplitude and resistance level from a 0.3 $cm^2$ field will be compared with that from a simultaneously recorded macroscopic site by a sampling technique. Total sweat gland count will also be made in this delineated area. A gross electrode will then be applied to this field and the magnitude of response and resistance level compared with that calculated from the individual data. Discrepancies will be examined for indications of non-sweat activity.

e) Experimental miliaria will be used to block sweat glands selectively. This method, [redacted] involves stimulation of keratin formation at the sweat pore by use of high currents. Affected areas will be compared with adjacent sweating areas.

f) Atropine has been shown to block all SCR activity but the effect is inconclusive for resolution of the present question since other effectors may also be cholinergic. Pilocarpine induces profuse sweating and may be considered to raise sweat gland output to a maximal level. Therefore any alteration in skin resistance after iontophoretic introduction of pilocarpine (30), may be considered as probably non-sudomotor. However, the complete abolition of electrodermal response would be somewhat inconclusive for the same reasons as stated for atropine.

g) The sweat gland may be having an indirect but important effect on SCR amplitude by virtue of the induced change in corneal hydration as postulated

by; [redacted]. If he is correct, one should expect SCR amplitude to be just as large with a constant current system as with a constant voltage system even with a relatively "dry" electrolyte such as 0.1 NaCl in 90 per cent glycerol. If change in hydration is relatively minor the constant voltage system will result in diminished amplitude, owing to a significant loss of the "constant" voltage across the non-varying corneal resistor.

2. Do the positive and negative components of the SPR originate in separate sites? Because of unavoidable electrical leaks one can always expect contamination of signals in one area by those in the adjacent area. Results of microelectrode surveys will therefore be suggestive rather than definitive. Moreover, the positive and negative components, though slightly out of phase, are to a great extent fused and subject to partial cancellation. In fact a positive wave may occur without the combined wave ever going positive (31). Resolution of the two components is understandably difficult.

a) Experiments on epidermal slabs (microelectrode) previously confined to conductance measurements will be extended to potential measurements. Wave forms from the two areas will be examined for predominance of either polarity.

b) The effect of $Ag^{+}$ inactivation of the sweat gland on microelectrode wave forms of response from various areas will be determined.

c) The application of an external load (shunt) will be used to determine whether the internal resistance of the positive and negative generators are different.

If the two waves are differentially attenuated when a low resistance shunt is used, this would be evidence for different internal resistances of these two components and therefore for different sites. It would be important to rule out temporal changes in the impedance of a single generator, as an alternative explanation. This would be done by comparing the magnitude of any difference in the internal resistance with the maximum variation in total resistance observed during the response. This latter can be determined by a simultaneous writeout of resistance using a 5 mv, low frequency AC source (32).

d) The report by [redacted] that high current density differentially affects the positive and negative components of the SPR will be followed up by a microelectrode study. High currents will be applied selectively to sweat glands and non-sweat gland areas to determine whether the waves from these are differentially affected by this treatment.

3. Are the potential responses observed from the nail bed epidermal or vascular in origin?

a) The nail will be exposed to electrolytes such as 1 M $CaCl_2$, known to have a marked effect on SPR amplitude on the skin. It is very unlikely that this agent is exerting any effect on blood vessels.

b) Vascular changes of short duration will be imposed by the use of venous and arterial cuffs and the effect on SPR will be noted. Naturally occurring vascular response in the nail bed, monitored by the reflectance plethysmograph, will be compared with the simultaneously monitored SPR. The same will be done on conventional skin sites.

c) The pharmacologic experiments by [redacted] which discounted the role of vascular responses in the SCR will be extended to SPR measurements.

d) The nail bed will be punctured to determine whether SPRs are still observable under the epidermis.

4. What is the biological significance of each component found?

a) Does the sweat gland secretion represent anticipation of a thermal load or does it serve primarily for moisturizing the skin or are both functions involved? The guiding hypothesis in this case is that both types of sweat glands function separately and according to the demands of the anticipated act. It is further hypothesized that in a well integrated organism, thermal sweating should be associated with cutaneous vasodilatation. Special attention will therefore be given to areas or to instances in which the electrodermal response is associated with dilatation as opposed to the vasoconstriction more commonly occurring. SPRs and SCRs respectively associated with these will be examined for characteristic differences. The effect of ambient thermal conditions on each will be examined.

b) Is the positive wave of the SPR causally related to epidermal absorption or transpiration of water as previously indicated (21)? Clarification of this relationship will be obtained by observing the concomitant effects of ischemia on the positive SPR and reabsorption activity; similarly for the effects of high current density.

c) What is the relationship of activity of specific electrodermal components to tactile sensitization? In a previous study (28) although there was a significant relation between skin conductance response and change in tactile threshold, there were many SCRs not associated with a tactile change. If there is, in fact, a peripheral sensitizing mechanism as previously postulated, it is possible that the threshold change is associated with one of the two components of the SPR. Tactile thresholds will be determined in conjunction with skin potential recordings. The separation of positive and negative potentials will be aided by the use of a newly developed electronic analyzer.

5. What are the principles of summation and interaction between component mechanisms and what rationale is indicated for correction of response amplitude for base-line differences?

a) The approach to this will depend on future methods developed to obtain separate measurement of the activity of each component. Such measurements will be applied to test the validity of various physiological and circuit models of the integrated system. Among these methods may be:

1) Measurement of SPR from the finger nail and from nearby skin. The differential factor here would be sweat gland activity.

2) Selective block of sweat glands by $Ag^{+}$ or experimental miliaria.

3) Microelectrode sampling of an entire skin field (sweat gland and non-sweat gland areas).

4) Simultaneous measurement of SCR and SPR from two equal areas having a different sweat gland count.

5) Measurement of vapor under standard conditions when the sweat glands are nonfunctioning, and when they are secreting. Simultaneous observation of SPR and SCR would be made.

b) The combined analysis of SCR and SPR data with the use of external shunts to determine the respective generator impedances will be used in an effort to build a unified model.

c) The predicted peripheral relation of response amplitude to base level under a variety of conditions will be tested. Relation to central level of activation is a separate matter. Frequently central activation is the variable sought for the indicator being base-line-corrected reflection of neural outflow. With this philosophy, it becomes clear that central variation must be avoided in this phase. Two methods are suggested:

1) Stimulation of the distal stump of the severed plantar nerve of the cat. This investigator has already done exploratory experiments in which base level conductance of the foot pad was brought to a high level by repetitive neural stimulation, followed by standard stimuli at 30 second intervals as the base conductance gradually fell (recovered) over a thirty minute period. These experiments will be continued.

2) Because human skin probably does not behave exactly as the cat foot pad, similar experiments will be performed on human paraplegic

patients, using a standard electrical stimulus to the foot and recording from the opposite foot. This spinal reflex system has many of the properties described in (1).

3) A final preparation of this nature is the use of a nerve block on the hand in the region of the ulnar nerve, with a standard electrical stimulus applied to the nerve distal to this block, using surface electrodes. Electrodermal responses will be measured from the tip of the fifth finger.

References


1. Richter, C. P. A study of the electric skin resistance and psychogalvanic reflex in a case of unilateral sweating. Brain, 1927, 50:216-235.
2. Leva, J. Ueber einige Körperliche Begleiterscheinungen psychischer Vorgänge mit besonderer Berücksichtigung des psychogalvanischer Reflex phänomens. Munchen. Med.-Wschr., 1913, 60:2386-2389.
3. Rothman, S. Physiology and Biochemistry of the Skin. Univ. of Chicago Press, Chicago, 1955.
4. Edelberg, R. Independence of galvanic skin response amplitude and sweat production. J. Invest. Dermat., 1964, 42:443-448.
5. Forbes, T. W. and Landis, C. The limiting A.C. frequency for the exhibition of the galvanic skin ("psychogalvanic") response. J. gen. Psychol., 1935, 13:188-193.
6. Edelberg, R., Greiner, T. and Burch, N. R. Some membrane properties of the effector in the galvanic skin response. J. App. Physiol., 1960, 15:691-696.
7. Gildemeister, M. Der sogenannte psycho-galvanische Reflex und seine physikalisch-chemische Deutung. Pfl. Arch. f. d. Ges. Physiol., 1915, 162:489-506.
8. Grings, W. W. Methodological considerations underlying electrodermal measurements. J. Psychol., 1953, 35:271-282.
9. Wilcott, R. C. Effects of local blood removal on the skin resistance and potential. J. comp. physiol. Psychol., 1958, 51:295-300.
10. Maulsby, R. L. and Edelberg, R. The interrelationship between the galvanic skin response, basal resistance and temperature. J. comp. physiol. Psychol., 1960, 53:475-479.

11. Lader, M. H. and Montagu, J. D. The psycho-galvanic reflex: a pharmacological study of the peripheral mechanism. J. Neurol. Neurosurg. and Psychiat., 1962, 25:126-133.

12. Wang, G. H. The galvanic skin reflex: A review of old and recent works from a physiologic point of view. Am. J. Physical Med., 1957, 36:295-320 and 1958, 37:35-57.

13. Wilcott, R. C. The partial independence of skin potential and skin resistance from sweating. Psychophysiology, 1964, 1:55-66.

14. Woodworth, R. S. and Schlosberg, H. Experimental Psychology. Holt, Rinehart and Winston, New York, 1964.

19. Lloyd, D. P. C. Action potential and secretory potential of sweat glands. Nat. Acad. of Sci. of the U. S. A. Proc., 1961, 47:351-358.

23. Yokota, T., Takahashi, T., Kondo, M., and Fujimori, B. Studies on the diphasic wave form of the galvanic skin reflex. EEG & Clin. Neurophysiol. J., 1959, 11:687-696.

24. Edelberg, R., and Wright, D. J. Two galvanic skin response effector organs and their stimulus specificity. Psychophysiology, 1964, 1:39-47.

25. Kuno, Yas. Human Perspiration. Charles C. Thomas, Springfield, 1956.

30. Gibson, L. E. and Cooke, R. E. A test for concentration of electrolytes in sweat in cystic fibrosis of the pancreas utilizing pilocarpine by iontophoresis. Pediatrics, 1959, 23:545-549.

31. Holmquest, D. and Edelberg, R. Problems in the analysis of the endosomatic galvanic skin response. Psychophysiology, 1964, 1:48-54.

32. Edelberg, R. Electrical properties of the skin. In Brown, C. C. (ed.) Methods in Psychophysiology, Williams & Wilkins, Baltimore, 1965.

33. Culp, W. C. and Edelberg, R. Regional response specificity in the electrodermal reflex. Submitted for publication, 1965.

Period of Work

This proposal would cover one year of effort. It is apparent that this is an inadequate period to accomplish all of the experiments described but it would be sufficient to complete over half of them. It would be hoped that continuation of support could be negotiated if appropriate, for a second year of effort.

Amount of Support

An approximate estimate of costs is itemized below. A fixed fee grant or contract would be most desirable but a cost-reimbursement contract on a non-profit basis would be acceptable.

Facilities

Among equipment on hand is a complete microelectrode set-up, a high-gain 6 channel, D. C. polygraph, free, however, only part-time, a neurophysiological set-up for nerve stimulation and recording, animal surgical equipment and diverse pieces of accessory and test equipment such as oscilloscopes, oscillators, etc. Animal sources are available

Costs

Principal Investigator (part-time) } including FICA

Research Assistant (full-time) }

Subjects

Animals

Stenographic Services

Reproduction

Expendables (Paper, Chemicals, Electronic Supplies)

Sub-total

Overhead at 20%

Total