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DETERMINANTS OF CEREBRAL RECOVERY

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There seems to be, presently, a swingback, in part, to older views of basic central nervous system maintenance and growth principles. Prior to Sperry's truly stunning long series of studies emphasizing the presence of a high degree of neurospecificity, the wildest claims had been made about the extent of functional recovery possible, following either central or peripheral nerve damage (Sperry 1965). For years, it was these studies, as well as Harlow's (1971) at a psychological level, that put a halt to the runaway interpretation that function precedes form. Recently research has again focused attention on the question of the degree of plasticity in the CNS - for example, the work on visual deprivation (Hirsch and Spinelli 1971; Blakemore and Cooper 1970). These studies have shown us how discrete visual experience during rearing modifies the basic organization of the primary visual system. Along with this work, of course, are the studies of Schneider (1973), Raisman (1969), Moore (1971) and others which detail the extent to which neural growth is possible following central neural lesions. As a result, the idea in everyone's mind is that we may now have a handle on the physical basis of recovery in the CNS - not to mention the insights such work affords us on the broader question of the physical basis of learning and memory.

Indeed, Hirsch and Jacobson (1974) have recently argued that adaptive behavior, in general, is the product of changes in the microneurons or Type II cells of Golgi. These cells, it is believed, remain adaptive while the long axon cells responsible for the major transmission of information into and out of the CNS are under early, and exacting, genetic control and specification. How long this state of flexibility obtains for the microneurons is not known. It supposedly extends into the teens, which thereby allows for the speculation that it is a process involved in the kind of speech and language recovery seen in the rehemispherization of these processes following early brain damage. It simultaneously could explain why the relocalization of speech and language rarely occurs after twelve years of age. In this regard, it is worth noting the studies of Nottebohm (1970) on the bird-song of canaries. He has shown that up to the age of one year, the song can be taught to birds deprived of hearing the song. Birds deprived for longer periods can not be so trained. Yet, if the birds are castrated when young, thus altering the testosterone level, they are able to learn the song well into the second year. Here we see an exciting model for the experimental manipulation of how and why the CNS at some time "wires out" adaptive changes in communicative behavior.

In my view, however, all of this fascinating basic work in neural development does not directly bear on the question of recovery of function in the CNS as the term is normally used in a clinical sense. Before proceeding, however, let us look at the stature of clinical functional recovery.

Clinical Recovery: There are a variety of claims on the mechanisms and extent of nervous system recovery. Luria feels that temporarily depressed areas can be "disinhibited" both by training and with the aid of pharmacological agents such as atropine and neostigmine. Yet most neurologists are skeptical of applying these methods to patients and, in general, believe the extent of long term recovery from a lesion is a function of the individual's capacity to realize repair and has little to do with external therapy. For example, in studies examing the value of rehabilitation on motility and other sensory-motor functions on stroke patients, it has been concluded that no more improvement is forthcoming than if the patient had been left alone (Stern *et al.* 1971). The same case can be made for speech and language rehabilitation following stroke (Sarno *et al.* 1970). Indeed, in the clinical setting it is hard to improve upon von Monakow's concept of diaschisis, where recovery is viewed as the reestablishment of temporarily impaired neural systems - not the vast reorganization of neural

systems through substitution, retraining or as the result of new growth. There have been, in recent years, both physiological and metabolic studies that support von Monakow's ideas. Recordings from cortical areas distant from cerebral lesions, for example, find the areas transiently depressed followed by return to normal levels of firing (Kempinsky 1958). In stroke, it is observed that there is a marked transient decrement in metabolic rate in the brain areas opposite the lesions (Hoedt-Rasmussen 1964).

Yet, even if the basic ideas of von Monakow prove correct, some clinical instances of recovery involving the higher cognitive processes following massive brain damage probably come about through other mechanisms and involve neither disinhibition or actual structural changes. In what follows, I will show instances of recovery of function which can be brought about quickly after a brain lesion or by prelesion prophylactic measures; it will also be demonstrated that recovery can be obtained by the use of proper behavioral training routines long after diaschistic processes are thought to be active.

In general, all of the data I will report leads me to the view that recovery in the adult, arising from nonphysiological improvement, is the result of preexisting behavioral mechanisms not necessarily previously routinely involved in a particular act now covering for the mental activity under question. For instance, I believe that the implicit functional syntactic mechanism present and active in decoding a meaningful pictorial array is probably able to come to the assistance of the organism when the syntactic mechanism for language has been destroyed through stroke or lesion. But before getting into the clinical work, let me lay a broader base for this view with recent work of ours in animals.

Animal Research: We believe that the behavioral dysfunction supposedly resulting from discrete lesions in the brain can frequently be quickly circumvented by changing environmental or behavioral contigencies (Gazzaniga *et al.* 1973). We recently pursued this idea in one of the most exhaustively studied systems in physiological psychology, the lateral hypothalamic area.

Bilateral lesions here, of course, produce an adipsic animal who will neither drink nor eat, and if left alone postoperatively, would die. Such animals are nursed for an extended period of time and with enough coaxing some will eventually be able to sustain life postoperatively. We, however, observed that within a few days after the lesions, most rats will have a higher probability of running than they have of drinking. Thus the adipsic rat will show essentially no probability of taking a lick from a water spout but within a half hour period will run between one hundred and one hundred and fifty seconds. We then made these two behavioral events contingent such that if the animal wanted the opportunity to run, he had to drink, which in turn released a brake on a wheel that allowed the animal to run. Dramatically, the adipsic rats immediately began to drink in order to have the opportunity to run.

Now let us consider the infero-temporal lobe syndrome in monkeys where it has been repeatedly shown lesions in this area dramatically impair learning and performance in visual discriminations (Clark and Gazzaniga 1974). Clark and I (1974) have recently extended the kind of insight afforded in the preceding experiment into this area where discrimination problems are trained to monkeys undergoing infero-temporal lesions. In the beginning we assumed caged monkeys were like rats and would relish the opportunity to run in a similar type of apparatus. Instead, we seemed to have discovered the phylogenetic origin of "don't rock the boat". Here, when the animal has the opportunity to run, a preferred response turned out to be to adopt a vertical spread-eagle position so as to minimize movement in the wheel. This required a change in contingencies such that if the monkey made a correct choice, the wheel would be locked so no movement was possible.

Specifically, three monkeys were trained on a pattern discrimination for food reward using a discrimination panel that was placed inside of a large activity wheel. When the discrimination was learned, an added contingency was introduced. The wheel, driven by a motor, would automatically start to turn at the onset of the stimulus. As described, if the correct choice was made, the wheel

locked during the intertrial interval. The animals, under these conditions, decreased their latency in making their responses and immediately made a perfect score even after all food reward was withdrawn.

All animals then underwent bilateral infero-temporal ablation. To our great surprise, the animals were instantly able to perform perfectly the discrimination to a food reward alone, as well, of course, as to the not-to-run contingency. Our expectation, of course, was that we would see a dissociation of performance between the food condition and the not-to-run contingency.

It would appear from the foregoing that the training of a visual task with two explicitly different kinds of rewards insulates the organism from showing the classic impairment following bitemporal lesions. It was as if the preoperative dual training encouraged the organism to use a number of conceptual strategies to solve the problem. These strategies then may have created a cerebral redundancy such that impairment to one part of the brain could in no way do exclusive damage to all of the paths used in problem solution. Indeed, the well known beneficial effects of preoperative overtraining has on postoperative scores may be the result of a similar mechanism. During the long overtraining period, the animals may well decide to solve the problem through a different kind of strategy than the one originally used. This, of course, could never be delineated by the present experimental design. At the same time, the strategy substitution interpretation is commonplace in complex discrimination training in humans. Here it has been shown, using other testing methods, that both children and adults are constantly changing their hypotheses along the way as they learn a particular visual discrimination (Levine 1966). In short, the old analysis of learning phenomena which urged simple behavioristic interpretations with the corresponding simplistic neurological models won't do anymore for the data are giving way to the view that distinctly separate mental processes are active during even the simplest kind of discrimination training.

Cognition Following Stroke: The problem of determining the amount and kind of cognitive function remaining after severe brain damage to the left dominant hemisphere is difficult. In the past, little credit has been given to what the remaining, largely undamaged, right hemisphere is capable of in this regard. Encouraged by our earlier studies on the cognitive capacity of the right hemisphere (Gazzaniga *et al.* 1965; 1967; Gazzaniga and Sperry 1967; Gazzaniga 1970) we commenced a series of studies on the severely left brain damaged patient in efforts to determine what, in fact, the cognitive limits were. We predicted that, with the right behavioral testing technique, much more extensive behavioral capacity would be evident than is usually claimed and this has indeed been our experience. Using Premack's (1970) language training system developed for the chimp, we ran a series of tests on global aphasic patients and quickly discovered these patients could learn to perform many language-like operations.

Before beginning language training, a viable social relationship must be established between the patient and the trainer. The importance of this phase can not be overemphasized for if the motivational setting is inappropriate, no learning will occur. In psychological parlance, if a patient is emotionally flat and shows no preference, then it is impossible to arrange a contingency where manipulating and learning X will produce desired reward Y. Indeed, it would seem fair to say that all too frequently neuropsychological assessment procedures ignore this factor. Tests are designed, norms are established on a normal population, and the relation all this has to testing a brain damaged patient who surely is in a complex ever changing motivational state is frequently remote.

Using paper cut-out symbols, errorless training procedures were administered in the initial training. For example, in teaching "same versus different", two similar objects, say two erasers, were placed on a table in front of the patient. Placed in between was another symbol, a question marker, which comes to mean "missing element". The subjects learned to slide the question marker out from between the two test objects and insert in its place the symbol meaning

"same". At first, this is the only response allowed. Subsequently, an eraser and a screwdriver are placed in front of the patient and the patient must remove the question marker and insert the symbol meaning "different". Following this training, the two symbols are both available on each trial and the subject must now make the correct response to the two varying, "same" or "different", stimuli. When the stimuli used in training are then changed, it is observed that the subjects can use the symbols correctly no matter what test objects are used by the examiner.

These procedures than enable one to teach any of a number of language operations to the global aphasic patient. The negative, yes, no, the question, and simple sentences were all successfully trained. Before teaching the sentences, the patients' lexicon was increased by teaching them a few nouns, verbs and personal names. Each of these words was taught by associating a symbol with an object, action or agent in the context of a simple social transaction. An object was placed before the patient along with the symbol for the object and the patient was required to place the symbol on the writing surface, after which he was given the object.

It is of interest to note that the training of symbols referent to actions (verbs) was consistently much more difficult than training in symbols referent to nouns. Noun symbols were learned in a few trials whereas verbs sometimes took weeks to learn. To some extent, of course, this is not too surprising. To know a verb is to know a whole context, subject and object, whereas to know a noun is simply to know a single object. The difficulty we experienced in training symbols referent to actions is also reminiscent of the finding that the right hemisphere of the split-brain patient was unable to process natural language verbs.

In a second series of cases examined on a whole battery of language tests, as well as a host of other cognitive tasks, artifical language training proved possible in most of the patients (Glass 1973). In those that failed, a series of simple cognitive assessment tests demonstrated that these patients did not possess to a normal extent, even the rudimentary aspects of cognitive life, such as a short term memory capability. In these tests, a pea placed under one of two different objects would not be reliably retrieved after a short delay. Without short term memory, it would seem very unlikely that the artificial language system could be learned.

These demonstrations of logical cognitive functions encourage one to examine more closely other dimensions of the cognitive content of the severely brain damaged individual. In all of the foregoing tests as well as those described in the following, the only criterion for accepting a global aphasic patient in the test was that he be alert and bright-eyed and in general, responsive to reward contingencies. With such a group, it has now been shown that a distinct cognitive capacity is remaining (Zangwill 1966). These tests, which are still preliminary in nature by and large, took a different approach from the standard tests which frequently require patients to manipulate symbols freshly presented at the time of testing. In our tests, pictures were used of common everyday objects or scenes. The patients were required to order them in a logical sequence or to complete a logical equation developed and posed solely with familiar pictorial material.

These studies clearly suggest that the severely left brain damaged patient can perform a wide variety of conceptual tasks. Because of the large extent of left damage, it would seem likely the intact right hemisphere is surely involved in many of these tasks. We know from other studies that the right hemisphere has enormous cognitive power (Gazzaniga and Sperry 1967; Bogen and Gazzaniga 1965; Levy, Trevarthen and Sperry 1972; Milner and Taylor 1972) and, indeed, the imagery mechanism associated with language behavior appears to be a right hemisphere process (Seamon and Gazzaniga 1973).

In these studies, use was made of Sternberg's (1966) serial processing model of short term memory processes. In brief, he found that as a memory set increased in size - for example, from one item to three items - a "probe word" examining whether that word was part of the set took longer to yield an answer the larger the memory set size.

Seamon reasoned that if the instructions to a subject were varied, different response patterns would be evident. Instead of instructing the subject to rehearse verbally the material, as is usually the case in the Sternberg design, he told them to create with the memory set words an interactive image, where all the words in the set "touched" one another in the image (Seamon 1962). Thus "tree" and "bird" should find the bird in the tree, not flying by it. Changing the instructions in this way found equivalent response times no matter how large the memory set.

This remarkable observation encouraged us, of course, to examine the possibility that there may be a left-right difference in hemisphere specialization for imagery processes. For years we had felt that it was the right hemisphere that was specialized for handling the visual abilities of mental life and, in this context, we examined whether different response times would be functioning as a feature of both our instructions for encoding the original material and the visual-field-hemisphere first receiving the probe.

Results of the study clearly showed it is the right hemisphere that is specialized in the image process and the left for verbal directions. For present purposes, these studies indicate how a cognitive system working in parallel with the language system might well come to the aid of a patient following severe left brain damage. In addition, and perhaps more importantly, we see how by manipulating the encoding instructions, wholly different brain systems are called upon to process information. In a sense, then, the idea here is that one can "shunt" around a brain lesion by setting up the environmental contingencies differently and thereby requiring a different part of the brain to be used in the solution of a problem.

Summary: For the present, we are faced with the problem of how to account for clinical improvement in terms of recovery of function. Does it reflect a process where the central and dominant language processing systems have repaired to the extent of allowing the observed behavior? Or, are these cognitive talents the product of other existing behavioral strategies that are capable of handling the job but have previously been involved in other more supportive roles? With the latter view, the recovery period becomes more the time needed to allow for the realignment of these cognitive processes than the time needed for physical repair.

While it is still too soon to say for sure, my guess is that once the motivational state of a brain damaged patient is defined and analyzed, correct manipulation of these variables will maximize the extent of recovery possible. Just as the adipsic rat will drink to run - the bright-eyed aphasic patient will learn an appropriate meta-language system in order to communicate meaningfully with the environment.

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