REVERSIBLE DISTURBANCES OF FUNCTION FOLLOWING CORTICAL INSULT

by

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TABLE OF CONTENTS

PREFACE

An experimental doctoral thesis is the product of many individuals, not solely of the one whose name adorns its front page. For direction of the experiments reported herein and for the editing of the following pages, I owe much to Professor D. O. Hebb. Dr. W. Penfield, Dr. H. L. Roberts and the staff of the Montreal Neurological Institute have given their maximum cooperation in the gathering of the clinical data. Professor G. A. Ferguson has given his time unselfishly for discussion of the statistical treatment employed. Miss Ruth Hoyt has been of aid in the sectioning and staining of rat brains. My wife, Janet Ruth Forgays, has offered her encouragement and has been of continual assistance throughout the two year course of this research. She has appropriately concluded her inestimable contribution to the present work by typing the final manuscript.

To the above people, I am in great debt.

HISTORICAL INTRODUCTION

Historically, there have been two main approaches to the analysis of cerebral function. From one point of view, it has been maintained that different psychological attributes or functions reside in different parts of the cerebrum. In contrast to this, the position has been held by many that there is no such localization of function.

It is now quite clear that many functions can be localized, in the sense that a loss of a limited region of cerebral tissue results in a qualitatively limited, or restricted, loss of function, and a loss of much cerebral tissue elsewhere in the brain does not produce the same loss. Destruction of Brodmann's Area 17, for example, or of a certain small region in the hypothalamus, results in a selective loss of vision or of temperature control. Larger destructions of other areas of brain tissue have no such effects.

On the other hand, it does not follow that all psychologically definable functions are localized in such a way. It seems highly probable that in this matter, as elsewhere in psychological theory, a half-way position will have to be adopted and that the extremist in localization theory is pursuing a will-o'-the-wisp.

Those who have attempted to maintain the more extreme point of view have long been in difficulty in attempting to explain the variation and divergency of symptoms after an injury has been sustained by the cerebral cortex. Negative cases have been properly emphasized by von Monakow (1914), Hebb (1945), Alford (1944) and others. Most of these

workers cite instances in which large quantities of cerebral tissue have been removed in man without any resultant gross changes of function; others have shown cases in which expected symptoms have not developed after known lesions. It seems, as Hebb (1945) points out, that "The case in which the fewest symptoms follow a known surgical removal is likely to be the one in which the truest picture of the effect, or lack of effect, of the removal is given, and for the localization of function the most weight must always be given to such a case" (page 15). Another problem, with which any adequate theory of cortical localization must deal, is the presence of recovery of function after complete destruction of its supposed site of localization in the cerebrum. Partial or complete recovery follows almost every loss of function subsequent to cerebral insult. It is usual for the lost function to return gradually and presumably retraining goes on during this recovery period. Some disturbances, however, recover quite suddenly and dramatically, even when long periods of time have elapsed after the cerebral damage was sustained. With a few exceptions, the time course of the recovery process in these cases would seem to preclude a retraining explanation.

The aim of the present report is to demonstrate the existence of an unrecognized source of confusion in the interpretation of the recovery of functions after brain damage. It is generally assumed that a function lost after cerebral damage depended wholly on the injured part of the brain, and the subsequent recovery occurs because some other undamaged part of the brain acquires the lost function. However, it can be shown that in some cases, at least, this interpretation is incorrect.

There have been rare reports in recent years of symptoms which appear not immediately after cerebral injury or ablation but after a brief post-damage interval of adequate functioning. In these cases the symptoms may last for a short or a long time, and it appears that they recover spontaneously. One of the purposes of this thesis is to subject this phenomenon to experimental examination. If it is verified, the data will necessitate a revision of current concepts of cortical localization and restitution of function. If part of the brain is damaged and specific functions are only temporarily impaired, to improve slowly, then some mechanism, such as vicarious functioning, must be postulated. This mechanism would allow the recovery to take place and still be in conformity with the rather rigid doctrine of cortical localization, if this notion is to be retained. If a spontaneous recovery follows the loss of function, again complicated mechanisms, such as spontaneous neural reorganization, must be postulated as being responsible. However, if injury is sustained by the central nervous system without any apparent effect for a period of time, the symptoms appearing later, it seems that instead of postulating further and more complicated mechanisms to 'explain' this phenomenon in accord with the doctrine of cortical localization, we should perhaps revise the basic tenets of the doctrine itself. Moreover, restitution of function theory and, indeed, any adequate theory of neural functioning would have to take this evidence into account.

It is generally agreed that restitution of a function, temporarily lost subsequent to cerebral injury, must be accompanied by organizational

changes in the central nervous system. To account for these changes, the mechanisms of regeneration, reeducation and diaschisis have been proposed. An attempt will be made in the following pages to show that regeneration plays an unimportant role in the human brain as regards restitution of function, that reeducation plays a part in the restitution of function process, but by no means the major part, and that a revised principle of diaschisis must be proposed to account for the presently reported phenomenon.

Regeneration

The first mechanism mentioned above which has been proposed to account for restitution of function is that of neural regeneration. The nature of regeneration of neurons in the central nervous system has been discussed for many years. Lee (1929) has reviewed the earlier work in this field and has come to the conclusion that the evidence for its existence is very weak indeed. His review examined work of the previous sixty years dealing with many species from various lower animal forms up to and including primates. In his appraisal, Lee commented that satisfactory tests of functional regeneration were lacking in the early studies and that most of the evidence for regeneration therein was morphological. In addition he feels that this morphological evidence is not readily acceptable because of the difficulty in differentiating between regeneration and degeneration.

More recently, however, Stone (1944) and Sperry (1944 and others) have presented data confirming earlier work which indicates that

functional regeneration <u>can</u> take place in the central nervous system of the amphibian. For example, Sperry has demonstrated a completely effective regeneration of the optic nerve (this is, of course, properly speaking not a nerve but a central neural tract).

In a very provocative report Brown and McCouch (1947) describe a series of spinal cord transections in the cat and dog. They found that a good growth of axons followed their experimental lesions, but apparently these axons were deflected from their true paths by a rapid growth of connective tissue. They conclude that regeneration is possible in the central nervous system but that it is abortive due to collagenous tissue growth. (However, one could infer from their study that if one could prevent the growth of connective tissue, functional regeneration could be effective in mammals as well as amphibia.)

In man abortive regeneration has been reported, but for all practical purposes at this level central nerve-fiber regeneration does not take place (Lichtenstein,1949; Ranson and Clark, 1947; Morgan, 1943; and others). On the basis of information available at the present time, therefore, regeneration cannot be accepted as explaining the recovery of function process.

Reeducation

The second mechanism which has been proposed to account for restitution of function is that of reeducation. According to the principle of reeducation, when functions are lost because of central

nervous injury, the individual adjusts to the circumstances through learning. The mechanisms which have been proposed for this relearning seem to be of three main types: first, substitution, in which the lost function is replaced by a new one which is a really different process fulfilling the same purpose as the original lost function, and in much the same way; secondly, a reorganization of the remaining parts of a neural system after a portion of it has been destroyed; and thirdly, a relearning due to the vicarious functioning of neural structures which previously were not directly concerned in the lost and re-acquired behavior. An example will help to clarify the rather subtile difference between the notions of substitution and vicarious functioning. Let us suppose that an individual manipulates a screw-driver with his right hand, thus making specific contractions of definite muscular patterns. After injury to the hand area of the left motor cortex, it is fair to assume that the individual will be rendered at least temporarily incapable of making these specific movements. According to vicarious functioning, these same contractions will again become available to the individual because cerebral tissue which previously had little to do with these definite motions now will mediate them. According to the substitution principle, the individual may still use his right hand to wield a screw-driver because he makes use of muscular contractions still available to him which are different from those previously employed, but which are, nevertheless, successful with practice. The three mechanisms of reeducation will have to be dealt with in some detail.

The conception of substitution is holistic because it implies that the individual reacts to cerebral injury as a totally integrated organism. As in the example cited above, the individual is not severely incapacitated by a rather specific limitation of muscular ability because there are many possible behavior patterns which will accomplish a desired action. To elaborate on the example, the person may continue to use his right hand in handling a screw-driver if he employs muscular patterns which he previously had not, or he may merely manipulate the instrument in his left hand.

The writer who has chiefly supported the conception of substitution is Kurt Goldstein. He believes that a <u>true</u> recovery of function can take place only if the cerebral tissue mediating the function is anatomically restored and thereby returned to normal service (Goldstein, 1931; 1932). This type of recovery will occur spontaneously without any special training (Goldstein, 1942; 1948). For Goldstein, however, the most likely method of recovery is a re-adaptation of the patient which enables him to live without the lost functions. This usually involves a slow learning, with tedious practice, of roundabout replacement functions, such as the use of the left hand in operating a screw-driver as mentioned above. These replacement functions are dependent upon the parts of the central nervous system which ordinarily mediate them. In other words, no true functional restitution follows the damage of cerebral tissue, but recovery is still possible through substitution. For example, in discussing his observations of brain-injured aphasic patients in whom the use of words

returned very slowly after months of practice, Goldstein says: "This, then, is obviously not a result of restitution of language through improved function of the left [damaged Broca's] area; nor can it be explained as a result of a taking over by the right corresponding area of an activity it had previously shared. We are probably dealing here with an entirely new activity slowly acquired by the right area" (Goldstein, 1948, page 205).

Sperry (1947) has helped to clarify the nature of substitute activity with his experiments of crossed muscular innervation in the monkey. He reports that the reversed movements brought about by his surgical procedure were replaced quickly in cage behavior by compensatory reactions. After a few months of practice, the original reversed movements could only be evoked under special conditions of testing which precluded the use of the substitute activity. It is interesting to note that "Positive readjustment in the function of the test muscles was eventually achieved in all cases, until the monkeys could actively flex and extend the elbow in an adaptive manner" (Sperry, 1947, pages 472-473).

The second of the three mechanisms of relearning is reorganization. It is difficult to distinguish this notion from that of substitution, in which there is a reorganization of the organism as a whole. It seems, however, that the substitution mechanism ordinarily involves a long retraining period; while according to the reorganization hypothesis, when functional nervous tissue is destroyed, there is a spontaneous change in the operation of the remaining parts of the

system of which the destroyed part was a member. This adjustment is not due to regeneration, and according to Foerster (1932) all afferent and efferent tracts which can aid in the reorganization are enlisted.

An example which we may consider under the heading of reorganization is the reported formation after occipital lobe injury of a new functional center of optimal vision, called a pseudofovea. Fuchs (1920) and Goldstein (1932, 1939, 1942) describe patients with visual cortex damage in one hemisphere whose perimetric tests disclosed complete hemianopsia but whose subjective field of vision extended in all directions, with optimal vision located in the center. The same phenomenon was later reported by Bender and Teuber (1947). The mechanisms underlying this process probably include a central completion of incompletely perceived objects (Poppelreuter, 1914-1916; 1917), and a shifting of the patient's fixation so that objects which would ordinarily fall upon the blind side now will fall upon a healthy part of the retina (Fuchs, 1920; Goldstein, 1923; 1927; Bender and Teuber, 1947). This change of fixation is what has been called the pseudofovea.

The formation of the pseudofovea is a spontaneous compensation or adjustment on the part of the individual to the damage of visual cortex. Apparently in many cases the patient is not even aware of his lack of vision. Properly speaking, this is a substitution phenomenon since there is no restitution of the damaged tissue. Thus the patient "learns" to live without the damaged part of the brain. Substitution usually implies, according to Goldstein, a long and tedious reeducative process, but the formation of the pseudofovea is

reported to be immediate. It is obvious that there is some difficulty in actually distinguishing between recoveries of function due to substitution and those due to a reorganization, since both mechanisms appear at times to be responsible for spontaneous recoveries.

Poppelreuter (1914-1916; 1917) reports experiments designed to test whether a central completion of incompletely perceived objects was a factor in the 'pseudofovea' phenomenon. He exposed incomplete figures to his patients so that the completed part of the figure fell on the good visual area and the incomplete part on the injured visual tissue. He reports closure or the perception of the entire figure by the patients under these circumstances. Recently, however, Bender and Teuber (1948) could not confirm this finding and they conclude that their patients, who were also hemianoptics, "could actually 'see' in those regions of the field which seemed blind according to perimetry ....under certain special conditions" (page 6). Studies will have to be made employing special perimetric techniques before any final conclusions can be reached as to the occurrence of central completion in these cases.

Spatz (1932) believes that supposed cases of reorganization have no corresponding changes in tissue and therefore cannot be explained from a morphological standpoint. The experiments of Sperry (1941; 1947) cast doubt upon the idea that central nervous reorganization can occur immediately without any practice. In some circumstances, where it might have been expected, it does not occur at all. His work dealt with the crossing of nerves to antagonistic muscles or actual

transplantation of the muscles in the rat (1941) and in the monkey (1947). He found that this procedure brought about disruption of motor function directly related to the operative transposition. In these cases the reversed movements occurred early after nerve regeneration and persisted for some months. Therefore, under the conditions of his experimentation at least, no spontaneous central nervous reorganization takes place to adjust to the altered peripheral relations.

Examples of substitute activities cannot be accepted as evidence of <u>true</u> recovery since they are accompanied by quite severe limitations of function. In cases of aphasia, the speech "never regains its normal premorbid promptness" (Goldstein, 1948; page 205); in cases of the formation of a pseudofovea, "The patient's field is restricted and his acuity is not quite as good as that of normal subjects" (Goldstein, 1942; page 51).

The third mechanism of relearning is that of vicarious functioning. After cerebral tissue is destroyed, it is possible, according to this conception, for other parts of the central nervous system to take over the functions of the destroyed area. This conception was first used by Fritsch and Hitzig (1870) to account for the recovery from paralysis of dogs from whom they had previously removed motor cortex unilaterally. They assumed that the motor cortex of the uninjured hemisphere had taken over the functions of the injured area. To test this assumption, they removed this supposedly "vicariously-functioning" area and produced no reappearance of the original paralysis.

Further evidence contradictory to the principle of vicarious functioning was obtained by Carville and Duret (1875), Leyton and Sherrington (1917), and by Franz and Oden (1917). The experiments of Bucy (1933; 1934) and of Bucy and Fulton (1933) indicated that recovery from paralysis produced by the destruction of the motor area will take place in the monkey if the corresponding premotor area is left intact, but that the paralysis will be complete if both the motor and the premotor areas are destroyed. However, recent work casts doubt upon the supposition that the premotor area, Brodmann's Area 6, acts vicariously for the motor area, Area 4, when this has been destroyed. Denny-Brown and Botterell (1948) feel that Bucy and Fulton had a false notion of the extent of Area 6, and that this affected the interpretation of their experimentation. Denny-Brown and Botterell showed that no additional loss was displayed in the monkey when the premotor area was removed some time after the original motor area ablation. This seems to show that Area 6 does not function vicariously for Area 4. However, there is still the possibility that subcortical mechanisms, for example, the corpus striatum, may be operating vicariously in these cases.

Lashley (1922) tested the usefulness of the concept of vicarious functioning. He ablated the area striata in rats and found a loss of a pre-operatively established light-darkness discrimination. After the rats were retrained to their original level of performance, he removed all the remaining areas of the cortex in various animals and found no disturbance in retention of this <u>simple</u> visual habit in any case.

Thus he concluded that no part of the cortex was operating vicariously for the habit tested. There is the possibility, however, that here too subcortical mechanisms may be taking over the function of the cortex. In reference to this experiment, Lashley (1929) later stated that the recovery in the retraining part of the study following the first ablation is so "clearly related to the learning process as to leave no doubt that it involves a reacquisition of the habits rather than a spontaneous recovery from diaschisis" (page 103).

In the history of the development of neurological and psychological thought, many writers have felt that the brain was entirely interchangeable and that there was therefore no limit to the amount of vicarious functioning possible (Flourens, 1842; Goltz, 1881; Franz, 1923). In addition many clinicians have believed that vicarious functioning could readily occur. Henschen (1920-22), for example, finding that unilateral damage to the site of Broca's area did not invariably result in aphasia while bilateral damage to the same area always did, judged that vicarious functioning must take place quite often. This viewpoint is supported to some degree by Franz (1923), Foerster (1930), Bethe and Fisher (1931), German and Fox (1934), Woodward (1945), and Nielsen (1947). The evidence contained in these reports is not readily acceptable as crucial to the endorsement of the postulation of vicarious functioning.

Even though many writers assume that vicarious functioning can occur readily and extensively, its limits have been determined only for the motor and the visual systems as outlined above. From this evidence

alone and from the lack of confirmatory evidence of a supposedly common phenomenon, we should perhaps conclude with Lashley (1938) that vicarious functioning only takes place within limited systems of interrelated cortical and subcortical structures. These structures are assumed to be both normally mediating the concerned functions and the subcortical mechanisms are able to take over a limited amount of the cortical function when the cortex is destroyed.

Diaschisis

The third mechanism mentioned above, of those proposed by various writers to account for restitution of function, is that of diaschisis. Von Monakow (1905; 1914) suggested this conception as an explanation of those spontaneous recoveries of function which are independent of relearning. According to him, clinical symptoms following cortical destruction can be due not only to the loss of the cortical tissue involved but also to the resultant curtailment of facilitation for another area which does not function effectively without it. Subsequently, neural reorganization may take place, so that the uninjured area can function properly even without the original facilitation. This is reflected by a spontaneous recovery of the clinical symptoms. Residual symptoms, and these alone, are due directly to the loss of the destroyed tissue.

According to the principle of diaschisis, then, loss of the injured area is only indirectly responsible for the transitory clinical symptoms, and, of course, conclusions concerning cortical

localization of function must be made only from the residual symptoms. This differentiation between transitory and residual symptoms has been stressed from the time of Goltz (1881) and Loeb (1900) up to the present.

While transitory symptoms cannot be accepted as evidence of localization of function, they cannot be ignored from a theoretical point of view. Mettler (1949) reminds us that "....there might be a tendency to disregard troublesome, early, fleeting phenomena [appearing after damage to the central nervous system] as inconsequential simply because they are difficult to explain. To shirk the task of analyzing these changes by attributing them to some hypothetical general cause--such as edema--is merely self-narcotization and actually may ignore one of the most promising opportunities which may present itself" (page 485).

Material which is relevant to the concept of diaschisis can be found in the reports of those workers who emphasize that a function can be disturbed by a lesion which is some distance from the supposed site of localization of that function in the brain. Dandy (1930), Head (1926), and Weisenburg and McBride (1935) were the first to suggest this possibility. More recently, evidence which supports the point has been presented by Alford (1940, 1944, 1948), Goldstein (1942), Woodward (1945), and Riese (1949 a and b). Alford, who is the most enthusiastic contemporary supporter of the action-at-a-distance conception, feels that this proposal helps to clarify many of the discrepancies in the field of cortical localization. Most of

the writers mentioned above suggest that the distance reaction acts through shock-effects, transmitted pressure, edema, and circulatory disturbances. Although the connection between the two concepts has not been stressed, the distance reaction seems directly related to the notion of diaschisis, and both appear to be contradictory to the vicarious-function postulate. The mechanism of vicarious functioning implies that a function resides in the tissue which is directly damaged, and that other cerebral tissue takes over the function, usually with a certain amount of reeducation. Diaschisis and the action-at-a-distance notions suggest that the disturbed function may not reside in the damaged tissue but at some distance away. The original injury leads to the disturbance of the function through secondary effects of the damage. Recovery may then be due to a cessation of these secondary effects and not to an assumption of the function by other cerebral tissue. The distance reaction was proposed mainly to account for differential results of similar cerebral lesions, and for changes of function following small specific lesions in areas of the brain supposedly not related to the disturbed function. The mechanism of this action also is unknown.

Lashley (1933) points out that no limit has been set to the time requisite for recovery from diaschisis effects. Presumably, it would be difficult to determine which are transitory and which are residual symptoms. Von Monakow (1905) has emphasized that the symptoms may last for weeks and pass very slowly, and so are not to be subsumed

under the concept of surgical shock. For von Monakow there is a spontaneous recovery from the diaschisis effects, but unfortunately he did not explain the mechanism of this process and he has been criticized for this by Lashley (1938), Crook (1940), Morgan (1943) and others. Perhaps a more serious criticism of the notion is that it is very difficult to differentiate between a true spontaneous recovery and restitution resulting from retraining. As Lashley describes this situation: "The spontaneous and re-educative improvements after cerebral lesions make it exceedingly difficult to draw final conclusions from any syndrome concerning cerebral function, since a gradual improvement may be ascribed to recovery from shock, even though it occurs during a post-operative retraining."

Evidence which is said to be opposed to a diaschisis effect includes the work of Franz and Oden (1917) and Lashley (1922). Franz and Oden demonstrated that enforced use of the limbs of monkeys after lesions to the motor area brought about recovery of some of the functions of the limbs, whereas passive massage of the limbs or the complete lack of treatment led to no improvement in the condition of the paralysis. Thus, although a recovery does not seem to come about spontaneously in these monkeys, systematic reeducation produces at least a partial recovery of function. Lashley studied the retention of visual habits in rats after ablations of the visual cortex. In his experiment, he varied the time of retraining a light-darkness discrimination post-operatively. One group of rats began retraining on the seventh post-operative day and a second group began on the

fourteenth. The former group had completely reacquired the discrimination by the fourteenth day while the latter group was, at that time, at the same level of performance as the recovered group was on the seventh day. From this, Lashley concludes that lost functions that would not otherwise recover spontaneously can recover with retraining.

These experiments are not really crucial evidence against the diaschisis concept. It is possible that a diaschisis effect may not occur after direct insult to the motor or visual cortex under the conditions of the experiments. Moreover, it is quite probable that retraining will expedite a recovery even though that recovery will occur spontaneously at a later time. This point will be discussed more thoroughly in another section.

Crook's Experiment

In a study designed especially to test the hypothesis that retraining is necessary for recovery, Crook (1940) performed on rats a complete sectioning of the left lateral funiculus of the spinal cord, usually at the level of the third cervical segment. After this, for approximately five days, he restrained the rats in various ways, permitting no movement of the limbs in one operated group, and movement of the hind limbs only in another operated group. A third operated group was unrestrained, while other control groups included unoperated restrained and sham-operated restrained rats. The sham-operated control animals received the same type of operation as the

experimental animals except that the spinal cord was left intact. This group of animals permitted the evaluation of muscle separation and traumatic consequences of the operation and restraint upon the tests of motor functions employed, separate from the effect of the spinal cord damage itself. After removal of the appropriate groups from the restriction, all the rats were tested periodically for about thirty days, on thirty-five measures of motor performance.

The results of the experiment indicated that "...in general both rate of recovery and final level are greatest for the OC's" (the operated unrestrained group). In addition Crook states "that neither restraint of normal animals nor sham operation plus restraint produces, in general, any but the slightest depression on the functions measured" (page 40).

It is important to note that the operated-restricted rats showed steady improvement in most of the measures of their motor performance. This recovery is indicated by the ascending slope of most of the individual test curves shown for these groups. Even though the thirty day level of recovery for the operated-restrained animals is not as marked as that of the animals with the same operation but unrestrained during convalescence, this is no indication that the two groups would not have become more closely approximated in their motor performance had the study been carried further. In short, the final level of recovery that Crook refers to applies only to the unrestrained group and not to the restrained group whose recovery curves on individual measures are ascending in slope even at the last periods of observation.

Because of this, Crook is not justified in saying that the operated-restricted groups "apparently never reach the OC (operated-unrestrained) recovery level, but permanently possess greater residual deficits" (page 55).

This study may be merely demonstrating that restriction of limb movement following damage to the spinal cord in rats delays the time of recovery of motor function. What the mechanism of this process might be is left open to speculation, but that there might be a delay of recovery under such conditions is not crucial evidence against a spontaneous-recovery hypothesis.

The only critical tests of the hypothesis that learning is necessary for restitution of function following insult to the central nervous system would be to demonstrate that the lost functions do not recover spontaneously when there is no possibility of retraining, or that lost functions which would not recover spontaneously do, in fact, recover with training. Under the latter circumstances it is important to establish that the regained functions are the same as those lost and not merely substitute activity. Moreover, since there is no known time limit for the appearance of the diaschisis effect, it is necessary that enough time be allowed after injury without the possibility of retraining.

Reports of Spontaneous Recovery

There have been a few reports which indicate that a spontaneous recovery of function may follow a loss due to cerebral damage when the

possibility of retraining has been more or less precluded.

Loeb (1900), for example, described earlier work in which he removed the left visual cortex of dogs who possessed only the right eye. Some of these animals apparently exhibited no obvious effects of the operative procedure while others became hemiamblyopic. Some of the hemiamblyopic dogs were placed soon after the operation in a light-proof room for six weeks. When they were removed from this environment and examined, their visual reactions were found to be entirely normal. Loeb concludes that their recovery was not due to the acquiring "....of new visual images of memory but to the fact that a purely physiological effect upon the irritability of the optical apparatus caused by the operation wears off after a certain time" (pages 272-273).

Marquis and Hilgard (1936) report the spontaneous recovery of an eyelid response conditioned in three dogs before they were subjected to bilateral occipital lobectomy. The conditioned response was not present in any of these dogs at the time of the first testing on the second post-operative day but had returned by the fifth post-operative day in two of the animals and by the thirtieth day in the third. The authors rule out anesthesia and general surgical shock as responsible factors with control animals. It seems that "this temporary absence must be a specific symptom of the occipital removal..." (page 166). The phenomenon would be very difficult to explain on the basis of vicarious functioning. According to this mechanism, the conditioned response should have been present at the time of the first post-operative

testing, and possibly mediated by new cerebral tissue. More probably, after having been lost because of the operative removal, the conditioned response should have been reacquired after post-operative retraining. Since the conditioned response was not present directly after the cerebral removal but appeared thereafter without formal retraining, it would be hard to invoke the concept of vicarious functioning to explain this phenomenon.

A report of a similar occurrence in the monkey has been made by Warden, Barrera and Galt (1942). They trained two five-year old Rhesus monkeys in a multiple platform instrumentation test and then subjected them to bilateral pre-frontal lobectomies. For one monkey, this was a one-stage operation; for the other, a two-stage operation with continued testing of the multiple platform problem during the intervening month. In the case of the monkey who had the two-stage operation, the learned habit was not present at the time of the first post-operative testings (two and five weeks) and little or no recovery was evidenced at the last testing (17 weeks). The monkey who had the one-stage removal showed a similar loss at the first post-operative testings but displayed a complete recovery up to the pre-operative level of functioning of the habit at the time of the last testing (twenty weeks). The monkey who recovered the learned habit had no tests between the first and second operation, and few test trials on the first post-operative testings. The monkey showing no recovery of the habit had interoperative testing and more test trials on the first post-operative testings. The authors point out that "these facts eliminate the possibility that the difference in recovery of the two

monkeys was due to practice effects arising from the previous tests" (page 160). They also state that the brain injury was approximately the same for both animals and the same cytoarchitectural areas had been ablated in each case.

The above illustrations indicate that spontaneous restitution of function is possible after extensive injury to the cerebrum in situations in which we cannot reasonably invoke the principle of reeducation as an explanatory concept. Moreover, a distinct problem is raised regarding the residence of specific functions in definite localized areas of the brain. The temporary loss of function could not have been due merely to the loss of cerebral tissue, since a spontaneous recovery follows without retraining, and since central nervous tissue does not display functional regeneration at the higher animal levels.

There are other studies which raise additional problems regarding cortical localization and which contribute to the understanding of the recovery process. As early as 1911 reports have appeared of losses of function which did not occur immediately after cerebral injury but at varying times thereafter. Franz, at that time, noted the case of a monkey whose occipital cortex had been cauterized bilaterally. Apparently the monkey's vision appeared normal for six post-operative days. After this the monkey began to make poor visual adaptations and by the tenth post-operative day, "...his movements became like those of a blind person" (page 81). Unfortunately this animal was killed on the eleventh post-operative day,

and any recovery of visual function that may have been possible after this time is not known.

Bucy (1944) describes two patients in whom evidence of sensory loss was not discovered soon after the removal of parts of the 'motor' area but was found within twenty-four hours. The loss progressed to a more extreme degree and remained in this condition for several days, recovering almost completely in from two (second case) to four weeks (first case). "These cases", writes Bucy, "strongly indicate that the sensory loss which develops following these operations is not the result of removal of the precentral motor cortex but appears later, after edema and vascular alterations have had an opportunity to interfere with the activity of the cortex lying posterior to the central fissure" (page 393).

In Malmo's (1948) recent communication is found the case of D.H. This patient underwent the bilateral removal of the inferior orbital surfaces of the frontal lobes. Immediately after the operation and for approximately five days, she attained normal limits on the Cameron Counting Test. She then showed a depression of score for ten days, reaching normal score limits again at the end of this time.

In these accounts a striking example can be seen of losses of function which could easily have been attributed to the localized damage, to the surgical injury as such, had not testing been done so soon after operation. It is rather unusual to test patients immediately after cerebral operation, and occurrences such as those described above might have been discovered quite frequently had post-operative

testing been done early enough. In the cases reported by Bucy and Malmo, at least, the particular losses could not be due directly to the loss of cortical tissue since the concerned functions were reported intact immediately after operation, that is, after the brain tissue had already been removed. This phenomenon not only adds one further problem to be taken into account when considering theories of cortical localization of function, but also casts some light on the recovery process. If the loss of function does not occur immediately after the loss of cerebral tissue, subsequent recovery of function, in some cases at least, cannot reasonably be considered to be due to a vicarious functioning of other cerebral tissue for that damaged. In addition the recovery of function cannot be attributed to a diaschisis effect, as this concept is normally interpreted. The mechanism of diaschisis implies an immediate loss of function after cerebral damage, and therefore a delayed disturbance of function would be contradictory to the mechanism as it is postulated. However, there are other aspects of the delayed disturbance of function and subsequent recovery pattern which more closely correspond to the diaschisis notion than to the other mechanisms of recovery. These will be discussed later.

The importance of verifying this delayed disturbance of function phenomenon and the subsequent recovery pattern is evident. The phenomena affect the interpretation of the theoretical issues of cerebral localization of function and restitution of function following cortical insult.

CLINICAL DATA: ANALYSIS OF CASE HISTORIES

If delayed disturbances of function take place after cerebral damage, then one would expect to find some evidence of this occurrence in the hospital records of patients receiving operative treatment for central nervous dysfunctioning.

Case histories of patients who were admitted to the Montreal Neurological Institute from 1930 to 1950 were made available to the writer for study. Fifty histories were selected randomly from the group of patients who underwent cerebral surgery. These were examined for the appearance of a delayed disturbance of function after brain operation: that is, for a disturbance which did not appear directly after removal of cerebral tissue but at some time thereafter. The subsequent course of recovery was also examined. Frequent testings are made in this hospital both pre- and post-operatively to determine the presence of aphasic, motor, and sensory defects.

The majority of patients whose histories were selected were seeking relief from epileptic seizures. The three exceptions were cases of muscular weakness and wasting, spastic paralysis, and athetoid movements.

The operation in most of the fifty cases was performed with the use of local anesthesia during the exploratory and removal phases: that is, while the brain was being explored visually and electrographically, and while cerebral tissue was being removed. Immediate effects of the actual removal could then be observed. General anesthesia was employed during closure of the wound.

For the purposes of the present analysis, cases were accepted as examples of delayed disturbance only when there were definite statements in their records to the effect that such disturbances were not present immediately following surgical intervention and for some time thereafter. Employing this criterion, evidence of delayed disturbance was found in thirty-nine of the fifty cases selected. One of these patients, however, died on the ninth post-operative day, and was excluded from the figures reported below. Six patients displayed no post-operative symptoms, while five developed symptoms on the operating table.

It must be noted that in the following outline the same cases may be represented in more than one subdivision of post-operative delayed disturbance.

Of the cases developing delayed symptoms, thirty-four involved operation on the side of the brain contralateral to the dominant hand. Four involved operation on the side of the brain ipsilateral to the dominant hand. In both instances, all major subdivisions of the brain, the frontal, temporal, parietal and the occipital lobes, were represented: that is, at least one case of cerebral removal from each of these parts of the brain was included. In addition, one patient underwent exploration only and suffered no loss of cerebral tissue during the operation. The delayed symptoms which followed cerebral operation are classified in terms of aphasic, motor, and sensory disturbances.

In the group of fifty patients represented in this analysis,

evidence of a delayed aphasic disturbance of some type was found in thirty-seven cases. These represent all the major subdivisions of the brain. The mean time for the appearance of this disturbance after operation is 36.9 hours, with a range of from 6 hours to 7 days. According to the records, twenty-two of these cases had recovered from the delayed disturbance at the mean time of 20.5 days post-operatively (range: 8-40 days). The remaining fifteen patients showed gradual improvement as regards the delayed disturbance during their stay in hospital, but still demonstrated residual symptoms at discharge time, which is taken to be twenty-one days in this analysis.

Evidence of a delayed motor disturbance of some type was found in eighteen of the total fifty cases. These cases also represent all the major subdivisions of the brain. This disturbance appeared at the mean post-operative time of 47.4 hours, with a range of from 7 hours to 6 days. Thirteen of these patients recovered from their delayed motor disturbances at the mean time of 16.4 days post-operatively (range: 2-37 days). The remaining five cases showed gradual improvement, but demonstrated residual symptoms at the time of discharge.

Six patients suffered a delayed sensory disturbance of one type or another. In this instance, also, all major subdivisions of the brain were represented. The mean time for the appearance of this type of disturbance was 105 hours post-operatively, with a range of from 5 hours to 8 days. Three of these patients had recovered from

the delayed sensory disturbance at the mean time of 23.6 days post-operatively (range: 13-37 days). The remaining cases showed gradual improvement as regards the delayed disturbance during their period of hospitalization, but still demonstrated residual symptoms at discharge time.

If the three symptom groups are combined and the patients taken as a whole, over seventy-five percent of the case histories examined demonstrate some type or types of delayed disturbance following cerebral surgery performed mainly for the relief of epileptic dysfunctioning. The mean time for the appearance of the combined delayed disturbances is 46.7 hours post-operatively, with a range of from 5 hours to 8 days. In over half of the delayed symptoms, there is a reported complete recovery at about the nineteenth post-operative day. In the remaining cases gradual improvement of the symptoms had occurred during convalescence of the patients in hospital, with only residual defects detected in most cases at the discharge examination.

According to the present analysis, the delayed disturbances reported above are not confined to any definitely localized cortical tissue, since all major subdivisions of the brain are represented in the group of patients manifesting the disturbances. It is particularly noteworthy, in this regard, that one patient who underwent cerebral operation without removal of cortical tissue also manifested delayed transient aphasic and motor symptoms. Complete recovery of the defects in this case was effected in about three weeks.

CLINICAL DATA: PRE- AND POST-OPERATIVE TESTS

After an examination of the results reported in the first clinical study of this thesis, it was felt that intellectual functions might display a delayed disturbance pattern similar to that of the aphasic, motor and sensory symptoms noted. That is, after cerebral operation, a delayed disturbance of intellectual functioning might occur, which is separate from aphasic, motor, or sensory defects. The present study was designed to test this assumption.

Epileptic patients under Dr. Wilder Penfield's service at the Montreal Neurological Institute who were selected for surgical therapy were tested both pre- and post-operatively with a battery of eight psychological tests. The tests were selected because of their ease and briefness of administration, susceptibility of rapid comprehension, acceptibility to the testee, and their supposed measurement of varied and general capacities. The battery included the following tests:

a. The Stanford-Binet Vocabulary Test (Terman, 1916),

b. The 4th. Word Series (analogies test: Hebb, 1942),

c. The Benton Visual Memory Test (Benton, 1945), using a multiple choice version of the test,

d. The Wechsler Information Test (Wechsler, 1944; 1946),

e. The Wechsler Digit Span Test (Wechsler, 1944; 1946),

f. The McGill Picture Anomaly Series (Hebb and Morton, 1943),

g. The Wechsler Block Design Test (Wechsler, 1944; 1946),

h. The Knox Cube Test (Knox, 1914; Weisenberg and McBride, 1935).

This group of tests was given to a number of patients at from twelve hours to seven days pre-operatively, from six to eighteen hours post-operatively, and on the third, seventh, thirteenth, and twentieth post-operative days. The latter time is the approximate discharge day of the patients. Test and retest forms of the various tests were used alternately. This meant that Form I of any test was given to the patients pre-operatively and on the third and thirteenth post-operative days. Form II of the tests was given in the immediate post-operative period and on the seventh and twentieth post-operative days. The motivation of the patients as a group appeared to be extremely high at all times. The seven patients selected for report here were those who were able to be completely tested in the immediate post-operative period, and who displayed no post-operative aphasic, motor or sensory disturbances. The patients who manifested such defects will be treated in separate communications. Those included in this report represent all major subdivisions of the brain.

The mean scores obtained on the various tests and the statistical significances (using Fisher's t for small correlated samples) between the pre-operative, immediate post-operative, and the second post-operative testing results are reported in Tables 1 and 2. The graphical representation of the mean scores obtained on all of the tests at each testing period is given in Figure 1.

From Tables 1 and 2, it can be seen that the mean scores obtained on all the tests at the immediate post-operative testing period were equal to or slightly higher than the mean scores achieved at the

TABLE I

Mean raw scores obtained on the various tests at the pre-operative, immediate post-operative and the next post-operative testing periods.

Test	Number of Cases	Mean Raw Scores: Pre-Operative	Immediate Post-Operative	Third Post-Operative Day
1. 4th. Word Series	7	21.00	21.57	16.71
2. McGill Picture Anomaly Test	7	23.85	24.00	23.28
3. Benton Memory Test	7	6.42	6.71	5.42
4. Stanford-Binet Vocabulary Test	7	27.28	27.28	26.28
5. Wechsler Digit Span Test	7	11.28	11.28	9.28
6. Wechsler Information Test	7	14.42	14.85	14.14
7. Knox Cube Test	7	6.28	6.57	6.14
8. Wechsler Block Design Test	7	16.57	17.28	15.00

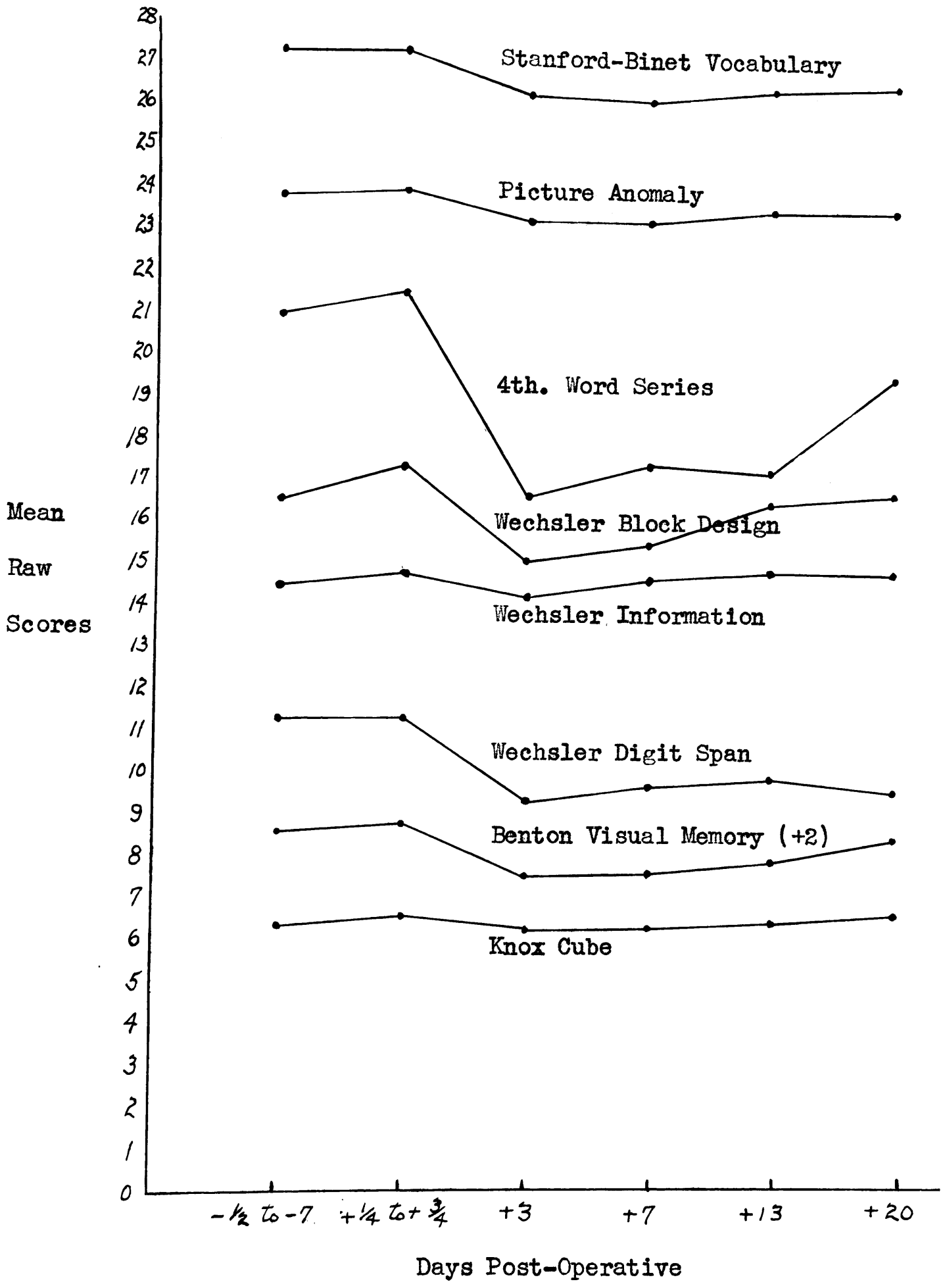
TABLE II

Significance of the differences between the mean raw scores obtained on the various tests at the pre-operative, immediate post-operative and the next post-operative testing periods.

Test	Number of Cases	Significance of the Difference Between Means of Correlated Samples: Between Pre-Operative and Immediate Post-Operative	Between Immediate Post-Operative and 3rd. Post-Operative Day	Between Pre-Operative and 3rd. Post-Operative Day
1. 4th. Word Series	7	t = 0.9313 p = < 0.4	t = 4.410 p = < 0.01	t = 3.079 p = < 0.03
2. McGill Picture Anomaly Test	7	t = 1.000 p = < 0.4	t = 3.875 p = < 0.01	t = 2.830 p = < 0.04
3. Benton Memory Test	7	t = 1.001 p = < 0.4	t = 3.058 p = < 0.03	t = 1.619 p = < 0.2
4. Stanford-Binet Vocabulary Test	7	$M_D = 0$*	t = 2.907 p = < 0.04	t = 2.644 p = < 0.05
5. Wechsler Digit Span Test	7	$M_D = 0$*	t = 2.898 p = < 0.04	t = 2.898 p = < 0.04
6. Wechsler Information Test	7	t = 2.127 p = < 0.09	t = 2.500 p = < 0.05	t = 1.001 p = < 0.4
7. Knox Cube Test	7	t = 1.015 p = < 0.4	t = 1.446 p = < 0.2	t = 0.304 p = < 0.8
8. Wechsler Block Design Test	7	t = 1.263 p = < 0.3	t = 1.456 p = < 0.2	t = 1.099 p = < 0.4

*When there is no difference between the means (M_D=0), there obviously can be no significant difference between the two groups of scores.

FIGURE 1: Diagramatic representation of the mean raw scores obtained by the seven patients on each test at each testing period. To separate the curves, two points were added to each mean score achieved on the Benton Visual Memory Test.



pre-operative testing period. None of the mean scores of the immediate post-operative period are significantly different (at the five percent level of confidence) from their counterparts of the pre-operative testing period. Any increase in mean score on the second testing is considered to be evidence of a slight practice effect.

On the third post-operative day, however, the majority of the seven patients made lower scores on all the tests used. At this time only one patient actually made a higher score, and this on just one test (Wechsler Block Design). The mean scores obtained at this testing period, on four tests, the 4th. Word Series, the McGill Picture Anomaly Test, the Stanford-Binet Vocabulary Test, and the Wechsler Digit Span Test, were significantly less than the mean scores gained on the same tests on the two previous testing periods. The mean scores obtained on the Benton Memory Test and the Wechsler Information Test on the third post-operative day were significantly lower than those secured on the immediate post-operative testing, but not significantly different from the mean scores achieved pre-operatively. No significant differences could be demonstrated between the mean scores achieved on the first three testing periods for the Knox Cube Test and the Wechsler Block Design Test.

From Figure 1 it can also be seen that the acute post-operative depression in the scores disappears, or nearly so. By the time of discharge from hospital, performance on at least half of the tests is about at its pre-operative level.

In summary, these results show a delayed intellectual defect following brain operation. The disturbance cannot be ascribed simply to the removal of cerebral tissue, for the level of intellectual functioning in the immediate post-operative period, after the tissue was removed, was equal to or better than that of the pre-operative period. Recovery from the defect apparently takes place spontaneously. Without special training, performance on many of the tests of intellectual functioning used returned to approximately its pre-operative level at the time of discharge from hospital.

ANIMAL DATA: GENERAL PROCEDURE

In order to secure more rigid experimental controls and a greater supply of available subjects than was possible in the preceding clinical study, a comparative study of the post-operative delayed loss of function after cerebral insult was undertaken.

Testing Methods

Groups of male hooded rats of the McGill colony were selected at ninety days of age and trained to run on the "Closed-field" test of rat intelligence (Hebb and Williams, 1946; Hebb, 1947; Rabinovitch, 1949). This test is essentially a variable maze, or series of 24 relatively easy maze problems. The apparatus consists of a box 30 by 30 by 4 inches, plus starting and food boxes at opposite corners. Quarter-inch mesh wire covers the entire structure. Stable barriers of four inch heights and of different lengths are put into the closed-field, or large center section. They vary in position from problem to problem. The object of each test is for the rat to begin in the starting-box, proceed through the section where the barriers are, and eventually arrive at the 'goal' box where freshly moistened ground mash is available. Each rat is tested after twenty-four hours of food deprivation. The shortest possible route from the starting-box to the food box is accepted as an errorless route. Any course which deviates from this route is assigned an error score which is the number of entries into previously marked off "error zones".

Preliminary training involves the acclimatization of the rats to the new environment of the closed-field test by placing them in it in groups of three to five for a few hours a day. At these times sample barrier problems are set up and food is placed in the 'goal' box, even though the rats are not food deprived. After three days of this type of exposure the rats are food deprived for twenty-four hours and put singly into the starting-box, with sample barrier-problems still being used. Each rat is given ten trials a day under these conditions. A trial is a complete excursion from the starting-box to the 'goal' box. A rat is considered to be ready for actual testing when any nine of his ten daily trials in the practice series are completed within one minute of running time. Testing of all the rats awaits reaching of this criterion by all of the rats in each particular group. This is normally achieved one to two weeks after the commencement of preliminary training.

The present study made use of closed-field problems standardized by Rabinovitch (1949). They consist of two series of twelve problems each. The two series of problems are roughly equated as to difficulty and they correlate highly with each other (Reliability of the total series is .75 to .80). When all of the rats in a particular group have met the criterion mentioned above, they are run for twelve days on the first series of test problems, ten trials on each problem and one problem per day. At the end of this time the total group of rats is then broken down into two equated groups. The equating is done so that the error scores of the two groups for the twelve tests are as

similar as possible. Through the process of selection it was possible in all cases to choose groups which had almost identical mean error scores, both for the twelve tests as a whole and for each individual test.

Operative Procedure

Both of the equated groups of rats in each experiment were then food deprived for twenty-four hours and subjected to operation. The operations were performed under aseptic conditions using ether as the anesthetic. An incision was made along the center line of the cranial epidermis, and the connective tissue thus exposed was separated so as to reveal almost the entire dorsal surface of the cranium. Trephine holes were made employing an electrically powered dentist's burr. With a few exceptions the dura was usually punctured at this time.

One of the equated groups in each experiment suffered removal of cortical tissue, while the other group received "sham" operations (Franz, 1907; Rey, 1938; Crook, 1940); that is, they underwent an operative procedure similar to that of the removal group except for the actual removal of cerebral tissue. Cortical tissue was removed by suction. All of the animals were sutured similarly and the closed wound covered with antiseptic powder. The length of the operation was kept the same for both groups, and, depending upon the type of operation, varied from six to twenty minutes.

After operation, each animal was put into a small wire mesh cage, 12 by 10 by 8 inches, where he could be easily observed. Normally in each experiment the rats of both groups were kept in large colony cages, 18 by 18 by 15 inches. For only six hours post-operatively were they kept individually in the smaller cages so that the immediate recovery process could be carefully observed. With the use of light ether anesthesia during operation, it was found that the rats were sufficiently recovered between one and two hours post-operatively so that they could continue their testing on the closed-field problems. Beginning two hours after operation, then, all rats were exposed to the second series of twelve problems of the closed-field test. These tests were run every few hours for a day or two. After this, the rats were run on a continuous repetition of the entire twenty-four problems, one or two per day, until they were tested for at least thirty days after operation. Accurate error score tabulations were kept for all testings. For a graphic record of the times of testings, please consult the figures accompanying the text of each experiment.

At about the sixtieth post-operative day all animals were sacrificed by prolonged ether exposure, and their brains were removed. Gross inspection revealed that individual lesions in any particular group were of about the same size, the amount of cortex underlying the standard size burr holes. The brains were fixed in celloidin, sectioned at 40 micra, and stained with thionin. A sampling from each experimental group (including control animals which were trephined,

but had no surgical removal of brain tissue) was taken. They were reconstructed histologically, according to Lashley's (1929) technique, affording a good estimation of the localization and extent of injury to the brain.

A diagram of the location of the cerebral tissue removed in the various experiments can be found in Figure 2. The lesions performed on any one experimental group will be described in the appropriate place.

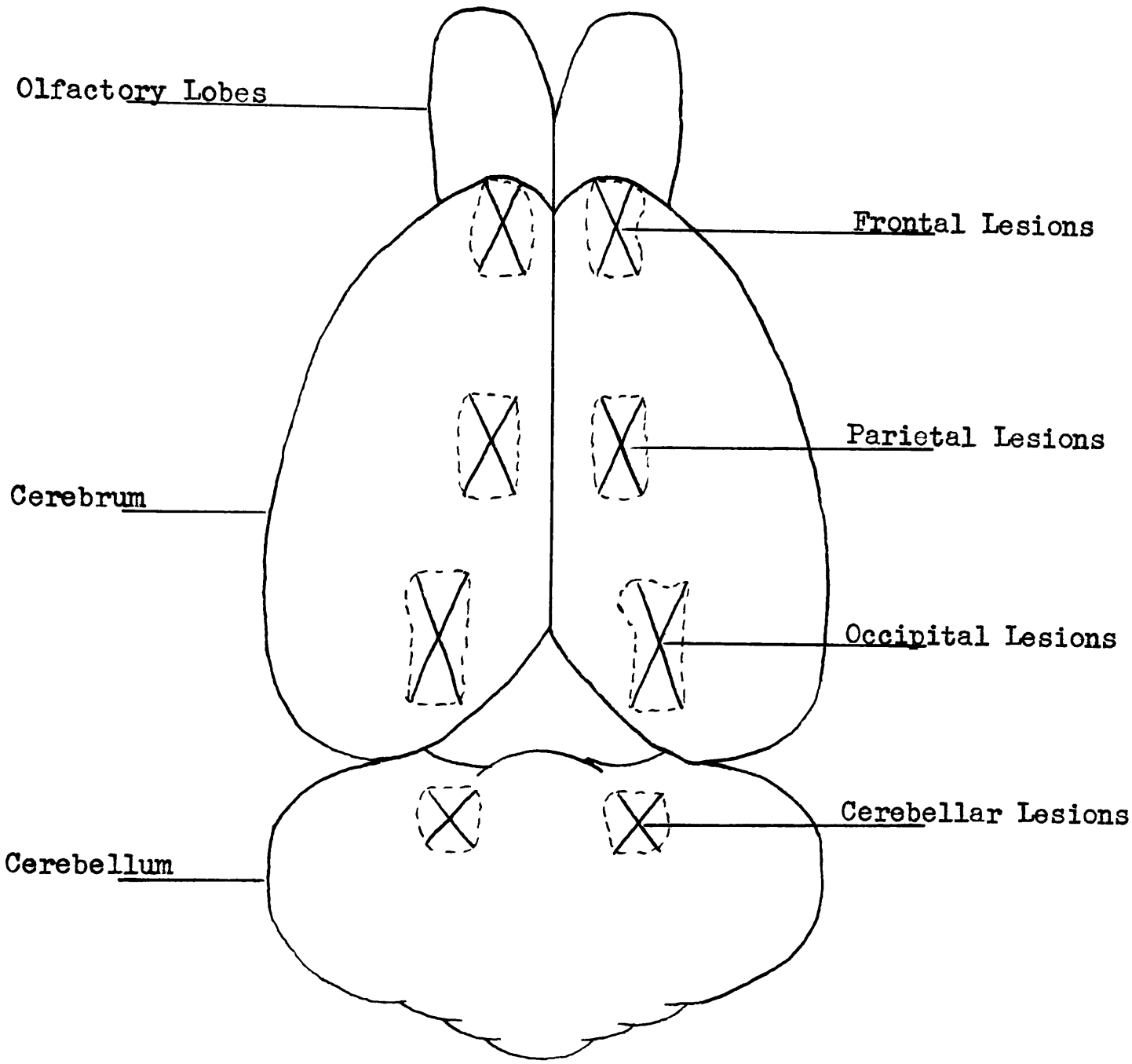


FIGURE 2: Diagram of the rat brain, adapted from Lashley (1929), showing the location of the ablations of Experiments 1 and 2. Crossing of the diagonal lines indicates the approximate placement of each lesion. Dotted lines indicate the total range of the ablations in the entire group of animals having tissue removed from that part of the brain.

EXPERIMENT 1: EFFECT OF BILATERAL FRONTAL AND PARIETAL REMOVALS

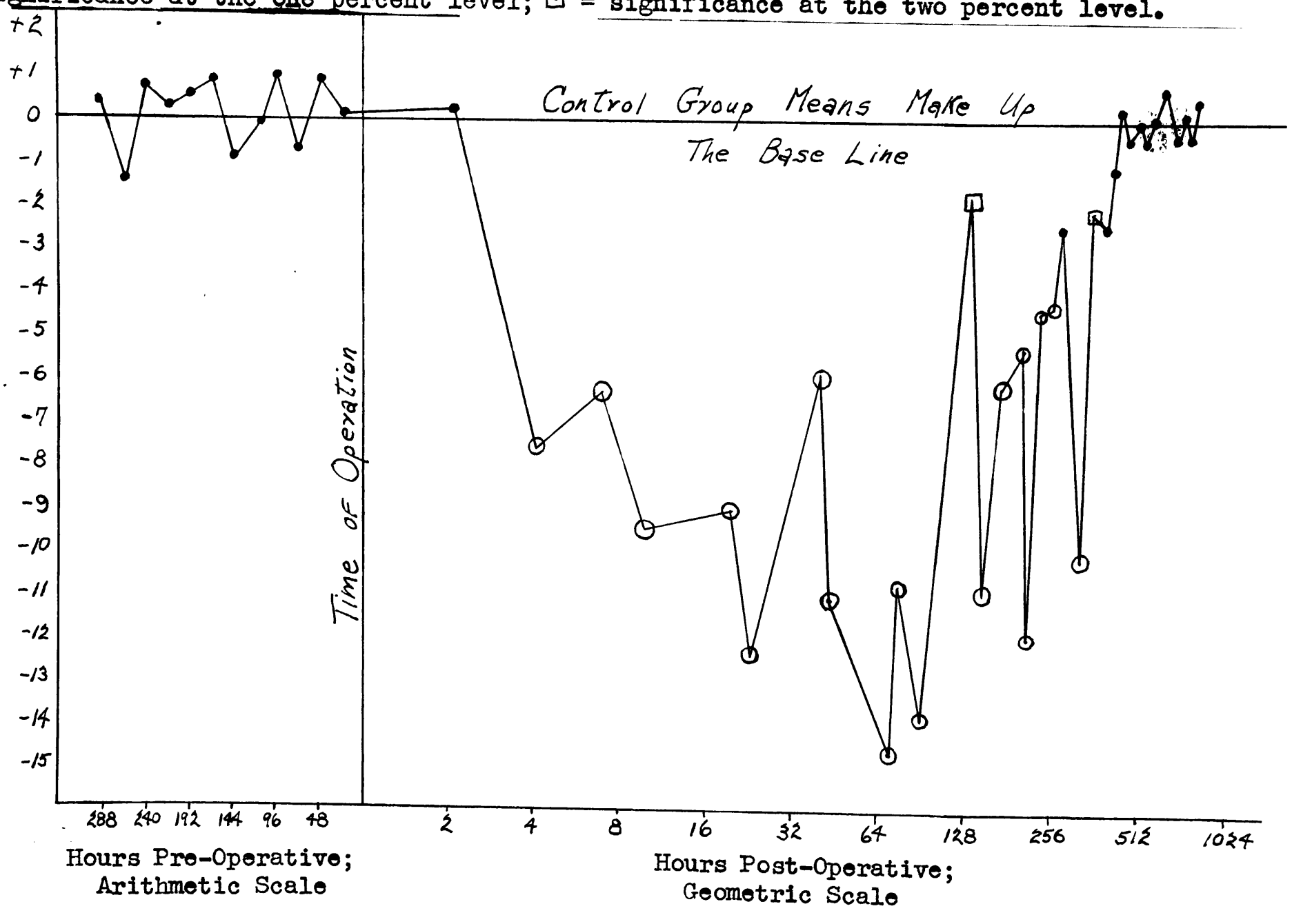
Procedure

This experiment was completed in three sections, one pilot study and two confirmatory studies. The three involved a total of twenty-four adult male rats, four in each of the separate control and experimental groups. Since the results of all are quite similar, they are combined, so that there are 12 animals in both the control and the experimental groups. After equation of the groups on the closed-field test of rat intelligence as described above, all of the rats received bilateral frontal and parietal burr holes. In addition, the experimental group was subjected to the removal of cerebral tissue beneath these burr holes. By reconstruction, the average total removal for the experimental group was estimated to be 5.2 percent of the entire cerebral cortex. No evidence of subcortical damage was found. The length of the operation was approximately twelve minutes for each animal. There were no deaths until all the animals were sacrificed.

Results

Mean error score differences between the two groups of rats on the closed-field problems run pre- and post-operatively and points of statistical significance, or lack of it, are pictured in Figure 3. The mean error scores of the two groups were not significantly different (using Fisher's *t* for small correlated samples) from each

FIGURE 3: Mean scores of the Experimental Group of Experiment 1 for each pre- and post-operative testing period, presented as subtractions from the comparable Control Group scores. N = 12 for each group. Legend: • = no significant difference between the mean scores of the two groups; ⊙ = significance at the one percent level; ⊡ = significance at the two percent level.



Control Group Mean Scores Minus Experimental Group Mean Scores

other for all of the pre-operative testings as well as for one testing at two hours post-operatively. At four hours post-operatively, however, a sharp, statistically significant increase in mean error score was found for the experimental (removal) group. This increase continued for a number of days. According to the pattern of the curve pictured in Figure 3, the two groups again became equated approximately on the seventeenth post-operative day. Actually, no statistical significance at the five percent level of confidence could be demonstrated between the mean error scores of the two groups after the fourteenth post-operative day.

Here, then, as in the clinical studies reported above, a delayed disturbance of function has been demonstrated. In the rat, under the conditions of this experiment, there is no immediate effect on closed-field testing of bilateral removal of small quantities of frontal and parietal cortex. At four hours post-operatively there appears a sharp significant increase in the mean error score of the experimental (removal) group over that of a previously equated group, and this lasts for about two weeks. The two groups of rats become equated again after this time, and remain so for the duration of testing.

EXPERIMENT 2: EFFECT OF LOCUS OF LESION, PRACTICE, AND AGE UPON THE DISTURBANCE OF FUNCTION

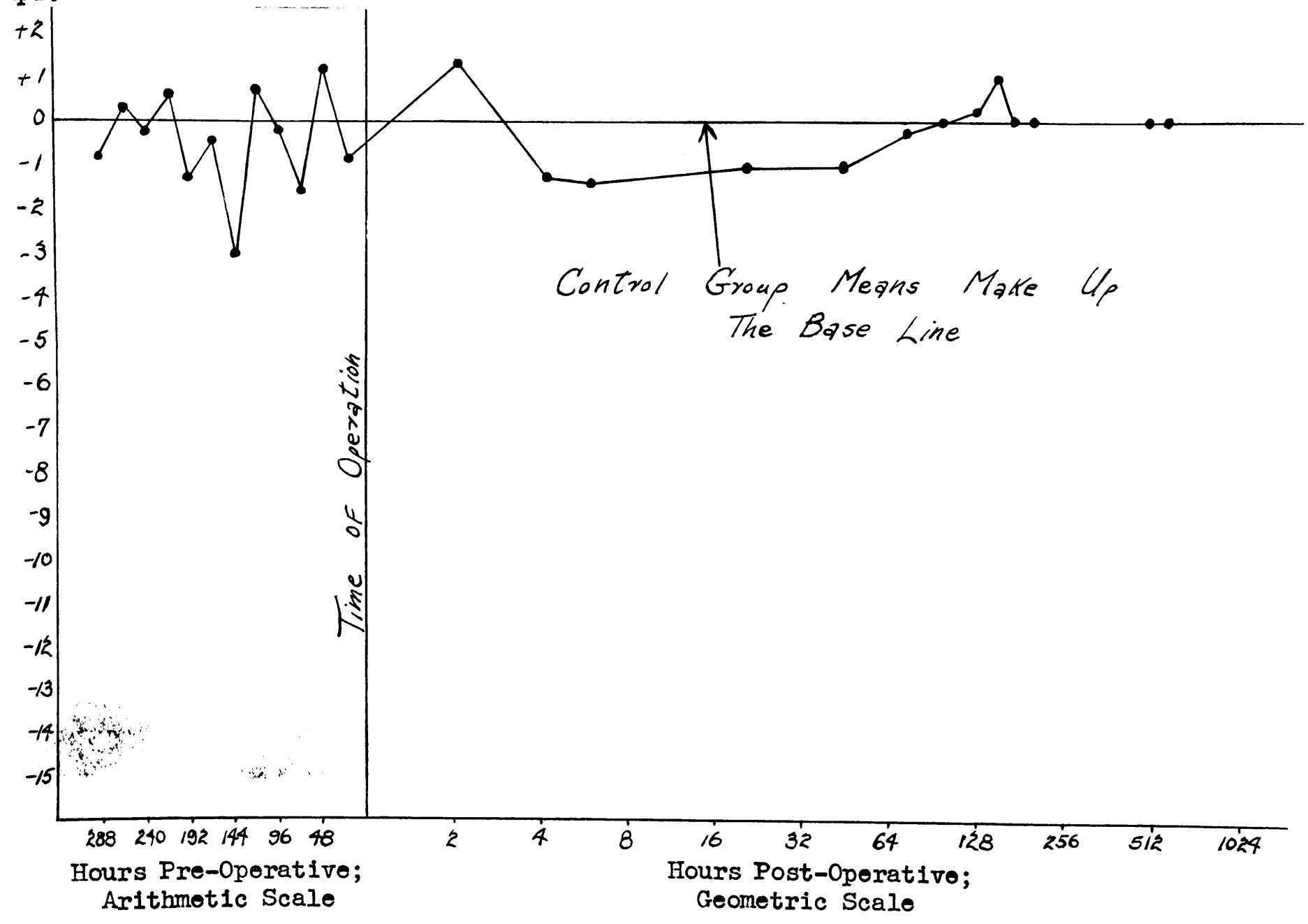
Locus of Lesion

Having found that a delayed disturbance of function could be demonstrated in the adult male rat on the closed-field test after bilateral frontal and parietal removals, it was decided to perform lesions with about the same total removal of cortical tissue as the four-lesion groups, but from varied bilateral locations in the brain. Thus, from anterior to posterior, four different locations were selected for study: the frontal, parietal, and occipital regions in the cerebrum, and the anterior portion of the cerebellum. The same methods of equation and testing of animals and of operative procedure were used as described above.

Results

Results on the closed-field test of bilateral frontal removal estimated to be 4.8 percent of the entire cerebral cortex are graphically presented in Figure 4. Two equated groups of 6 rats each were run pre-operatively, two hours post-operatively, and frequently thereafter. At no point in the pre- or post-operative testing could any statistical significance (at the five percent level of confidence) be demonstrated between the mean error scores of the two groups. However, the mean error score of the experimental (removal) group increased slightly from about four to seventy hours post-operatively.

FIGURE 4: Mean scores of the Frontal Ablation Group of Experiment 2 for each pre- and post-operative testing period, presented as subtractions from the comparable Control Group scores. N = 6 for each group. Legend: • = no significant difference between the mean scores of the two groups.



Bilateral parietal lesions were estimated to be 4.9 percent of the cerebral cortex. Pre-operatively and for one testing at two hours post-operatively, no significant difference was found between the mean error scores achieved by the two groups of six adult rats each. After this the experimental (removal) group displayed a sharp significant increase in mean error score, and this lasted for a number of days. According to the curve pictured in Figure 5, in which the results of this study are presented, the two groups of rats again become equated at about seventeen days post-operatively. Actually, no further statistical significance could be demonstrated after the ninth post-operative day.

Mean score differences and the corresponding statistical significances of the occipital removal study are presented in Figure 6. The lesions in the 6 adult male experimental rats were estimated to be 4.6 percent of the entire cerebral cortex. The 6 control rats, of course, received only the burr holes. No statistical significance could be demonstrated between the mean error scores achieved by the two groups of rats either pre- or post-operatively on the closed-field test. In the post-operative period, there was no consistent increase, however slight, in the mean error score of the experimental group.

The cerebellum study also involves a total of 12 adult male rats, 6 in each of the two groups. The lesions were estimated to be 4.6 percent of the entire cerebellar cortex. The mean score differences between the two groups on the closed-field test and relative statistical

FIGURE 5: Mean scores of the Parietal Ablation Group of Experiment 2 for each pre- and post-operative testing period, presented as subtractions from the comparable Control Group scores. N = 6 for each group. Legend: • = no significant difference between the mean scores of the two groups; ⊙ = significance at the one percent level; ⊡ = significance at the two percent level; ♦ = significance at the five percent level.

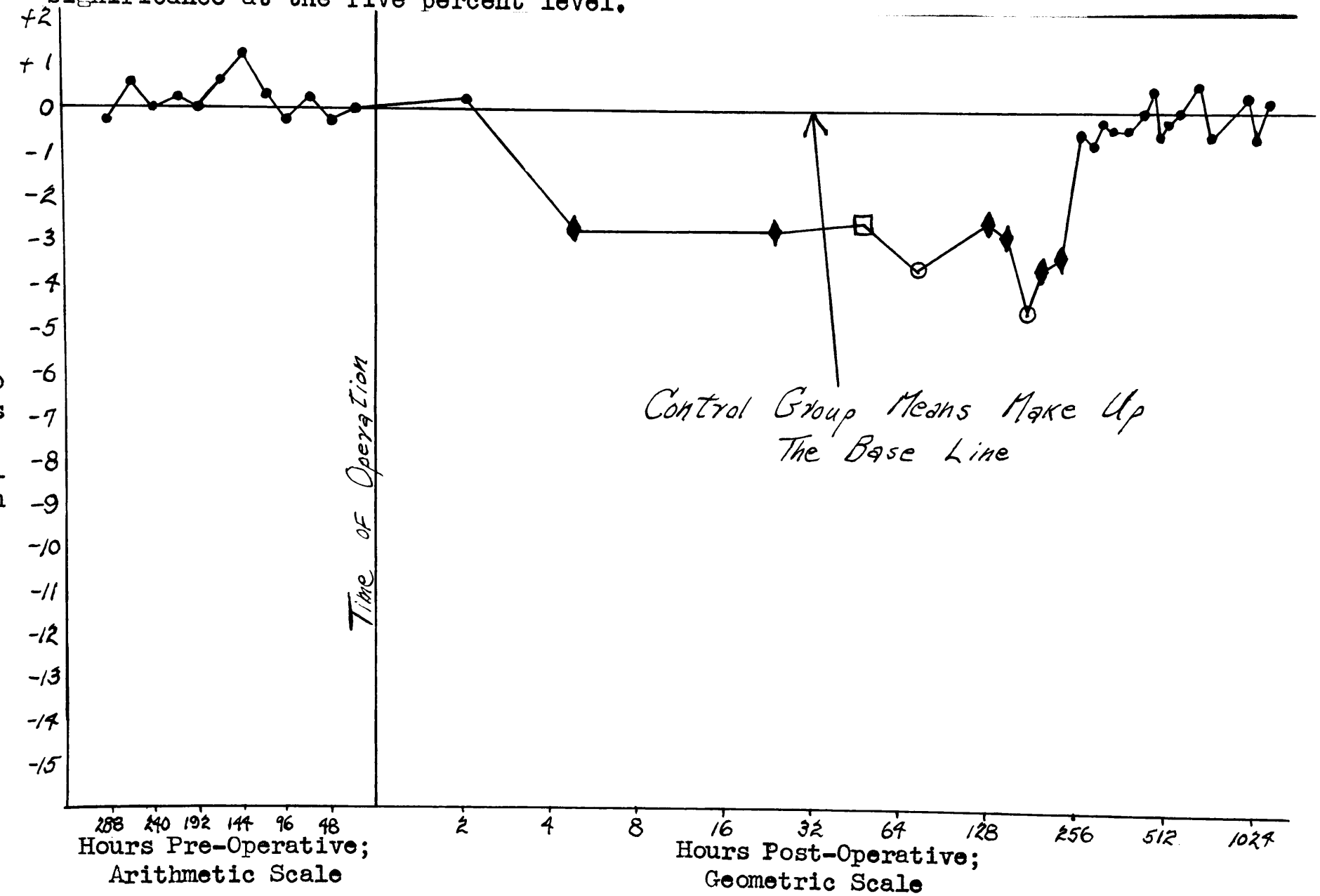


FIGURE 6: Mean scores of the Occipital Ablation Group of Experiment 2 for each pre- and post-operative testing period, presented as subtractions from the comparable Control Group scores. N = 6 for each group. Legend: ● = no significant difference between the mean scores of the two groups.

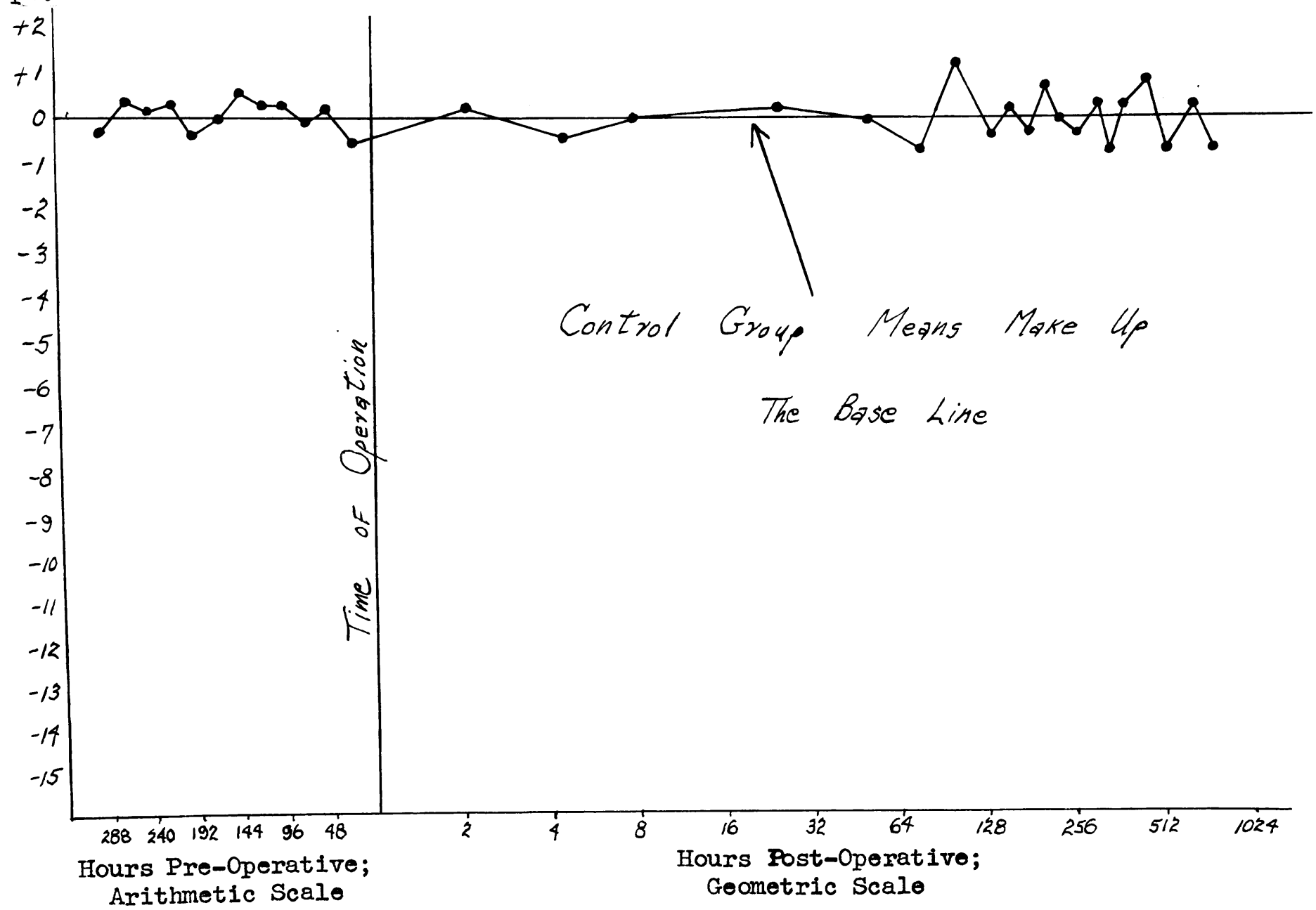
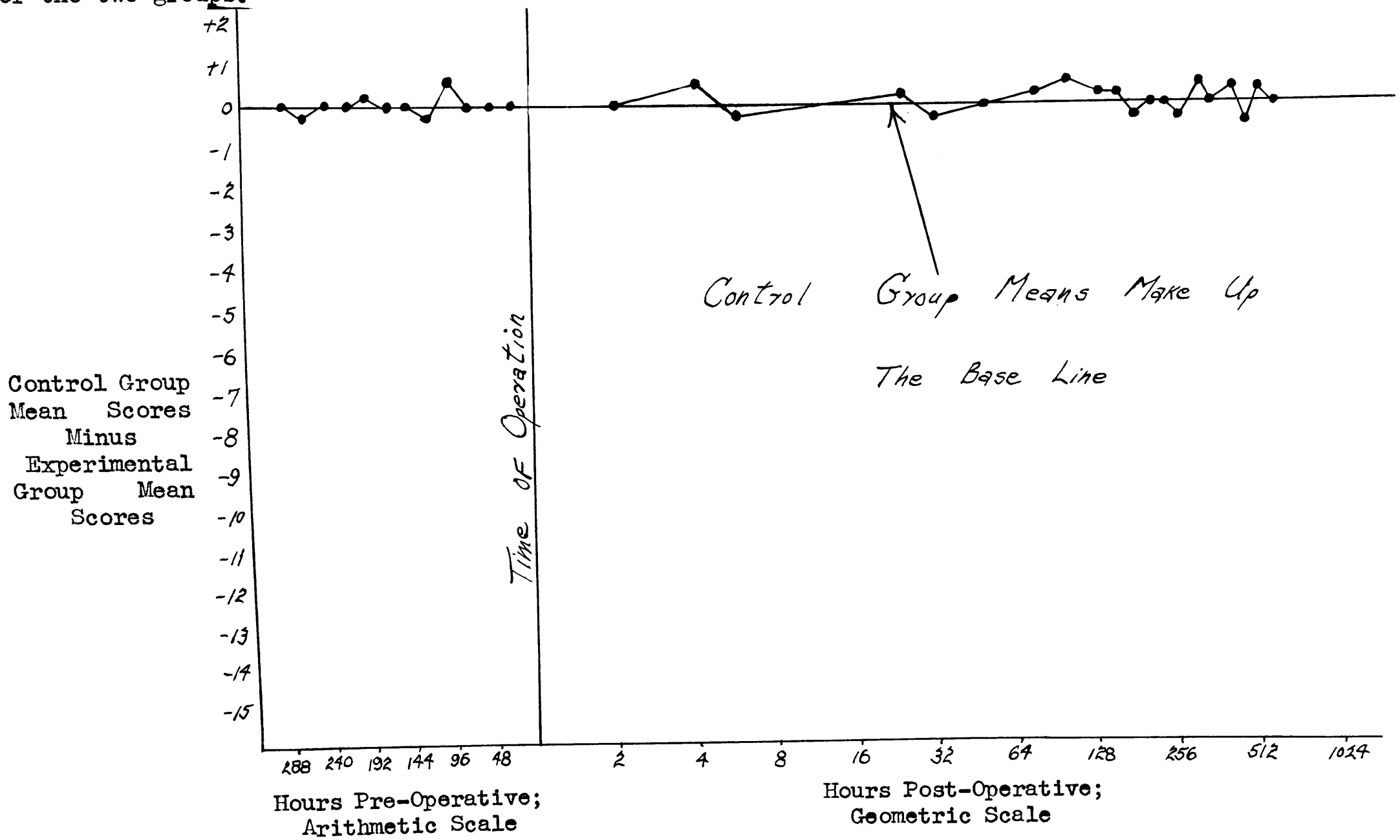


FIGURE 7: Mean Scores of the Cerebellum Ablation Group of Experiment 2 for each pre- and post-operative testing period, presented as subtractions from the comparable Control Group scores. N = 6 for each group. Legend: • = no significant difference between the mean scores of the two groups.



data are presented in Figure 7. At no point, either pre- or post-operatively, could any statistical significance be demonstrated between the mean error scores of the two groups. As in the occipital study above, there was no consistent increase, however slight, in the mean error score of the experimental group in the post-operative period.

Upon reconstruction of the lesions, no subcortical involvement was found in any of the brains of the rats in the experiments described above.

According to the present studies, then, the delayed disturbance of function as measured by the closed-field test of rat intelligence follows bilateral lesions in a limited area of the rat brain, that is, in the parietal region. No defect, which was statistically significant, was found after bilateral lesions in the frontal and occipital areas of the cerebrum and in the anterior portion of the cerebellum. The delayed effect in the parietal removal group lasted statistically for only nine days as compared to a more profound effect over a longer period of time in the bilateral frontal and parietal lesion groups reported in Experiment 1. This would indicate that the bilateral frontal lesions do contribute to the extent of a disturbance produced by lesions elsewhere. Moreover a delayed increase in mean error score which lasted a few days was displayed by the frontal removal group. Perhaps a delayed disturbance does occur after frontal tissue damage. If it is slight, it would take a larger number of animals than used here before it could be established significantly.

Practice

It will be recalled that the greatest and longest delayed disturbance of function found in the present experiments followed bilateral lesions in the frontal and parietal areas of the rat brain. The delayed defect, shown as an increase in error score on the closed-field test, began at approximately four hours post-operatively and lasted for about two weeks. Since testing on the closed-field problems began within a few hours after operation and continued throughout the course of the experiments, the effect of this testing upon the subsequent recovery, or return to equation of the two groups, is unknown. It could be maintained that without this continued testing post-operatively, any delayed disturbance following specific ablations might last much longer than the two week period reported above. In other words, a recovery following a delayed disturbance after specific lesions in the cerebral cortex might not come about spontaneously, but might depend upon repeated testings in a situation similar to the one provided the rats pre-operatively. Without further testing in the immediate post-operative period, testing at a later date would perhaps disclose an effect which is more permanent than that indicated in the experiments outlined above.

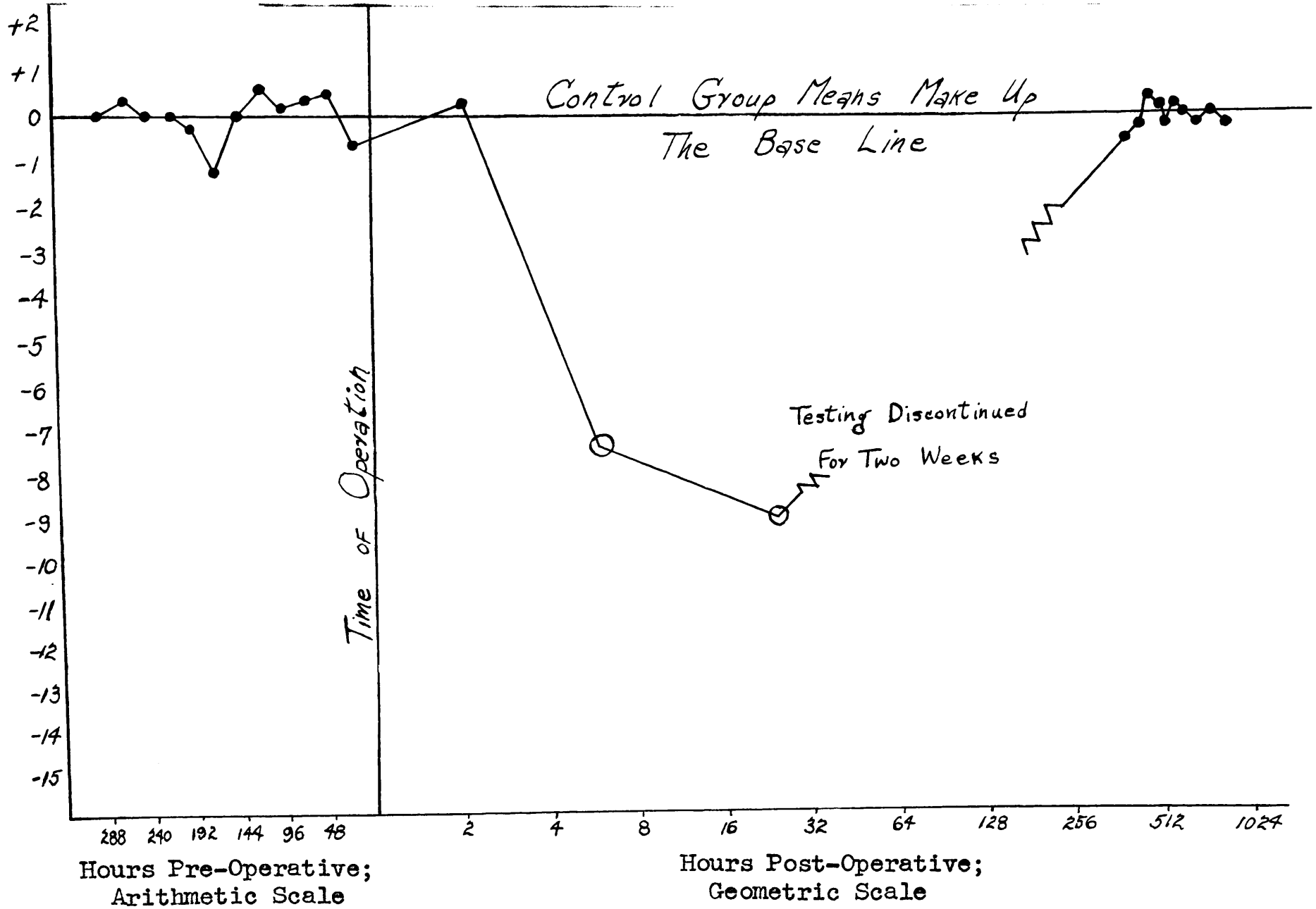
The present study was designed to test the hypothesis that a spontaneous recovery would follow the delayed disturbance of function after bilateral frontal and parietal lesions in the cerebral cortex of the rat.

The equation of the two groups of 6 adult male rats each and the operative and the testing procedure remain as described above. The bilateral frontal and parietal removals in the experimental group were estimated to be 5.0 percent of the entire cerebral cortex. The rats were tested on 3 closed-field problems only in the immediate post-operative period of twenty-four hours. Testing was then discontinued for two weeks, commencing again on the fifteenth post-operative day.

The mean error score differences between the two groups as well as the points of statistical significance, or lack of it, are presented in Figure 8. There was no statistical significance between the mean error scores of the two groups on the closed-field problems run pre-operatively and at two hours post-operatively. For the next two testings, six and twenty-four hours post-operatively, the experimental group displayed a sharp and significant increase in mean error score. In the period which followed the resumption of testing on the fifteenth post-operative day, no evidence of statistical significance was found between the mean error scores of the two groups.

This experiment confirms the results reported above that a delayed disturbance of function takes place after bilateral frontal and parietal lesions in the cerebral cortex of the rat. It also indicates that a recovery will follow this defect even if no further testing takes place in the period between the appearance of the delayed disturbance and the observed time of recovery with continual post-operative testing.

FIGURE 8: Mean scores of the Practice-Check Group of Experiment 2 for each pre- and post-operative testing period, presented as subtractions from the comparable Control Group scores. N = 6 for each group. Legend: • = no significant difference between the mean scores of the two groups; ⊙ = significance at the one percent level.



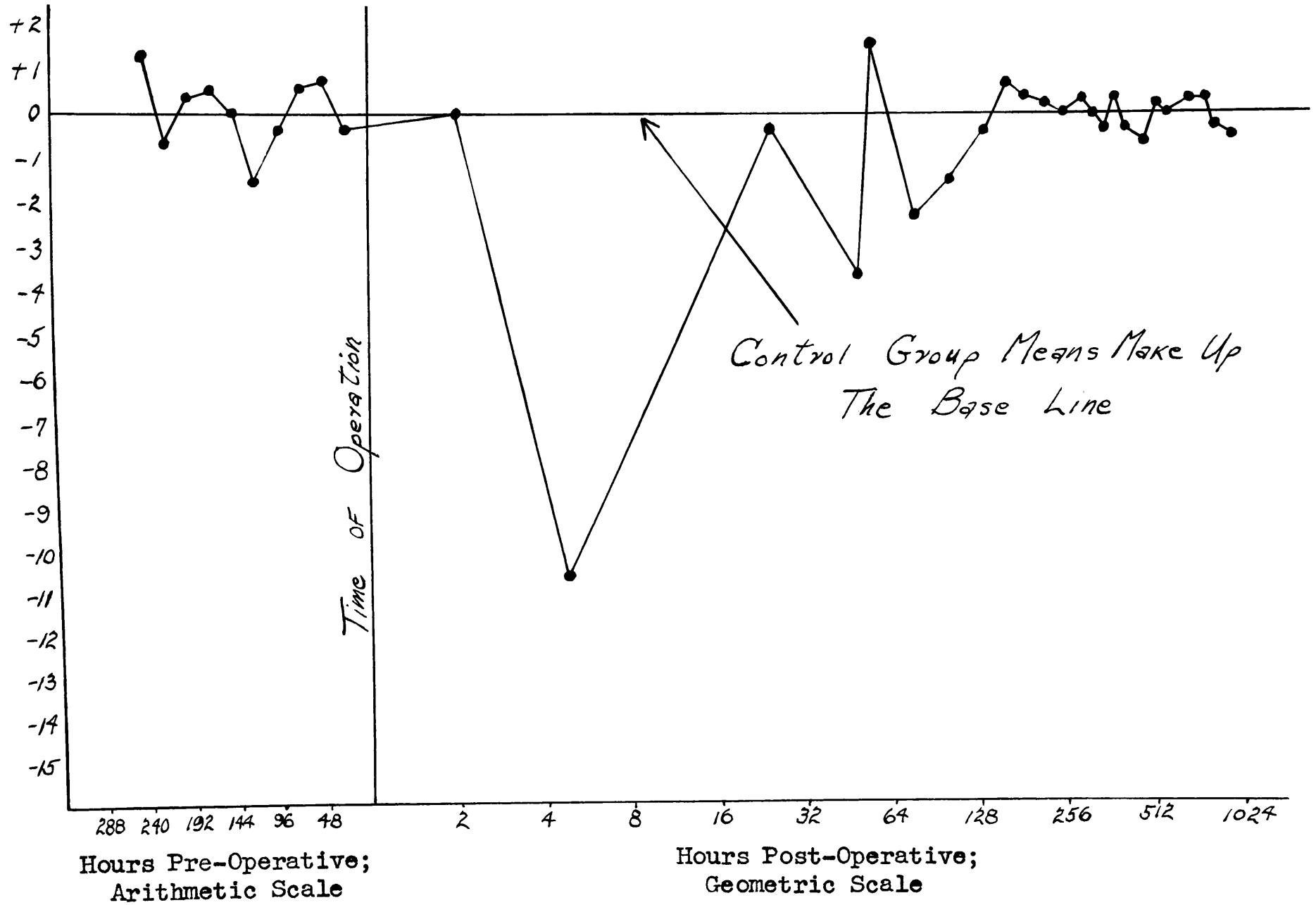
Age

Because experimentation currently in progress in the McGill psychological laboratory indicated that the effects of cortical destruction upon error score on the closed-field test may depend upon the age of the rat at the time of operation, the present study was undertaken.

It will be recalled that in the experiments reported above, adult male hooded rats were employed as subjects. They were subjected to operative procedure at about the age of 120 days. In the present study 12 male hooded rats were selected and trained on the closed-field test at about the twenty-fifth day of age. Actual testing began on the thirty-first day of age and the first series of twelve problems were completed at the rate of one per day by the time these rats were forty-two days old. At that time, two groups of 6 rats each were equated as outlined above. At forty-three days of age, all of the rats underwent operative procedure. The control group received burr holes bilaterally in the frontal and parietal regions. The experimental group had cortical tissue removed from beneath similar burr holes. The lesions were estimated to be 5.5 percent of the entire cerebral cortex. The post-operative testing procedure remained as outlined in the other experiments.

Mean error score differences between the two groups of rats and relative statistical data are presented in Figure 9. At no point in the pre- or post-operative testing periods could any statistical

FIGURE 9: Mean scores of the Immature Group of Experiment 2 for each pre- and post-operative testing period, presented as subtractions from the comparable Control Group scores. N = 6 for each group. Legend: • = no significant difference between the mean scores of the two groups.



significance be demonstrated between the mean error scores achieved by the two groups of rats. At two hours post-operatively the mean error scores of the two groups were identical. At five hours post-operatively, there was a sharp increase in the mean error score of the experimental group. This difference was significant, however, only at about the ten percent level of confidence. The testings following this could not establish the presence of a consistent trend, even though statistically not significant, in the direction of an increase in mean error score of the experimental group.

All bilateral removals of frontal and parietal cortical tissue from adult rats in the present report resulted in statistically significant delayed disturbances of function. The younger immature rats of this study did not display this defect. It is possible that here, too, there may be a slight delayed defect which would require far larger groups of animals before it could be statistically established.

SUMMARY OF RESULTS

The purpose of this investigation was to learn more about the delayed disturbances which frequently follow cortical operations, in order to see if any explanation can be found for the peculiar time course taken by the disturbance, and to show the relationship of this phenomenon to other, better-known phenomena of deterioration and recovery following operation. In the first of the two clinical studies, it was shown that delayed aphasic, motor, or sensory symptoms may follow cerebral operation performed in most of the cases under local anesthesia for the relief of epileptic dysfunctioning. Such delayed disturbances were detected in thirty-nine of the fifty case histories examined. The delayed symptoms usually appear about two days after operation. In the majority of cases, a complete recovery of function takes place within a month without any special training. Gradual improvement was noted in the remaining cases. All major subdivisions of the brain were represented in this group of patients. It was pointed out also that one patient had an exploratory operation only, with no cortical tissue actually removed. (This is not an unusual result. There are a number of other case histories in the Montreal Neurological Institute which show that severe symptoms may follow prolonged exploration as well as surgical removal of cerebral tissue.)

In the second of the clinical studies, in seven patients who had no aphasic, motor or sensory defects, it was found that intellectual

functions display a pattern of delayed disturbance with approximately the same time course as that found in the case histories. That is, compared to the pre-operative level of intellectual functioning, no loss was detected immediately after cerebral operation. Three days later, at the time of the next testing period, there were significant losses on six of the eight tests employed. With further testing in the convalescence period, mean scores on the tests approached the pre-operative level.

In the animal study, it was demonstrated that some lesions (bilateral parietal alone or in combination with bilateral frontal) produced no evident disturbance of function on the closed-field test at two hours after cerebral operation, but a marked defect about four hours after operation. The disturbance lasted for about two weeks in the parietal plus frontal group, and for a few days less than this in the parietal group. The extent of the defect was also considerably less in the parietal lesion group. This would indicate that the frontal lesions were contributing to the effect. Bilateral frontal lesions in other animals produced no delayed losses which were statistically significant. The experimental animals, however, displayed delayed increases in error score which lasted a few days. Thus it is probable that damage to frontal cerebral tissue does lead to a delayed disturbance of function, even though it is slight and not readily demonstrated.

No increase in mean error score followed small bilateral lesions to the occipital region of the cerebrum or to the anterior portion of the cerebellum in the rat.

To test the importance of practice for the recovery which follows the disturbance, another group of adult rats was subjected to small bilateral removals of frontal and parietal tissue. The typical delayed loss was present from about five to twenty-four hours after operation. Testing was then discontinued. Two weeks later it was resumed. At this time no difference between the error scores of the control and the experimental groups was found. Hence, a recovery occurs as quickly without daily practice on the tests as with it. To this extent, at least, the recovery is spontaneous.

It was also shown that with small bilateral frontal and parietal lesions in the immature rat of forty days of age, no delayed disturbance which was statistically significant could be found. However, in this study, also, there was a delayed increase in error score in the experimental group which lasted a few days. Thus, it is possible that a delayed disturbance does occur but that it is slight and not readily demonstrated in animals of this age.

THE MECHANISM OF RECOVERY AFTER DAMAGE TO THE BRAIN

The clinical and experimental data which have been presented raise some question about existing conceptions of neural function, by supplying a need for reinterpreting some of the evidence on which the conceptions are based.

If part of the cerebral cortex is lost and specific functions are lost at the same time, then it is reasonable to assume, as the advocates of specific cortical localization have assumed, that the disturbed functions were residing in the area of the brain which was lost. If the impairment proves only temporary, it could be further assumed that, as recovery proceeds, some other neural tissue is taking over the functions of the lost tissue. Supposedly, the remaining tissue, before injury, was not directly concerned with the functions which it is now taking over. For obvious reasons, such a conception of recovery is called vicarious functioning.

There is a question, however, whether this is the real course of events. In the earlier work concerning loss and recovery of function after removal of cerebral tissue, the evidence is inadequate because testing of the functions concerned was rarely done until a few days, and usually much longer, had elapsed after the damage had been sustained. Hence, one cannot be certain that the functions reported lost were not actually intact immediately after the injury. Bucy (1944) and Malmo (1948) report such occurrences, and the present data demonstrate that a delayed disturbance not only <u>can</u> follow cerebral injury but quite often does.

If functions are intact immediately after the brain is damaged but are disturbed a short time later, the conclusion cannot reasonably be made that these functions directly resided, or were localized, in the tissue that had been lost. Thus when recovery follows in due course, it would be illogical to maintain that it is because new cerebral tissue is functioning vicariously for that lost. It is not argued that vicarious functioning never occurs; but it becomes clear that for many cases in which vicarious functioning at first seems a good explanation, we must seek some other explanation of recovery.

The presence of a delayed disturbance of function after exploration of the brain only, without an actual removal of cerebral tissue, raises a further point. If the brain is merely exposed to air and ultraviolet radiation (operating-room antiseptic agent), there is no loss of cerebral tissue, but the same loss of function and slow recovery follows this procedure. The recovery certainly is not because of vicariously functioning tissue, since no tissue was removed.

If it were not for the fact that the defect follows exploration of the brain alone, an explanation of delayed disturbances could be offered which would still be in accord with the notion of vicarious functioning. It could be argued that the original cerebral loss is followed by further injury to the brain through scar formation or other means. The subsequently lost function would reside, according to this explanation, in the tissue which was damaged by the scar formation. Thus, a function could be intact immediately after cerebral

removal and be disturbed at some later time. Recovery which takes place after this could then be due to new tissue functioning vicariously for the tissue incapacitated only secondarily by the original injury.

If so, the functions concerned could still be considered as localized in specific limited areas of the brain. It would be expected that at some times, then, this specific tissue itself would be damaged and a loss of the function residing therein would follow immediately.

The present data do not negate this argument completely, but make it seem highly unlikely, since a delayed disturbance of the same functions was found to occur after damage to widely dispersed areas of the human brain. One would also expect, from the point of view of the argument in defence of vicarious functioning, that delayed disturbances of function would occur far less frequently than reported in the present study. Moreover, if tissue not directly concerned with a function until the brain is damaged, suddenly is called upon to assume that function, one would expect that some amount of practice or reeducation, and probably a good deal of it, would be necessary before this could take place. It will be remembered that in both of the clinical studies and in the rat study of the present report, delayed disturbances of function improved considerably or completely within a short period of time without any special training. In the rat experiment designed to control practice effects, a recovery still took place, and was therefore considered a spontaneous recovery

of function. These points, plus the fact that the defect follows exploration of the brain only, make it unsatisfactory to explain the delayed disturbances of function and the subsequent recovery in terms of vicarious functioning.

The same objections hold for the other reeducative conceptions mentioned in the introduction as possible mechanisms of recovery. This does not mean that reeducation has no part in the recovery process, but that its significance for recovery has yet to be completely understood.

What of the mechanism of diaschisis as an explanation of delayed disturbances of function? It will be recalled that, according to the theory of diaschisis, symptoms following cortical destruction may be due not to the loss of tissue as such, but to the resultant curtailment of facilitation for another area which does not function effectively without it. Again, one would expect the curtailment to occur directly after the cerebral damage and the functions dependent upon the facilitation to be disturbed immediately.

This aspect of the principle of diaschisis is inconsistent with the data outlined in the present report. According to the present evidence, any curtailment of facilitation brought about by cerebral damage and resulting in the disturbance of a function not directly residing in the injured area is not immediate but occurs a short time after the damage is sustained.

The principle of diaschisis also implies that the uninjured area of the brain which is suffering a lack of facilitation because of damage

to another area may eventually function properly even without the original facilitation. This will be reflected by a spontaneous recovery of the functions. No intelligible mechanism of such a recovery has yet been proposed. The present data indicate that a spontaneous recovery of function can take place, or, at least, that no special formal training is necessary for recovery. How may the function return, however, without a direct replacement of the lost facilitation?

It is possible that the original injury is to a part of the brain which mediates a function. This may cut off a certain amount of facilitation within the area, but perhaps not enough to bring about a disruption of the function. However, the cerebral insult may be followed by pathological changes, such as edema and shock-effects, glial tissue formation, pressure or circulatory alterations. These secondary changes may take a little time to develop, and they may cut off enough facilitation to produce the clinical symptom of the loss of the function concerned. In due course, the complicating pathological factors may reverse. Recovery, of course, would occur without a return of the facilitation originally cut off by the cerebral insult, and also without any special training of the function.

Another possibility is that the original injury is to tissue which adjoins an area of the brain mediating a specific function. The injured region and the area adjacent to it need not be a functional unit facilitating each other. Damage to a non-functional area, then, may precipitate pathological changes in another area, producing a delayed disturbance of the function residing therein. Perhaps this is what

occurs in cases such as those outlined by Bucy (1944). Bucy found that lesions to the precentral motor cortex resulted in delayed sensory losses. There are other examples of an apparent action-at-a-distance disturbance (Alford, 1940; 1944; 1948; Goldstein, 1942; Woodward, 1945; and Riese, 1949b).

Reversible pathological changes in the brain brought about by cerebral insult have been proposed here as a possible explanation of the delayed disturbance phenomenon and the recovery which follows. Elaborating somewhat will make it more possible to judge the plausibility of the proposal.

After brain operation, the presence of cerebral edema and pressure is seen clinically as a swelling of the scalp and face, and a discoloration of the skin surrounding one or both of the eyes. Every patient in the second clinical study had, in fact, at least one black eye post-operatively. The swelling is widespread but it seems to be concentrated in the region of the operation and more on that side of the head and face. It is interesting that these physical signs of the presence of edema and pressure in the brain usually do not appear until a few hours or even a day or two after operation. In other words, they may occur in man at about the same time that the delayed disturbance of function is observed. These signs ordinarily disappear after a few days and certainly after a week or two. If edema and pressure were the only causal factors of the delayed disturbance, their disappearance should result in a spontaneous recovery of a function fairly soon after its loss. Edema itself must be accompanied

by pressure and circulatory changes. Also, if part of the brain is removed, the circulatory system in that region is going to be somewhat disrupted. This may lead to further progressive disturbances of circulation if thrombi, for example, spread from the local area of injury to other areas, thereby interfering with the proper circulation in cerebral tissue not originally injured.

If circulatory alterations or scar tissue formation were at least partly responsible for the delayed defect, a longer period of time would have to be assumed before the complete absorption of the degenerative tissue or rerouting in the circulatory system (anastomosis) could take place. Thus, recovery of function might not come about until some time after the original cerebral injury. In such circumstances, of course, the gradual recovery seems like a slow learning process.

If a delayed disturbance of function is present in all cases of cerebral insult, and this is a possibility, it would still be masked in most. The defect would not be readily detectable except in the special circumstances of cerebral operation under local anesthesia. In cases of trauma to the head, the cerebral damage that by itself would produce a delayed disturbance is also accompanied by concussion, so that there is little opportunity to observe what can be observed under other conditions. In tumor cases, development of the lesion is gradual, and the increasing cerebral destruction is accompanied by a spreading vascular disturbance. Thus, the delayed disturbance could have occurred before the patient reached the operating table, and so

gradually that it could not be recognized as such.

The explanation of the delayed disturbance proposed above is in keeping with the distinction between dysfunctioning and a loss of function. That is, a disturbance of function after cerebral insult may not be a direct result of the original loss of tissue, but of the resultant dysfunctioning of other cerebral tissue. The dysfunctioning would be due to pathological processes in which neural cells do not actually die, though firing rates and so on are changed. The spontaneous recovery which appears to be possible after delayed disturbance would seem to be consistent with a reversal of the causes of the dysfunctioning.

The dysfunctioning of the brain brought about by cerebral insult could be very brief, or of rather long duration; conceivably, it could be permanent. The first type has been described by Hebb and Penfield (1940) and by Hunt, Wittson and Harris (1942). It is probably due to a temporary misfiring of neural circuits, and it can be reflected by a brief disturbance of intellectual functioning. Hebb and Penfield report that during the pre-operative intelligence testing of their patient, responses on year X items of the Stanford-Binet test were slow and of a poor quality. This was followed by better and quicker responses on year XI of the test. The day after this examination, the year X items on which he had failed were given again, and the responses of the patient were satisfactory. The writers state that this was "a transient epileptoid state, of which the patient seemed unaware" (page 431). Hunt, Wittson, and Harris report the

mental testing of a subject while he was apparently undergoing a petit mal attack. Before the attack, which was seen clinically as a brief flutter of the eyelids and a temporary fine head tremor, the subject performed at a dull normal level on two subtests. Directly after the attack, the performance on the next two subtests bordered on feeblemindedness. That is, there was a considerable drop in the level of performance. The subject was tested later on the same day and passed all four of the subtests at the dull normal level. Thus, there was a short period of intellectual disturbance which probably occurred during a period of cerebral dysfunctioning seen clinically as the petit mal attack.

The more permanent type of cerebral dysfunctioning, which possibly is the type responsible for the delayed disturbances of the present report, has been described by Blum, Blum and Chow (1948). They found that a monkey who had prefrontal cortical tissue excised bilaterally was hyper-active and failed in a test of delayed response post-operatively. No fits or seizures were observed until, two months later, the monkey was injected subcutaneously with benzedrine. A series of convulsions were witnessed until the animal was sacrificed about thirty hours later. The writers conclude that "irritative lesions, though insufficient to produce epileptic discharge, may be present after cerebral excisions; benzedrine may increase sensitivity to these irritative effects; and observed abnormalities of behavior, such as hyperactivity and failure in the delayed response test, following brain lesions may be due to the irritative action of pathological

tissue which is subliminal for fits" (page 561).

Experiments which support the conclusions of Blum, Blum and Chow have been reported by Kopeloff, Kopeloff and Pacella (1947), Pollack and Kark (1948), Pollack and Silver (1948), and Ransohoff (1949). Most of these writers have shown that a focus of irritation in the cortex of animals may not cause seizures until some sensitizing agent is introduced.

The problem remains to account for disturbance of function following exploration of the brain only, without removal. If the delayed defect is thought to be due to dysfunctioning of the brain rather than to a loss of cerebral tissue as such, how could this occur after exploration only? An answer seems provided by the experiments of Prados, Strowger and Feindel (1945). In confirming earlier work of Echlin (1939), they found that mere exposure of the brain during operation produced serious consequences. They exposed to air part of one hemisphere of the brains of 40 cats. The exposure period, measured from the time that the dura was opened, varied from four to seven hours. The writers report finding circulatory changes which were more pronounced in the exposure area, but which also occurred in more remote parts of <u>both</u> hemispheres and in subcortical structures. The circulatory changes consisted mainly of vasodilitation and the cellular changes of swelling and chromatolysis or shrinkage and homogenization. In addition some neurons were completely destroyed. Physiological changes also took place. These included changes in the the electrical activity of the cerebral cortex and alterations in the

permeability of the capillary endothelium. All of the changes were considered to be secondary to the circulatory alterations.

Both pathological and physiological changes are present in the brain shortly after exposure. That is, there is a certain amount of swelling and a depression of electrical activity which is obvious almost immediately. Other changes, however, take longer to develop. Areas of ischemia were found throughout the whole cortex about twenty-four hours after exposure. A generalized increase in the amplitude of the electrical activity was found on the third post-operative day. This, incidently, occurred at about the same time that the circulation was practically reestablished.

By the seventh day after the exposure almost all the changes were reversed and the brain of the animal was back to its pre-operative condition. The neurons that are destroyed do not recover, of course, but the rest of the picture may be completely normal.

The reaction of the brain to air is a good deal like its reaction to ultraviolet exposure. When the brains of various animals are exposed to ultraviolet radiation, with the air factor controlled, the pathological and physiological changes are similar to those described above (Odom, Dratz and Kristoff, 1949; Elvidge and Morris, 1949).

It appears, then, that there may be reasons for clinical symptoms to occur after a human brain has been subjected only to air and ultraviolet radiation exposure during exploration. Exposure alone may lead to edema-like and vascular alterations, neuronal and circulatory alterations. The time course of these effects would seem to be consistent

with the time course of a delayed disturbance of function. Some of the changes due to exposure do not occur immediately, but take from a few hours to a few days to develop. Moreover, some of the alterations, such as neuronal destruction, may not be reversible. Others may be reversed only after some time has elapsed after the exposure.

Thus, when the brain is exposed and subjected to ablation or merely to exploration or when the brain is insulted in other ways, there may be no immediate disturbance of function. There may be, however, a delayed disturbance of function. This disturbance would presumably be related to pathological changes in the brain. The pathological changes may be brought about either by traumatic injury to the brain or by exposure with or without ablation at the time of operative therapy. The function which is subsequently disturbed may reside in cerebral tissue at or close to the site of injury or at some distance from it. Recovery from the defect may come about quickly or it may take a long time. In either case it may not be due to re-education but may occur spontaneously. The recovery would be due to the cessation or reversal of the pathological changes in the brain brought about by the original insult.

However, the question of explaining the delayed disturbance appears to be a pathological, not a psychological problem. The essential point of the present investigation is the relation of the phenomena to the theories of cortical localization and restitution of function. The fact that losses can be demonstrated which do not occur immediately after cortical insult but at some time thereafter would seem to impose

one further barrier over which those who maintain extreme cortical localization of function must climb. The time course of loss and recovery of function reported here after cortical insult indicates that the mechanism of vicarious functioning cannot reasonably, in these cases at least, explain the restitution which takes place. In addition, the phenomena indicate that the importance of reeducation to recovery of function has yet to be understood completely. The possibility of a revised principle of diaschisis explaining the present data will have to be investigated further.

SUMMARY

The chief objectives of this investigation were: to demonstrate the existence of a delayed disturbance of function after cerebral insult, to learn something about its properties in order to see if any explanation is available, and to see what relation the phenomenon has to other types of disturbance following brain injury already reported.

A delayed disturbance of function was demonstrated in man and in the rat. Immediately after cerebral injury no loss of function was detected. At some time later, a sharp and significant disturbance took place. Recovery from the defect in most of the human and in all of the rat cases occurred in a few weeks and apparently without the necessity of retraining. In the remaining human cases, gradual improvement was noted.

The probable explanation of the delayed disturbance is in the nature of the pathological changes which are secondary to the original injury. This problem, however, is a pathological and not a psychological one. The essential point emphasized here is the relation of the phenomena to the theories of cortical localization and restitution of function. The fact that losses can be demonstrated that do not occur immediately after cortical insult but at some time thereafter, would seem to necessitate a reexamination of current conceptions of cortical localization of function. The time course of loss and recovery of function reported here after cortical insult indicates that the mechanism of

vicarious functioning cannot reasonably, in these cases at least, explain the restitution which takes place. In addition, the phenomena indicate that the importance of reeducation to recovery of function has yet to be understood completely. The possibility of a revised principle of diaschisis explaining the present data will have to be investigated further.

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